Replies

This issue is an interesting one, and I appreciate Drs. Stenn and Scott for addressing it. I would like to state from the outset that I am an anatomic pathologist/dermatopathologist by training, that I practice cutaneous pathology exclusively, and that I know little about the technical aspects of the genetic approach to the diagnosis of cutaneous disease, other than in the most general sense. Much of what I have to say, therefore, is philosophical, which is to say: pre-scientific in nature, dealing with fundamental ideas involved in the advancement of knowledge and technology in any medical field, including cutaneous pathology.

At the risk of looking, or actually being, foolish in my approach to this question of "whither dermatopathology?" I would like to observe that many competent creators of knowledge and new technology have floundered magnificently in trying to predict the extent of the future applications of their discoveries to their or other industries. With this in mind, I would like to begin by considering the very nature of what comprises a diagnosis in order to gain insight about why microscopes were ever used in the first place to assist in the diagnostic process. Perhaps such an overview will aid in predicting the future usefulness of the knowledge of genetic information as applied to the future of cutaneous pathology.

What is a diagnosis? The term means literally to "know across." The Oxford English Dictionary defines it as the "determination of the nature of a diseased condition; identification of disease by careful investigation of its symptoms and history; also the opinion (formally stated) resulting from such investigation." In the modern era of medicine, the "tried and true" approach to understanding a disease consists of observation, comparison, more observation, more comparison, review of previously gathered data, review of literature, acquisition of additional data, rereview, and, at some point, integration of all the data into a cohesive whole.

In the process of investigation, the history of medical knowledge has been one of induction to a principle, then the application of the principle to new observations, comparison of the new observations to the established principle, modifying it if necessary, and so on. The systematic and formal process of this act is the scientific method. Thus, what began historically as a philosophic approach to data, primarily an empiric one, developed into a formal systematic approach to classifying the data, resulting ultimately in scientific principles about how a biologic system (in the case of medicine) worked.

In this context, the microscope was simply a logical extension of one's eyes in the process of classifying a different aspect of the same clinical observation in the skin. The microscope did not supercede clinical observation; it served rather as an adjunctive device, yielding a new body of data that had to be integrated into an ever expanding body of concepts or principles. Similarly, the discovery and application of immunologic principles as well as the applications of electron microscopy to morphology-based diagnosis have also been adjuncts to the process of establishing a diagnosis when applied with a thorough knowledge of dermatopathology, in turn applied in a proper clinical context.

Clearly, it was no accident that knowledge of cutaneous pathology arose from clinical dermatology; applying the microscope to the observation of clinically abnormal skin was merely an extended observation of the senses that could not have been reversed with any consistent and scientific meaning.

Of course, it is true that many students of dermatopathology attempt to reverse the process, especially while in training, but it simply cannot be done; reality and the nature of the diagnostic process will not allow it. In point of fact, a clinical context will always be required for a histologic diagnosis, no matter what the diagnosis is, because a diagnosis consists of every aspect of the disease.

With this principle in mind, I believe that Drs. Stenn and Scott are asking whether or not a radical difference in the way that a diagnosis is made in humans will necessarily eliminate light microscopy from the diagnostic process. I interpret this as asking whether it is possible that the process of diagnosis could switch from:

> Observation → data collection → microscopic evaluation when relevant → other data (including genetic) → integration → diagnosis
>
> To:
>
> Genetic data collection → diagnosis

My answer: in some circumstances, genetic data may, especially in cases of screening for structural and humoral gene abnormalities or products, lead directly to a diagnostic conclusion. However, I doubt that this information will eliminate the need for clinical and microscopic data that are fundamental in establishing the way the concept of disease enters the minds of physicians. In fact, I strongly suspect that the understanding of genetics will result in a whole new body of knowledge that will not replace the need for clinical medicine and the use of microscopes in the helping to formulate diagnoses, but will provide new insights that must be integrated into existing knowledge. Even if a tumor can be dissected and genotyped, for example, it will still require clinical observation and histologic diagnosis to establish the need for and application of such a procedure.

Clinical dermatology and dermatopathology are fundamentally cognitive professions; therefore, they require the ability of concept formation, concept integration, and complex interpretation of data that cannot be replaced easily by the introduction of a new technology as such. A diagnosis requires a highly sophisticated type of data processor and data integrator: an extensively trained and experienced rational human mind.

The answer(s) to the question raised by Drs. Stenn and Scott will be forthcoming eventually for genetic as well as other technical diagnostic issues that few can imagine easily today. Additionally, the application of these techniques will be influenced by the markets of medicine and governmental regulation of medicine. Technologies have not arisen and do not arise without an established context that influences tremendously the final interpretation that is a diagnosis. When technologies are proven useful, dermatopathologists should attempt to embrace them as additional tools to complement existing diagnostic approaches, replacing them when necessary. Only time will tell when or if this happens and to what extent.

Whither dermatopathology? Dermatopathologists are physicians; as such we owe it to ourselves to become educated in the history of our profession, to master current technologies, and to exploit relevant newer technologies while holding a proper context, in order to learn as much as possible about the natural history of disease – likely with microscopes, but without them if necessary – as a rational use of technology will offer us more insight into the diagnostic process.

We and our patients deserve no less.

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The fact that molecular biology advances are markedly influencing the practice of diagnostic pathology in general and dermatopathology in particular cannot be denied, coupled with the expectation that we are only witnessing the beginning of the revolution. Therefore, as Drs. Stenn and Scott aptly point out in their letter, it would be very unwise for dermatopathologists to ignore those advances, or to fail to incorporate those techniques into their armamentarium once they have proved their utility. Parenthetically, in so doing, they would not be behaving any differently from previous pathologists when faced with special techniques over the course of this century, such as electron microscopy, immunohistochemistry, or *in situ* hybridization.

Having said that, I must confess I find the enthusiasm of the authors of this letter toward molecular technology a little overwhelming, and their predictions about the demise of light microscopy perhaps a little premature. Their comment about the fact that "... it will take a while to figure out how these genes actually function and cause disease" is a bit of an understatement, and their sense of wonder at the speed of molecular techniques (a 2–4 h analysis) a little excessive. As seasoned pathologists, they surely know that in that same length of time (or in 2–4 min if necessary – I am thinking of frozen sections), one can give the clinician a lot of information about the disease with the light microscope. Actually, I doubt whether there is at present a technique in the whole of medicine that provides so much information so quickly and at such a little cost as the H&E technique.[1] Therefore, let us merrily join the molecular revolution but without discarding too quickly something that has proved so remarkably informative and efficient to us over the years. As the author of an editorial in a recent issue of *The Economist* entitled "In praise of old technology; Sometimes the traditional ways can be the best" said, "The lesson of history is, in short, that even apparent moribund technologies [...] have a persistent habit of, well, springing back to life. That is worth remembering next time you hear the death-knell being sounded for a supposedly outmoded way of doing things."[2] For light microscopy, that death knell has been sounding for an awfully long time. Suffice to quote in this regard the Harveian Oration given in 1912 at the Royal College of Physicians in London by Sir James Goodhart on "the passing of anatomic pathology."[3] As José Zorrilla would have told him and his followers: "Los muertos que vos matais gozan de buena salud."

References

1. Rosai J. The H&E technique. Old mistress apologue [Editorial]. Pathologica (Italy) 1998; 90: 739.
2. In praise of old technology [Editorial]. The Economist 1999; April 17: 20.
3. Goodhart J. Harveian Oration at the Royal College of Physicians, 1912. In: Lockyer C, ed. Fibroids and allied tumours (myoma and adenomyoma). Their pathology, clinical features and surgical treatment. London: MacMillon, 1918.

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