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EDITORIAL

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Classification of Leprosy: A Full Color Spectrum, or Black and White?

Proper classification of a disease is one of the fundamental tools of modern medicine in selecting treatment, evaluating prognosis, measuring overall progress, and furthering the understanding of that disease. Classification is an essential tool in our approach to a disease, much as a good map is necessary tool for developing and navigating a country. The development of a comprehensive, practical classification system for leprosy may rate as one of the most important accomplishments in the extraordinary progress against this disease in the 20th century. While the more obvious, essential accomplishment was the discovery of effective anti-microbial agents to treat this infection, the availability of effective treatment does not, by itself, guarantee success against a disease. The value of classification is not only historical; continued application of the best classification system is essential in the efforts to better understand a disease and to clearly and intelligently develop a strategy to combat it and, ideally, prevent it.

The struggles against leukemia and lymphoma provide a useful example of the continuing value of classification. Several effective agents were available for these malignancies long before many of the current successes in treatment. Greater success has been brought about in part by a better understanding of how to use these agents in combination, but also—and very importantly—by better classification systems that enable physicians to know which types of leukemia or lymphoma will respond to particular medicines or combinations. Recognition of this has stimulated continued, vigorous research to refine the methods and concepts of classification of many malignancies. Such studies enhance the understanding of these diseases, with implications not only for treatment but also for early detection and prevention. Today, no cancer researcher would consider conducting a study, or publishing results of a study, using a primitive or technically outmoded classification system. And no professional journal would accept such a report.

Yet, in current leprosy research, a disturbing trend is to do exactly that: to abandon the best classification system (one that uses clinical assessment plus histopathologic examination of a skin biopsy), and choose instead to group patients into only 2 groups, multibacillary (MB) or paucibacillary (PB), according to their bacterial load, or to disregard the bacilli altogether and classify according to the number of skin lesions on a patient's body. This last approach, which disregards the bacteria entirely, seems highly ironic for research on an infectious disease. These approaches are technically inferior ones that assume, and accept as satisfactory, a higher degree of inaccuracy than is readily available with standard technology. Such over-simplification of this complex host-pathogen relationship is unfortunate and unacceptable. It is as if some have grown intellectually weary of

trying to understand the full-color immunopathologic spectrum, and have decided to settle for a black and white outline.

Why is this done? Two related reasons are generally given—cost and expertise. The MB/PB categorization was promulgated by the World Health Organization in the global campaign to eliminate leprosy as a public health problem. For some treatment and control programs, where access to expertise and other resources is severely limited, the use of a simplified system of classification is reasonable, just as paramedical workers deliver medical care where there are no doctors. It has become too easy, however, to use this as an excuse to justify a non-critical acceptance of oversimplification that does a disservice to our basic research endeavors.

Research always requires substantial expertise and is inherently costly, and is nearly always conducted with specifically allocated research funds. Nevertheless, we have watched with dismay as some investigators and collaborative groups apply sophisticated molecular and immunologic techniques to specimens from patients who are classified only as MB or PB, or are classified only according to the number of skin lesions. Some of these manuscripts arrive at our office, and some are published in other journals. The multiple authorship and acknowledgments of support in most of these papers clearly indicate that financial resources and sophisticated expertise have been brought to bear, and funds have been allocated for expensive instruments and reagents. Experienced clinical leprologists are virtually always involved in these studies, implying an availability of sufficient resources, and it is not acceptable that they do not take the effort also to obtain skin biopsies and have them examined by an experienced professional.

In some instances the pressure to publish quickly appears to play a role. The Ridley-Jopling classification system ([1]) divides patients into five groups, whereas MB/PB schemes divide into only two groups. It is much easier (and faster) to obtain enough patients for a 2-group protocol than for one with 4 or 5 groups. But is this better? Is knowledge really advanced by such a simplification? We are very skeptical. No self-respecting academic research advisor will accept such an excuse from a student, and the research community should not make an exception and settle for this with respect to research on leprosy.

Any classification system must be applied thoughtfully, and in some circumstances a simpler system truly will suffice. For example, in epidemiologic or implementation field studies, simplified classification may be justified.

The diversity inherent in the immunologic spectrum of leprosy may not be reflected in all biological parameters we set out to measure. In some instances, the results may reveal that patients fall into only 2 or 3 groups. To discover this is not a failure, nor is it wasted effort. Once such findings are established, a 2- or 3-part classification scheme for that parameter is acceptable. But if the hypothesis is not first evaluated against the full spectrum, we will not know if there were more than 2 or 3 groups. The burden remains on the investigators, however, to explain why better classification was impractical and why a simplified system is actually acceptable in testing their hypothesis. If we do not look, we will not know conditions as they truly exist, and we may thus overlook important connections and implications.

Researchers in leprosy have before them, at all times, one of the great immunological models in nature. An essential part of the foundation of our understanding of leprosy is the recognition that—clinically, histologically and immunologically—polar lepromatous (LL) differs from borderline lepromatous (BL), and borderline tuberculoid (BT) differs from polar tuberculoid leprosy (TT). From their first publication in the mid-1960's, the soundness of the theoretical basis for this classification system ([2]), and the description of practical, straightforward criteria to accomplish such classification anywhere in the world ([1]), were hailed as major accomplishments by workers within and beyond the field of leprosy. Both the theory and the practical criteria recognize the natural diversity of the immune response in leprosy that has challenged immunology for nearly half a century. A more complete understanding of the basis for this diversity and its underlying mechanisms will most probably be required before this disease can be eliminated (i.e., before a highly effective vaccine can be developed).

The questions posed by this complex immunopathologic spectrum have perplexed more than a few great minds who have attempted to tackle them. Although support for leprosy research has declined, it seems a grave mistake for those of us who continue to work on leprosy to surrender one of our best scientific assets—a practical and theoretically sound classification system for leprosy. Oversimplification fosters the illusion that this disease is simpler than it appears, and easy to understand (or eliminate). Infection with *Mycobacterium leprae* elicits the full range of human immunologic responses; this is a natural phenomenon and, like the metastasis of cancer, it will not go away if ignored, but will be ignored at our peril.

Today, although the prevalence of leprosy has declined worldwide, the number of new cases diagnosed annually has not. This paradox raises new, important, and interesting questions. Answering these and the other still unanswered questions about leprosy will require application of the best scientific methods available. It is common knowledge that funds for leprosy research are in much shorter supply than they were a few years ago, and that fewer individuals are engaged in leprosy research. This, however, is not an excuse for us to be less rigorous. To do so would be a travesty to the hundreds of thousands of patients still diagnosed every year, to those with lasting disabilities from this disease, and to all of those who have gone before us, who did not shrink from a rigorous attempt to understand the complexity of leprosy even though they worked without many of the technical advantages we have today.

—DMS

REFERENCES

1. Ridley, D. S., and Jopling, W. H. Classification of leprosy according to immunity, a five-group system. Int. J. Lepr. **34** (1966) 255–273.
2. Skinsnes, O. K. "The immunological spectrum of leprosy." In: *Leprosy in Theory and Practice*. Baltimore: Williams and Wilkins, 1964, pp. 156–162.