Features of the Ridley-Jopling Classification

To the Editor:

Dr. S. K. Kundu (Int. J. Lepr. **47** [1979] 64–65) asserts that different lesions produce different classifications, a view which has been expressed quite frequently in the past. My own experience is based on receiving double biopsy specimens, taken concurrently from two lesions, which has been the routine practice of several of the clinicians who have sent me material over many years. In addition, I have carried out comparative assessments of the specimens of some other workers who have shared Dr. Kundu's opinion. The results are discussed in previous publications. In tuberculoid, borderline, and lepromatous leprosy, it has been exceptional to find even insignificant differences in classification between a pair of biopsies, and not infrequently the histological classification has been the same for two lesions that were clinically discrepant.

There are two provisos:

a) during reversal reactions, reacting lesions may sometimes develop at different speeds.
b) during the process of upgrading or downgrading, there may occasionally be a confusing mixture of features of BT and BL, but reactions apart, no difference, I believe, between lesions.

It is simply not true, in any general sense, that this system of classification produces different answers for each lesion. A symposium to test the views of "eminent experts," which Dr. Kundu asks for, was organized by Dr. Chapman Binford and held at the Armed Forces Institute of Pathology, Washington, in 1971, and again at Bergen before the Congress in 1973. On each occasion, agreement among the histologists participating was almost unanimous.

Neither Dr. Jopling nor I would accept that "it might better be called a slide classification." It is (opportunity permitting) a joint clinical-histological classification. Histology sometimes has the advantage on points of detail because it reflects directly the underlying immune mechanism. But the clinical assessment is always and at least a useful counterpart to histology, and in the absence of a biopsy, it stands by itself. The reason why more has been written about the histological aspects is that they are less widely understood.

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To the Editor:

I have read the interesting comments by Dr. Kundu about the Ridley-Jopling classification (Int. J. Lepr. **47** [1979] 64–65). It is a fact that borderline leprosy often presents varied and pleomorphic clinical and histopathological features in the same patient. Marked variation in the LTT and immunoglobulin levels have also been noticed in borderline patients. I do agree that for field purposes the WHO classification into tuberculoid, borderline, and lepromatous is more easy and practical. However, it still remains important to have these subdivisions, which create better understanding of the disease and which make it easier to realize the concept of the leprosy spectrum. The subdivisions, which still represent the state of the patient at a certain time, are needed for follow-up of patients and for evaluation of drug therapy. In fact, when doing research, one comes to the conclusion that there is need for further subdivisions. The borderline tuberculoid (BT) or borderline lepromatous (BL) subdivision still represent different clinical, histopathological, and immunological manifestations. This has led some leprologists to in-

troduce further subdivisions (TT/BT, BT/BB). However, even these subdivisions could not replace a thorough, detailed clinical description of the lesions in the individual patient. Hence I feel that there is need for these subdivisions.

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The Effect on Pregnant Mice of 0.05% B1912 Fed in the Diet

To the Editor:

Morrison and Marley stated, in a Letter to the Editor ([2]), that B1912, like clofazimine (B663), interacted with DNA's with "upfield red shifts" at 482 nm. The degree of this shift was found to be 4 to 5.7 times greater for B1912 than for B663. While it was not stated as such, apparently the extent of this shift for B1912, as opposed to B663, necessitated an expression of precaution as to the "implications of the data for testing of B1912 in human volunteers." The precaution was inferred on the basis that B1912 vs. DNA interaction, indicated by the upfield red shift, was assumed to be accountable for the strong antimitotic effects seen in tissue culture in the authors' laboratory. The antimitotic effects were not described in the letter nor was there any reference to the B663 effect in tissue culture under similar conditions.

Some time later, the same authors made a similar report to the Twelfth Joint Leprosy Research Conference, U.S.–Japan Cooperative Medical Science Program. The abstract of this presentation ([3]) clarified the antimitotic effects by offering the suggestion that "B1912 acts as a metaphase inhibitor producing lethal effects in rapidly dividing cells" at concentrations that could be attained in human serum. This effect was termed "nucleotoxicity," and the authors stated this property to be consistent with the formation of stable complexes between B1912 and human DNA, as indicated in their earlier data. Nucleotoxicity was confirmed by their finding that complete interrruption of pregnancy occurred in pregnant mice fed 0.05% B1912 in the diet for five days during mid pregnancy. No details were presented to document or describe these results, but fetal death, resorption and at least one abortion was mentioned. Again, the authors offered a precaution that a considerable amount of preclinical testing will be required before B1912 can be safely tested in human volunteers.

Apparently most leprosy workers feel that, since B663 is available, there is little need for urgency in the evaluation of its analog, B1912. However, Barry, *et al.* ([1]), after comparing B663 and B1912 reported that there were differences between these compounds in growth-inhibitory activity against certain mycobacteria. Differences were also observed in the "*in vivo*" tissue distribution of the two compounds. They concluded that B1912 had potential as a potent compound for leprosy and tuberculosis. For this reason, we felt that the claims of Morrison and Marley merited further investigation.

We decided to investigate the report that B1912 induced abortion in laboratory mice. Three successive attempts were made to repeat this observation using our NAMRU (Naval Medical Research Unit) inbred strain of mice.

In the first attempt, five pairs of mice were fed 0.05% B1912 in the diet from the date of pairing until parturition. All five females delivered a total of 41 weanlings (17 males, 24 females). All birth processes and offspring were normal except for an obvious red discoloration of parents, offspring, and fetal tissue. This discoloration disappeared in 6 to 8 weeks and all weanlings matured into normal adults.

In the second trial, three pairs of mice were fed 0.05% B1912 in their diet starting 2 weeks after pairing. Two additional pairings were maintained as controls, without B1912, under otherwise identical circumstances. All females were routinely weighed during the course of the observations. All five females produced healthy lit-