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EDITORIALS

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THE SUPPOSED LAG IN BACTERIOLOGICAL IMPROVEMENT

The statement is being encountered constantly, in one form or another, that in patients under sulfone treatment—those with lepromatous leprosy, that is—bacteriological improvement lags far behind clinical improvement. Is that really true? Would it not, perhaps, be more correct to say that clinical improvement of the lepromatous lesions is more than bacteriological *clearance*, meaning consistent negativity of smears made by the standard method?

Let us consider a prominent lepromatous infiltration or nodule in an untreated case, a standard smear from which is graded as—let us say—3+ for bacilli in a 4+ (or more) scale. Take into account its thickness, and therefore the total bulk for a given surface area, and with that in mind try to appreciate the total number of bacilli in that mass.

In a recent note[1] it was estimated that it takes a minimum of about 10,000 tubercle bacilli per cubic centimeter of sputum before the ordinary direct smear search can reveal enough for any given specimen to be considered positive. (The calculation, briefly, was as follows: About 0.01 cc. is used to make the smear; an examiner, in 10 minutes, can cover an area of about 2 x 3 cm. (about 1,000 fields), or 1/75th of the slide; that area involves about 1/7,500 cc. of the material. Thus 10,000 bacilli per cc. is about the smallest number which will permit on the average finding 1 bacillus in the usual allotted time.)

When the large—even tremendous—numbers of bacilli that are often present per field in smears of tissue pulp from lepromas are considered,

[1] EDITORIAL. Searching for tubercle bacilli. *J. American Med. Assoc.* **154** (1954) 1424.

some degree of appreciation can be gained of the myriad of them that the patient must get rid of in recovering from lepromatous leprosy. Hanks[2] once estimated that the numbers average 2.5 billions—two thousand five hundred millions—per milligram of leproma tissue.

After a certain period of treatment the leproma is reduced greatly in thickness—the infiltration much less marked, the nodule perhaps quite subsided in the infiltrated zone in which it arose. A smear is again graded as 3+, the same as before; in actual fact it may be 2+ or even less, but for the sake of the argument, let us say that it remains at 3+. This signifies that the number *as it now exists* has not greatly changed, but it also means that the total number of bacilli present in the lesion mass as it then exists is less than at first, proportional to the reduction of its bulk.

The clinical improvement, the subsidence and lessening of bulk of the lesion, means that in some way not understood the number of lepra cells present has been reduced. There is no other explanation, since the bulk of an ordinary leproma does not depend upon edemato-congestive elements, and since the supporting collagen-reticulin stroma tends to persist.

Now, if it were that these lepra cells merely die off and disintegrate, the bacilli all dumped *in situ*, and persisting, their concentration per unit of tissue volume (or unit of material scraped for the smears) would be correspondingly increased, and consequently the bacillus count should be much higher.[3] That is not the case.

By the time a lepromatous infiltration has subsided, or receded, to the point where the clinician may hope a smear may prove negative, it is usually far from negative. But biopsy will reveal a persistent histological lesion, perhaps more or less similar in degree to the "inapparent" lesions which were often demonstrated in the days when methylene blue and other dyes were being used, and which provide the sites of the so-called erythema nodosum leprosum. Various workers have pointed this out, showing that these deposits of old, sudanophilic, foamy cells long contain bacilli or bacillary elements—which, it may be said, are more likely to appear as rods in the clinician's smears than in the pathologist's sections.

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[2] HANKS, J. H. A note on the numbers of leprosy bacilli which may occur in leprous nodules. *Internat. J. Leprohy* **13** (1954) 25-26.

[3] That condition was once seen in our experience many years ago when thick earlobes were subjected to ultraviolet irradiation from a quartz lamp, under pressure by a quartz contact rod. In several instances the earlobes shrank in a striking manner, but smears showed greatly increased numbers of bacilli per field and the experiment was discontinued. No biopsies were made. Furthermore, in biopsy sections many bacilli should be found in groups and masses lying free in the tissue spaces where left by the dissolution of the host cells, unless taken up by new wandering monocytes and macrophages, in which case the lesion would be perpetuated. We have not seen that condition ourselves, nor have we seen any record of an observation of it.

Finally, however, these elements may disappear completely, although the cell foci may remain. In the meantime, in the long intervening period, the clinician and patient are liable to be discouraged — and to wonder how long these long persisting bacillary forms remain viable.

Be all this as it may, considering the tremendous number of bacilli that were present at the outset to be disposed of, and considering the resistance of even dead acid-fast bacilli to such deleterious influences as exist in the tissues of normal animals, let alone lepromatous patients, the wonder is that leprosy lesions ever clear up at all. At any rate, we should seriously ask ourselves if the current attitude that the bacilli in the lesions do not decrease as they should under sulfone treatment should not be reconsidered. The situation may be viewed with an attitude less discouraging to the physician and the patient. —H. W. WADE