Is Leprosy Treatment Ineffective?

Good, practical reasons require that most evaluations of the effectiveness of specific therapy in leprosy be based on results achieved in the treatment of lepromatous leprosy. Indeed, generally accepted programs for the evaluation of drug effectiveness in human leprosy are based on their testing in controlled series of lepromatous patients. This is as it should be, because lepromatous leprosy presents the major therapeutic problem in this disease. Nevertheless, the practice imposes unusually difficult circumstances, obscures certain comparative differences relative to therapy in other infectious diseases and lends an aura of relative ineffectiveness to all current therapeutic efforts. Thus one often hears or reads statements to the effect that, "The sulfone drugs, while useful in preventing lepromatous leprosy from advancing, must be taken for years before the disease can be considered arrested,"[1] and the word "arrest" is preferred to "cured" by many.

The question arises as to whether or not the therapeutic results in leprosy are actually ineffective relative to results, for example, in the treatment of tuberculosis.

A recent, five year survey of tuberculosis treatment results in Taiwan[2] may be regarded as being set against field conditions similar to those prevailing in many areas of leprosy work. The results may be summarized by the following table.

Tuberculosis (Taiwan 1963-68)
1292 cases after 5 years treatment

Healed	213	16.5%	27.1%
Inactive	137	10.6%	
Active	130	10.1%	
Defectors	571	44.2%	
Died	241	18.6%	

This summary is in many respects less dissimilar to those often noted with leprosy than is commonly appreciated, though most leprosy series do not acknowledge death as being caused by leprosy per se.

The comparison, however, is not a true comparison. Indeed, no true comparison between effectiveness of treatment in tuberculosis and leprosy is feasible on the bases of the leprosy treatment trial conditions noted above. To be comparable, results of treatment in tuberculosis should be compared with the results obtained in the treatment of tuberculoid and intermediate (dimorphous, borderline) leprosy only. If this were done, in all probability the results in tuberculosis would appear less effective than those in leprosy, for the relatively greater virulence of the tubercle bacillus would shine through. The reason for the inequity in comparisons lies in the fact that, in the human, there is no naturally occurring lepromatoid tuberculosis and the whole naturally occurring immunopathologic spectrum in tuberculosis relates only to that portion of the leprosy spectrum represented by the tuberculoid and intermediate section.[3]

In all effective specific therapy of bacterial infections two major factors are operative. One is the inhibiting effect of the therapeutic agent on the pathogen, the other the effectiveness of the host phagocytes in disposing of the pathogen. In the early years of penicillin availability we essayed a series of experiments involving the effect of penicillin therapy in mice severely debilitated by dietary protein deprivation and infected with a strain of virulent but markedly penicillin susceptible pneumococci.[4] The protein deprived mice had virtually no ability to deploy phagocytic cells to the infected tissues, such cells being unavailable because of the lack of protein needed for their production. As a result, despite more than adequate penicillin therapy, viable pneumococci persisted far longer in the blood stream and tissues of the deprived as compared to the control animals, as depicted in Figure 1.

---

1 Binford, C. H. Remarks on receiving the Damien-Dutton Award, 1971.

2 Luan, H. W. A five year observation of tuberculous patients in central Taiwan. Asian J. Med. 7 (1971) 327-336.

3 Skinsnes, O. K. Comparative pathogenesis of the mycobacterioses. Ann. N.Y. Acad. Science **154** (1968) 19-31.

4 Skinsnes, O. K. and Woolridge, R. L. The relationship of biological defense mechanisms to the antibiotic activity of penicillin. I. The modifying influence of penicillin on the pattern of pneumococcic infection and the immune response in the protein depleted rat. Jour. Infect. Dis. **83** (1948) 78-86.

Influence of Protein-depletion on Antibiotic Therapy

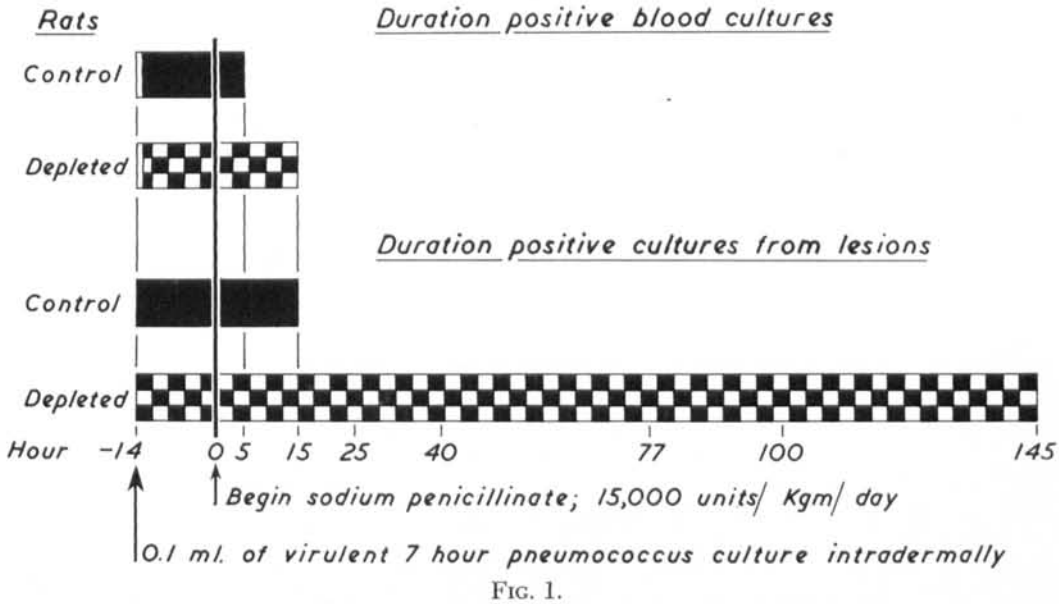

FIG. 1.

Every instance of lepromatous leprosy presents as a problem of therapy in an immunologically deprived host. The lepromatous macrophage, as demonstrated by its storage of lipids to give rise to the "foam cell" as well as its high content of viable as well as slowly degenerating bacilli, is markedly deficient functionally with respect to this pathogen, though perhaps not totally incapable. Therefore, unlike the therapeutic problem in tuberculosis and tuperculoid leprosy, the problem set by lepromatous leprosy places virtually the whole therapeutic burden on the therapeutic agent. That these are quite effective is indicated by a number of factors including the finding by Shepard *et al*[5] that infectiousness of *M. leprae* from DDS treated lepromatous patients, as tested in the mouse foot pad, was not detectable after approximately 90-100 days and the finding of Worth[6] that Hong Kong children born after their DDS-treated parents, with whom they continued to live, began treatment did not develop leprosy.

Current therapeutic results can therefore, comparatively considered, be regarded as remarkably good in leprosy even though they are far from that desired in lepromatous leprosy. Results in lepromatous leprosy cannot be expected to be rapid even if an instantly bactericidal agent were to be found, for the problem would remain of disposing of the mass of dead bacilli and their products. These materials may in themselves have irritative and immunologically deleterious effects on the host. Their removal by deficient macrophages is slow, to which the storage phenomenon is witness.

Unsatisfactory as the treatment of leprosy is, particularly when measured against considerations relative to lepromatous leprosy alone, it is well to recognize why this is so and not to be overly discouraged by comparisons with results in tuberculosis and other bacterial infections. The therapeutic problem in lepromatous leprosy is different.—O. K. SKINSNES

[5] Shepard, C. C., Levy, L. and Fasal, P. The death of *Mycobacterium leprae* during treatment with 4,4'-diaminodiphenylsulfone (DDS). Amer. J. Trop. Med. & Hyg. **17** (1968) 769-775.

[6] Worth, R. M. Is it safe to treat the lepromatous patient at home? Internat. J. Leprosy **36** (1968) 296-302.