THE COMPARATIVE ACTION OF CHEMOTHERAPY ON *M. leprae* IN SUPERFICIAL TISSUES AND IN THE RETICULO-ENDOTHELIAL SYSTEM

D. S. RIDLEY, B.Sc., M.D.
Hospital for Tropical Diseases, London

That the reticulo-endothelial system (RES) is heavily involved in leprosy has been widely recognized for many years, but there have been few studies of the effects of treatment on leprosy bacilli in the RES. Ferrand (1954) and Benhamou *et al.* (1956) found leprosy bacilli and lesions in liver and marrow unchanged after 8–10 months treatment, and Furniss (1953) found bacilli in a lymph gland when the skin had for long been nearly clear. Powell and Swan (1955) sometimes found bacilli in other tissues after they had disappeared from skin. The question has been raised whether the reticulo-endothelial system acts as a reservoir of bacilli and possibly as a source of re-infection after treatment. This paper reports the incidence of bacilli in different parts of the body at different stages of treatment of lepromatous leprosy.

Material and Method

Post-mortem material of four cases of untreated lepromatous leprosy and of eight cases at different stages of treatment has been examined for acid-fast bacilli; in some instances two or more specimens of one type of tissue were examined. All the patients, except one, were at the Jordan Hospital, Redhill, England or at Sungei Buloh Settlement, Malaya. Treatment in all cases had been by sulphones.

Cases 11 and 12 differ from the others in that treatment had been severely interrupted by reactions, and full doses of the drugs were never maintained; Case 11 had received no treatment for eighteen months prior to death; these two cases, therefore, are considered separately. The method of histological preparation was that described by Lowy (1956). The number of bacilli was assessed as the average per field according to a bacterial index with a range of 1 to 6, in which each unit represents a ten-fold difference in actual numbers. The granularity of bacilli was assessed by an index previously described (Ridley, 1960); in the range of 0 to 10, 0 represents all solid bacilli and 10 all granular.

Results

The results are summarized in the Table. Before treatment and during the first six months, numbers of bacilli in the RES were comparable with those in skin. By twelve months there was a signifi-

cant decline in the RES compared with the skin and after three or more years of treatment no bacilli were found in any of the organs of the RES, although they were still abundant in some cases in skin. Case 7 suggests that bacilli may persist longer in lymph glands than in liver or spleen but there is not enough information to establish this point.

Bacilli in superficial nerves (the ulnar nerve in Cases 3 and 10, and the auricular nerves in Case 7) were comparable with those in skin, before and after treatment. In other organs, bacilli were very scanty, apart from the testis.

Bacilli in the RES were more granular than those in skin or nerve. Before treatment the index ranged from 4 to 9 in the RES sections, compared with a mean of 2.5 for skin bacilli in another series of comparable cases; (the only case, No. 3, in this series for which the index for skin was available before treatment was not typical because the patient was undergoing a reaction). After treatment bacilli in the RES were more granular in every instance than those in skin or nerve.

In the two cases (11 and 12) in which treatment was interrupted and inadequate, the bacteriological state of the RES was closer to that of the untreated than the treated cases. In Case 11 there was clear evidence of regeneration of bacilli in one at least of the skin sections; there was no sign of recrudescence of the bacilli in the RES.

Discussion

These few cases demonstrate that under chemotherapy bacilli generally disappear from the RES before the skin or other superficial tissues (nerve or testis). The RES is not a reservoir of bacilli which threatens re-infection after the skin has been cleared.

Brand (1959) has pointed out that leprosy is a disease of superficial tissues, possibly because *M. leprae* is favoured by a lower temperature than that of the internal environment. To this the only exception is the RES. It is known that the primary function of the RES is the collecting and disposing of foreign particles and noxious agents. The macrophages or related cells in which leprosy bacilli are to be found, whether in skin, liver, spleen or elsewhere, are members of the same physiological system. It is reasonable to assume, therefore, that bacilli in the liver and spleen are there only because they have been filtered off from the blood stream. The results of this investigation indicate that they do not thrive. In lepromatous leprosy, in which the tissue reaction to *M. leprae* is quite passive, it is likely that the RES is the principal site of destruction of the bacterial bodies. When infection is arrested and the inflow of bacilli to the liver and spleen is reduced, numbers rapidly decline.

Summary

A series of necropsies showed that in lepromatous leprosy numbers

TABLE

The number and condition of bacilli (Bacterial/Granularity indices) of bacilli in different tissues at different periods of treatment.

Case No.	*Race*	*Treatment (months)*	*Skin*	*Lymph glands*	*Liver*		*Spleen*	*Marrow*	*Nerve (superficial)*	*Other Organs*
					Portal Tracts	*Parenchyma*				
1	I	0		4.6/7 2.1/6 4.5/7	4.7/5	3.8/4	4.0/8			
2	C	0		2.5/8 3.3/6	5.3/9	3.8/9	3.8/9 4.0/9			
3	C	0	4.0/7 4.2/8	2.1/9	3.4/9	3.4/9	3.4/9		4.1/8	Lung <1
4	N	0	4.5/–	2.2/9	3.5/9	1.3/9	2.0/9	2.0/–		
5	EA	1½	4.4/5		4.0/9	2.6/9				
6	E	6	2.4/3		3.0/7	1.0/9	2.0/9			
7	E	12	4.8/8	3.8/9	2.0/10	0.3/10	1.2/10		4.4/8 4.6/8	Adrenal <1
8	C	36	0		0	0	0			
9	E	55	2.5/7	0	0	0	0	0		
10	C	60	1.1/10		0 0	0 0	0		0.4/10	
11	E	(66)	2.4/5 3.8/2		1.0/6	1.0/6	1.8/6	0		
12	E	(156)	3.7/8	3.0/6	3.7/5	2.5/4	3.4/5			Testis: (superficial)4.4/2 (deep) 2.2/2 Adrenal <1

C = Chinese E = European EA = Eurasian I = Indian N = Negro

of bacilli in the reticulo-endothelial system declined rapidly after twelve months' treatment, and disappeared long before those in the skin or other superficial tissues. Bacilli in the RES were more granular than those in skin or nerve.

These findings support the view that leprosy bacilli find their way to lymph glands, liver and spleen only as a result of filtration of lymph and blood streams; and that in lepromatous leprosy the RES is the main site of destruction of bacilli.

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