

Renal Alterations in Murine Leprosy

TO THE EDITOR:

In 1988, a paper describing a patient with borderline lepromatous (BL) leprosy and erythema nodosum leprosum (ENL) that showed mesangial proliferative glomerulonephritis secondary to the deposition of circulating immune complexes (CIC) and epithelioid granulomas free of acid-fast bacilli (AFB) in the renal interstitium was published (1). On reviewing the literature, the authors of that paper did not find any report of AFB-positive granulomas in the kidney, although they found some reports of cases with renal granulomas with AFB (8, 10). Although it had been noticed already (3, 6), the above paper emphasizes the particular resistance of the renal tissue to infection by *Mycobacterium leprae*. The reason for this higher resistance to mycobacterial infections in general is not obvious, but it has been related to the high amount of spermine and spermidine in renal tissue (4, 5) and to the relative lack of macrophages in the renal interstitium.

In murine leprosy, despite the fact that it is a systemic mycobacteriosis, the renal tissue is, as in human leprosy, seldomly affected. While the liver, spleen, skin, lymph nodes, and other target structures are extensively parasitized in the advanced disease, the renal parenchyma remains virtually free of infection. Bacilliferous granulomas may appear, however, at the hilar zone and on the renal capsule (Figs. 1 and 2). Because of this peculiar resistance of the renal tissue to infection by *M. leprae-murium* (MLM), it was noteworthy to find discrete, isolated, bacilliferous granulomas (or clumps?) in a couple of glomeruli in 2 out of 10 albino NIH mice with an advanced (6 months) MLM-infection. This contrasted with the large proportion of granulomas found in the target organs of all of the examined animals. Thus, renal tissue in the mouse seems to be as resistant to infection by *M. leprae*.

The other aspect of the paper by Al-Mohaya, *et al.* (1) refers to the development of glomerulonephritis in their lepromatous patient. Glomerulonephritis, one of several re-

nal lesions that have been described in human leprosy, although relatively common is not a general complication of the disease. Most frequently, it has been observed in those lepromatous cases with recurrent leprosy reactions (2), and it has been related to the chronic deposition of CIC. In patients with long-lasting disease, however, CIC involve mycobacterial antigens, but they also involve self-antigens. Thus, glomerulonephritis may result from the deposition of mycobacterial-related CIC, but it may also result from the deposition of other microbial-related CIC (from associated infections), from the deposition of self-related CIC, or as a result of autoantibodies reacting with glomerular structures, since a variety of autoantibodies have been reported in lep-

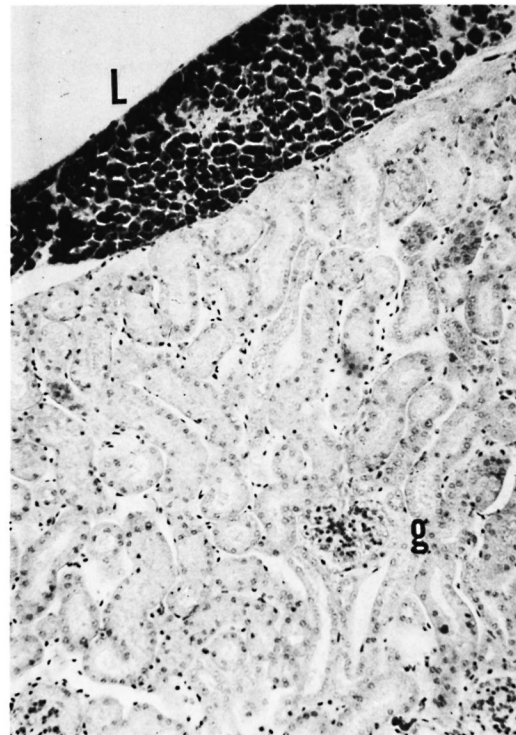


FIG. 1. A highly bacilliferous leproma (L) associated with the renal capsule of a mouse with more than 6 months of MLM infection. Despite the advanced stage of the infection, no granulomas or other major alterations are seen in the renal interstitium nor in the three glomeruli (g) shown (Ziehl-Neelsen and H&E $\times 100$).

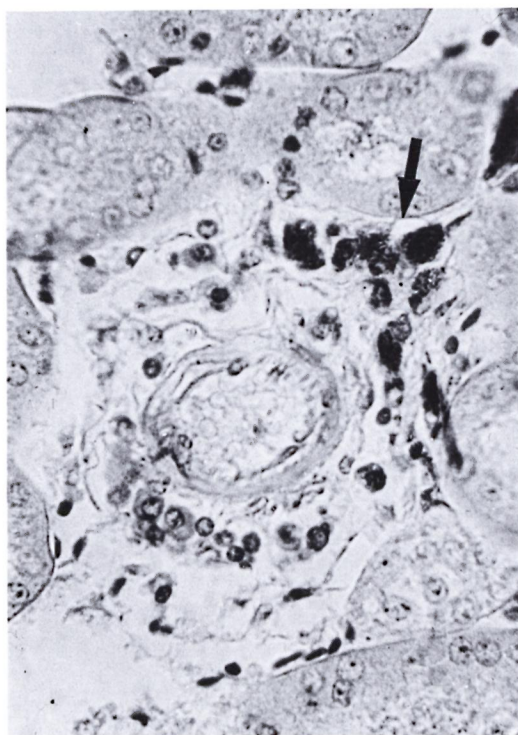


FIG. 2. Bacilliferous granulomas of moderate size (arrow) frequently seen around blood vessels of the hilar zone in the kidneys of mice with advanced MLM infection. Beyond this region, isolated bacilli or bacilli-containing granulomas are rarely found (Ziehl-Neelsen and H&E $\times 400$).

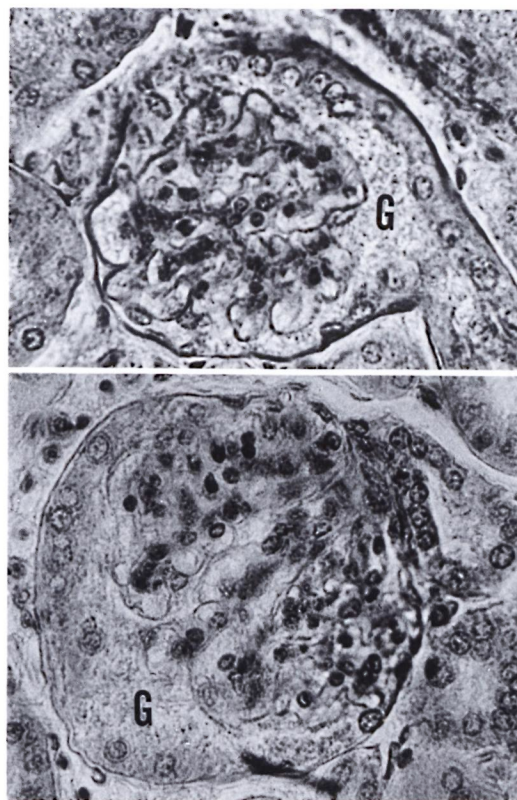


FIG. 3. Glomeruli in murine leprosy often present nondestructive alterations such as increases in volume, hypertrophy of the connecting proximal tubules (notice nucleated cell layer lining the glomerular capsule), and the presence of amorphous granular material (G) filling up the increased subcapsular space (H&E $\times 400$).

romatous leprosy (¹¹). Therefore, since multiple etiologies may give rise to CIC in leprosy (and these, in turn, may lead to diverse renal lesions), it is not clear to what extent leprosy itself accounts for the renal pathology reported in the literature (for a short, comprehensive review see ⁷).

Murine leprosy (a disease similar in some aspects, different in others, to human leprosy), on the other hand, being susceptible to all sorts of controls (homogeneity in sex, age, and weight of the host population; knowledge of the exact infecting doses and time of infection; exclusion of other associated infections; and adequate housing and nourishment), is appropriate for the study of renal pathology resulting from a chronic mycobacterial disease. In the murine infections, abundant antibodies to mycobacterial antigens, hence very likely CIC, are produced. CIC that deposit on glomerular structures give rise to lesions that do not

involve the participation of polymorphonuclear (PMN) leukocytes and, hence, do not become destructive. The thickening of the mesangial matrix (PAS and Mallory stains), hypertrophy of the very proximal renal tubules that alters the morphology of the Bowman's capsule giving the impression of glomerular retraction, and the appearance of an amorphous granular material filling up both the enlarged subcapsular space and the lumen of the adjacent proximal renal tubules, are the most frequent anomalies noticed (Fig. 3). Amyloid (methyl-violet and Congo red stains) was not a component of the glomerular lesion.

The lack of tissue destruction, even in the presence of immune complexes (we have previously demonstrated the heavy deposition of IgG and IgM immunoglobulins in the glomeruli of mice with advanced murine

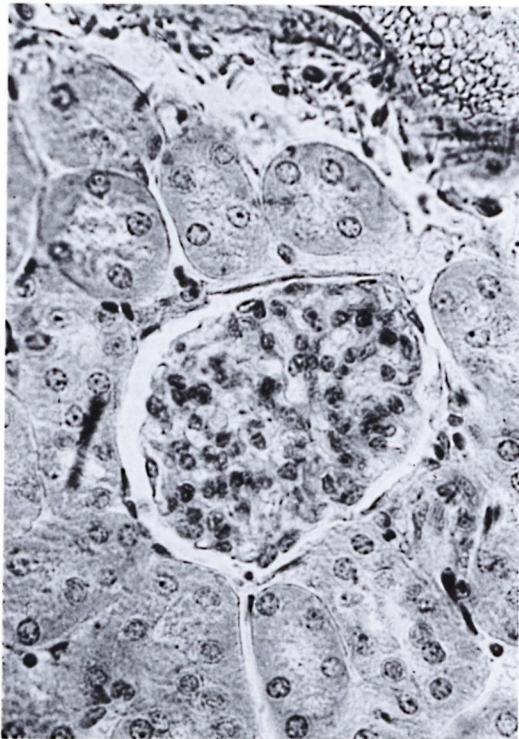


FIG. 4. A normal glomerulus showing average size and cellularity, the neat Bowman's capsule, and clear subcapsular space (H&E $\times 400$).

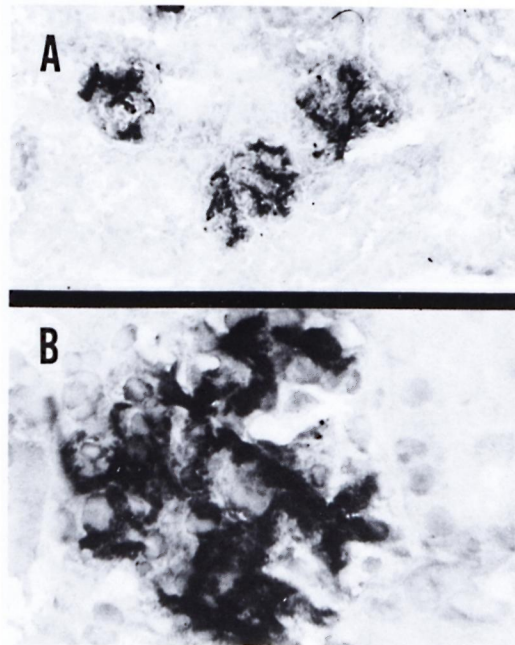


FIG. 5. A kidney section from a mouse with 7 months of MLM infection showing a heavy deposition of IgG. A similar but less-intense reaction was observed

leprosy; Figures 4 and 5), is probably due to the lowered complement activity which, in turn, might account for the absence of PMN infiltration. The low complement activity observed in the infected animals seems to be due to the production of a certain factor that very likely inhibits activation of either C1, C4, or C2 since the alternative route remains almost unaffected (Rojas-Espinosa, *et al.*, submitted for publication). This inactivation of complement that appears and increases during the course of the infection minimizes the general tissue damage and delays the eventually lethal outcome of the disease, allowing the bacilli to preserve their host longer. We do not know whether this is a particular characteristic of murine leprosy or if it also happens in human leprosy, although here this situation might be masked by pathological factors secondary to the mycobacterial disease.

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when the renal section was reacted with an antibody to mouse IgM. This particular specimen showed negligible deposition of murine C3 (Immunoperoxidase stain $\times 100$ (A) $\times 400$ (B).

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