

Serum Complement (C3) in Leprosy*

TIN SHWE

*Department of Clinical Tropical Medicine,
London School of Hygiene and Tropical Medicine
and
Burma Leprosy Service*

Serum complement (C3) was estimated in fresh sera of 45 leprosy patients and 10 healthy controls. Most of the patients with lepromatous leprosy showed an elevated complement level, but 4 out of 6 patients during the first 2 weeks of acute erythema nodosum leprosum (ENL), with or without proteinuria, showed a depressed complement level. Follow-up of one of the latter patients showed that such reduction in complement is only temporary. This suggests that there is an antigen-antibody reaction, with utilization of complement, during the early stage of ENL, which is often associated with proteinuria.

Introduction

Evidence that antigen-antibody reactions may be occurring in a patient can be gained from the amount of complement present in the serum. Thus in serum sickness, acute nephritis, and systemic lupus erythematosus, diseases in which antigen-antibody reactions presumably occur *in vivo*, complement titres are depressed (Boltax & Fischel, 1956; Gewurz *et al.*, 1966). However, complement titres are raised in a number of acute inflammatory conditions, such as acute infectious diseases, rheumatic fever, rheumatoid arthritis, and myocardial infarction (Gewurz *et al.*, 1966; Rapp & Borsos, 1966).

While most authors (Sheagren *et al.*, 1967, 1969; Saitz *et al.*, 1968; Wemambu *et al.*, 1969; Sacher *et al.*, 1970; Mayama, 1971) have reported complement to be elevated in leprosy, others have reported it to be absent (Eliasberg, 1911), normal or slightly depressed (Bonatti & Castro, 1945), or depressed in many patients undergoing severe leprosy reactions (Azevedo & Melo, 1966; Bonomo & Dammacco, 1968, 1969; Meneghini C-Trimigliozzi *et al.*, 1969). The study on serum complement in leprosy was therefore repeated, special emphasis being accorded to its presence in different stages of the lepra reaction.

Materials and Methods

Serum complement (C 3) (β ic- β ia) estimations were carried out on fresh sera collected from 45 leprosy patients at the Hospital for Tropical Diseases, London. The sera of 10 normal healthy subjects (also from the tropics) were included in the study as controls. One patient with acute erythema nodosum leprosum (ENL) and proteinuria, in whom the level of complement was found to be depressed, was

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followed at monthly intervals for 3 months. The estimation of complement (C 3) was carried out by the radial diffusion method (Mancini *et al.*, 1963), using the specific antibody in agar gel plates, and the standard C 3 complement purchased from Hyland Laboratories, California, U.S.A. Sera were diluted for retesting when the diameter of the precipitation zones was greater than that of the highest standard complement. The levels of complement are expressed in mg per 100 ml.

Results

The patients with non-lepromatous leprosy had a mean serum complement level close to that of the controls, viz: 133.0 and 139.4 mg per 100 ml respectively.

Among patients with lepromatous leprosy a wide range of the level of complement was recorded. Most of the patients, with or without ENL reaction, had a raised serum complement level, but among the patients with acute and severe reaction of recent onset there was a reduction in serum complement in 4 out of 6 patients. The difference is significant when this group of patients is compared with other lepromatous leprosy patients with no reaction or to those with chronic ENL ($P < 0.01$) The results are summarized in Table 1 and Fig. 1.

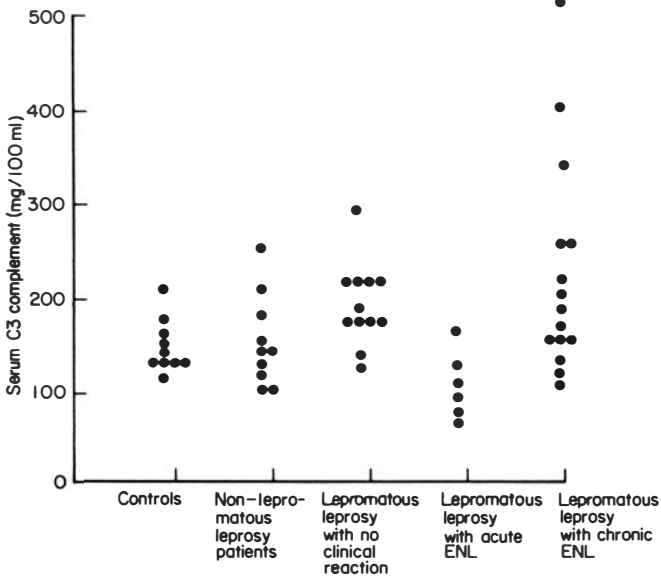


Fig. 1. Serum complement (C3) in different groups of leprosy.

A follow-up study of one patient showed that serum complement was reduced (to 65 mg per 100 ml) only in the early stage of ENL and proteinuria. During the course of the reaction the serum complement level rose again (Figs 2 and 3).

TABLE 1
Serum complement (C3) in different leprosy groups

Group	No. of patients studied	Serum complement level mean (standard deviation) (mg/100 ml)	
Controls	10	134.9	(34.9)
Non-lepromatous leprosy	10	133.0	(48.2)
Lepromatous leprosy with no lepra reactions	12*	183.1	(41.2)
Lepromatous leprosy with chronic lepra reactions	17**	222.4	(120.1)
Lepromatous leprosy with acute lepra reaction	6***	100.0	(37.2)

* includes 2 patients with chronic renal failure.

** includes 7 patients with proteinuria.

*** includes 3 patients with proteinuria.

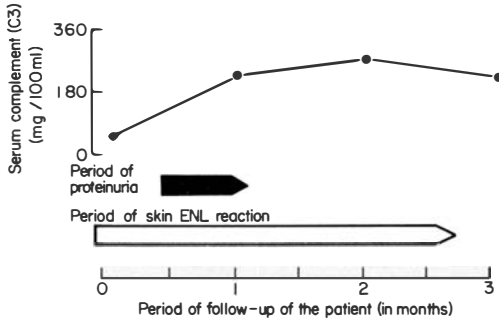


Fig. 2. Follow-up study of a patient showing the relation between the fall in serum complement, ENL, and proteinuria.

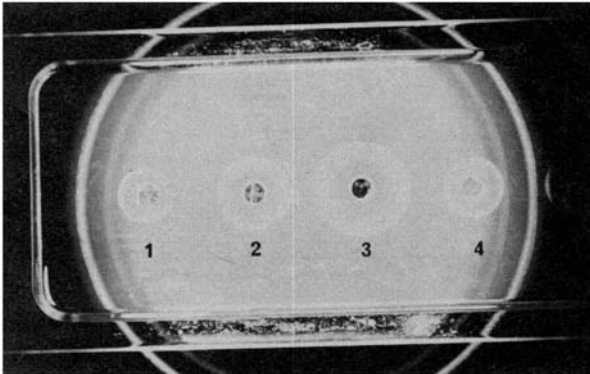


Fig. 3. Immuno-diffusion plate for assay of human complement C3 (β ic- β ia) after incubation with 3 reference standards and serum from a patient with lepromatous leprosy during the first 2 weeks of reactions and proteinuria, showing the fall in complement level of patient's serum. The first 3 wells belong to reference standards 60, 185 and 360 mg per 100 ml respectively. The 4th well, which contains the patient's serum showed the diameter of the precipitation ring equivalent to 65 mg per 100 ml.

Discussion

In this study a depressed level of complement (below 90 mg per 100 ml) was recorded in 4 out of 6 patients within the first 2 weeks of acute ENL, with or without proteinuria. Among other patients with lepromatous leprosy, including those with no lepra reactions, the serum complement value was raised in most cases.

In leprosy, conflicting results have been reported as regards the level of serum complement. Sheagren *et al.* (1967, 1969) reported the concentration of C 3 complement as normal in all patients with uncomplicated leprosy, but found it elevated in lepromatous leprosy patients with ENL or amyloidosis. Saitz *et al.* (1968) reported that C 2 complement levels were within the normal range among lepromatous leprosy patients without ENL, but the titres were distinctly raised in most borderline cases and in cases with an ENL type of reaction. Wemambu *et al.* (1969) reported that 5 out of 17 patients with ENL had a serum complement value (C 3) over 250 mg per 100 ml, and none of them had levels below those found in normal subjects. Sagher *et al.* (1970), in their study on more than 300 sera, reported that complement levels tended to be elevated in patients with active lepromatous leprosy, as well as in patients suffering from lepra reactions, though they tended to be lower during the quiescent phase of reaction. Mayama (1971), in a study of 38 patients with leprosy, also found a marked increase in serum complement in lepromatous leprosy patients with ENL.

On the other hand, other workers have reported serum complement in patients with leprosy as absent (Eliasberg, 1911) or normal or slightly diminished (Bonatti & Castro, 1945). More recently Bonomo and Dammacco (1968, 1969) reported that 50% of lepromatous leprosy patients had low complement levels, and Meneghini C-Trimigliozzi *et al.* (1969) in their study on 80 leprosy patients found low complement levels as measured by serum haemolytic activity, in many cases with strong leprosy reactions.

Such differences could be due to the differences in the method of estimating serum complement, and also to the stage of the ENL reaction. In the present study the fall in serum complement during the early stage of ENL and proteinuria provides indirect evidence that an antigen-antibody reaction, with utilization of complement, occurs in patients with lepromatous leprosy. Serum complement is raised in a number of inflammatory conditions, and therefore the increase in serum complement which is found in most patients with lepromatous leprosy is not altogether surprising.

This finding is in agreement with the reports of Wemambu *et al.* (1969) who demonstrated granular deposits of immunoglobulins and complement in the skin of patients with acute ENL and suggested that ENL reaction is a manifestation of the Arthus phenomenon; and also of Tin Shwe (1971) who has demonstrated granular deposits of immunoglobulins and complement in the glomeruli of 3 out of 7 patients with lepromatous leprosy and proteinuria, and suggested that the chronic renal failure so common in leprosy is possibly due to deposition of antigen-antibody complexes in the kidney. It also confirms the findings of Tin Shwe and Petty (1971) who demonstrated activation of complement (C 3) by immuno-electrophoresis in fresh plasma of 6 lepromatous leprosy patients with proteinuria, and suggested that in lepromatous leprosy there is a stage of antigen-antibody complex formations.

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