REVIEW OF LITERATURE
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INTRODUCTION AND HISTORY

Leprosy is known since antiquity, but where it took its origin remains obscure. Possibly this disease started in Africa and spread through out the world including India via routes of pilgrimage and travel (Scott, 1943). In "Shushrut Samhita" (600 BC), leprosy has been described as "Vat rakt" or "Vat shonita" and "Kushta". Though these conditions probably included psoriasis and vitiligo, leprosy was certainly described. "Kushta" was also mentioned in Vedas and the disease leprosy in our country is present at least since 1400 BC, if the contention of Roger and Muir (1940) and Lowe (1942) is correct.

In European countries this disease was recognised from second century A.D. (Anderson, 1969). One finds a reasonably good account of leprosy at several places in Bible but it is doubtful whether the word has reference to the same disease what we know today as leprosy- (Lie, 1938; Lendrum, 1952). "Zaraath" in Jewish and 'Lepra' in Arabic literature stand for scaly and fungal diseases. The term Zaraath in old test-a-ment and term 'lepra' in new test-a-ment has been considered by many authors to refer to leprosy, and in all Biblical translations has been rendered as leprosy.
The exact number of leprosy patients around the world is not definite. WHO estimated leprosy patients to be over 12 millions including 4 millions in Africa, 7 millions in Asia and about 0.5 millions in America. In India 1971 census showed it to be 3.2 millions, and 1981 census about 4 millions. Uttar Pradesh is moderately endemic state with about 0.05 millions of estimated cases.

**IMMUNOLOGY OF LEPROSY**

Leprosy is an infectious disease caused by *Mycobacterium leprae* (M. leprae). It presents itself in the form of a clinical, pathological, bacteriological and immunological spectrum (Ridley and Jopling, 1966; Skinsnes, 1973). At one end of the spectrum is the tuberculoid (TT) leprosy with high resistance and strong delayed hypersensitivity. At the other pole of the spectrum is a low resistance form the lepromatous leprosy, characterised by multiplicity of lesions abounding in *Mycobacterium leprae*.

**GENETIC FACTORS**

The host resistance can vary because of various interacting factors including constitutional and environmental. Earlier circumstantial evidence suggested that it was the host factor variation rather than existence of different types of disease. Varied forms of leprosy occur in the same family
where strains of *Mycobacterium leprae*, are expected to be the same (Newell, 1966). Secondly, there is high incidence of concordance for leprosy in monozygotic twins than in dizygotic twins (Ali, 1966; Chakraborty and Vogel, 1972). Lack of variation in the virulence of different strains of lepra bacilli was confirmed by Rees (1969). He demonstrated that leprosy bacilli from patients with different types of leprosy all behave in the same way when injected into susceptible mice.

A number of other studies, Viz., taste sensitivity to phenyl thiourea (Beiguelman and Marques, 1964), correlation with A.B.O. blood group system (Hsuen, Thomas and Jesudian, 1963; Lechat et al, 1968), glucose-6-phosphatase dehydrogenase deficiency (Beiguelman, 1966), the frequency of Australia antigen (Blumberg and Melartin, 1967; Samuel, Samuel and Godal, 1974; Bedi, Sama and Bhutani, 1975) and the distribution patterns of HLA antigens (Godal and Myrvang, 1973; Kreisler et al, 1974; Das Gupta et al, 1975; Smith et al, 1975) have been done to assess the role of genetics in leprosy. These studies have given conflicting reports and the role played by genetics in leprosy even today, remains controversial.

**HUMORAL IMMUNITY**

*Mycobacterium leprae* is an intracellular parasite. It is well known that the circulating antibodies can not eliminate intracellular parasites (Mackaness, Blanden and
Collins, 1966). The intracellular organisms, therefore, require cell-mediated immune (CMI) mechanism for the control of infection (Mackaness et al., 1966). The variation in the host resistance to *M. leprae* is thus related to cell-mediated rather than the humoral antibody response which may in fact be enhanced in lepromatous (low resistance) form of the disease. Various types of immunoglobulins in the sera of leprosy patients have been shown to be raised by various workers. Much more higher levels were demonstrated among lepromatous than the tuberculoid (Uhr and Moller, 1968; Bullock, Ho and Chen, 1970; Jha et al., 1971; Young chaiyud et al., 1975). Non specific mycobacterium antibody against protein antigens of *M. leprae* have been shown to be raised in lepromatous leprosy (Abe et al., 1972). The production of antibodies to unrelated antigens such as typhoid and paratyphoid appears to be normal in both types of leprosy (de Almeida, Bandao and de Lima, 1964; Sheasgren et al., 1969; Jha et al., 1971). A number of autoantibodies have also been demonstrated in the sera of patients with lepromatous leprosy (Matthews and Trautman, 1965; Bonomo and Dammacco, 1968; Wager, 1969; Saha and Mittal, 1972; Rea et al., 1974).

**ANTIGENIC CHARACTERIZATION OF M. LEPRAE**

Characterization of *Mycobacterium leprae* antigens and demonstration of specific anti *M. leprae* antibody
remained difficult till recent time. Harboe et al. (1978) carried out immunochemical characterization of *M. leprae* by crossed immune electrophoretic analysis but failed to identify any specific antigen. All the seven antigens which they had isolated from *M. leprae* cross reacted very strongly with other mycobacteria. With the newer methods like iso electric focussing, various protein antigens have been identified. Navalkar (1984) demonstrated that only *M. leprae* bands extended to pH 6.5 while other mycobacterial bands were seen between pH 4 and 5 on polyacrylamide gel plates. Similarly phenolic glycolipid antigen of *M. leprae* have been found to be specific (Brett, 1984). Other recent developments, the monoclonal antibody and the enzyme linked immuno assay (ELISA) helped (Sinha et al., 1983). It has been shown that monoclonal antibodies recognised specific and non specific epitopes of *M. leprae* antigens (Ivanji et al., 1983) and also one of the monoclonal antibodies (ML04) has been used for an specific serological assay for the detection of *M. leprae* antibody (Sinha et al., 1983). ML06 is another specific monoclonal antibody. Recently Narayana et al. (1983) demonstrated both these monoclonal antibodies in both tuberculoid and lepromatous granulomas while no staining with these antibodies could be obtained in lesions of tubercular lymphnode, psoritic skin or normal skin. Further, the *M. leprae* in lepromatous lesions also could not be stained. The lymphocytes and macrophages in both the tuberculoid and lepromatous
granulomas showed membranous staining with the above antibodies.

ROLE OF CELL MEDIATED IMMUNITY

Cell mediated immunity can be assessed by a number of in-vivo and in vitro parameters. Lepromin and tuberculin skin reactivity, ability to develop contact sensitivity, survival of skin homografts, architecture of lymphnodes and ratio of B and T cells all help in the study of CMI responses. CMI can also be assessed by in vitro tests like lymphocyte response to various mitogens and antigens and production of lymphokines (MIF) by lymphocytes.

LEPROMIN REACTIVITY

Some of the earliest studies to assess the immune status of leprosy patients were understandably concerned with the skin reactivity to lepromin. Lepromin skin reaction is reported to parallel the host resistance to _M. leprae_ (Mitsuda, 1953; Hayashi, 1933) and are therefore negative in BL, LI and LL leprosy; moderate in BB and BT and strongly positive in TT leprosy (Ridley and Jopling, 1966). Talwar et al. (1972) have studied the lepromin test in the spectrum of leprosy and they found that both early and late reactions were negative in LL but early reaction was positive in some BL. Further, BB patients had only positive early reactions while late reaction was negative. In TT and BT patients
both early as well as late reactions were found to be positive. Other workers have noted similar observation (Bedi et al., 1976; Job et al., 1976; Rea et al., 1976; Sharma et al., 1979; Kumar et al., 1980; Rao and Rao, 1981; Singh et al., 1985).

The lepromin negativity in lepromatous leprosy is more or less specific (Turk and Brycesson, 1971; Chatterjee, 1976). In lepromatous patients non-specific depression of responses to other intradermal antigens (tuberculin, trichophytin and odiomycin) has also been reported (Rotberg, 1938; Lima and Mogaroa, 1962; Bullock, 1968; Waters, 1971; Mendes et al., 1974). Lowe and Mc Nulty (1953) however, did not find difference in tuberculin reactivity among lepromatous and tuberculoid patients. Rea et al., (1974) using streptokinase/ streptodornase, mumps antigens, trichophytin, candida antigens or histoplasmin also failed to find any difference between lepromatous leprosy patients and a control group of dermatological patients.

CUTANEOUS HYPERSENSITIVITY

The reduced capacity in lepromatous leprosy patients to develop cutaneous hypersensitivity to such chemical sensitizers, as picryl chloride and dinitrochlorobenzene (DNCB) also reflects a non specific depression of the host's CMI. Most of the workers (Waldorf et al., 1966;
Turk and Waters, 1969; Saha and Mittal, 1971) have shown a lowering in the rate of sensitization to DNFB and picryl chloride in leprosy as compared to normals. The depression is of greater magnitude among lepromatous leprosy patients and less in the tuberculoid patients. However, Mendes et al., (1974) and Rea et al., (1974) observed near normal contact sensitivity to DNFB among lepromatous patients. Both Waldorf et al., (1966) and Bullock (1968) observed a lack of correlation between the impaired ability to develop contact sensitivity and tuberculin reactivity. This lack of correlation suggested that failure to chemical contact sensitivity probably detected only a partial failure of CMI was further evidenced by the work of Turk and Waters (1969), who were able to induce sensitivity to key-hole-limpet hemocyanin (KLH) in all the nine lepromatous sensitized with DNFB.

**GRAFTS**

In-vivo, prolonged survival of skin homografts is regarded as a non-specific indicator of cell mediated immunity depression. Prolonged survival of skin homografts has been observed in lepromatous patients (Job and Karat, 1967; Han, Weiser and Kau, 1971). Han, Weiser and Kau (1971) noticed a similar though less pronounced survival of the graft in tuberculoid patients. Ptak et al., (1970) reported a prolonged survival of skin allografts in mice infected with M. Lèpremumurium.
ARCHITECTURE OF LYMPH NODES

Another change which may be seen in vivo with a depression of cell mediated immunity is the depletion of lymphocytes from paracortical areas of lymphnodes. Such changes are seen in Wiskott-Aldrich syndrome a disease with decreased CMI (Cooper et al., 1968) and in animals treated with antilymphocyte serum (Turk and Willoughby, 1967). Desiken and Job (1966) and Turk and Waters (1968, 1971) reported similar finding in lymphnodes among lepromatous leprosy patients; the lymphocytes were replaced by bacilli laden macrophages. Turk and Waters (1971) further observed that the histiocytes became epitheloid along with an increase in number of lymphocytes in paracortical areas as resistance to infection increases across the leprosy spectrum. Ptak et al., (1970) found a similar depletion of paracortical areas of lymphnodes in mice infected with M. leprae murium.

LYMPHOCYTE TRANSFORMATION (LTT)

Various in vitro parameters corroborate the in vivo findings of depressed CMI in lepromatous leprosy. A severe depression of phytohaemagglutinin (PHA) induced lymphocyte transformation in lepromatous leprosy has been demonstrated (Rodriguez- Paradisi, de Bonaparte and Morgenfeld, 1967, 1968; Bullock and Fasal, 1968, 1971; Dierks and Shepard, 1968; Han, Weiser and Lin, 1972; Yamada and Fuzimoto, 1974). In tuberculoid leprosy also, some of the
studies suggest that the lymphocyte response may be depressed though this is neither that pronounced nor consistant (Bullock and Fasal, 1968, 1971; Dierks and Shepard, 1968; Han, Weiser and Lin, 1971; Wong et al, 1971). While some authors (Sheagren et al, 1969; Nelson et al, 1971; Ulrich et al, 1972; Jacob et al, 1974; Rea et al, 1974) failed to demonstrate a depression of lymphocyte response to PHA in lepromatous leprosy also, the evidence in favour of depressed lymphocyte response to PHA is sufficiently convincing. Further studies by Kaklamanis et al,(1977) have revealed that the depressed response to PHA was associated with the reduction in circulating T-lymphocytes. Other workers also observed the same response (Rea et al, 1976; Nath et al, 1977; Sharma et al, 1979; Ghei et al, 1980; Dubey et al, 1981).

Other non-specific mitogens- pokeweed mitogens, and antigens - streptolysin - 'O' and PPD have given similar results (Sheagren et al, 1969; Bullock and Fasal, 1971; Talwar, 1972; Ulrich et al, 1972). All these mitogens and antigens show a non-specific depression of CMI.

The lymphocyte response to specific M. leprae antigens is also significantly depressed (Bullock and Fasal, 1971; Godal et al, 1971; Talwar et al, 1972; Myrvang et al, 1973). A continuous decrease in lymphocyte response
to *M. leprae* from the TT to LL end of the spectrum by both morphological and tritiated thymidine uptake methods had been reported (Myrvang et al, 1973).

LYMPHOCYTES (T AND B)

From the above it is obviously clear that humoral immunity is intact and CMI is impaired among leprosy patients, more so among lepromatous group. Lymphocytes are involved in immunological mechanism (Harris et al, 1945). The thymus dependent (T-cells) appear to be concerned with CMI and bursa dependent (B-cells) with the humoral immunity (Clamen et al, 1966; Roitt et al, 1969; Greves et al, 1973). Thus assessment of T-cells status is important while considering CMI.

Various workers have shown that the T-cell count in the peripheral blood had decreased gradually in the spectrum of leprosy from tuberculoid pole to lepromatous pole; maximum fall being in lepromatous and minimum being in tuberculoid pole; contrary to this B-cell count is found to be increased towards lepromatous pole than tuberculoid pole (Dwyer et al, 1973; Gazlpeczalska et al, 1973; Lim et al, 1974; Chogle et al, 1977; Sharma et al, 1979; Sachdev et al, 1980). In contrast, in the tuberculoid type of leprosy the number of E-rosetting T-cells remain at normal level (Nath et al, 1973; Manimakalai et al, 1982).
Similarly in the lymphnodes of lepromatous leprosy patients, it has been demonstrated that number of B-cells is high in comparison to B-cells in lymphnodes of normal human beings (Verma et al, 1971). This is similar to what one finds of B-cells in peripheral blood of leprosy patients.

Mendes et al., (1974) have studied T and B cells in peripheral blood as well as in lymphnode of lepromatous leprosy cases. A significant decrease in proportion of T-cells was observed in peripheral blood and depletion of T-cells in para cortical areas of involved lymphnodes indicating impaired CMI. B-cells were found to be increased in peripheral blood as well as preservation of B-cells areas was seen in lymphnodes. Similar observations have been made by Methias et al (1980) in the study of cellular changes in spleen.

Studies of infiltrating cells in cutaneous lesions of leprosy have shown similar findings. Kaplan et al., (1984) demonstrated that cutaneous infiltrates of patients of lepromatous leprosy (LL and BL) contained only small numbers of scattered lymphocytes, mostly of the Leu 2a/OKT8 T-cells subset. In borderline patients (BL and BB) and increase in the number of lymphoid cells specifically of the Leu 3a/OKT4 T-cells subset was observed. At the tuberculoid pole of the spectrum (BT and TT), large
numbers of T-cells with extremely long and complex filipodia were found closely associated with epitheloid cells and multinucleated giant cells.

**CMI SUPPRESSION**

The failure of CMI in leprosy, more so among lepromatous leprosy patients has been explained either because of suppressor cells (suppressor T-cells), serum factors of impaired macrophage functions. A number of workers (Bullock et al, 1968; Nelson et al, 1971; and Jaswaney et al, 1982) demonstrated the presence of suppressor factor(s) clearly in lepromatous serum. Jaswaney et al,(1982) have shown that lowering in the numbers of T-cells in lepromatous leprosy can reverse to normal levels by incubating the lymphocytes in foetal calf serum (FCS). However, Patel et al,(1984) could not obtain this stimulatory effect of foetal calf serum on the number of T-cells after 24 hours of incubation. Further, when FCS treated cells were incubated for another 24 hours for rosetting in normal healthy serum, tuberculoid (TT/BT) serum, lepromatous (BL/LL) serum respectively, a very stimulatory effect was noted in T-cells numbers in all the sera. It has been ampl$^\text{d}$ demonstrated that such "suppressor" factor in the serum of lepromatous patients comes from infected macrophages (Salgame et al, 1984; Satish and Nath, 1983). This factor initiate suppressor function of lymphocyte transformation tests (LTT) to both
specific *M. leprae* mediated antigen stimulation and non specific (con A stimulation) mitogens.

As mentioned earlier the unresponsiveness of lepromatous patients to antigens of lepra bacillus, and there partial responsiveness to related antigens for example tubercle bacillus, would be due to the presence of a specific population of suppressor lymphocytes capable of being triggered by at least one unique antigen of *M. leprae*. Mehra et al, (1980, 1982, 1984) have shown that: (i) Dharmendra lepromin induced in vitro suppression of the con A response of lepromatous and borderline, but not tuberculoid patients or normals (ii) two cell populations contribute to the suppression, monocytes and T-cells (iii) all the lepromin induced T cells activity was associated with a 20-30% subpopulation of T-cells defined by the thymidine, monoclonal OKT5 or OKT8 antibodies (iv) a high percentage of the T-cells subset expressed activation markers, Ia and Fc receptors (v) some T-cells recognised the unique phenolic glycolipid I of *M. leprae*, which could induce suppression of mitogenic responses in vitro as well as lepromin and (vi) no significant suppression in vitro was found with lymphocytes from 60 lepromatous patients after immunotherapy with BCG + killed *M. leprae*, and the number of a Ia + OKT8 + cell returned to normal levels.
In this context it is interesting to note that Salgame et al., (1984) have shown that exposure of suppressor factor to T-cell make them as suppressor cells by altering membrane of T-cells, since colchicin treatment reverses the suppressor activity of T-cells.

MACROPHAGES-STATUS IN LEPROSY

Role of macrophages in CMI is mentioned earlier for effective CMI the co-operation of antigen presenting cells and responding lymphocytes is essential. The macrophages process the antigen and present it to the lymphocytes. They also produce factors (Monokines) which may stimulate or inhibit the lymphocytes and may have cytotoxic properties also (Mackaness, 1969 and Territo and Clind, 1975).

The functional status of macrophages has been investigated. In 1967, Barbieri and Correa reported that macrophages from Mistuda - Negative individuals were inactive in vitro against M. leprae, while macrophages from Mistuda - positive persons caused the haemolysis of bacillus in vitro. Similar results have been observed by Beiguelman (1967) and Pisani et al, (1973). Recently Sharp, Calston and Benerjee (1985) showed that M. leprae are not killed by peritoneal macrophages of Nude mice, However, macrophage activity (killing) parallels infection in normal mice. There appears to be defective macrophage population in lepromatous patients that is unable to process M. leprae antigen and initiate the CMI response.
M. leprae on entering into the macrophages of "susceptible" individual produce product(s) that alter metabolism of host cells and also alter the membrane chemical architecture of the cells. Salgame et al., (1980) showed that entry of M. leprae into the macrophages of lepromatous patients, reduced the level of protein synthesis of the host. This has been confirmed to be true even for lysosomal enzymes (Marolia and Mahadevan, 1984). Birdi et al., (1980) demonstrated the occurrence of membrane charges in "susceptible" macrophages by the entry of live M. leprae by monitoring Fc receptors, HLA Dr-antigens. Similar changes have been demonstrated by monitoring con A receptors (Salgame et al., 1983). Lad et al., (1983) have done the same with the adherence receptors that enable M. leprae to adhere to the cell.

Birdi et al., (1980) also demonstrated that there is an inability of the macrophages from leprosy patients to undergo antigen mediated (dead or live M. leprae) physical attraction with lymphocytes, unlike the macrophages from the "resistant" normals or tuberculoid leprosy individuals. This is also most probably, due to membrane perturbation in the susceptible macrophages.

REACTION IN LEPROSY:

Leprosy is a chronic disease with the slow and gradual progression spread over a number of years. However, during the placid course of the disease, abrupt changes in
the clinical stability of the disease or acute outbursts of activity occur and these are termed reactions (Ridley, 1969; Bedi and Bhutani, 1975; Jolliffe, 1977). These are different from mere extension or regression of disease. These acute inflammatory reactions have immunological basis.

Reactions are characterised by certain clinical, pathological, immunological and possibly bacteriological changes. Considerable confusions has, in the past, been caused by use of different terminology to describe the reactions; probably, the most misinterpreted term having been "lepra-reaction" which has variously been used to denote either the entire group of reactions or the progressive lepra reaction in lepromatous leprosy (Jopling, 1971). Yet, another interpretation (Cochrane, 1964) given to lepra reaction in reactions in lepromatous leprosy only. Waters, Turk and Wemambu (1971) suggested that the majority of these reactions may be classified into two aetiological groups, type I and type II reactions. This classification has been followed by other workers and accepted generally (Jolliffe, 1977).

**TYPE I REACTIONS:**

This type of reaction is found in patients with nonpolar type of leprosy (BT, BB and BL) whether treated or untreated. These type I reactions may be divided into
two sub types; namely reversal or upgraded and down graded reactions depending upon the changes in the CMI. Evidence that this reaction is caused by alteration in CMI is provided by the following (1) Changes in the Mistuda reaction; (2) Altered reactivity of lymphocyte transformation tests using whole *M. leprae* antigen (Barnetson, Pearson and Pus, 1976); (3) Histopathological evidence in reacting skin and nerve lesions of changes in the numbers of defending cells such as lymphocytes, epitheloid and giant cells and changes in the numbers of viable bacilli (Ridley, 1969); (4) Lymphnode histological evidence of changes in the cell types occupying the T-cell, paracortical areas. Polar lepromatous (LL) sub polar lepromatous (LI) and the normal lymphocyte population is replaced by macrophages full of bacteria. In reversal reactions the lymphocytes reappear, suggesting return of T-cell activity (Turk and Waters, 1971).

The type I reactions are precipitated by the sudden change in the hypersensitivity in the individual to antigens (Skinsnes, 1973). The exact mechanism is not clear. The change in CMI may be in any direction. Occasionally, however, there may be no change in the CMI. It is usually not possible to differentiate clinically the shift of the immunological status even when new lesions appear. Thus down grading reactions are associated with a decline of immunity and a corresponding increase in the number of bacilli and extension
of infection in near tuberculoid and borderline patients. By their nature these reactions are likely to be found only in untreated patients. Reversal reaction are the opposite. They occur in near lepromatous and borderline patients when the bacterial load is diminished as a result of treatment, and they are associated with a corresponding increase of immunity (Fernadez et al, 1962).

Godal et al., (1973) have also shown concomitant changes in CMI in reversal reactions through various in vitro tests viz. lymphocyte transformation test (LTT) and leucocyte migration inhibition test to *M. leprae* antigens. In this reversal type of reaction the number of lymphocytes is increased in the cutaneous lesions as well as in the lymphnode. Such reactions have been experimentally produced in immunologically suppressed mice with lepromatous leprosy on infusions of syngeneic lymphoid cells (Rees, 1970).

**TYPE II REACTIONS**: This second type of reaction (Type II) or so-called ENL reactions usually manifest itself by the end of first year of sulfone therapy in about 50% of polar and sub polar lepromatous patients and less frequently in borderline cases. Rea and Levan (1980) reviewed 32 patients with this form of reaction and less than a third of them had received any form of anti leprosy therapy prior to its
onset. They stressed that this reaction is a manifestation of the disease and not always a complication of its therapy.

The typical cutaneous and subcutaneous crops of tender erythematous papules or nodules (Erythema nodosum leprosy, ENL) may be associated clinically with rigor and fever. Sometimes this may be complicated by neuritis, arthritis, iridocyclitis, orchitis, proteinuria and lymphadenopathy. Histologically the lesions resembles, Arthus reaction. The centre of ENL lesion comprised disintegration of macrophages with release of bacterial (M. lepra) antigens. There is intense perivascular bacteria free polymorphonuclear leucocytic (PMN) infiltration along with intense vasculitis with fibrinoid necrosis in deep dermal vessels and capillary necrosis in more superficial vessels (Ridley, 1969; Job, Gude and Macadin, 1964). The bacilli are usually relatively sparse in lesions of ENL.

The ENL reactions are believed to result from a combination of mycobacterial antigens with circulating antibodies. Wemambu et al, (1969) demonstrated immunoglobulins and complements in ENL lesions. Electron microscopic studies have proved successful in localizing the M. leprae antigen in the cytoplasmic fraction which forms immune complexes with circulating antibodies (Humoral antibodies are raised in sera of lepromatous patients). In fact such circulating immune complexes have been demonstrated in sera of patients
suffering from ENL by Moran et al, (1972). Furthermore, Lin Shwe (1971) has shown that serum complement is utilized in these immune reactions. The findings of impaired fibrinolytic activity and increased serum histaminase levels in ENL patients are also in conformity with this being an Arthus phenomenon.

Recently, Mshana (1982) however, proposed that ENL is initiated by a decrease, absolute or relative of suppressor T-cells. He based this hypothesis on the following:

(i) Contact sensitivity to dinitro-chlorobenzene (DNCB) is depressed in lepromatous leprosy but greatly attenuated or not at all impaired during ENL (Rea and Levan, 1980).

(ii) Bach et al, (1980) using monoclonal antibodies demonstrated that there is a depression of suppressor T-cells during ENL with a concomitant increase in vitro phytohaemagglutinin (PHA) response, although vivo responses to M.lepraeg were not affected. (iii) Despite circulating M.lepraeg antibodies, not all patient develope ENL as a complication.

(iv) Various factors known to precipitate ENL seem to share little in common in terms of immune complexes. In their view most of the factors associated with precipitation of ENL are causing a disturbance in the T-cell balance thus favouring a drop in the suppressor cells. The observation of Saha
ét al., (1973) on ENL occurring after small pox vaccination is taken as a support suggesting that ENL in this instance is precipitated by the T-cell sub population starting with an increase in suppressor cells, as in common with viral infections, and then followed by a decrease of this population which results in ENL precipitation. Further work on this hypothesis is awaited for confirmation.