DISCUSSION
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It is well established that leprosy is an infectious disease caused by M. leprae. Despite this, majority of the people though exposed to infection do not show any signs and symptoms of leprosy and only a minor group is affected. This fact clearly indicates the difference in the immunological phenomenon in two groups of population. Previous studies by different workers have revealed that due to some unknown mechanism, majority of the population have good immunity against M. leprae and escape from clinical disease whereas others have low resistance. Recently, Mahadevan (1985) has proposed a hypothesis that genetic susceptibility is responsible for lepromatous type of disease. The concept is based on the idea that there is significant quantum of host pathogen interaction before the disease can manifest and clinically identified. In view of interaction between the phagocytic cell and susceptible individuals live M. leprae leads to negative modulation of immune competence of the susceptible individuals. Such negative modulation is mediated through structural alterations of infected cells and production of soluble factors that immuno-modulates the response of the host to the pathogens.
During the chronic course of the disease, however, in some cases, there is a sudden spurt of disease activity, quite different from the normal progression and this is termed reaction. The reactions are very common in different types of leprosy. The exact mechanism of reaction is not definite but seems to be immunological. The type I reactions occur because of changes in cell mediated immunity (CMI) (Godal et al., 1973; Barnetson, 1976), while type II reactions probably occur because of immune complexes (Bedi and Bhutani, 1975).

The present study was undertaken to study the status of T and B lymphocytes in different types of leprosy patients with and without reactions. The study included 60 subjects in total. Out of which 15 were normal healthy volunteers (relations of patients or hospital employees) forming the control group and 45 cases of different types of leprosy both with reaction and without reactions. The leprosy cases were classified according to Ridley and Jopling's (1966) classification. The maximum patients were clinically of the lepromatous group (28.88%), Borderline type (24.44%) and Tuberculoid type (24.44%) (Table II).

Out of 45 leprosy cases 62.30% were males while 37.70% were females. This may be because males are more exposed to the external environment thus infection and reinfection are common. The majority of males in the sample
suffered from lepromatous leprosy while majority of females had borderline leprosy (Table V). The maximum patients were in the age range of 21 years to 40 years (Table II and IV). About 50% cases of lepromatous leprosy suffered from fever. Out of 45 cases, 13 cases diagnosed clinically as lepromatous leprosy were confirmed histopathologically while in tuberculoid type 11 cases were diagnosed clinically but only 5 were proved so histopathologically. The difference or the lack of correlation between the clinical type of disease and histologically described variety of the disease is understandable. This difference may occur because of the fact that tuberculoid group included cases with TT or BT type of clinical picture. In some of the BT cases during reactions the histological picture may mimic the BL or BB. There is an obvious overlap in the borderline group (BT, BB and BL) as these are not well defined type of disease but a part continuous spectrum (Ridley and Jopling, 1962). Further, different types of lesions can occur simultaneously in a patient (Ganpati and Desikan, 1974). More lymphocytes were observed in tuberculoid lesions with reaction than those without reaction. There was also presence of oedema. In BB and BL patients with reactions there was also marked oedema of dermal connective tissue. The cells were polymorphs as well as lymphocytes. A free subepidermal zone was observed in two patients of BB leprosy with reaction. Similar clear subepidermal zone has been described by Skinsnes (1973).
In the present study follow up could not be done following the subsidence of reactions, neither lepromin test was performed during, before or after the reaction. Thus it is very difficult to say that type I reactions observed in this study were of down grading or reversal type. Influx of lymphocytes in the lesion during type I reactions has been described (Ridley, 1969). However, number of these infiltrating lymphocytes subsequently decrease in down grading reactions and the granuloma opens up much more. In contrast, though the number of infiltrating lymphocytes may decrease the granuloma becomes more compact with high number of epitheloid cells. Erythema nodosum leprosy (ENL) - type II reaction presents features of acute vasculitis often associated with fibrinoid swelling of collagen fibres with focal areas of necrosis with numerous inflammatory cells, predominantly polymorphonuclear. In our study, six out of nine LL patients with reactions, one BL case with reaction and two out of eight cases of BB type II reaction showed intracellular oedema as well as extracellular oedema along with fibrinoid necrosis. Evidence of vasculitis was present in all these cases. This is similar to what has been previously described (Bedi and Bhutani, 1975; Job et al., 1964; and Ridley, 1969).

Among the controls in the present study mean (±SE) absolute T cell count was 1435 ± 236.4 while the mean T cell percentage was 57 ± 1.7, this was little less than what has been reported by Rea et al. (1976). In their study mean T cell
percentage was 68.8 ± 7.7 however mean T cell percentage
as reported by other workers has varied from 40.8 to 77
percent. (Dwyer et al, 1973; Lim et al, 1974; Chogle et al,
1977; Sharma et al, 1979). The differences in mean cell
count among normal people have been studied by Mendes et al,
(1974). Variation can occur because of the population diffe-
rence and also in the donor when tested on different days.
The reactive rosette formation of T cells and sheep red
blood cells is temperature dependent. The maximum values
are obtained between 10°C and 25°C and no rosette formation
occurs at 37°C. Jhansi, the place of study is a warm dry
area. The high temperature from March to July-August might
have affected the cells during the transporation from the
leprosy clinic to laboratory. Storage of blood and lympho-
cytes is known to affect T cell number. However, in the
present study while comparing the data from controls and
test subjects these factors are not applicable as climatic
conditions are similar for both the groups. The minor and
insignificant difference in the T cell count of this study
and other studies may be due to above mentioned factors.
The mean absolute lymphocyte count among the controls and
different types of leprosy cases is depicted in Table XI.
It is almost equal in all types of disease. This indicates
that there is no correlation between the absolute lymphocyte
count and the type of leprosy the patient has the mean T cell
percentage among control was 57.00 ± 1.7, similar figures
were obtained for TT and BT group. The T cell percent was 48.90 ± 2.35 in BB, 50.4 ± 3.37 in BL and only 42.0 ± 3.20 among the lepromatous patients. Thus the mean T cells percentage was lowest among the lepromatous group when compared to control, the difference was highly significant. Similarly when compared to TT group the mean T cell percentage was very significantly low (p < 0.001). In other groups also the mean T cell percentage was significantly low when compared to controls, though the significance gradually declined from lowest values of lepromatous to maximum value of tuberculoid. Other workers have also reported similar findings showing the decrease in mean T cell percent from control to LL (Dwyer et al., 1973; Lim et al., 1974; Chogle et al., 1977; Kaklamanis et al., 1977). Recently Sharma et al., (1979) and Singh et al., (1983) made similar observations. These studies also indicated that there is gradual decrease in the mean T cell percent from control to LL group. In contrast to the above, no difference in mean T cell percent among the control and LL leprosy subjects was observed by Rea et al., (1976). They found mean T cell percent 70.4 ± 6.3 and 68.8 ± 7.7 among the controls and LL patients respectively. Our findings are further corroborated by Mendes et al., (1974). He studied T and B cells in peripheral blood and lymphnodes of lepromatous leprosy cases and found a significant decrease of T cells in the blood as well as the paracortical areas of
lymphnodes. Turk and Waters (1971) also made similar observation.

The mean B cell percentage (Table XIII) was 36.46 \pm 2.54 among the controls. Similar value was obtained for borderline cases and borderline tuberculoid cases. In the tuberculoid group the mean B cell percentage was only 30.54 \pm 3.82 (range 34 to 45). The difference was significant in comparison to control. Contrary to this, B cell count was raised in borderline lepromatous and lepromatous patients 44.2 \pm 1.49 and 48.38 \pm 2.90 respectively. The increase in B cell count in comparison to control in both these groups was very highly significant (p \leq 0.001). The same was true when compared with tuberculoid group. The differences were again significant between tuberculoid and BT/BB groups with tuberculoid patients showing the lowest value as mentioned.

Gazl-Paczalska et al, (1973) had reported marked increase in B cell percentage 60% to 85% of B cell in peripheral blood. Sharma et al, (1979) had studied B cell percentage in complete spectrum of leprosy and observed slight increase in B cell percentages. They observed mean \pm SE of B cell percentage in control, TT, BT, BB, BL and LL which was 27.67 \pm 3.77, 28.50 \pm 5.71, 30.23 \pm 7.89, 31.85 \pm 7.81 and 29.97 \pm 7.79 respectively and concluded that there was very minimal increase in B cell percentage which was statistically not significant. Rea et al, (1976) had also observed no significant increase in B cells in lepromatous leprosy.
Dwyer et al, (1973) had studied B cell percentage only in control and lepromatous groups and found significant increase in B cell percentage in peripheral blood in lepromatous group. They observed 27 percent in control and 35 percent B cell in lepromatous group which are similar to the observations of present study. Other workers also had shown that patients with lepromatous leprosy had high proportion of circulating lymphocytes possessing membrane bound immunoglobulin (B cells). It has been proposed that such increase in B cell might represent over compensation for a deficiency of T lymphocytes.

The findings of present study were also in accordance with Chogle et al, (1977), who studied mean ± SE of B cell percentage in control, TT, BB and LL groups and found 27 ± 5.4, 36 ± 8.6, 37 ± 6.6 and 56 ± 10.7 respectively.

The findings of present study are supported by the study of Verma et al, (1971) who had observed significant increase in B cell percentage among lymphocytes obtained from crushing the lymphnode.

As B-lymphocytes are involved in antibody production, Abe et al, (1972) had reported anti M. leprae antibodies with indirect fluorescent technique in both lepromatous, tuberculoid, and indeterminate sera but the proportion of positive sera titre observed was highest in lepromatous sera.
B cell percentage was confirmed between the leprosy patients with reaction and without reaction. There was no significant difference between these two groups, neither there was any correlation of mean B cell percentage during reaction to the type of disease patient had. This can be explained because of the fact that type I reactions occur due to changes in CMI (Bedi and Bhutani, 1975) and type II reaction which occur in multibacillary patients are immune complex mediated (Gelber et al, 1973). In the later group the humoral activity is already increased and various types of immunoglobulin sera have been demonstrated to be raised. (Uhr and Moller, 1968; Young Chaigud et al, 1975). Similarly the B cell count has also been demonstrated to be raised towards lepromatous pole than tuberculoid pole (Dwyer et al, 1973; Sharma et al, 1979; Sachdev et al, 1980).

The cell count was low among patients of all types with reactions when compared to patients without reactions (Table XI and XII). In the two tuberculoid patients it was 52% and 58% respectively (absolute T cell count 884 and 881). Among the borderline patients with reaction, three patients had T cell percent between 38 and 40% while two patients each had count of 48 and 50% respectively. Only one patient had count as high as 58% (absolute T cell count 1928). In contrast two reacting lepromatous patients had very low
T cell count that is 28% (absolute values 582, 1117 respectively). Other four patients had also low values between 35 and 41%. Three lepromatous patients with reaction had count around 50% and only one had high count about 60% (absolute value 1104).

The T cell count was not different among TT patients whether with reaction or without reaction. Though improvement of CMI is expected during reversal reaction, it is not necessary that T cell count in sera will increase. The changes in CMI are well documented by the influx of lymphocyte in lesions during reacting phase. The other parameters like lepromin test, blast transformation, macrophage inhibition studies were not done in this study. Further, patients could not be studied before, during and after the reactions, thus it is difficult to corroborate reversal nature of the reaction in these two tuberculoid patients.

The recent development of monoclonal antibodies had helped in identifying various phenotypes of T cells in leprosy infiltrates. This may distinguish different reaction states such as ENL from upgrading or borderline (Wesley et al, 1982).

The nature and histological pattern of the cutaneous infiltrates of 17 leprosy patients in reversal patient (Type I) and ENL, (Type II) were compared with tissue from 18 non reactional borderline leprosy (BT and BL) and lepromatous leprosy (LL) patients using monoclonal antibodies and
immunofluorescence. Reactional BT lesions showed a mild increase in OKT-11 + Pan T cells as compared to non reac-
tional tissues and a significant influx of OKT-8 + (Suppressor/
Cytotoxic) cells which were peripherally localised in the
lymphocytes mantle surrounding the epitheloid cells. The
leu 3a + (helper inducer) cells were scattered amongst the
lymphocytes and macrophages. The mean ratio ± SE of leu 3a +/
OKT-8 + cells was 1.88 ± 0.64 in BT reactions as compared to
2.95 ± 0.95 in BT lesions. In contrast, lesions of BL reversal
reactions and ENL showed a more marked increase in Pan T cells
with a preponderance of helper/inducer subset, leu 3a +/OKT-8 +
ratio being 2.26 ± 0.61 and 0.93 ± 0.57 in BL reactional and
non reactional lesions, respectively. Interestingly, this
increase in number of T cells reached levels observed in BT
lesions. The distribution pattern of OKT-8 + cell was similar
to leu 3a +, both being diffusely scattered on the bacilli
laden macrophages. Ia like antigens were present in all granu-
lomas and were abundant on lymphocytes and macrophases and
less conspicuous on epitheloid cells. T6 + langerhams cell
were uniformly increased in all reactional lesions. It would
appear that the changes observed in both type I and type II
reactions are similar in the lepromatous group of patients.
They differ significantly from the BT reversal reaction in
terms of the dominant T cells subset and the microanatomical
distribution of the OKT-8 + cells in the lesions (Narayana
et al, 1983).
Similar observation was made from the borderline patients with reactions, also it was difficult to differentiate, nature of reaction whether reversal or downgrading.

All the ten lepromatous patients and sole BL patient with reaction had type II reaction. The low T cell count observed among these were comparable to those observed in patients without reactions. The course of ENL is proposed to be immuno-complex mediated mechanism (Wemambu et al, 1969). It is akin to type III arthus reaction (Waters and Turk, 1971; Gelber, 1973). Demonstration of immune complexes in and around blood vessels is not universally found in ENL lesions (Faber et al, 1978). A cell mediated immune pathogenesis has also been proposed (Waldorf et al, 1966; Grean, 1971).

Mshana (1982) also proposed that ENL reaction is initiated by changes in the cell mediated immune reaction, that is, decrease in absolute or relative suppressor T cells. This is based on certain clinical observations, for example, not all LL patients develop ENL though all of them have high bacillary load and anti M. leprae antibodies. It has also recently been shown that, whereas, contact sensitivity to dinitro-chlorobenzene (DNBC) is depressed in lepromatous leprosy, it is, on the other hand, not impaired or greatly attenuated during ENL (Rea et al, 1980), indicating a depression of suppression. Depression of suppressor cell during
ENL with a concomitant increase in in-vitro phyhaemagglutinin (PHA) response has been demonstrated by Bach et al. (1980). However, in-vivo responses to *M. leprae* were not affected in their studies. It is interesting to note that Wesley (1982) in his study was able to demonstrate only few OKT-4/leu - 3a cells, T cells in the infiltrate of patients with erythema nodosum leprosum, while the sole patient whose disease had changed from borderline to tuberculoid leprosy had large number of OKT-4 Len-za cells, similar to that found in tuberculoid lesion.

Keeping in view the work of other authors and the present study, one can establish that there is gradual depression of CMI among leprosy patients from the tuberculoid pole to lepromatous pole. This is evident from lepromin test, lymphocyte transformation test and cutaneous delayed hypersensitivity reaction. The borderline group bridges the two poles with varying intermediate results. The B cell percentage gradually increases from tuberculoid to lepromatous end. While T cells in the peripheral blood though normal in number among tuberculoid patients are significantly low in lepromatous group. T cell percentage was significantly low among BB and BL patients also but the fall in the number was much less than that in LL patients. No difference was observed in the number of B cells in blood from patients with reaction and without reaction. Similarly the T cell percentage was similar among TT patients with reaction and without reaction. However,
in contrast to this a low T cell count was observed among lepromatous (LL and BL) patients with reaction in comparison to those who did not have reaction. The difference was not significant. Among the borderline patients with reaction highly varied T cell count was observed in the blood, in some significantly low and in others equal to that seen among borderline patients without reaction. However, it was never high. Thus, we can say that T cell count alone does not affect the nature of reaction, and other parameters for assessing immunity should be carried out.

Modlin et al. (1985) also observed statistically fewer cells of the suppressor cytotoxic pheno type and a greater number of cells of the helper induced phenotype in patients with ENL as compared with those without ENL. Patients without ENL had a tissue helper suppressor ratio of 0.6 to 0.1 as compared with those with ENL, whose ratio was 2.1 ± 0.4. Prior therapy had no affect on the results. Their work further supports that cell mediated immuno response is important in the pathogenesis of ENL, either directly or by permitting production of the antibody critical to the formation of immune complex. They also observed a lack of relationship between tissue and peripheral blood helper suppressor ratio. This finding is consistent with a process of selectivity of entry, retention or exit, or some combination of these rather than a passive diffusion of lymphocytes from the vascular component of tissues.