Measles in one of the important exanthemous viral infections of childhood. The disease has been defined as "a eruptive fever caused by a specific virus and clinically characterized by fever and catarrhal symptoms followed by typical rash."

Measles is a "pediatric priority" in the developing countries (Morley, D. 1973). The outcome of the disease depends upon the cell mediated immune system of the host (Burnet, F.M. 1968).

**NOMENCLATURE AND HISTORY**

There is some doubt about the origin of the name measles most probably it comes from the Latin term misellus or misella itself a diminutive of the Latin miser, meaning miserable. It was John Caddesden who identified, quite unjustifiably, the non specific leprous sore with disease called in Latin morbilli. This term was a diminutive of morbus, meaning disease, which referred to the major disease. In the anglicized form of misellus, namely measles, the word hence forward became applied to the specific disease morbilli (Wilson G.S. 1962).
The disease was probably first recognized by Rhazes, a tenth century Arabian Physician and its identity as a specific disease was fully established by sydenham in the 17th century. Koplik in 1896, was able to establish a definite clinical basis for differentiating measles from rubella and other exanthems. Enders et al (1959), succeeded in cultivating measles virus and thus providing a reliable procedure for diagnosis and for preparation of vaccine. The vaccine was first used in clinical trial in U.S.A. in 1959.

MAGNITUDE OF THE PROBLEM

Measles is truly a universal disease, endemic throughout the world, sporadic cases occur throughout the year in all countries but epidemics are most frequent during the late winter and early spring. In large cities it is common for it to show a biennial peak, dependent presumably on the accumulation of susceptible persons. In Britain, Europe and the United States, measles has been a disease mainly of winter and spring. In India the peak incidence has been reported from March to June every year (Taneja, P.N. 1962).
EPIDEMIOLOGICAL OBSERVATIONS

Panum did classical studies on the epidemiology of measles in 1947. The attack rate in measles is higher than for any other infectious disease (Wilson, C.S., 1962). The disease is fairly mild in itself unless complicated by respiratory infectious when it becomes severe or even fatal. In virgin population that have not experienced a previous visitation, more than 90% of that population will be infected, Morley David (1973). Most children exposed to the infection for the first time contract the disease, with an infection to illness ratio almost one. Secondary attack rates over 90% was observed by Krugman and Ward in 1975, after intimate household exposure. However in the periodic epidemics of measles, in rural communities in India, attack rate in children born subsequent to the previous epidemics have been much lower (Pereira and Benjamin 1972, Siddique et al, 1974, Sinha, 3. 1977, John T.J. et al., 1980). This may be due partly to limited exposure.

MORBIDITY AND MORTALITY PATTERN IN MEASLES

There have been reported a high morbidity and mortality in measles and a number of complications later on. Children with measles who do not recover may succumb to acute complications (mainly respiratory) or chronic disease (respiratory and neurological) may develop.
Despite the reduction in mortality morbidity is still high with 90-95% affected by the age of 10. Harin, J.F. (1967) reported a mortality of .2 per 10,000 notified cases in developed countries.

Measles is still a major cause of death in developing countries (Harley, D. 1969). In Africa mortality among hospital ranges from 5-25%. Hendrickse, R.C. (1975) has claimed a case fatality rate of 5% or more from developing countries. Kester, F.T. (1981) observed a case fatality rate of 3.7% in his study on measles in Bangladesh. In other developing countries the reported data are Guatemala (6.6%), Nigeria (5%), Tanzania (13.7%) while in developed countries such as U.S.A. (0.02%).

Studies from Asian countries and particularly from India, have shown, measles to be less severe as compared to serious countries from a rural community in India, Falghar Shah and Udani, P.M. (1969) have reported only 1.5% of the deaths due to measles, while Krishnamurthy, K.P., Devaj Rajan, R. (1979) observed a mortality rate of 11.76%. In a recent study Thomas cherian, Abraham Joseph and John T.J. (1984), while
carrying out their study in a measles epidemic in Tamilnadu (Dec. 79-March, 80), observed an attack rate of 54% and case fatality rate of 10%.

**Passive Immunity in Measles**

Infants under 3 months of age are absolutely immune to measles and those between three and six or eight months are relatively immune. Infants acquire immunity transplacentally from mothers, who have had measles. Infants born to mothers immune to measles are protected against infection during their first 6 or 7 months after birth (Mehata, N.A., 1972). With the decline of maternal antibodies, babies become increasingly susceptible after 6 months of age and may on exposure develop disease varying severity. Those with modified or occult illnesses are thought to be examples of partial protection by residual transplacentally acquired antibody. The infants of rare mothers who has never had measles or vaccine is susceptible at birth and may acquire the infection at any time postnatally.

**Age Relation to Measles**

The incidence of disease is usually highest in the second, third and fourth years of life (Wilson 63, 1962).
The peak incidence of the disease in developing countries is between 1 and 3 years. While in United Kingdom and Europe it is 5 years and above, and in United States it is 10-14 years (Morley D. 1969).

The extent of the prevalence of disease, the immune status of the population, and the susceptible age at which infection generally occurs in India are unknown. In India median age of measles has been found to be different by different workers. Mehta, N.A. (1972) while conducting the seroepidemiology of measles in Bombay found 48% positivity by 4 years of age and 100% by 7 years of age. Thus highest susceptibility and attack rate was seen in the preschool and early school years.

Krishnamurthy and Anantharaman (1974) found highest incidence in between 1 and 3 years of age. RamaKrishnan et al (1976) observed maximum incidence in the age group of 0-1 years. Bhan et al (1979) observed, onset of measles infection at preschool age (2-4 years) with the maximum rate of infection in school going age group 6-7 years. Bhaskaran P. et al (1984) found maximum incidence (45%) in children between 1 and 3 years, 22% in the age group less than one year, 20% in 3-5 years age group and rest above 5 years.
The pathologic agent causing measles is the paracyxovirus belonging to the group of myxoviruses. It's internal component of ribonucleic acid (RNA) with in a helicole protein capsid is enclosed by an outer membrane of a lipid and protein. It is about 140nm in diameter only one antigenic type is known. During the prodromal period and for a short period after the rash appears, it is found in nasopharyngeal secretions, blood and urine. It can remain active for at least 34 hours at room temperature.

The virus has been cultured in human and monkey leucocytes (Berg and Rosenthal, 1961).

Epidemiologically measles has been considered to be a respiratory disease since Famm (1938-39) and Babbet F.L. and Gordon J.E. (1954) first presented evidence for this point of view. It is assumed that infectious droplets of nasopharyngeal secretions from a patient land upon the respiratory epithelial cells of the new host. Infection occurs and the chain of events resulting in disease is initiated. It has been proposed particularly by Papp, K. (1926) that the primary site of infection is conjunctiva and evidence has been presented that the introduction of immune serum into this area or covering the eyes will protect against natural infection (Robbins, Fredrick, 1962).
PATHOGENESIS OF DISEASE

The classic investigations of Fenner, P. (1950) on the pathogenesis of measles in mouse pox, provide an experimental model with general applicability.

The sequence of events based on the Fenner scheme and making the proper adaptations for measles would be as follows.

Day 0  1- Invasion of respiratory epithelial cells and multiplication.

Day1+  2- Extension to regional lymph nodes.

Day2   3- Primary viremia - This has not been conclusively demonstrated for measles.

Day3-5 4- Multiplication in lymphoid tissues and respiratory epithelium with formation of giant cells; infection of respiratory tract probably mediated through the blood.

Day 5   5- Secondary viremia.

Day7+  6- Establishment of infection in skin, involvement of brain may result from virus reaching it, through the blood.

Day 11+ 7- Onset of prodromata.
Day 14+ 8- Development of rash.

Day 15+ 9- Antibody appears, viremia ceases and viral content in organs diminishes.

Day 17+ 10- Symptoms ameliorate, and rash begins to fade.

CLINICAL MANIFESTATIONS OF ILLNESS

Measles is characterized by three well recognized stages:

1- An incubation period of approximately 10-12 days with few, if any signs and symptoms.

2- A prodromal stage with an exanthem (Koplik spots) on the buccal and pharyngeal mucosa, mild to moderate fever, slight conjunctivitis, Coryza and an increasingly severe cough, and

3- A final stage with a maculopapular rash erupting successfully over the neck and face, body arms and legs and accompanied by high fever.

MEASLES ANERGY, AND PROVOKING EFFECT OF THE DISEASE

The altered reactivity of the patient during measles is expressed in the state known as measles anergy.

Before the appearance of rash till the late convalescent, passive tuberculin reaction disappears,
(Von Pirquet 1908, Starr and Barkevitch 1964), the titre of immune bodies falls, the complement titre falls, the immunization capacity of the patient diminishes, and a negative schick reaction changes to positive. As a result measles can light up latent infections (tuberculosis, dysentry, whooping cough etc.). The protective reaction of the child is lowered, the mild infections can become lethal. This provoking effect is particularly pronounced in children.

Tuberculosis and malnutrition infections normally controlled by cell mediated immune response are known to follow measles (Beck 1962, Smythe et al 1971).

MEASLES AND MALNUTRITION: ITS SYNERGISTIC ROLE AND COMPLICATIONS

Several clinical studies have high-lighted the synergistic effects of measles and malnutrition on the host (Corden, J.E. 1965, Morley, D. 1969). Defense reactions are suppressed in malnutrition and mild infections can become lethal (Smythe P.M. et al., 1971). Children with measles who do not recover, may succumb to acute complications (mainly respiratory) or chronic disease (respiratory and neurological) may develop (Cosvadia, N.M. et al., 1977). Prolonged
mortality due to secondary infection is frequent especially in malnourished children and this has been attributed to immuno-suppression.

Measles and its complications

Measles virus infections are associated with a number of complications accredited to immune phenomenon of giant cell pneumonia due to direct viral invasion of the pulmonary parenchyma is seen primarily in previously immunocompromised children (Maccarthy K., Mitus F., Cheathan W. et al., 1988). Secondary bacterial pneumonia and otitis media are frequent complications in otherwise normal children and are thought to related to virus induced immunosuppression (Miller, D.L. 1964), on the other hand the encephalitis seen in measles has been suggested to have an autoimmune basis (Koprowski, H.J. 1960, Lachmann, P.J. 1974).

Bhaskaram P. et al (1984) concluded that morbidity due to measles show two distinct phases. The children may develop complications in the acute stage of measles or during the subsequent period. The follow up study showed that the children suffered from frequent infections even after the attack of measles. This could be due to prolonged immuno-suppression induced by the disease.
IMMUNOLOGIC SYSTEM

Immunologic system is the part of host defence, its primary function is to protect against invasion by infectious agent. The major cost of this protection are allergy, autoimmunity and rejection of organ transplant. There are four major limbs of immunologic system, T lymphocyte B lymphocyte, phagocyte and complement.

T AND B CELL LYMPHOCYTE

Harris et al (1945) had shown that the lymphocytes were involved in the immunological mechanism. It is now recognised that lymphocytes form an indispensable component of body immune status and embodies that precursor of cells that will give rise both cell mediated immunity and humoral immunity.

Study of Claman et al (1966), Devis et al (1967) Miller and Michel (1968) indicated that at least two population of lymphocytes were involved in most of immune response. These two population of lymphocytes are currently known as T cell (Thymus dependent), and B cell (Burma equivalent derived), Rittet et al (1969), Graves et al (1973) had shown that T cell appear to be concern with cell mediated
immunity (CHI) and B cell with humoral immunity.

T lymphocytes play a major role in immune response to facultative organisms, tissue or organ graft and certain infections with viruses. B lymphocytes mature to become antibody producing plasma cells and play a role in humoral immunity response (Rowland (1975) lymphocytes circulate 4 to 6 times a day. T cells accounts for as many as 70% of peripheral blood lymphocytes while 20-25% are B cells (Lukes et al., 1974).

T lymphocytes are grouped broadly into modulator cells, effector cells, and cell producing lymphokines, modulator cells are further devided in to two categories. Those that initints (helper or inducer) and those that tends to terminate (supressor cells) immune response (Reinherz and Schlossman 1980). The production of antibody by B lymphocytes requires the participation of helper T cells. A possible mechanism for subsequent termination of antibody production is the activity of suppressor cells. There appears to be a subpopulation of inducer T lymphocyte required to induce the function of the T suppressor lymphocyte (Morimoto et al., 1981). In addition to modulatory lymphocyte there are the T lymphocytes called cytotoxic effector cells. These cells are able to recognise
foreign or altered self antigen, on the surface of cell
and to destroy the cells (Paul K.S. 1980). The other
function of T lymphocytes is secretion of lymphokines, these
low molecular weight substance secreted by activated
T lymphocytes, affect the function of other cells in
the surrounding environment. T cells secretes one type
of interferon, a lymphokine that stimulates other cells
to develop anti viral activity. Macrophage migration
inhibition factor secreted by stimulated T cells causes
activation and immobilization of macrophages at the
site of an inflammatory response (Rocklin at 1980). Inter
leukin-2 is lymphokine that promotes activation and
division of other T lymphocytes (Gillis 1983).

B lymphocytes has immunoglobulin molecules of
a single antigenic specificity on its surface, when
exposed to the relevant antigen usually processed by
a macrophage, and under the influence of signals from
an antigen specific T lymphocyte, B lymphocytes differentiate
into plasma cells which secretes antibody of same
specificity as originally found in its progenitor.
B cells are commonly identified by immune globulin
on SI-gm marker. Approximately 10% cell carry these
markers along with IgD. The most commonly employed test
for B cell function is quantitative measurement of serum immunoglobulin by single radial diffusion.

T AND B CELL COUNT

T and B lymphocytes can be identified by various methods, antibodies against T and B cells have been prepared. But the most widely used method at present for identifying human T cell depends upon their ability to bind sheep RBC spontaneously in characteristic morphological configuration termed as rosette (Fundenberg 1975). Human B cell possess surface immunoglobulin detectable by direct immunofluorescence. They also possess receptor for aggregated immunoglobulins. For antigen–antibody complex and for the third component of complement. These receptor are detected by erythrocyte coated with antibody or complement that surround B lymphocyte in cluster (Wybran and Fundenberg 1973).

Presently the spontaneous formation of rosette with sheep erythrocytes appears to be a specific property of T lymphocytes, and membrane bound immunoglobulin detectable by immunofluorescence constitute the most reliable marker of B cells, (Saligman 1974). However the fundamental nature of rosette formation is not known. They also possess receptor aggregated immunoglobins
for antigen and antibody complex and for the complement C₃, surrounded by B lymphocyte in cluster (Mendas et al 1973). These receptor are detected by erythrocyte coated with antibody and complement.

Steel, C.M. et al (1974) noted that T lymphocyte and B lymphocyte rosette formation are affected by temperature, incubation time, red cell to lymphocyte ratio, and sheep from which RBC are obtained. A short incubation time between the sheep RBC, and human lymphocyte result in rosette formation of only some of T cell whereas a longer incubation time permits all T cell to bind. Thus the studies using longer incubation time usually have higher value of percentage of cell which form rosette. Fundenbergs and associates (1975) termed the population detected by short incubation period, active cells because they appears to be a subpopulation of more actively envolved in cellular immunity than total T cell population.

It is believed that rosette are formed by rapid release or metabolised receptor substance on the living cell surface. Positive bivalent ion are required since ethylene diamine tetra acetic acid will block to rosette formation (Jendal 1972), although comparable result using either ethylene diamine tetra acetic acid (EDTA)
or heparin a anticoagulant for rosette testing have been reported. Fairbanks (1976) and Hadfield and associates (1975) reported that as the concentration of heparin was increased in the test system the percentage of T lymphocyte rosette decreased. Normally there are more than 1500 circulating T cell/mm$^3$ each having less than 10 u in diameter. In some T cell deficiency, number of lymphocyte count is normal or even elevated but the lymphocyte are larger than 10 u in diameter, monocytosis and eosinophilia are commonly associated with T cell deficiency (Nelson 12th edition).

**VARIATION OF LYMPHOCYTES COUNT WITH AGE AND SEX**

In study of deviation of T lymphocyte and B lymphocyte counts in disease, most report compared the data from so called normal population without specifying their normal characteristics though Elhilali and associates (1976) emphasized that importance of using age matched control in their study.

Zacharski and co-workers (1971) noted that there are no significant variation of lymphocyte count with sex or at various period of age. Wytran et al (1972) found that there is no difference in T and B cell percentage of infants and children. Wheeler and
Lutteroth (1974) found no difference in total lymphocyte and relative number of T lymphocyte in peripheral blood of young children and adult individuals.

NORMAL DISTRIBUTION OF T AND B LYMPHOCYTE

Neiburger et al in 1976 studied the distribution of T and B lymphocyte in peripheral blood of children and adult and found the following distributions:

<table>
<thead>
<tr>
<th></th>
<th>T Cell %</th>
<th>B Cell %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children</td>
<td>44±4.2</td>
<td>30.4±3.1</td>
</tr>
<tr>
<td>Adult</td>
<td>46.3±1.8</td>
<td>26.5±2.3</td>
</tr>
</tbody>
</table>

Fleisher, T.A. et al (1973) studied the sub-population of lymphocyte in children and adult using E and EAC rosette assays. Children under 18 month of age were found to have less percentage of E binding T lymphocyte and an more percentage of EAC binding. B lymphocyte as compared to older children (18 month to 10 years) and adult. The absolute number of both E binding and EAC binding lymphocyte was more in children under 18 month of age than older children and adult, observation was as following.
### T (\& Binding) Cell

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Percentage Mean±SD</th>
<th>Range</th>
<th>Absolute Mean±SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤18 month</td>
<td>50.2±9.7</td>
<td>33-67</td>
<td>2.97±0.99</td>
<td>16.20-4.330</td>
</tr>
<tr>
<td>18 month -10 years</td>
<td>56.9±5.9</td>
<td>45-69</td>
<td>1840±640</td>
<td>530-3290</td>
</tr>
<tr>
<td>Adult</td>
<td>64±69</td>
<td>51-78</td>
<td>1910±590</td>
<td>750-3070</td>
</tr>
</tbody>
</table>

### B (FAC Binding) Cell

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Percentage Mean±SD</th>
<th>Range</th>
<th>Absolute Mean±SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤18 month</td>
<td>26.2±6.3</td>
<td>14-39</td>
<td>1530±540</td>
<td>470-2,590</td>
</tr>
<tr>
<td>18 month -10 years</td>
<td>22.7±3.4</td>
<td>16-29</td>
<td>720±280</td>
<td>170-1270</td>
</tr>
<tr>
<td>≤70 years</td>
<td>17.2±3.1</td>
<td>11-23</td>
<td>540-170</td>
<td>170-510</td>
</tr>
</tbody>
</table>

### T AND B LYMPHOCYTES IN INFECTIONS

Niklasson et al (1974) found that patients with acute bacterial diseases and viral diseases have low percentage of T cells in their study of T and B lymphocytes in acute infections. The decrease of T cell in viral infections however was much more marked than bacterial infections. The active T lymphocyte values were usually decreased in viral illnesses but remain normal in bacterial illnesses.

B lymphocyte were found raised in both viral and bacterial illnesses, but the rise of B cell was earlier (1st week) than bacterial illnesses (11th week).
MEASLES AS AN INDEX OF IMMUNOLOGICAL FUNCTION

The measles virus has long been known to suppress immunological responses. Natural measles infection suppresses both cell mediated and humoral immune response (Whittle, H.C. and Bradley Moore et al., 1973), and this coupled with malnutrition, leads to the death of many children from secondary infection (Morley, D. 1969). In 1908 Von Pirquet reported that the tuberculin reaction was suppressed in children with measles who had previously been positive to this test. Subsequent studies have also shown that extensive immunosuppression exists during acute measles (Coovadia et al., 1978).

White, R.C. and Boyd, J.F. (1973) attributed this immunosuppression to the widespread aggregative destruction of thymocytes seen in the cortex and medulla on the fourth day of disease. Tuberculin hypersensitivity can disappear before the date of onset of measles rash and be absent after measles vaccination for an average of 18 days (Starr and Berkovitch, 1964). According to Smithwick and Berkovitch (1966), transformation of lymphocytes from Mantoux-positive subjects by tuberculin FPD was depressed by addition of measles virus to the tissue culture. However, PHA could affect transformation
in a normal fashion of the same virus treated cells. (Csunkoya et al., 1974). Finkel and Dent (1973) noted impairment of lymphocyte response to sub-optimal dose of PHA.

Other hypothesis for depression of cell mediated immune response has been advanced.

Csunkoya et al., (1974) have revealed the presence of measles virus in lymphocyte during acute infection judged by immunoflorescence. They also suggested that depression of CMI response could be cause of a transient reduction in number of T lymphocyte as a result of cytopathic destruction.

Joseph et al., (1975) have shown that in vitro both T and B cells and monocytes can be infected by measles virus. Kantor, F.S., (1975) raised the possibility that the virus might stimulate some lymphocyte to release a suppressor of cell mediated immunity.

Whittle, H.C. and Dessetor, J. (1979) were able to recover virus directly from lymphocytes which support the impairment of CMI response. Palton, B.K., Hylton Winsome et al., (1982) have shown that a small percentage of both T and B lymphocytes are infected, but like HSV, measles virus only suppress the inductive stage of a
specific antibody or immunoglobulin response.

Controversies still exist regarding the mechanism of immunosuppression, especially in young children. A decrease in helper/inducer (H) to suppressor/cytotoxic (S) T-cell subpopulation ratio (H/S ratio) resulting from a decrease in H counts was found in adults (Alpert et al., 1985) and in one study in well nourished African children (Jaffe et al., 1983) during acute measles infection. In contrast, other did not find any change in H/S ratio during acute measles in older children and young adults despite a decrease in both H and S counts (Arheborn and Biberfeld 1983).

It is now well established that cell mediated immunity is important not only for recovery from measles but also for resistance other bacterial and viral infection (Bhaskaram and Reddy, V., 1983). They have shown that cell mediated immune response was observed to be significantly depressed in children following measles.

It is concluded from above studies that measles process can itself demolish a preexisting state of cell mediated immunity. The resulting deficiency of thymus dependent lymphocyte, as a result of replication of virus within or cytopathic destruction or loss of discernible
cortex from the thymus (White, K.G. and Boyd, J.F., 1973), may be sufficient to impair the specific immunological attack on the virus and allow persistence of large amount of virus in the thymus (Burnet 1968). Indeed the extensive destruction of thymocytes in the thymus gland may be the major factor in development of a state of tolerance to measles-antigens predominantly in respect of cell mediated immunity as was postulated by Burnet (1968).

It has also been reported that a preexisting state of malnutrition might produce diminution of cell mediated immunity via reduction in the population of thymus-dependent lymphocytes (Smythe, et al., 1971), which could predispose to severe or fatal measles.

The whole process of the eruptive stage of measles and subsequent immunity is mediated by the thymus dependent system. Burnet, F.M. (1968) hypothesized that in the course of the generalized delayed hypersensitivity reaction which we see as the measles rash, there is discharge and exhaustion of all these local cells probably including mast cells, which can contribute pharmacologically to the local reaction. He further added that it could also be assumed that the
regions from which large number of T-D (Thymus-dependent) cells are liberated, have been temporarily exhausted. Taken together these are responsible for the failure of the classical Montoux reaction to be elicited in the weeks following measles. He stated that this phenomenon is a clear indication of the fact that the measles rash is itself a diffuse delayed hypersensitivity reaction. The whole pattern of measles pathogenesis and immunity is clearly based on thymus dependent immunocytes. Measles is in fact a complex and severe delayed hypersensitivity reaction. The Gut dependent (GD) system and its antibody are side effects epiphenomenon of minimal or no importance.

T AND B CELL STUDIES IN MEASLES

Various studies have shown the effect of measles on number of circulating T and B lymphocytes, null cells, Complement C₃ and antibodies and immunoglobins. Lymphocyte studies have been done using different surface markers on T and B lymphocytes namely E and EAC rosette technique, monoclonal antibodies OKT-3 and C3d antigen beads etc.

Cocovadia et al (1977) have found that the profound immune-suppression during the first few days of the rash in measles which can determine prognosis has
been shown to affect chiefly the T and B cell subpopulations with less severe effects on C3 and T cell function assessed by PHA transformation of lymphocytes. They have carried out the immunological studies in two groups of measles patients. Group A in which there was severe lymphopenia (≤2000/mm³) and Group B in which lymphocyte count was (72000/mm³). Subpopulations of lymphocytes were counted in a single preparation by means of sheep rosette formation and by an immunofluorescence method for detecting immunoglobins. Peripheral lymphocytes were classified as rosetting cells (T), florescing cells (B), cells with no markers (null) and those with both markers (FT). The distinguishing pattern in absolute lymphocyte counts, T, B, null and FT cells was observed. The mean initial absolute lymphocyte counts in Group A (1318±318/mm³) and Group B (4232±314/mm³) were lower than that in healthy control (6833±553/mm³).

Lymphocyte subpopulation except for null cells had reached the levels of normal controls at the third week after onset of rash in those who recovered. At the third week of the rash lymphocyte subpopulation except for F.T. cells, were still significantly below normal in children who did not recover. At the sixth week only the T cells in addition had reached normal in these children.
where as the absolute lymphocyte counts, B cell and null cells were still significantly depressed.

Whittle, H.C. and Dossetor et al. (1978) have shown in their study of 25 children with natural measles that the number and proportion of circulating T lymphocytes was low in the acute stage of measles. 37% of T cell showed positive immunofluorescent staining for measles virus after stimulation with PHA. 7% of the B cells were shown to contain virus, but their number did not alter significantly during the infection.

<table>
<thead>
<tr>
<th>Group</th>
<th>T cells</th>
<th>B cells</th>
<th>Null cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute measles</td>
<td>38.7±13.8</td>
<td>32.7±8.4</td>
<td>26.7±16.5</td>
</tr>
<tr>
<td>4 weeks later</td>
<td>42.2±7.1</td>
<td>29.9±6.0</td>
<td>27.9±9.5</td>
</tr>
<tr>
<td>Controls</td>
<td>53.3±10</td>
<td>32.3±9</td>
<td>14.4±10.3</td>
</tr>
</tbody>
</table>

Pelton, Winsome Hylton (1982) have shown that both T and B cells are infected in disease process and both cell types support measles virus replication.

Joffe, Max I and Sukha Nagin, R. et al. (1983) observed a depression in circulating T lymphocytes using monoclonal OKT 3 antibody and Quantigenbeads, as well as enumerating E-rossette forming cells.
<table>
<thead>
<tr>
<th>Measles patient</th>
<th>Lymphocytes</th>
<th>E rosette %</th>
<th>OKT 3% Monoclonal-antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4400</td>
<td>41</td>
<td>38</td>
</tr>
<tr>
<td>2</td>
<td>1240</td>
<td>52</td>
<td>48</td>
</tr>
<tr>
<td>3</td>
<td>4030</td>
<td>44</td>
<td>44</td>
</tr>
<tr>
<td>4</td>
<td>1350</td>
<td>50</td>
<td>43</td>
</tr>
<tr>
<td>5</td>
<td>1100</td>
<td>32</td>
<td>34</td>
</tr>
</tbody>
</table>

**Controls**

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2400</td>
<td>70</td>
<td>66</td>
</tr>
<tr>
<td>2</td>
<td>3750</td>
<td>57</td>
<td>62</td>
</tr>
<tr>
<td>3</td>
<td>2850</td>
<td>65</td>
<td>62</td>
</tr>
<tr>
<td>4</td>
<td>3300</td>
<td>68</td>
<td>65</td>
</tr>
<tr>
<td>5</td>
<td>2950</td>
<td>60</td>
<td>68</td>
</tr>
</tbody>
</table>

Bhaskaran, P. et al. (1983) studied 34 children aged between 6 months and four years. Cell mediated immune response was observed to be significantly depressed in children following measles. The degree of immunosuppression was found to be significantly depressed (31.1±1.55% T cells) in well nourished children and 32.4±2.21 in under nourished children.

<table>
<thead>
<tr>
<th>Nutritional status</th>
<th>No. of children studied</th>
<th>Initial 5 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal controls</td>
<td>22</td>
<td>% Rosette 49.0±1.94</td>
<td></td>
</tr>
<tr>
<td>Well nourished children with measles</td>
<td>20</td>
<td>31.1±1.55</td>
<td>31.3±0.97</td>
</tr>
<tr>
<td>Under nourished children with measles</td>
<td>11</td>
<td>32.4±2.21</td>
<td>32.8±1.21</td>
</tr>
</tbody>
</table>
Arnborn and Biberfeld (1983) observed a depression in total T subsets (leu 4) during the acute phase of measles as compared to normal controls.

Monoclonal antibodies
Leu 2a - suppressor/cytotoxic
Leu 3a - Helper subset of T lymphocytes
Leu 4 identifies Total T cells.

<table>
<thead>
<tr>
<th>Measles It.</th>
<th>Leu 2a</th>
<th>Leu 3a</th>
<th>Leu 4(Total T cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15</td>
<td>23</td>
<td>44</td>
</tr>
<tr>
<td>2</td>
<td>14</td>
<td>49</td>
<td>69</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>42</td>
<td>58</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>42</td>
<td>64</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
<td>40</td>
<td>68</td>
</tr>
<tr>
<td>6</td>
<td>23</td>
<td>32</td>
<td>51</td>
</tr>
<tr>
<td>7</td>
<td>28</td>
<td>41</td>
<td>61</td>
</tr>
<tr>
<td>8</td>
<td>17</td>
<td>45</td>
<td>63</td>
</tr>
<tr>
<td>Controls</td>
<td>25</td>
<td>45</td>
<td>79</td>
</tr>
<tr>
<td>Median</td>
<td>16-38</td>
<td>38-59</td>
<td>66-83</td>
</tr>
</tbody>
</table>

Per Arnborn and Gunnel Biberfeld (1983) have found that in acute phase of measles, there was T lymphocytopenia but no change of the ratio between T lymphocytes of helper and suppressor/cytotoxic cell phenotypes.

Robert, L., Hirsch et al (1984) have shown that lymphocytes from patient with measles showed profound and prolonged suppression of proliferative response to mitogens. The degree of suppression was similar in patients
with uncomplicated measles virus infection and in those with pneumonia or post infectious encephalitis.

**IMMUNE RESPONSE IN MALNOURISHED VS WELL NOURISHED CHILDREN**

In malnourished children measles is often severe and can be fatal in up to 50% of cases (Whittle et al. 1980, Dossetor et al., 1977). Many speculate that this phenomenon is due (Anonymous 1982, 1983) at least in part, to the impairment in cellular immunity observed in malnourished children especially during measles. However Whittle has demonstrated that in malnourished children although peripheral blood mononuclear cells (PMN) support a higher replication of measles virus, their cellular immunity does not seem to differ from that in well nourished children (Dossetor et al., 1977). It has been suggested (Whittle et al., 1980, Dossetor et al., 1977) that lymphocytes of children with malnutrition are abnormally susceptible to infection by measles virus. The infection is followed by a normal cellular and humoral immune response and this response generates immunosuppressive factors in the patients plasma, thus making the child susceptible to secondary infection (Ron Dagon et al., 1987, Bhaskaran, P. and Radda, V., 1986) investigated the effect of PEM on the clinical course, outcome and immune status of 50 children with different
nutritional status. The duration and complication of measles were found to be similar in well nourished and malnourished children.

<table>
<thead>
<tr>
<th>Nutritional status</th>
<th>% of standard weight</th>
<th>% of T cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight/age</td>
<td>No.</td>
<td></td>
</tr>
<tr>
<td>790% Measles (8)</td>
<td>31.2±0.84</td>
<td>62.5±1.87</td>
</tr>
<tr>
<td>Control (12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>76-90 Measles (15)</td>
<td>29.8±0.98</td>
<td>60.8±1.94</td>
</tr>
<tr>
<td>Control (15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 60% Measles (12)</td>
<td>25.1±1.76</td>
<td>28.6±1.22</td>
</tr>
<tr>
<td>Control (15)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The immunological parameter showed that the percentage of circulating T lymphocytes was significantly lower in severely malnourished compared to those of other nutritional grades. However, children with measles irrespective of nutritional status showed a significant decrease in the circulating T cell number compared to the controls. Severely malnourished children with measles did not show any further decrease in the T cell number compared to their matched controls.
Ron Dagon et al (1987) investigated the effect of measles in malnourished and well nourished children, and observed that malnourished infants showed a trend towards a deeper depression in both helper and suppressor T cells during the acute phase than well nourished children where as the helpersuppressor ratio remained similar in two groups.

There was a more impressive decrease in mean T lymphocyte counts than in B lymphocyte count in children with measles.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients acute phase</th>
<th>Patients Convalescent phase</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 26</td>
<td>N = 19</td>
<td>N = 22</td>
</tr>
<tr>
<td>WBC</td>
<td>8.561±3.290</td>
<td>9.795±2500</td>
<td></td>
</tr>
<tr>
<td>Total lymphocytes</td>
<td>3.444±2065</td>
<td>4.765±1545</td>
<td></td>
</tr>
<tr>
<td>B lymphocyte Mean %±S.D.</td>
<td>16±6</td>
<td>21±8</td>
<td>14±3</td>
</tr>
<tr>
<td>T lymphocyte Mean %±S.D.</td>
<td>54±10</td>
<td>60±14</td>
<td>64±14</td>
</tr>
</tbody>
</table>

REVIEW OF T CELL FUNCTION

Human T lymphocytes are endowed with the capacity to recognize specific antigens, execute effector functions and regulate the type and intensity of virtually all
cellular and humoral immune responses (Reinherz, E.L.,
chloosman, S.F. 1980).

Two major functionally distinct subsets of T
cells have been defined with heteroantiserums, autoantibodies
and monoclonal antibodies directed at stable cell surface
antigens (Evans, R.L. et al., 1976, Reinherz, E.L. et al.,
1980).

The human immune system, therefore consists of
discrete subsets of T cells that are critical for immune
homeostasis. It is the balance between effector and
regulatory subsets that governs the outcome of antigen
triggering. The inducer subset is central for the
activation of T and B cells, and macrophages, as well
as for haematopoietic differentiation. This inductive
influence is regulated by the presence of suppressor
T cells that function to inactivate the inducer subset
or alternatively, the effector itself population. Loss
of activation of these subsets leads to a variety of
immunologic disorders characterized by autoimmunity or
immunodeficiency. Immune homeostasis results from a
delicate balance of inducer and suppressor subsets with
in the human T cell circuit.
A popular method to assess the function of T cells in vitro is to quantitate the amount of cell division (Plastogenesis). They undergo the process in response to stimulation in vivo by specific antigen or by mitogen (Plant derived material) that perturb the lymphocyte membrane and triggers the cell division. In vivo T lymphocyte function can be measured by delayed hypersensitivity reaction using variety of antigen to which majority of older children and adult have been sensitized. The most generally useful skin test antigens are 1:100 dilution of tetanus toxoid, PPD, histoplasmin mumps, extract of candida, trichophyton, PHA and DNCE.

Skin tests are more important test for GMC assessment in vivo, appropriate antigen skin test were evaluated by different observers to assess erythema, oedema in course of time as well as size of reaction, they can provide the valuable information. Positive skin test are of value in establishing the presence of normal T cell function but negative skin test are inconclusive evidence of deficient T cell function.
CUTANEOUS HYPERSENSITIVITY REACTIONS FOLLOWING MEASLES

Many workers have studied the effect of different mitogens PHA, PPD, streptococcal antigen, PWM etc. on lymphocyte transformation in measles.

Bellamayer Eric, Bhattacharyya H. et al (1972) studied 7 patient of measles and observed, lymphocyte transformation to be more depressed in measles patient than in other diseases. The responses in the measles group were uniformly low and significantly less than in the controls (P<0.001).

Whittle, H.C. and Bradley Moore et al (1973) have demonstrated that delayed hypersensitivity to specific antigens like PPD and candida and streptococcal antigens is temporarily suppressed in measles. However when the expression of delayed hypersensitivity was suppressed the patient could still be sensitized normally to DNFB and PHA. 31 of the 33 patient (94%) previously sensitized with 2mg DNFB responded to a challenge of 200 μg DNFB and their lymphocytes responded to stimulation with PHA.
<table>
<thead>
<tr>
<th>Group</th>
<th>PPD Day</th>
<th>Cond. Day</th>
<th>Strept. Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles (No. 33)</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td><em>P&lt;0.05</em></td>
<td><em>P&lt;0.01</em></td>
<td><em>P&lt;0.01</em></td>
</tr>
<tr>
<td>Control (No. 34)</td>
<td>4</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td></td>
<td>ND</td>
<td>21</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td><em>P&lt;0.01</em></td>
<td><em>P&lt;0.02</em></td>
<td></td>
</tr>
</tbody>
</table>

On day 3rd after measles rash no patient responded to PPD. 6 patient responded to candida and only 3 patient to streptococcal antigen. After repeat skin testing; read on day 16 the number of reactions in the measles group was comparable to controls.

Bhaskaran, P. et al (1983) investigated the effect of measles infection on the nonspecific response to mitogens and observed a significant reduction of PHA induced lymphocyte response as judged by DNA synthesis.

Arneborn - Per and Gunnel Biberfeld (1983) found a low proliferative response to PHA during the acute phase of measles and varicella. The response to PPD was also low in all measles patient tested and in some of the varicella patient.

Hirsch Robert, L. et al (1984) in their study observed that lymphocyte from patients with measles showed
profound and prolonged suppression of proliferative responses to mitogens (PHA, PWM and PBS). The degree of suppression was similar in patients with uncomplicated measles virus infection and in those with pneumonia or post infectious encephalitis.

Madhusudan and Bhaskaran, P. (1986) studied the response of T cells to PHA and to measles antigen and found a low CHI response to PHA in children with measles irrespective of their nutritional status indicating the affect of measles per se on immune status.

Ren Dagon, Moshe Philip et al (1987) observed a reduced response to mitogens (PHA, ConA and PWM) during the acute phase of measles mean % of stimulation (±SE) by PHA ConA and PWM were 81±3, 71±11 and 58±11 respectively during the acute period most of the workers have shown mitogen stimulation response to lymphocyte, to be reduced. However Whittle, H.C. et al have shown PHA stimulation to be normal.

As a test for cellular immunity, contact sensitization to 1-nitro, 2,4-dichlorobenzene ( DNCB) offers several advantages over intradermal tests. Reliance upon previous exposure to the allergan is unnecessary since both sensitization and challenge are controlled and approximately 95% of normal people can be sensitized to
this agent, (Krupan, A.M.1 Spatein, W.L. 1959). Furthermore circulating antibodies do not develop with contact sensitization (Waksman, B.M., 1960) which renders it a more exact test of cellular immunity.

The sensitizing properties of DNCE are related to its ability to act a hapten forming covalent bands with lysine groups of epidermal protein (Eisen 1958). A threshold concentration of DNCE is required for sensitization. Less than 1% of the applied DNCE becomes bound and a relatively brief duration of binding in the skin is necessary. Sensitization takes place in the regional lymph nodes and is mediated by circulating lymphocytes. The development of sensitization requires seven to twenty one days.

The capacity to become sensitized to DNCE may be tested by application of DNCE to the skin, followed 2 weeks later by patch testing at different sites. Thus ability of an individual to develop CMI denovo can be determined by applying DNCE directly to the skin. The chemical combines with skin proteins to form immunogenic substance that stimulate sensitization of T cells to DNCE, 10-14 following this initial exposure to DNCE the reapplication of DNCE on skin will result positive skin test if CMI is intact.
Sanjeev, Rai P. Krishnamurthy, P.N. et al (1981) carried out DNBC skin sensitization test in 170 malnourished children and compared it with control group, their studies have shown DNBC reaction, positive only in 54.1% of malnourished children compared to 86.7% in control group.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Control group</th>
<th>Study group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.   %</td>
<td>No.   %</td>
</tr>
<tr>
<td>3+</td>
<td>11  36.7</td>
<td>31  18.2</td>
</tr>
<tr>
<td>2+</td>
<td>12  40</td>
<td>49  28.9</td>
</tr>
<tr>
<td>1+</td>
<td>3   10</td>
<td>12  7.0</td>
</tr>
<tr>
<td>Negative</td>
<td>4   13.3</td>
<td>78  45.9</td>
</tr>
</tbody>
</table>

Simultaneously they have also studied the pattern of reaction in various groups of malnourished children. The reaction was related to the degree malnutrition severe the malnutrition, more the negative reaction.

For DNBC skin test 1000ug/0.1 ml concentration were used for sensitizing dose and 50 ug/10.1 ml for challenge dose. Reaction was graded as under (Sanjeev Rai, P. and Krishnamurthy, P.N. et al., 1981).
3. Contaneous flare occurring at both sensitizing dose and challenge dose sites.

2+ Spontaneous flare occurring at sensitizing dose site.

1+ Absence of spontaneous flare, but on reapplication of challenge dose an equivocal delayed hypersensitivity reaction.

Negative—No reaction, no spontaneous flare occurring even after reapplication of challenge dose.