DISCUSSION

The present study was conducted on 27 children with malnutrition of various grades excepting those with grade I malnutrition (according to I.A.P. classification) and 12 healthy age matched control children. Presence of overt infection was excluded by clinical examination. These children were chosen from outpatient department, well baby clinic of department of Pediatrics and from those admitted to Pediatrics ward of M.L.B. Medical College, Hospital, Jhansi from January, 1991 to January, 1992.

Malnutrition is the most common cause of secondary immunodeficiency. The causal interaction between nutritional status and immunologic function is a complex one and not exactly known. The most prominent effects of nutritional deficiencies have been observed on cell mediated immunity, number of T lymphocytes, helper T cell function, complement system, mucosal IgA response, neutrophil bacterial killing capacity and antibody affinity.

The impact of protein energy malnutrition is greatest and universal on T cell number and function and on cell mediated immunity. Polymorphonuclear leukocytes
(PMN) and macrophages constitute an integral part of non specific barrier to infections. On comparing malnourished patients, with the patients of chronic granulomatous disease (CGD), a genetically determined disease of defective microbicidal capacity; Similarities have been found between the infecting organisms. Moreover, pulmonary infections of patients with chronic granulomatous disease typified by their chronicity, tendency to encapsulation and enlargement of the hilar shadows, are reminiscent of the pneumonias seen in severely malnourished children (Wolfson et al, 1968).

Nitroblue tetrazolium reduction test is now reliably used for diagnosis of chronic granulomatous disease, where NBT reducing capacity is found to be virtually absent, transient abnormalities of a lesser degree have been reported in patients on treatment with corticosteroids (Miller and Kaplan, 1970).

The NBT reduction values in our study were found to be lower in children with grade III and IV malnutrition as compared to control children and the difference among them was found to be significant.
The NBT reduction values found in control children in our study were similar to those found in control children of study by Raghu Raman (1992). In this study evidence of altered intraneutrophilic metabolic function was found in protein energy malnourished children without infection. They also found a reduced NBT score in PEM, which was found to be significantly reduced in children with kwashiorkor as compared to control children. Similar inference was drawn by Shousha et al (1972) also, but the factor of infection was not excluded in their study.

Results obtained by Kendal and Nolan (1972) were also similar, but in their study a wide scatter of values was seen, indicating that the histochemical abnormality observed although related to malnutrition was expressed only in some children.

Contrary to this Altay et al (1972) and Rosen et al (1975) did not observe any difference in NBT reduction between healthy and PEM children. In the study by Rosen et al (1975) the NBT reduction was found to be raised in malnourished children with infection. Whereas in a study by Schopfer and Douglas (1976) the NBT reduction score was found to be significantly higher for cells from children with kwashiorkor than for controls.
Candidacidal assay was performed in our work to study the PMN dysfunction more precisely. As it has been reported to be more sensitive by Rao et al (1984) also from their study on neutrophil functions in children with repeated infections. Particle ingestion and phagocytosis test was done by them by using killed candida albicans suspension, they termed the test as candida avidity index. In our study viable candida albicans suspensions were used and then the capacity of neutrophils to kill them was assessed by counting percentage of killed candida.

The results of candidacidal assay in our study were similar to the results of most of previous studies which have shown impaired microbicidal activity in PEM. The candidacidal assay values were found to be significantly lower in malnourished children with grade II, III and IV malnutrition as compared to control children.

Similar results were obtained by Solberg and Hellum (1972) i.e. decreased bactericidal activity of polymorphs in malnourished patients.

Selvaraj and Bhat (1972) studied metabolic and bactericidal activities of leukocytes in PEM and found
the bactericidal activity to be significantly lower in children with PEM than those of control children. They also found other evidences of decreased microbicidal activity by studying other metabolic activities. They found low in vitro glycolytic activity and complete failure of leukocytes to show an increase in lactate production in response to particle challenge. Further they also found these leukocytes to fail to show an adequate stimulation of Hexose - monophosphate shunt, which supplies $\text{H}_2\text{O}_2$ for microbicidal activity.

Seth and Chandra (1972) also studied bactericidal activities and reported a significant decrease in killing ability of neutrophils from children with kwashiorkor. Their deductions, however, were based on the results of a group of patients in whom infection was not taken into account. Later in 1975, such comparison was shown to be invalid by Rosen et al as they found the infection to be an important factor to alter the microbicidal capacity of neutrophils. In their study they reported no difference in the bactericidal activity of infected control and uninfected kwashiorkor children. Infected control as well as
kwashiorkor patients were found to have impaired killing ability. The impairment of bactericidal ability in both infected groups was statistically significant when compared with uninfected groups. Thus they explained depressed antimicrobial activity to be primarily due to infection and not due to protein depletion.

In 1974, Douglas and Schopfer reported the bactericidal capacity of phagocytes from kwashiorkor children to be normal in the early phase (first 30 minutes) and significantly reduced during the last phase (after 60 minutes) of the assay as compared with cells from healthy children.

In 1976 again they studied PMN's function in children with kwashiorkor, when they analysed the in vitro chemotactic response and candidacidal activity of PMN's along with kinetic assays of glycolysis and of hexose monophosphate shunt in resting and phagocytizing cells. The chemotactic response of PMN's from children with kwashiorkor was found to be significantly reduced at the early incubation intervals in comparison to PMN's from control children and after 180 minutes there was no longer
a difference found between PMN's from kwashiorkor and control children. They demonstrated impairment of candidacidal activity for the PMN's from kwashiorkor children. HMS activity for resting PMN's of malnourished children was found to be significantly higher than for controls during the 60 minutes incubation period but no difference was found in the maximum level of stimulation of the HMS during particle ingestion.

In contrast to above studies Bhaskaram and Reddy (1982) found bactericidal function to be unaltered in kwashiorkor children. They suggested further studies to be done to evaluate other factors that are known to influence in vivo macrophage function.

Humoral immunity also is one of the type of primary host resistance, in which resistance to microorganisms is mediated by circulating immunoglobulins. In our study the difference in the serum levels of IgA, IgG and IgM of the two groups, control and malnourished was found to be statistically insignificant. Similar results have been reported by some other workers also. Mcfarlane et al (1970) reported that serum levels of all three serum
immunoglobulins (IgG, IgM and IgA) were similar to those in age matched controls. In three children in their study the serum IgG concentration rose immediately before death. They suggested that the reason for high serum IgG may be related to infection.

Reddy et al (1976) also reported similar levels of IgG, IgM and IgA in the serum of severely malnourished children and mild to moderate malnourished and normal children.

In a study by Puri et al (1980) no significant change was found in the values of IgG and IgM in either severe or mild to moderate PCM group as compared to controls, except in the presence of infection, where they found statistically significant increase in IgG levels.

In our study the children chosen were from those without any evidence of infection. Children having clinical evidence of infection were excluded from the study. Thus normal serum immunoglobulin levels obtained could be due to this reason.

In some other studies on malnourished children with infections, higher serum immunoglobulin levels have been reported. Chandra (1971) found IgG, IgA and IgM to
be raised tremendously in malnourished children with concurrent or recent history of infection. In malnourished children without evidence of infection he found very significant lowering of IgG and to a lesser extent of IgA. Thus he suggested that the capacity of malnourished children to respond to bacterial challenge seems to be intact.

(1975)

Similarly Neumann et al also found significantly higher serum levels of IgG, IgM, IgA and IgE in severely malnourished children as compared to moderately malnourished or control children. In their study also almost all children had infections (control as well as study group). Marked elevation in serum IgE levels found in their study was explained by them on the basis of possibly disordered T cell function.

In some other studies serum levels of IgG and IgM were found to be normal but serum levels of IgA were found to be raised. In 1969, Keet and Thom found no significant difference between the serum levels of IgG and IgM in kwashiorkor cases as compared to control children and serum IgA levels were found to be much higher in
kwashiorkor group. The difference in the values of serum IgA of kwashiorkor and control children was found to be statistically significant. They suggested that high IgA values found in kwashiorkor cases needed further confirmation and explanation. They further explained that though the mean age of the kwashiorkor cases in their series was higher than that of the control group, but it seemed unlikely that age factor alone could be held responsible for the higher IgA levels.

In the study by Alvarado and Luthringer (1971) on edematous protein calorie malnourished children no significant difference was reported in IgG and IgM serum levels of malnourished and healthy children, but serum IgA values were reported to be significantly higher in malnourished group. They suggested that an abnormal permeability of the gastrointestinal mucosa, if present could facilitate the entry of the IgA secreted by the plasma cells in the lamina propria, into the blood stream.

Similarly Seth et al (1985) studied children with severe malnutrition without infection and found that serum
IgG and IgM levels in severely malnourished children were comparable to the healthy children, but serum IgA levels were found to be increased. They suggested that this rise in serum IgA levels could be due to respiratory and gastrointestinal infections, as it was explained by Chandra also in 1977 in his study on malnutrition and immune response. However, it has not been worked out as yet for how long IgA levels remain elevated after an episode of infection.

Contrary to above reports Kielmann et al (1976) found in their study that of the three immunoglobulins (IgG, IgM and IgA) only serum IgA was directly related to a variety of anthropometric indices of nutritional status. They suggested that this might be a phenomenon both of reduced production owing to low nutritional status and of increased utilization caused by frequent and prolonged infection.

One more group of investigators (McMurray et al, 1976) found statistically significant reduction in IgA concentrations in the tears of malnourished children. They suggested that the reduced IgA activity might be due to reduced synthesis.
Reddy et al (1976) also found significantly lower IgA concentrations in duodenal fluid, saliva, nasal washings and tears as compared to normal children. They suggested, since the total protein concentration of these secretions was not found to be much altered, a low level of secretory IgA could be considered a selective deficiency. They further suggested that more severe and prolonged diarrhoea in malnourished children may be related to secretory IgA deficiency.

Similarly Chandra (1971) found reduction in nasopharyngeal IgA and impaired secretory antibody response in malnourished children and suggested such response mostly to be selective since total protein and albumin concentrations in the nasal washings, from malnourished children did not differ significantly from values in healthy children. They also reported that there was no evidence of reabsorption of secretory IgA, since the serum did not react with antiserum raised against secretory component.

Different to all above studies Gholy et al (1970) in their study of seventeen cases of marasmic children found serum IgM levels to be much higher than
that of normal cases. Whereas IgG and IgA serum levels were found to simulate more or less the normal pattern. They found a direct relationship to exist between the size of the spleen and the degree of increase of IgM in their study. They suggested that splenomegaly found in their study could be a part of a generalised reticulo-endothelial hyperplasia which in the absence of causative infections and septic foci in the investigated cases could be considered a part of the body response called for by the marked dystrophy and emaciation.