CHANGES IN LYMPHOCYTIC SUB-POPULATIONS IN PROTEIN CALORIE DEFICIENT CHILDREN

THESIS

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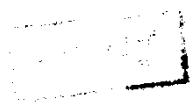

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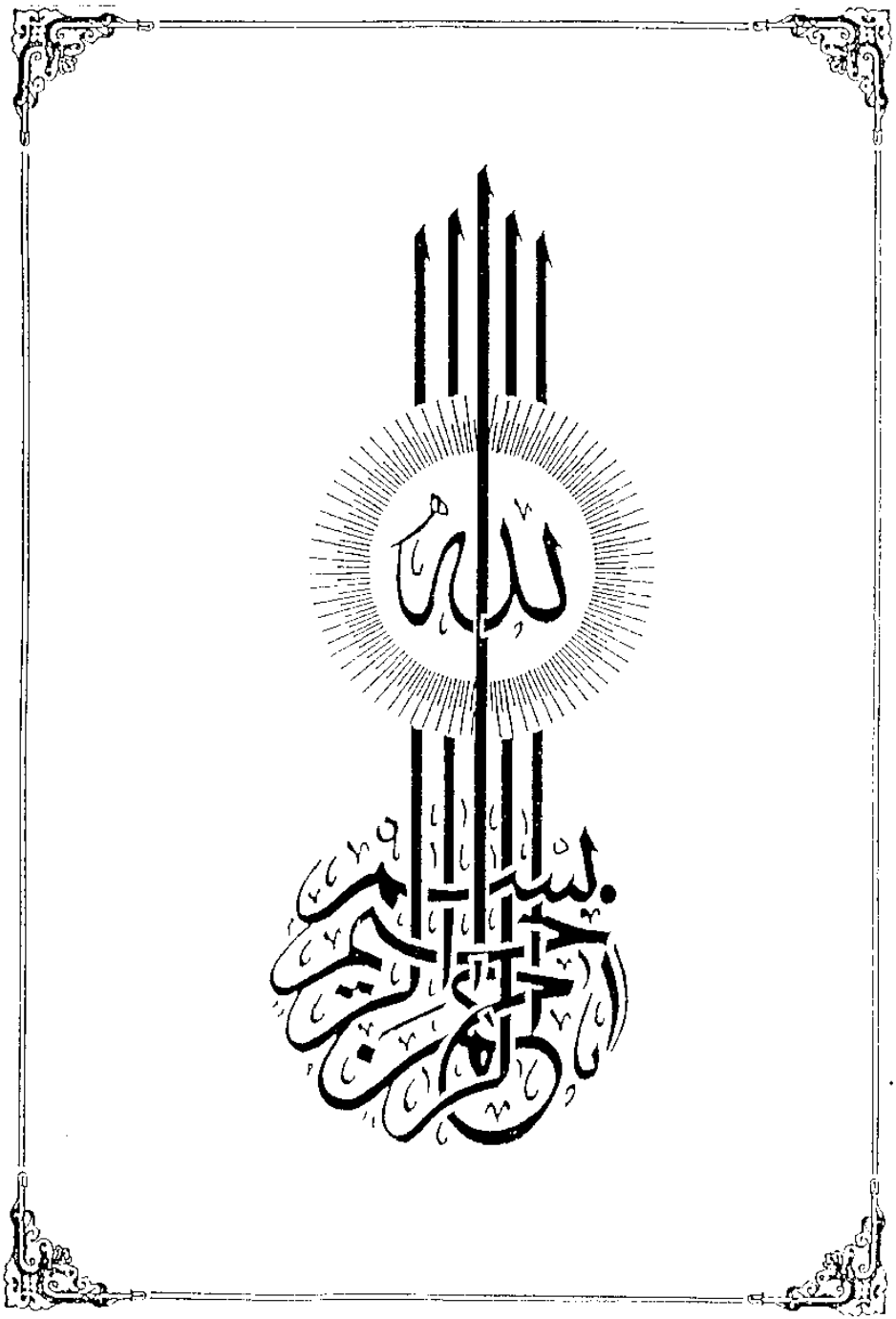

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AIM OF THE WORK

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Protein calorie malnutrition causes a major health problem among children in developing countries including Egypt. The problem concerning this disease is magnified by the great susceptibility of these patients to repeated attacks of infection. Nutritional deficiencies generally reduce the capacity of the host to resist infection and its consequences, so aggrevation of the disease is the expected result.

Many investigators have shown defective immunological mechanisms in protein calorie malnutrition. These defects include impairment of complement functions, cell-mediated immunity and other aspects of host resistance.

Recently, the effect of protein calorie malnutrition on lymphocyte subpopulations has given significant result among experimental animals.

In this work, a trial will be done to identify the effect of protein calorie malnutrition on lymphocyte subpopulations.

REVIEW OF LITERATURE

INTRODUCTION

Malnutrition is a major public health problem. Although this is more obvious in developing countries, malnutrition occurs throughout the world. A conservative estimate by the World Health Organization (W.H.O.) is that 100 million children below the age of five years suffer from moderate to severe malnutrition manifesting as marasmus and kwashiorkor; many more have subclinical problems. Deficiencies of iron, folate and vitamins affect several million individuals (Chandra, 1980).

Infection is a common complication of malnutrition, causing high morbidity and mortality. The frequent occurrence of undernutrition and infection together has led to the logical hypothesis that malnutrition robs the host of some of his defense mechanisms against infection. At the same time, infection itself interferes with normal immune responses and depletes the body of metabolic energy. It is essential therefore, to recognize these complex interactions between nutrition, immunity and infection (Fig. 1; Chandra, 1979a).

An increased frequency and enhanced severity of infectious diseases are often observed in young children with the characteristic clinical syndromes of marasmus and kwashiorkor. Infection itself causes an actual loss of nutrients as a result of vomiting, diarrhea and increased urinary nitrogen, as well as functional nutritional wastage

due to overutilization, diversion for preferential synthesis of protective proteins and vital enzymes (Beisel, 1977).

The commonly encountered pathogens in malnourished groups include bacteria (e.g. Staphylococcus, Streptococcus, Pneumococcus, Escherichia coli, Klebsiella, Mycobacterium tuberculosis), viruses (measles, herpes simplex, varicella) and fungi (Candida, aspergillus). Most of these organisms also plague patients with primary immunodeficiency disorders. Most malnourished individuals bear a heavy burden of parasites (hookworm, ascaris, malaria) that contribute to additional metabolic and gastro-intestinal loss of nutrients and malabsorption (Chandra, 1980).

The general characteristics of infection in children with malnourishment include absent or mild fever, variable leucocyte count, tendency to systemic spread and presence of necrotizing apurulent lesions yet, pyogenic micro-organisms are often found (Thompson, 1977).

Malnutrition is usually a composite of deficiencies of calories and many specific nutrients including protein, minerals, vitamins and trace metals. It is logical to suspect the possibility of alteration of immune response due to changes in the bioavailability of individual substances, such as iron, folic acid, vitamin A, pyridoxine or zinc (Chandra, 1980).

As protein calorie malnutrition is a major public health problem, many recent studies have included an analysis of the immune system in children suffering from protein calorie malnutrition. These studies have included investigations of the phagocytic system, humoral and cell-mediated immunity, the complement system, and non-specific host defence mechanisms. In this review we shall try to summarize the present knowledge of immunological alterations in those children. It should be emphasized that this is a very difficult group of subjects to deal with in that one can not separate, usually, the effects of malnutrition from that of infection (Jackson and Zaman, 1980).

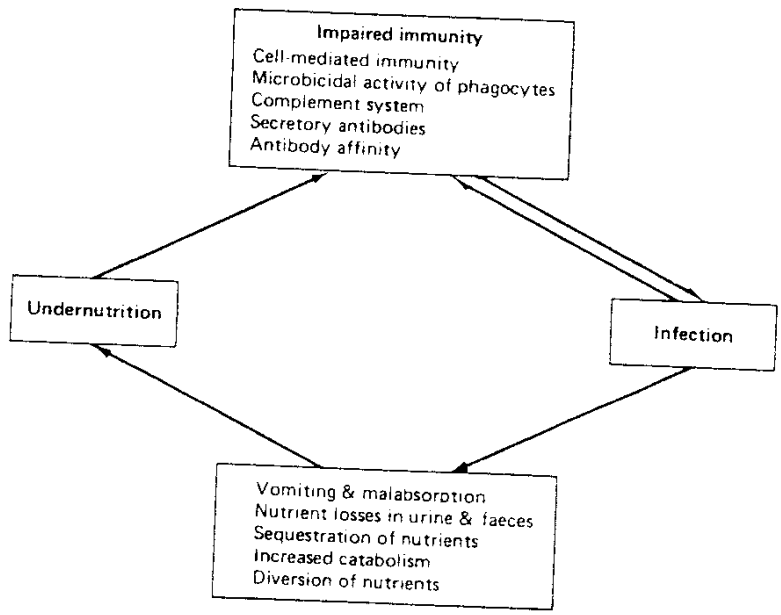

Fig. 1. Main immunologic deficits observed in protein energy malnutrition and pathogenetic mechanisms by which infection can increase nutritional deficiencies.

PROTEIN CALORIE MALNUTRITION

Protein calorie malnutrition is a sociomedical problem resulting from two main factors, a diet that is quantitatively and qualitatively inadequate and superimposed stress usually of infectious origin (Scrimshaw and Moises, 1965).

Syndromes of Protein Calorie Malnutrition

According to the variability in the clinical and biochemical presentations, protein energy malnutrition includes kwashiorkor, marasmus and marasmic kwashiorkor (Thompson, 1977).

Waterlow (1972) said that his criteria for kwashiorkor include that the child be at a minimum weight of not less than 60 per cent of the expected weight for age, in association with oedema and either hepatomegaly or dermatosis. Children with kwashiorkor show skin lesions which include dyspigmentation, desquamation and frequently extensive exfoliation. There is oedema of varying degree ranging from mild localized form in the feet and ankle to severe and generalized form. Hepatomegaly is a variable feature in kwashiorkor. Psychic changes in the form of apathy, irritability and anorexia are also present (Thompson, 1977; Behrman and Vaughan, 1983).

There are many biochemical changes in kwashiorkor. There is a low total serum protein due to hypoalbuminaemia (Heyworth et al., 1975).

Increased urinary nitrogen excretion also occurs due to increase in cellular breakdown (Thompson, 1977). There are electrolyte and mineral disturbances. Potassium depletion is a major biochemical characteristic feature of kwashiorkor. Although there is sodium retention in the body, serum sodium is decreased due to water retention (Waterlow and Alleyne, 1971). Serum iron, copper and zinc are found to be low in cases of kwashiorkor (Chandra, 1980).

Waterlow (1972) stated that his criteria for marasmus are that the child should be less than 60 percent of the expected weight for age and has no oedema or other specific signs. Marasmic children have severe wasting of muscle and adipose tissue. They are generally somewhat younger than kwashiorkor patients (Thompson, 1977; Behrman and Voughan, 1983). Biochemical changes in marasmus are usually not so serious except in cases with severe vomiting and diarrhea where electrolyte disturbances occur (Besson et al., 1979).

The sudden development of kwashiorkor in a marasmic infant is usually associated with the stress of infection where infections are known to decrease nitrogen retention by increasing the urinary nitrogen excretion (Kariks, 1962). Also, faulty dietary correction of marasmic infants with a diet containing a relatively low concentration of protein

relative to carbohydrates plays an important role in development of kwashiorkor in a marasmic infant (Scrimshaw and Moises, 1961).

Infection and Protein Calorie Malnutrition

Infection is usually a common association with protein energy malnutrition. The stress which accompanies infection leads to mobilization of aminoacids from the tissues with an increased need for nitrogen to replace protein loss. Moreover, anorexia, vomiting and diarrhea are often concomitants of infection thus perpetuating major dietary restrictions during infection. Infection and protein energy malnutrition may form a vicious cycle and it may be particularly difficult to distinguish initiating versus secondary factors (Thompson, 1977).

IMMUNOLOGICAL CHANGES IN PROTEIN CALORIE MALNUTRITION

I. Morphological Features of Immune System

Bell et al. (1976) studied the effect of dietary protein restriction on the lymphoid tissue. Weaning mice fed a 4% protein diet showed a generalized loss of lymphoid tissue which was greater than the loss of total body weight. This effect was greatest in thymus > spleen > mesenteric lymph nodes. Histopathological assessment of lymphoid organ structure confirmed the progressive lymphopenia evident in lymphoid organ weights and cell yields. It also showed that these changes were initially evenly distributed between the different structural compartments of each organ.

This cell loss was most pronounced during the first week on diets, then remained at stable levels for three weeks and showed a gradual rise thereafter. The effect was shown to be mediated partly by a cessation of growth in lymphoid organs due to low protein intake and, secondly, an adrenal corticosteroid induced lympholysis which actually reduced cell numbers. Elevated plasma cortisol levels have been reported in protein energy malnutrition and are thought to play an important role in physiological adaptation to restricted diet (Mc Farlane and Hamid, 1973; Rao, 1974). During nutritional repletion the spleen, thymus and mesenteric lymph nodes showed different and characteristic regrowth. The spleen was most active initially and rapidly reconstituted haemopoietic cells and B cells. This was

followed by the thymus which showed a delayed reinitiation of its normal growth kinetics which had been interrupted by the diet. The evidence suggested that full rehabilitation of the immune apparatus took place even after two months of nutritional deprivation. Of the numerous other reports of experimental undernutrition, that of Cooper et al. (1974) is similar in methodology and results to the experiments reported above.

Histopathological examination of tissues from the immunological system of malnourished children revealed morphological abnormalities of both central and peripheral lymphoid tissue (Thompson, 1977).

Histopathological changes in the thymus vary with the degree of malnutrition (Watts, 1969; Mugerwa, 1971). In intermediate stages of malnutrition there is a loss of corticomedullary differentiation and depletion of lymphocytes. In advanced stages of malnutrition the thymus is markedly decreased in size and weight, and interlobular spaces are increased and filled with fibrous connective tissue (Faulk et al., 1975). In extremely advanced cases even almost total "thymectomy" occurs, the organ being replaced by firbrofatty tissue which is difficult to differentiate from the fascia in that site (Chandra, 1980). On the other hand, an increased number of plasma cells have been reported in the bone marrow in protein calorie malnutrition (Awdeh et al., 1972). In his studies of kwashiorkor children, Thompson (1977)