

Polymorphonuclear Leucocytic Activity in Malnourished Children

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INTRODUCTION

Many observers have drawn attention to the increased mortality in both viral and bacterial infections in tropical and sub-tropical countries and related this not to an increased virulence of the organisms concerned, but to the diminished resistance of the host. There can now remain little doubt that malnutrition plays an important role in this diminished resistance (Morley, 1969). In recent years the immune responses have been intensively studied, the various processes involved have been described and in many instances quantitated. These recent advances which have been the subject of several reviews (Janeway, 1969), have shown that primary host resistance is of three types, humoral in which resistance to micro-organisms is mediated by circulating immunoglobulins, secondly the immune cellular response of thymic dependant lymphocytes, and thirdly,

polymorphonuclear leucocyte activity. Isolated defects of each of these systems have been described and studies of these patients have shown that the common infecting organisms may be grouped according to the type of immune response which they specifically evoke (Mudd, 1970) (see Table I).

Table I
PATHOGENS AND IMMUNE RESPONSE THEY SPECIFICALLY EVOKE

Primary Host Defence	Pathogenic Organisms
HUMORAL	Pneumococcus H. Influenzae Streptococcus Meningococcus sp. Pseudomonas aeruginosa Hepatitis virus Pneumocystis carinii
CELLULAR	Rubeola Varicella Vaccinia Cytomegalic inclusion body virus Mycobacterium tuberculosis Candida albicans Histoplasmosis
POLYMPHONUCLEAR LEUCOCYTIC ACTIVITY	Staphylococcus Klebsiella sp. Aerobacter aerogenes Serratia marcescens Candida albicans Aspergillus Nocardia

Investigations of the immune response have, until recently, thrown little light on the reasons for the increased severity of infections in malnourished children. It has been established that in these children levels of immunoglobulins are at least as high as in well-nourished children, which suggests that there is no defect in the humoral response (Watson and Freesmann, 1970). However, by measuring antibody production it was shown in 12 of 15 children suffering from Kwashiorkor that the injection of typhoid vaccine failed to cause a rise in antibody titre (Budiansky and da Silva, 1957), and a similar observation was made in relation to yellow fever vaccination (Katz and Brown, 1966). It is possible, therefore, that the immunoglobulins of severely malnourished children may not be fully competent and further work to clarify this is indicated.

There is evidence that in states of malnutrition the immune cellular response is deficient. Malnutrition diminishes resistance to tuberculosis, an adequate diet increases resistance (Brock, 1961). Tuberculin sensitivity in tuberculous patients, a reaction which is also dependant on the same immunological response is diminished in malnourished children and full sensitivity can be restored by a short period of high protein feeding (Phillips and Wharton, 1968). It has been shown that in Kwashiorkor there is not only a reduction in size of the thymus and thymic dependant lymphatic tissues, but also a functional depression of this system. Allogeneic skin grafts are rejected more slowly and the response to dinitrofluorobenzene and the transformation of lymphocytes in response to stimulation with phytohaemagglutinin are both diminished (Smythe, 1970).

Bacterial infections are frequent and often fatal in patients suffering from Kwashiorkor. In one reported series of 78 patients blood cultures were taken on admission. The organisms recovered were staphylococcus aureus on five occasions, salmonellae on six, paracolon and coliforms in three, and streptococcus pneumoniae in two (Smythe and Campbell, 1959). Thus staphylococci and enterobacteriaceae accounted for 14 of 16 positive cultures and a similar pattern of infecting organisms has been found by lung puncture aspiration in the pneumonias of malnourished children (Axton). Resistance to these groups of organisms is dependant upon polymorphonuclear (P.M.N.) activity, a process which has been shown to be defective in the genetically determined condition, chronic granulomatous disease (C.G.D.) (Good, *et al.*, 1968). Studies of patients with this condition have shown that the persisting

infections and the ultimate fatal outcome are due to an inability of the P.M.N.'s to destroy staphylococci and organisms of the enterobacteriaceae group.

In comparing patients suffering from C.G.D. with those suffering from Kwashiorkor not only are there similarities between the infecting organisms, but the pulmonary infections of patients with C.G.D. typified by their chronicity, tendency to encapsulation and enlargement of the hilar shadows (Wolfson, *et al.*, 1968), are reminiscent of the pneumonias seen in severely malnourished children. These considerations suggest that P.M.N. activity may be defective in malnutrition. Studies of the way in which the P.M.N.'s destroy certain pathogenic bacteria have shown that two stages are involved. The first is phagocytic ingestion, the second enzymatic killing and digestion of the intracellular bacteria. Phagocytic activity of P.M.N.'s from malnourished persons using staphylococcus albus as the test organism has been reported as being normal (Tejada, *et al.*, 1964). The possibility remains that the severity of these bacterial infections in malnourished children may be the result of an inadequate leucocytosis or a defect in bacteriocidal capacity of the P.M.N.'s. A method has been described recently by which using staphylococcus aureus as a test organism the phagocytic and bacteriocidal functions of the P.M.N.'s can be estimated separately (Alexander, *et al.*, 1968). Unfortunately, this investigation is difficult and complex, the author reports that he and his two colleagues worked on it for a year before reliable results were obtained. A simpler method suggested itself in that the P.M.N.'s of patients with chronic granulomatous disease show a constant histochemical abnormality, an inability to reduce tetrazolium dyes (Baehner and Nelson, 1968). During phagocytic activity normal P.M.N.'s reduce nitroblue-tetrazolium to readily visible intracellular deposits of formazan, the P.M.N.'s from affected persons show only very slight activity in this respect. Although the relationship between the histochemical abnormality and the enzymatic defect is not clear the test is now reliably used for the diagnosis of C.G.D. While the tetrazolium reducing capacity of P.M.N.'s from patients with chronic granulomatous disease is virtually absent, transient abnormalities of a lesser degree have been reported in patients on treatment with corticosteroids (Miller and Kaplan, 1970). The present investigation was undertaken to see whether similar histochemical abnormalities could be demonstrated in malnutrition.

these antibiotics do not penetrate the cell wall of the P.M.N. On the other hand the cell wall does not exclude chloramphenicol and this antibiotic is therefore effective against viable intracellular bacteria. In treating the infections of severely malnourished children it may be advantageous to consider this property of the chosen antibiotic in addition to the results of sensitivity tests.

SUMMARY

Investigations have shown an abnormality of enzymatic activity within the P.M.N.'s of some malnourished children. This offers an explanation of their known susceptibility to certain bacterial infections and of the clinical features of these infections.

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