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Serum thymic hormone activity in protein–energy malnutrition

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SUMMARY

To characterize the underlying mechanisms of impaired cell-mediated immunity in protein-energy malnutrition, thymic hormone activity was measured in the serum samples of undernourished children and was found to be reduced in the majority. This indicates that the cellular immunological deficit in nutritional deficiency may be due to reduced thymic inductive activity.

INTRODUCTION

Data in man and laboratory animals suggest that protein-energy malnutrition favours the development of infectious diseases, particularly in young children (Chandra, 1979a; Scrimshaw, Taylor & Gordon, 1968). Impaired immune responses contribute to such vulnerability to infection (Chandra, 1979b; Chandra & Newberne, 1977; Suskind, 1977). Cell-mediated immunity is almost invariably decreased in moderate to severe deficits of energy and protein (Chandra, 1972; Neumann *et al.*, 1975; Smythe *et al.*, 1971). To delineate the underlying mechanisms of impaired cellular immunity, thymic hormone activity was measured in the blood samples of malnourished children.

MATERIAL AND METHODS

Subjects. Peripheral venous blood samples were obtained from nine children aged between 9 and 30 months admitted for moderate to severe protein-energy malnutrition and from age- and sex-matched healthy children. Clinical features of nutritional deficiency included growth failure, hair and skin changes, reduced subcutaneous tissue and irritability or lethargy. Two patients showed pedal oedema. Weight-for-age was between 50 and 70% of the Harvard standard. Serum albumin concentration was less than 3·0 g/dl in two children. Serum transferrin concentration was less than 162 mg/dl in eight patients. None of the subjects had any evidence of gross infection at the time of study. The status of cell-mediated immunity in these patients has been described elsewhere (Chandra, 1977; 1979c).

Serum thymic hormone activity. This was detected according to the method of Bach & Dardenne (1973). Serial dilutions of serum were incubated with 3×10^6 spleen cells from adult C57Bl/6J mice thymectomized 14 days before. The incubation was carried out at 37°C for 90 min in the presence of azathioprine at a concentration of 5 μg/ml. Then, 12×10^6 sheep red blood cells were added, the mixture was centrifuged at 200 *g* for 5 min at 4°C and gently resuspended on a slow rotator. Rosette-forming cells were counted in haemocytometer chambers. Thymic hormone activity was expressed as the $\log_{-2}$ reciprocal titre.

RESULTS AND DISCUSSION

Serum thymic hormone activity in children with protein–energy malnutrition and age- and sex-matched well nourished controls is shown in Fig. 1. The activity was markedly lower in the undernourished group. This provides an additional facet to the mechanisms underlying impaired cell-mediated immunity in nutritional deficiency.

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Depressed cell-mediated immunity can be the result of a variety of factors. These include dysmorphogenesis of the thymus, inadequate inductive influence of thymic factors with qualitative or quantitative deficiencies, reduced number of T lymphocytes, alterations in T cell subpopulations with helper or suppressor activity, intrinsic defects of T cell differentiation, activation and proliferation, impaired production of lymphokines, lymphocytotoxic factors, serum inhibitors, etc. A number of thymic factors have been proposed as putative thymic hormones, including thymopoietin, ubiquitin, factor thymique serique, thymosin, thymic humoral factor and other substances (Goldstein, 1977). These are believed to promote the differentiation of T lymphocytes. More than one sequential signal is probably involved in T cell maturation. Thymic hormone(s) produced by epithelial cells is considered to be essential for the normal differentiation of thymocytes from prothymocytes, this action being mediated by cyclic nucleotides. Bioassays for thymic hormone activity are plagued by problems of specificity since non-thymus-related substances can mimic the action of thymic hormone. However, most non-specific factors promoting T cell induction also induce B cell differentiation. Recently, there has been considerable interest in the detection of thymic hormone activity in immunodeficiency disorders. The activity is high in early childhood and declines progressively after the fifth decade of life (R. K. Chandra, unpublished data). Subnormal levels of thymic hormone have been observed in primary specific immunodeficiency syndromes (Lewis *et al.*, 1977).

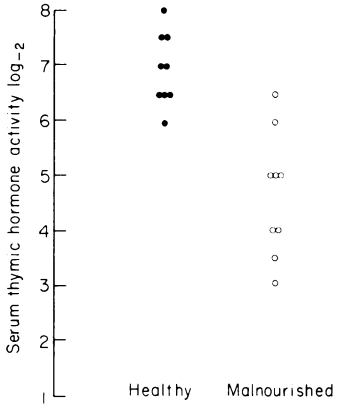

FIG. 1. Serum thymic hormone activity in children with protein-energy malnutrition (○) and age- and sex-matched healthy controls (●).

The hallmark of nutritional deficiency is reduced cellular regeneration, differentiation and repair. There is involution of many lymphoid organs, particularly the thymus and tonsils. Lymphocyte depletion is seen in T-dependent areas of lymphoid aggregates. The number of rosette-forming T lymphocytes in the blood is reduced (Chandra, 1974; Ferguson *et al.*, 1974). There is an increase in the number of 'null' cells without the conventional surface markers of T and B lymphocytes. The recent observation of elevated leucocyte terminal deoxynucleotidyl-transferase activity and its correlation with alterations in lymphocyte subsets in malnutrition (Chandra, 1979c), suggests that null cells may be immature and incompletely differentiated T lymphocytes. The decreased thymic hormone activity noted in the present study indicates that protein–energy undernutrition is associated with a deficiency of thymic inductive capacity which may result in impaired differentiation and maturation of T cells, thereby reducing cell-mediated immune responsiveness.

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