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MALNUTRITION AND IMMUNITY

Biological Interactions Between Infection, Malignancy and Host Immunity in Protein-Calorie Malnutrition

Studies of Australian Aboriginal Children

and Laboratory Animal Models

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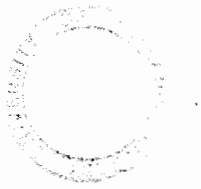

SYNOPSIS

The classic association between famine and pestilence represents a biological interaction of great historical significance to mankind. Aboriginal Australians, isolated from the rest of the world for over 30,000 years, developed a nomadic culture rich in social custom and mythology and a stable population living in close harmony with its natural environment. The European migration caused widespread famine from disruption of the natural food supplies and introduced new organisms which flourished in the virgin soil population, reducing the Aboriginal people to near extinction in 100 years.

The first part of this study provided the first published mortality and morbidity data for Queensland Aboriginal children. A relatively constant association between growth retardation, anaemia, chronic sino-pulmonary infection, parasitic infestation of the bowel and multiple nutritional deficiencies was described as the "protein-calorie malnutrition syndrome" of Aboriginal children, and was considered the major environmental factor predisposing to high mortality and morbidity rates in these communities. Children who were severely malnourished during infancy had persisting high loads of bowel parasites and chronic respiratory infection when examined as school children. Measurement of humoral and cellular immune responses in these children showed depression of both antibody and lymphocyte responses, which were partly corrected by reduction of the infecting load of organisms. Paradoxical increases in lymphocyte responses to some antigens were found in these children.

In the second part of this study the various mechanisms of host defence to infections and malignant neoplasms are briefly reviewed, and

the known influences of malnutrition upon these mechanisms considered.

A series of laboratory experiments using animal models in well defined protein and calorie deficient states, demonstrated a quantitative relationship between nutritional status, and the development of humoral and cellular immune responses to grafted tumours of different transplantation-antigenic strength. Cytotoxic cellular immunity, assessed by a sensitive in-vitro test, developed normally following inoculation of the tumour in all animals fed a diet containing more than 3% protein-calories. Humoral responses to the tumour, measured as cytotoxic, haemagglutinating and blocking antibody, showed marked dimunition in animals fed a diet containing less than 10% protein-calories. Hence the incubation of both serum and lymphoid cells from immunised animals, fed a diet with between 5% and 10% protein-calories, with labelled tumour target cells in-vitro, resulted in greatly increased lysis of target cells. Cellular immune responses may operate more efficiently in moderate protein deficiency due to the failure to develop serum inhibition by blocking antibody. This phenomenon may provide one explanation for the lower incidence of spontaneous tumours found in malnourished animals, and may account for their apparent increased resistance to certain viral infections and intracellular bacterial pathogens. Using a diet in which the protein content was duplicated entirely by synthetic amino-acids, selective depression of the antibody response alone, or of both antibody and cellular responses to tumour grafts, could be induced by specific amino-acid reduction in the diet. Minimal dietary requirements for each essential amino-acid were defined for both humoral and cellular immune responses. Blocking activity in mouse serum was found in tumour-specific IgG gamma 2a antibody fractions, and coincided with in vivo

tumour enhancing activity.

Animals subjected to a period of severe protein deprivation about the time of weaning were found to have persisting deficits in cytotoxic cellular immunity, and decreased numbers of thymus dependent lymphocytes in their spleens. These data, together with our previous findings in Aboriginal school children, suggest that malnutrition in infancy may result in long lasting immunological deficits. These findings have important implications in the understanding of host resistance to both infection and malignancy, and suggest the profound influences of protein-calorie malnutrition on the epidemiology and natural history of many diseases in populations where infant nutrition is sub-optimal.