

BIOCHEMICAL AND PHYSIOLOGICAL FACTORS OF THE IMMUNE RESPONSE

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SUMMARY OF RESULTS

Our studies of the inter-relationships of environmental extremes and endocrine imbalance on the immune response have been continued during the past year.

Our high-altitude studies at the Denver University High Altitude Station at Mt. Evans this past year were restricted to the Echo Lake facility at 10,600 ft. Late snows during May and June prevented utilization of the Summit Laboratory at 14,200 ft until late June. The time remaining would not have been sufficient for the experiments which had been planned.

Antibody formation in adrenalectomized rabbits at high altitude is under study. A group of rabbits were acclimatized for 30 days to 10,600 feet at Echo Lake, then bilaterally adrenalectomized. A control group of adrenalectomized rabbits was maintained in Denver. After four weeks of recuperation both groups were given a primary i.v. immunization with bovine serum albumin (BSA). Seven weeks later a secondary immunization with BSA was given. Serum samples were obtained at appropriate intervals and analyzed for precipitating antibody. High-altitude adapted and adrenalectomized rabbits exhibit a depressed primary immune response which reaches maximum titers later than high-altitude controls; the time sequence of the secondary response is similar to controls but the titers achieved are lower.

Our studies of the immune response in cold-exposed animals are continuing. A group of 10 rabbits were adapted to -15°C during a period of 10 weeks. The environmental temperature was gradually lowered from 8°C to -15°C during the first six weeks and the pelage progressively removed until only the head, feet and a one inch strip on the ventral surface remained. The rabbits were maintained under these conditions and immunized at the end of the 10-week period (10 mg BSA/kg i.v.). Titers of circulating precipitins were depressed. Hemagglutination titers have not been completed.

Two colonies of closed stock random-bred guinea pigs are being used in our studies of altitude and the immune response. Both colonies originated from the same stock; one colony is kept in Denver (altitude = 5,280 ft) and the other at Echo Lake (altitude = 10,600 ft). During the end of last summer and early fall, the colony at Echo Lake was struck by an epidemic of bacterial enteritis of unknown origin. Despite intensive antibiotic therapy, over 95% of the high-altitude colony was lost. The few remaining animals are being bred as a nucleus of a new colony, but a sufficient number of high-altitude-bred animals may not be available for use until the summer of 1967. Antiserums obtained from animals of this colony during the summer of 1965 are still to be analyzed for qualitative changes in antibody production.

As a result of experiments done several years ago, we are re-examining the question of inhibition of antibody formation by pre-immunization treatment with homologous γ -globulin. The ability of rabbits to produce anti-BSA precipitins is decreased by the prior injection of homologous γ -globulin but there is no decrease in the total quantity of γ -globulin produced. Thus, there appears to be a qualitative change in the synthesis of antibody protein. Experiments are in progress to determine the distribution of anti-BSA antibodies among the immunoglobulins and whether or not any aberrant immunoglobulins were synthesized as a result of the treatment with homologous γ -globulins.

Even though our work has progressed satisfactorily during the past year, there is not a great mass of data accumulated at this time to report. It is anticipated that the work of the current year will "fill in the gaps" and enable us to present a clearer picture of certain of the events of the immune response which occur in stressed animals.

Plans for the future

The long range plans of our research program are to investigate in detail the molecular basis of changes which occur in the immune response of animals subjected to stress of various types. As a consequence, we hope to elucidate some of the complexity of antibody synthesis and decay at a molecular level.

Our immediate plans are to continue with our studies of: a) determination of the distribution of antibodies among various fractions of serum from immunized animals subjected to stress; b) evaluation of possible relationships between the stress situation and observed alteration in antibody distribution; c) determination of possible differences in the immunological and physico-chemical properties of antibody produced by stressed animals; d) to investigate the possible relationship between the molecular properties of antibody produced and the ability of the animals to resist disease; and e) to establish the possibility of increasing the resistance of stressed animals to infection.

Techniques such as immunoelectrophoresis, immunodiffusion, starch gel electrophoresis, moving boundary electrophoresis, quantitative precipitin analysis and hemagglutination techniques for the quantitation and characterization of antibody in serum and serum fractions are being used. The serum fractions are obtained by column chromatography and other suitable methods.

It is anticipated that a clearer understanding of the immunochemical events at a molecular level will enable us to explain better the overall immune response. If it can be shown that the influence of stress and/or endocrines act on the immunological mechanism in a particular way, as evidenced by molecular changes which can be distinguished, it may be feasible to circumvent or overcome in part an adverse situation and its effect on the host-parasite relationship.

REPORTS

1. "Biochemical and Physiological Factors of the Immune Response", Contract Nonr 3545(00), NR 108-599, I.L. Trapani
 - a) Biochemistry Branch Progress Report Abstracts, 1966
 - b) Annual Progress Report for period 1 May 1964 to 30 April 1965, submitted 1 May 1965

PUBLICATIONS

1. "Altitude, temperature and the immune response", I.L. Trapani. International Symposium on Environmental Physiology - Kyoto, Japan. Smith, R.E., Ed., Federation Proceedings, 1966. In Press.
2. "The immune response at high altitude", I.L. Trapani. (Abstr.) Proceedings Fourth International Biometeorological Congress, Rutgers University, New Jersey, August, 1966. In Press.
3. Three manuscripts in preparation.