Analysis of the sera from both R.A. and the control group on a Technicon SMA 12/60 revealed no abnormality of liver or kidney function which might have suggested difference in immunoglobulin metabolism. The Gm phenotype distributions were also similar, indicating that the Gm groupings were not associated with the configurational differences observed.

Several workers have commented on the stability of immunoglobulin levels in a given individual. There is also evidence that the subclass proportions themselves are equally stable and this may imply a difference in the capacity of each individual to respond to a particular antigen. This preliminary study indicates that differences in molecular configuration may also occur. The presence of molecular species in the yG-globulins of rheumatoid patients, differing configurationally from 'normal' yG-globulins may be clinically highly significant since their presence may be highly favourable to the initiation of autoimmune phenomena.

4. IMMUNOGLOBULIN AND SPECIFIC ANTIBODY RESPONSES TO ANTIGENIC STIMULATION IN ADULT COELIAC DISEASE

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(Introduced by J. Anderson)

Fourteen patients with established adult coeliac disease were studied together with fourteen apparently healthy control subjects matched for age, sex and racial origin. Each subject received two doses of 0-5 ml adsorbed tetanus toxoid (Burroughs Wellcome) at an interval of 4 weeks, and blood samples were collected at weekly intervals after the first injection, for 6 weeks. Immunoglobulins G, A and M were measured using the single radial diffusion technique, and specific antitoxin titres were measured using passive haemagglutination and the bioassay method of Glenny & Stevens (1938). The results indicated that there was a significant difference in the immunoglobulin pattern observed in coeliac patients compared to controls, and there was also a depression in the antitoxin levels achieved in coeliac patients compared to the controls, both in those undergoing primary immunization and in those who were re-immunized. These observations support the concept that the humoral immune response is impaired in some coeliac patients, and that IgM synthesis is diminished. Correlations between antitoxin titres and immunoglobulin levels were observed to occur most frequently with IgG, but some large increases in immunoglobulin levels occurred without a corresponding rise in antitoxin titre. It is suggested that the immunoglobulin changes observed could have resulted in part from a non-specific adjuvant effect of the antigen.

5. WHAT IS TISSUE FLUID?

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A method for repeated sampling of tissue fluid has been developed, by implanting inert capsules beneath the skin, initially in rabbits and dogs and more recently in humans (Guyton, A., 1963, Circulation Research, 12, 399–413). These capsules have been in place for up to 11 months and are found to be surrounded by a fine capsule lined by an endothelial layer. The validity of this method of obtaining tissue fluid will be examined.

The normal interstitial pressure has been found to be negative and by plasmaphoresis the degree of negativity could be reduced. Other factors affecting the negative pressure will be discussed.

The ratio of serum to tissue fluid proteins was estimated, and relatively less globulin was found in the tissue fluid. The serum electrolytes were also estimated and a significantly lower potassium but higher chloride content was found in the tissue fluid. Examples of the application of this technique will be given.

6. SIMULTANEOUS MEASUREMENT OF BIDIRECTIONAL FLUXES OF SODIUM AND CHLORIDE ACROSS EPITHELIAL MEMBRANES

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(Introduced by J. Anderson)

The epithelia studied are the urinary bladder and skin of the toad, Bufo marinus. Net movement of ions across these membranes is given by the ‘short circuit current’ (s.c.c.).

There exist conditions where the s.c.c. does not equal the net sodium flux given by the difference between the unidirectional fluxes measured with $^{24}$Na and $^{22}$Na. At the same time, it is necessary to know the magnitude and ratio of chloride fluxes and the changes produced in these by pharmacological agents or electrochemical constraints.

It is convenient to measure the bidirectional chloride fluxes at the same time as those of sodium. The isotopes $^{24}$Na and $^{38}$Cl are produced by neutron activation of solid sodium chloride, which is added to the bathing solution on one side of the membrane, so that the final concentration of NaCl is appropriate to toad Ringer’s solution. The Ringer’s solution on the other side of the membrane contains previously added long-lived $^{22}$Na and $^{36}$Cl. These interdiffuse, and the contributions from the four isotopes in samples taken at subsequent times are differentiated.