A STUDY OF THE PATHOGENESIS AND IMMUNOBIOLOGY OF PYELONEPHRITIS

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SHORT ABSTRACT

The experiments carried out during this investigation have studiedthe pathogenesis and immunobiology of pyelonephritis. Two experimental models of the disease were developed in laboratory animals and several new analytical procedures for studying biological changes during the course of the disease were established. In particular, methods for the determination of glomerular filtration rates in small animals, the automated analysis of antibacterial antibody and the in-vitro determination of the response of rat lymphocytes to phytohaemagglutinin (PHA) were established.

The effect of chronic active pyelonephritis on renal function was studied and the effect of antibiotic treatment and elimination of infection on the pathological changes in pyelonephritis was determined. Eradication of infection did not affect the gross pathology and histopathological changes found at autopsy. These experiments have also investigated the role of bacterial interference as a determinant in the epidemiology of renal infection. It was shown that mixed renal infections with E.coli were uncommon and that the pattern of infection was determined by the resident pathogen. The relationship between bacterial infection of the renal parenchyma with E.coli and the establishment of pathological lesions was investigated and the conclusion reached that infection of the kidney is not always associated with pathological changes. The term "acquiescent infection" was then used to describe the host parasite relationship in which active persistent bacterial infection is not associated with pathological lesions.

Antigen presentation as a factor in the protective immune response to renal infection was also studied and experiments carried out which demonstrated that immunological memory to the somatic antigen of E.coli persisted for at least six months after primary immunization and appeared to be carried by the B lymphocytes. The distribution of B lymphocytes in the peripheral blood and lymphoid sites and the functional capacity of T cells during the course of pyelonephritis were also investigated. Lymphocytes forming the lymphocytic infiltrate in the kidney were identified as thymus derived lymphocytes by their surface labelling characteristics but further experiments showed that T lymphocytes in the kidney, which would normally respond to stimulation with PHA in-vitro, were non-responsive and presumably non-functional. A unique factor associated with renal cells was found to be capable of blocking the PHA response of T lymphocytes, suggesting that ablation of cell-mediated immune mechanisms in the kidney may contribute to the persistence of infection in pyelonephritis. This concept was investigated by studying the effect of a selective deficiency of thymus derived lymphocytes on the course of pyelonephritis. The experiments showed, however, that ablation of T lymphocytes did not appreciably alter the course of the disease. Further experiments were then carried out investigating the role of B lymphocytes in the immune response by manipulation of the hosts immune capacity using immunosuppressive drugs. Animals with pyelonephritis did not produce antibacterial antibody but were able to eliminate organisms more readily from the infected kidney than untreated animals with a normal immune response. This suggests that blocking of the phenomenon of immunologic

enhancement may explain these unexpected results and that the immune response to renal infection could have an enhancing role, protecting the bacterial cell from otherwise effective host defense mechanisms.

Clinical aspects of antimicrobial resistance in pyelonephritis were also investigated in a study of urinary tract pathogens from 120 patients. The results showed that standard methods for testing antibiotic sensitivity may reject potentially useful antibiotics and that up to 75% of microorganisms considered resistant to individual antibiotics may in fact be sensitive to concentrations of antibiotic attainable in the tubular lumen. In certain circumstances the determination of minimum inhibitory concentration of selected antibiotics may be of considerable value in patient management.