HOST-BACTERIA RELATIONSHIPS AT THE SECRETORY SURFACES
OF THE LUNG

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SUMMARY

The development of immunity in the mouse to intra-nasal infection with *Klebsiella pneumoniae* was investigated with regard to cellular and humoral aspects of immunity. Particular attention was paid to the possible role of local, humoral immunity in resistance to this organism.

Experiments were designed to investigate the role of antibody in the expression of cellular immunity due to the importance of the alveolar macrophage in the lung. Studies on the killing of *Salmonella typhimurium* and *Listeria monocytogenes* by normal and activated peritoneal macrophages revealed that antibody was required for the destruction of *Salmonella* but not *Listeria* by macrophages, irrespective of the degree of activation. The requirement of antibody for killing of *Salmonella* was related to the inability of this organism to bind to macrophages in the absence of antiserum. *Listeria* bound to macrophages in the total absence of serum. The binding of *Listeria* was dependent on the presence of Mg\(^{++}\) and Ca\(^{++}\) ions, while the antibody dependent binding of *Salmonella* was not. Thus the binding of *Listeria* was not due to the presence of cytophilic antibody. Acquired cellular immunity therefore does not change the requirement of antibody for macrophages in the destruction of certain organisms.

Humoral immunity was shown to protect mice to intra-nasal challenge with *Klebsiella pneumoniae*. Immunity could be produced by actively immunising mice intra-venously with vaccines or by passive
transfer of antiserum with the infecting dose of organisms. Both IgG and IgM derived from serum were shown to be effective in protection. Differences were observed between the protection mediated by these classes of antibody dependent on the nature of immunising vaccine used to raise the anti-serum. While antibody directed against capsular polysaccharide efficiently protected mice, a second non-capsular antigen that was heat-labile was also able to induce the production of protective antibodies. Antibodies to this antigen appeared in the IgG class and not the IgM class. The antigen was present in other strains of Klebsiella.

As humoral immunity was shown to be critical in resistance to this organism, and as cellular activation could not alter the requirement for antibody, it was decided to investigate the possible contribution of local humoral factors. Local immunisation of the respiratory tract produced immunity in the absence of high titres of serum antibody. Antibody could be detected in pulmonary secretions. Antibody in both IgA and IgG classes was detected and shown to be protective when passively transferred. While serum antibodies could promote the clearance of an avirulent organism from the lung following aerosol exposure, sIgA had no such effect. Fc receptors for IgG were detected on alveolar macrophages but no receptor for IgA was found. Protection mediated by IgA was probably not dependent on alveolar macrophage function. The possible contribution of polymorphonuclear leukocytes was investigated. IgA was not able to promote killing by these cells.
The protection mediated by IgA in the lung does not appear to rely on cellular events in the lower respiratory tract, the site of pathology in infection with Klebsiella. It is proposed that IgA functions solely in the upper respiratory tract in preventing temporary colonisation from occurring and inhibiting the spread of infection to the lower airways. A similar function for IgA and local immunity can be envisaged in human disease where colonisation of the upper respiratory tract by Klebsiella or other gram-negative bacteria appears to be the initiating event in nosocomially acquired infections.