A Puzzling Respiratory Virus

Respiratory syncytial virus is the most important respiratory pathogen of early childhood. It is because it causes bronchiolitis and pneumonia in infants less than 6 months old and especially in those aged 1-2 months. This is surprising because infants of this age are usually protected by maternal antibody—usually, the majority of infants have detectable antibody against the respiratory syncytial virus. In older children and adults it is known that infection with this virus can take place despite the presence of neutralizing antibody.1,2

Thus respiratory syncytial virus is unusual among viruses in that neutralizing antibodies do not protect against it. Consequently the preparation of an effective vaccine against it might be thought difficult, but an even stranger situation was disclosed by the results of trials of inactivated virus vaccine in the U.S.A. Not only were vaccinated children not protected, but among them a higher proportion of those who later became infected with the virus developed pneumonia or bronchiolitis than did the children in comparable control groups.3,11 Vaccination against the virus, therefore, both failed to produce immunity and actually increased the severity of the disease produced in those children who afterwards became naturally infected with it.

This unexpected result suggested that antibody produced in the serum by vaccination—or possibly also by previous infection or passive transfer from the mother—had in some way enhanced the severity of naturally acquired infection with the virus. A somewhat similar situation to this has been found with the vaccine made from inactivated measles virus, since a few of the children given this vaccine have developed an atypical, severe disease when they later became naturally infected with measles.12,13 In the case of measles this complication has been attributed to delayed hypersensitivity.14 But delayed hypersensitivity is almost certainly not responsible for lower respiratory tract disease in respiratory syncytial virus infection, because it is mediated by cells, which do not pass from mother to fetus. Chanock’s team15 has postulated that respiratory syncytial virus bronchiolitis and pneumonia, whether acquired as a natural infection in infancy or induced by vaccination, may be due to a type 3 or Arthus-type allergic reaction in the lungs.15 In this type of reaction an acute immunological injury results from the formation of complexes between antibody and virus which are toxic to cells and thus give rise to tissue damage. Imbalance between the presence of serum antibody and the lack or relative lack of local IgA antibody in respiratory secretions was also suggested as a possible additional factor.

At page 327 of this issue of the B.M.J., Dr. P. S. Gardner, Miss J. McQuillan, and Professor S. D. M. Court make some speculative observations on this interesting and important topic. They found that virus antigen was abundant in the lungs in one case of respiratory syncytial virus pneumonia but was scanty in two cases of bronchiolitis. Human globulin, on the other hand, was present, though sparsely, in bronchiolitis but could not be found in the lungs of the patient with pneumonia. If these observations are typical, they make it unlikely that either bronchiolitis or pneumonia are due to a type 3 reaction, since this would require the presence of excess virus antigen and antibody in the lungs, leading to the formation of antigen-antibody complexes.

The authors suggest that a type 1 or anaphylactic reaction16 is a more likely explanation of the pathogenesis of bronchiolitis. In this type of reaction the cells of the lung would be sensitized by reagin, or IgE antibody, formed as a result of a primary encounter with the virus or by vaccination. The sensitized cells would then suffer immunological injury if virus antigen were later introduced again during reinfection. Since reagins are not passively transferred from mother to fetus, this explanation would mean that in the absence of vaccination infants with bronchiolitis—even those under 3 months of age—must have undergone an earlier infection with respiratory syncytial virus which resulted in sensitization. Though at first sight this seems unlikely, Dr. Gardner and his colleagues point out that infections with this virus are so common that infants of this age might have been twice infected with the virus.

Some indication that this may indeed be the case comes from the observations of H. W. Kim and her colleagues17 that infants in the acute phase of respiratory syncytial virus infection of the lower respiratory tract had moderately high levels of neutralizing antibody, presumably largely IgA, in their nasal secretions. Dr. Gardner and his co-workers point out that this early nasal antibody may well have been the result of previous infection with the virus. They also suggest that the pathogenesis of respiratory syncytial virus pneumonia is different from that of bronchiolitis in that in pneumonia there is a widespread and primary virus infection of the lungs in the absence of IgA antibody.

Further work is necessary to see if the findings of the three cases described here are typical of most cases of respiratory syncytial virus bronchiolitis and pneumonia and also to investigate, perhaps by immunological as well as virological techniques, the pathogenesis of both diseases. The role of IgA antibodies in these diseases certainly requires further study.

Compression of Coeliac Axis

The introduction of relatively safe techniques of aortography has focused increasing attention on segmental areas of narrowing or occlusion of the aorta’s visceral branches, particularly since advances in vascular surgery now enable arterial reconstruction to be carried out. The clinical picture of intestinal angina, comprising abdominal pain after meals,