

body or complexes; (2) excess of antigen and presence of antigen-antibody complex; (3) excess of antibody and persistence of anaphylactogenic immune complexes. When there is free antigen, the patient is healthy, but with the development of antibody, hepatic function becomes abnormal.

Using the electron microscope, various investigators have seen Dane particles (42 nm), which are composed of an outer core and an inner, spherical (27-nm diameter) component. The outer core appears to be antigenically related to HAA, and the inner core bears some morphologic resemblance to the rhinovirus. The Dane particle can be disrupted with Tween 80 treatment into these two components, but the inner component may be unstable. Antibody to HAA and antibody to the inner core of the Dane particle might be associated with hepatitis B, although the role of these two antibodies in immune-complex formation or in protective immunity to hepatitis B infection is yet to be determined. Cell-mediated immune responses may also be involved in the conferral of immunity to hepatitis B. Cyclic adenosine 3',5' monophosphate and prostaglandins might also play a role in controlling the immune response to hepatitis B.

Based on different forms of evidence, the participants at the workshop agreed that hepatitis B disease may be complicated in certain cases by the formation of immune complexes. When these immune complexes lodge in the tissue, they initiate the typical immune-complex syndrome already outlined. It has been shown by various investigators that administration of certain gamma-globulin preparations can help prevent hepatitis B infection. It is not known whether the antibody to HAA or some other antibody, such as antibody to the inner core of the Dane particle, is the protective antibody. The effect of administration of gamma globulin with high titers of antiserum to HAA on immune-complex formation is not yet known. Particular caution should be exercised in administering gamma globulin to persons positive for hepatitis-B antigen.

JUNE DUNNICK, PH.D.

*Infectious Disease Branch  
National Institute of Allergy  
and Infectious Diseases  
National Institutes of Health  
Bethesda, Maryland*

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#### Workshop on Coronaviruses

Research during the past few years has shown that members of the newly defined coronavirus group have many properties in common. Although coronaviruses cause illness in man, chickens, swine, mice, and rats, approaches to basic and comparative virology are seldom separable on the basis of species.

On January 31, 1972, the National Institute of Allergy and Infectious Diseases (NIAID) sponsored an international workshop to review the relevance and relationship of the presently known coronaviruses, to identify specific problem areas of mutual concern and interest, and to offer an opportunity for free exchange of knowledge. Nearly 20 investigators participated in the workshop, which was organized by the Collaborative Program of NIAID under the direction of Dr. Robert J. Byrne and was held at the National Institutes of Health, Bethesda, Maryland. Dr. B. C. Easterday, University of Wisconsin, Madison, served as chairman.

In a discussion of comparative methods and problems, Dr. M. Tajima of the Nippon Institute for Biological Sciences, Tokyo, described the fine structure of the nucleocapsid and the character of the nucleic acid of one of the coronaviruses, avian infectious bronchitis virus (IBV). He reported that, in his studies, most surface projections on IBV particles were lost during the process of purification. Many particles contained spherical corelike structures corresponding in size, shape, and location to amorphous material in two other coronaviruses, strain 29 E human coronavirus and the transmissible gastroenteritis virus of swine. Purified virus treated with lipid solvents was completely disrupted with release of the contents of the virus, but corelike structures could not be identified.

Dr. J. D. Almeida, electron microscopist at the Royal Post Graduate Medical School, London, England, described studies of antigen-antibody coronavirus reactions. Dr. Almeida reported that it is possible to distinguish virus and host antigens on the surface of avian IBV. How-

ever, when attempts were made to reproduce these findings with human coronaviruses, it was found that all guinea-pig sera tested contained antibody to these viruses. The presence of this antibody in guinea-pig serum might explain why some serologic tests (CF) with human coronaviruses have yielded unsatisfactory results. These findings have opened an entirely new concept of the role of the various reagents in serologic tests.

Problems of antigenic relationship among coronaviruses were discussed by Dr. T. Estola of Finland. Many coronaviruses require rather exacting methods of cultivation. Titers of virus are generally low, and the limited range of infected tissues and the strong species specificity make serologic comparisons of uncertain value. In addition, there are no common antigens that cross-react with all coronaviruses in complement-fixation tests.

Human coronaviruses can be divided into at least three serologic types or groups in which the strains are closely related. Among the avian coronaviruses, there are at least 11 different strains that have common antigens detectable in gel diffusion but that differ in cross-neutralization tests to the extent that they are frequently regarded as separate serotypes. There are no significant cross-reactions thus far between avian and human coronaviruses, but there is an antigenic relationship between mouse-hepatitis viruses (MHV) and certain human coronaviruses. Transmissible gastroenteritis (TGE) viral strains of swine seem to be antigenically identical or similar, but their relationships to coronaviruses of other species have not been analyzed.

In discussing the clinical, epidemiologic, and

laboratory aspects of human coronaviruses, Dr. A. Z. Kapikian (NIAID) identified them as probable important etiologic agents of acute illness of the upper respiratory tract in adults. Their role in the respiratory illnesses of infancy and childhood is not presently known. Most knowledge of the clinical syndromes associated with these infections has come from studies in adult volunteers and from seroepidemiologic investigations, since the isolation of these agents has been so difficult.

In addition to recovery in cultures of human embryonic tracheal organs, coronaviruses have been recovered in monolayer cultures of human embryonic kidney cells, WI-38 cells, diploid fibroblasts of the human embryonic intestine, and a few others. Cell-culture monolayers have apparently been less sensitive for primary isolation than the tracheal-organ cultures.

A memorandum from Dr. D. A. J. Tyrrell, chairman of the Study Group on Coronaviruses for the International Commission for the Nomenclature of Viruses, was read at the workshop. The study group is soliciting additional information on the internal structure of coronaviruses, the number of polypeptides and pieces of RNA, the nature of the host component (which might also be separated during chemical fractionation), serologic cross-reactions between species and types, and the relationship of the viruses to various diseases.

Dr. B. C. Easterday reported on a pilot study devoted to collecting, storing, and retrieving information on the coronaviruses and paramyxoviruses. This information is being fed into a computer system at the University of Wisconsin.