Global Distribution and Molecular Biological Characteristics of Hantaviruses

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It was long believed that Hemorrhagic fever with renal syndrome (HFRS) case occur only in rural areas where farmers and soldiers stationed in the fields were the most likely victims. Districts infected with Hantaan virus were also thought to be limited to certain designated areas infecting only its inhabitants and travellers. Recent findings, however, show that HFRS patients are widely distributed throughout the Republic of Korea with urban cities having great number of patients. In Korea several hundreds HFRS cases occur in rural and urban areas every year with approximately 7% fatality.

In the past few years, it has become clear that urban rats in many parts of the world carry Seoul virus (1,2) as do laboratory bred white rats in the Republic of Korea, Japan, Malaysia, Belgium and Hong Kong. It now appears likely that viruses of Hantavirus (3) group will be recognized as a worldwide human disease problem.

Global center for HFRS serology and virus isolation

As WHO Collaborating Centre for Research on HFRS, we have provided serological diagnosis for suspect HFRS in sera from throughout the world, but especially from the Asian region. In addition, we have collaborated with a number of investigators conducting small mammal surveys for evidence of Hantavirus infection and isolation of strains from host animal tissues. Results of these preliminary studies indicate that human disease due to Hantavirus infection is present is several areas where HFRS had not been previously diagnosed. The results of the serosurvey of Hantaan (4,5) and related virus among rats and human populations in many parts of the world where HFRS patients are not known to exist are shown in Table 2.

Human sera from 12 countries; 7 countries in Pacific Ocean, 1 country in North America, 1 country in South America and 2 countries in Africa were found to have IF antibodies to Hantaan virus as shown in the table. The prevalence rate of antibodies to Hantaan virus was between 1.1%-9.5%, data much higher than those of residents of Seoul, the endemic area of HFRS. Very recently, we have confirmed HFRS patients serologically among hospitalized patients in Hong Kong, Singapore and India.

Urban rat sera from the Philippines, Hong Kong, Malaysia, Singapore, Fiji, Hawaii, Egypt, Sudan and Uganda were also found to have IF antibodies to Hantaan virus with a high prevalence rate of 51.5% among philippine rats and 20.0% in Egypt rats.

Forty two out of 154 laboratory-bred white rats from two institutions in Malaysia and several Wistar rats from Hong Kong and Singapore were sero-positive against Hantaan virus. Five out of 71 house mice from Egypt were also positive to Hantaan virus.

Recent studies have demonstrated a near global distribution of Seoul virus among urban rats and the presence of this or other Hantaviruses among
several different species and genera of small mammals. Clearly the genus Hantavirus(3) is widely distributed and maintained in a variety of different ecological settings. The degree to which Hantaviruses cause human disease, especially in areas where HFRS has not been traditionally recognized, is presently unknown.

**Antigenic and pathogenic characterization of Hantaviruses**

HFRS is caused by a number of serologically related viruses. From a recent biochemical analysis the viruses contain genomes consisting of three segments of single stranded RNA and have an RNA-protein structure consistent with classification in the family Bunyaviridae(7, 8). Numerous viruses have been described but not all have been associated with the disease. Studies using monoclonal antibodies have revealed significant antigenic variation within the group of viruses as shown in Table 3. Conservation of the 3' terminal sequences of each of the genome segments in all viruses examined has led to the proposal that they be classified as a distinct genus of the family Bunyaviridae. Hantaan and Seoul viruses are pathogenic to suckling mice with the virus is inoculated intracerebrally(9). There is no animal model yet that produces clinical symptoms similar to those of HFRS patients.

Preliminary results indicate that 4 distinct viruses compose the genus Hantavirus(3):Hantaan, Puumala (6), Seoul and Prospect Hill viruses. It appears that several subtypes of strains exist within each virus type(10) and epidemiological evidence suggests that other Hantaviruses still exist unrecognized in nature. Our preliminary experiments suggest that there are two serotypes of Hantaan virus in Korea: human isolates from HFRS patients and isolates from naturally infected Apodemus mice. There are also three serotypes of Seoul virus in Asia: the first represented by isolates from HFRS patients and urban rats in Seoul, the second from HFRS in China, and the third from Incheon and Tokyo rats. Our recent experience with virus isolates from Egypt and Hong Kong suggests that multiple antigenic serotypes exist. Our preliminary experiments have shown that the HI test(9) with Hantaan and Seoul virus hemagglutinins can differentiate antibodies against the two viruses.

A serologic classification is thus needed to clearly differentiate specific Hantaviruses and to aid in the recognition of new viruses. A total of 49 strains of Hantaviruses is presently on hand in our laboratory as shown in Table 4 and available for serological characterization. Using these viruses and those isolated in future studies, we will identify serological groupings of viruses generating a formal classification scheme using standard serological tests such as IFA, HAI, PRNT and EIA. This information will be useful in establishing which viruses are responsible for human disease and will insure that diagnostic tests and developed vaccines are reactive with all Hantaviruses.

**REFERENCE**

5) Information Exchange Subcommittee, Ft.: Collins, Co. 80522, 1980.