# CANINE HEPATITIS VIRUS AND HUMAN ADENOVIRUS

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INCREASING awareness of human infectious hepatitis and the common occurrence of infectious canine hepatitis in the United States have precipitated queries about the possible transmission of the canine disease to man, particularly when illness occurs simultaneously or has similar manifestations in a pet and in a family member.

Perhaps the name "hepatitis" in the designation of the canine disease is unfortunate since it suggests a relationship to human hepatitis. Actually the virus infects the reticuloendothelial system in general, and hepatitis is not a primary lesion. Frequently hepatitis is not manifested clinically, but lymphadenopathy, tonsillitis, and endothelial invasion are more constant lesions. Since infectious canine hepatitis virus was first described by Rubarth in 1947 (*1*), a great deal has been learned about the disease in its natural host and about its causal agent. Although the virus was known to cause an encephalitis in the fox, there was no suggestion in the early literature that man was also a host. However, at least one later study suggested that canine hepatitis virus can cause hepatic complications in man (*2*).

This report reviews the literature on infectious canine hepatitis virus to help clarify its position in relation to human disease.

## Serologic Studies

That humans carried serologic titers to the virus of infectious canine hepatitis was demonstrated in 1956 (*3*). These reactions, obtained in complement fixation tests, suggested a serologic relationship of the canine virus to poliovirus. Serums from patients with clinically diagnosed respiratory, neurotropic, or poliomyelitis infections showed some antibodies to canine hepatitis in all these groups, but those from patients with poliomyelitis showed a much higher percentage. A misleading point in this study was that type-specific poliovirus antiserums from rabbits showed cross reactions with the canine virus. It was later realized that monkey kidney epithelium used for propagation of poliovirus can be simultaneously contaminated with a variety of viruses, including adenoviruses. Such a situation was suspected, however, and it was stated that "A more acceptable conjecture might be that the ICH virus and another virus infective for man bear some common antigenic property."

This hypothesis was proved in 1959 when Kapsenberg demonstrated that a common complement-fixing antigen was shared by infectious canine hepatitis virus and human adenovirus (*4*). That these two viruses are not identical was also demonstrated by the observation that anti-infectious canine hepatitis serum was not reactive with human adenovirus. This also explains the recent observations of Govaerts (*5*) concerning canine hepatitis virus antibodies in human serums.

The serologic relationship of the viruses was also confirmed by Carmichael and Barnes (*6*), using gel-diffusion techniques. These authors and Prier (*7*), at the same time, suggested that the adenovirus group include the related animal parasites for taxonomic purposes. Prier suggested further that a classification include adenovirus group A types of human origin and adenovirus group B types of animal origin. Group B would then be broken down further as to species of origin: canine adenovirus, bovine adenovirus, or other.

In serologic studies by Bech (*8*) no antigenic

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relationship between the canine virus and the human hepatitis viruses could be established. No evidence existed, therefore, to link liver pathology of the human with a viral etiologic factor of canine origin.

On the other hand, the possibility that human hepatitis viruses are capable of causing infection in the dog was suggested by the work of Martin and Goret (*9*) which demonstrated the experimental passage of two human virus strains in dogs. However, since the true identity of these strains was not clear, more convincing data must be sought to justify this theory.

### Characteristics of Adenoviruses

In addition to serologic similarities, human adenovirus and canine adenovirus (infectious canine hepatitis) share other common characteristics. Both viruses are approximately the same size, as determined by electron photomicrographic studies (*10,11*). Also, typical intranuclear changes in cells infected with adenovirus (*10,12,13*) are almost identical with nuclear alterations associated with canine virus (*7,14–16*).

Other similarities of these viruses include the intranuclear site of multiplication and the specific growth pattern in controlled systems (*12,13*). Also common to both viruses is their ability to cause infections such as tonsillitis, keratoconjunctivitis, pharyngitis, and lymphadenopathy, in their respective natural hosts.

The agents may persist in their hosts long after infection. Initial isolation of adenoviruses was from adenoidal tissue of persons with no manifestation of acute disease. Similarly, the canine virus has been found in tissues from asymptomatic dogs (*4*). There are some clinical differences, however, including an appreciable mortality rate in dogs and predilection of the canine virus for hepatic and endothelial cells.

### Interspecial Transmission

Since the characteristics of the two viruses are nearly parallel, it is not impossible that the canine adenovirus may cause a respiratory disease in man or that human adenoviruses may have an affinity for the respiratory-enteric tracts of the dog. However, adenoviruses are peculiarly host specific, even for primary growth of the agents in tissue culture. Thus, the human viruses grow in human and primate cell cultures, the canine isolates in dog cells, and the bovine strains in calf kidney, but the agents are not heterotrophic for the cells of various species in culture.

An interesting concept by Klein (*17*) is that although animal viruses may cause individual human infections, they do not establish themselves as responsible factors in epidemic diseases. Obviously, the presence of certain subtle factors of the host or virus, or both, prevents free transmission of the parasites between two species, even though both species have been equally exposed to similar agents. Accurate identification of specific virus types or strains is therefore essential before the existence of multiple host species can be presumed. The many serologic similarities among the causative viruses of various diseases (canine distemper and measles, parainfluenza and bovine shipping fever, smallpox and cowpox, human adenovirus and infectious canine hepatitis) point up the reservations one must assume when considering the specific identity of viruses.

The presence of serologic antibodies for infectious canine hepatitis virus in man cannot lead to the conclusion that this virus is a human parasite. The logical conclusion would be that the human from whom the serum was obtained had been exposed to adenovirus. In fact, the specific adenovirus titer will undoubtedly be higher than that against the canine virus. It is quite possible, of course, that the canine agent may be capable of causing some type of illness in man, but proof will consist of isolation and identification of the specific virus.

### Summary

A review of the literature indicates that the infectious canine hepatitis and human adenoviruses share many common characteristics. Serologic and morphologic studies of infected cells have determined that these adenoviruses are members of a group which is peculiarly host specific. No conclusive evidence has been reported to indicate that the canine virus is capable of infecting man.

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## Cancer Sites of Husbands and Wives

A pioneering study of 231 husband-wife and sibling pairs who died of cancer shows that 43 of the pairs died of cancer of the same site, twice the number that would be expected by chance. The excess of 10 matches for cancer site among 51 husband-wife pairs implicates common environment rather than common heredity in the causation of cancer in these cases. The study was made from the 4,015 death certificates giving cancer as cause of death in Washington County, Md., between 1900 and 1960.

The study, "Site Distribution of Cancer Deaths in Husband-Wife and Sibling Pairs," was published in the October 1961 issue of the *Journal of the National Cancer Institute.* The paper carries an appendix which provides chi-square formulas for testing the deviations of the observed number of matched pairs from the expected.

The investigators in the study were Dr. William Y. Chen, Dr. Lyman B. Crittenden, and Dr. Nathan Mantel of the National Cancer Institute, Public Health Service, and Dr. W. Ross Cameron of the Washington County Department of Health, Hagerstown, Md.