Susceptibility of Gibbons, Rhesus Monkeys, and Cynomologous Monkeys to Infection with the Hepatitis A Virus (HAV)

Principal Investigators : Donald S. Burke, MAJ, MC
Rapin Snitbhan, M.D.
Markapol Tingpalpongse, DVM

Associate Investigators : Frank E. Chapple, MAJ, VC
Richard E. Whitmire, LTC, VC

Assistant Investigator : Choompun Manomuth, B.Sc

OBJECTIVES

1. To determine if gibbons, rhesus monkeys, and cynomologous monkeys have naturally acquired circulating serum antibodies to human HAV.

2. To determine which if any of these species could be used as an experimental model for HAV infection.

BACKGROUND: Anti-HAV activity has been detected in serum speciments from several primate species. Miller et al. (1) detected anti-HAV by the immune adherence method in 14 of 23 chimpanzees, 9 of 40 grivets, 1 of 17 rhesus, 0 of 6 baboons, 0 of 1 gibbons, and 0 of 82 marmosets. Purcell et al. (2) detected anti-HAV by the immune electron-microscopy method in 8 of 8 jungle-caught chimpanzees, 0 of 16 colony-born chimpanzees, 4 of 12 rhesus, 4 of 4 patus monkeys, 1 of 5 African green monkeys, 0 of 4 baboons, and 0 of 14 coebus monkeys. Before the development of serologic tests for HAV, it had been determined that only marmosets and chimpanzees were good models of acute infection with HAV (3).

The finding of antibody to HAV in other primate species suggests that perhaps these species also are susceptible to infection.

METHODS : Serum specimens were obtained from 6 gibbons, 10 cynomologous monkeys, and 92 rhesus monkeys caged at the AFRIMS Veterinary Medicine facility. The history of each primate was reviewed to determine if the animal was : (1) colony born or wild captured, (2) individually caged or gang caged. Specimens were tested for anti-HAV by the HAVAB (R) solid phase competition radioimmunoassay. The sera of two rhesus monkeys was precipitated by addition of ammonium sulfate to 33% saturation, the precipitate resuspended in PBS and dialyzed against PBS.

RESULTS : Results of anti-HAV screening of AFRIMS primate sera are presented in Table 1. Overall 2/6 (33%) of gibbons, 6/10 (60%) of cynomologous monkeys and 13/92 (14%) of rhesus monkeys had detectable anti-HAV activity in their sera. Mean % blocking for positive specimens for each species were 76%, 95%, and 87% respectively, well above the cut-off value of the test of 50%.

Ammonium sulfate precipitation of two rhesus sera showed that blocking activity was associated with the protein globulin fraction in both.

Historical data of individual antibody positive and antibody negative primates suggests (1) that gibbons and perhaps rhesus monkeys can contract HAV in the wild, and (2) that HAV infection may have spread through the colony of gang caged cynomologous monkeys.

Currently, challenge studies are underway in which animals of each species have been inoculated with known HAV infectious stool filtrates. These animals are being followed for the appearance of liver function test abnormalities, antigen shedding in the stool, and anti-HAV antibody response.

REFERENCES :

1. Miller, W.J., Provost, P.J., McAleer, W.J., Ittensohn, O.L., Villarejos, V.M., Hilleman, M.R.: Specific Immune Adherence Assay for Human Hepatitis A Antibody. Application to Diagnostic and Epidemiologic Investigations. Proc. Soc. Exp. Biol. Med. 149: 254-61, 1975.

2. Purcell, R.H., Dienstag, J.L., Feinstone, S.M., Kapikian, A.Z.: Relationship of Hepatitis A Antigen to Viral Hepatitis. Amer. J. Med. Sci. 270:61-71, 1975.

3. Hilleman, M.R., Provost, P.S., Villarejos, V.M., Buynak, E.B., Miller, W.J., Ittensohn, O.L., Wolanski, B.S., McAleer, W.J.: Infectious Hepatitis (Hepatitis A) Research in Non-Human Primates, PAHO, Bulletin, 11:140-52, 1977.

Table 1. Anti-HAV in AFRIMS Primates - 1979

Species	Rearing History		Caging History		Total
	Colony born	Captured	Individual	Gang	
Gibbon	0/4	2/2	2/6	0/0	2/6(33%)
Cynomologous	5/5	1/5	0/0	6/10	6/10(60%)
Rhesus	0/0	13/92	13/92	0/0	13/92(14%)