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Serologic Response of Primates to Influenza Viruses (40360)

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The appearance of a new strain of influenza A at Fort Dix, NJ, in February of 1976, was of interest, principally because of its antigenic relatedness to the virus presumed to be etiologically responsible for the 1918 pandemic, a varient of swine influenza. Very little is known regarding the interrelationships between human and animal influenza, although it has been clearly demonstrated that this virus does exist in a wide variety of animal and avian species. Only limited information, however, is available on influenza in primates other than man, and these data have generally resulted from experimental rather than natural infections (1–7), although an epidemic of influenza with high mortality was reported in baboons during the 1918–19 pandemic (WHO Ref. Z2/180/11, 16 July 1971). Other investigators (8, 9) have also reported influenza in simians, with death and clinical disease noted. Easterday (WHO Ref. Z2/180/11 and Z2/87/5, 10 January 1973) reported antibody in primates to A/FMI at the San Diego Zoological Gardens.

Serological surveys have indicated that antibody to influenza A (PR8, FM1, Hong Kong) and influenza B (Lee) exists to varying extents in "normal" colonies of gorillas, chimpanzees, orangutans, gibbons, baboons in Africa, captive baboons, Japanese macaques, African green monkeys, marmosets, squirrel monkeys, and capuchin monkeys. Owl, howler, and spider monkeys were generally serologically negative, although the number of animals examined was very small (7).

In 1974, an outbreak of respiratory disease occurred in a group of newly imported baboons (*Papio cynocephalus*). An isolate was obtained from seven of 20 animals, which appeared to be identical to A/Mayo Clinic/4/75 (H3N2). (Dr. F. Lief, personal communication). The seven animals from which virus isolations were made had high antibody titers; of the remaining 13 animals, six had antibody titers to the virus and seven had no antibody to the isolate but developed titers later. The serologic data suggested that infection had occurred just prior to shipment from Kenya in the late spring of 1974.

Since the data indicated the susceptibility of nonhuman primates to influenza virus following contact with infected humans, occurrence of a new strain of influenza virus offered the opportunity to examine representative simian sera in order to ascertain the possible role nonhuman primates may play in this virus infection. Reported herein are results obtained by examining human, captive-chimpanzee, and baboon sera collected each month for the year immediately following the outbreak of the A/New Jersey/76 (Hsw_1N_1) virus.

Materials and methods. Sera. Human, chimpanzee (*Pan troglodytes*), and baboon (*P. cynocephalus*) sera were obtained from randomly selected populations each month in the usual manner. Sera were so selected in order to avoid the following of animals with high titers and the possibility of not detecting seroconversions. Human donors were questioned regarding influenza vaccinations in order to distinguish vaccinees from cases (Table I). Most of the human volunteers were animal personnel or laboratory staff engaged in either the daily handling of the animals or in collecting specimens from these animals. Since the number of staff and chimpanzees is limited, over the 10-month study period of number of these were sampled on more than one occasion.

Antigens. Two influenza antigens supplied by CDC, Atlanta, Georgia, were used throughout the study. These consisted of chicken egg preparations of allantoic fluid and included strains A/Victoria A/3/75 (H3N2) and A/New Jersey/8/76 (Hsw_1N_1). Control chicken antisera to each virus, also provided by CDC, were routinely and simultaneously tested each month.

Antibody determination. A micro-HI test using 0.025 ml volumes and 4 HA units of antigen with 0.8% chicken erythrocytes was

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TABLE I. HEMAGGLUTINATION INHIBITION (HI) RESULTS ON PRIMATE SERA TESTED AGAINST INFLUENZA ANTIGENS.

			Number of sera with HI titer (Cumulative numbers)							
Date	Antigen	Primate Sera	<10	≥10	≥20	≥40	≥80	≥160	≥320	>320
Sept. '76	Victoria	Human	0	16	14	9	3			
		Chimpanzee				NOT	DONE			
		Baboon	0	10	8	5	3	1		
	New Jersey	Human	3	12	7	3				
		Chimpanzee				NOT	DONE			
		Baboon	7	3						
Oct. '76	Victoria	Human	1	9	7	4	1	1		
		Chimpanzee	7	10	1					
		Baboon	5	38	26	10	3			
	New Jersey	Human	5	5	3	3	1			
		Chimpanzee	17							
		Baboon	42							
Nov. '76	Victoria	Human	2	11	6	2				
		Chimpanzee	4	9	7	2				
		Baboon	10	18	7	2				
	New Jersey	Human	4	9	9	7	6(2)[a]	2	2	2(1)
		Chimpanzee	8	3						
		Baboon	28							
Dec. '76	Victoria	Human	2	9	8	6	3	3	1	1
		Chimpanzee	11	6	2	1				
		Baboon	1	21	16	9	7	6		
	New Jersey	Human	1	10(1)	6(1)	4	2	2(2)		
		Chimpanzee	17							
		Baboon	22							
Jan. '77	Victoria	Human	1	9	3					
		Chimpanzee	9	8	2					
		Baboon	8	15	5	5	5	4	3	
	New Jersey	Human	6	2(1)	1(1)					
		Chimpanzee	17							
		Baboon	22	1						
Feb. '77	Victoria	Human	2	13	13	8	1			
		Chimpanzee	13	4	1					
		Baboon	13	29	26	21	12	5	1	
	New Jersey	Human	7	8	7	6	6	4(2)	2(2)	
		Chimpanzee	16	1						
		Baboon	42	1						
March '77	Victoria	Human	0	17(3)	8(1)	5	5(2)	2	2	2(1)
		Chimpanzee	10	7	2					
		Baboon	8	29	21	10	4	1		
	New Jersey	Human	8	9	6(2)	4(1)	3(1)	2	2	2(2)
		Chimpanzee	17							
		Baboon	37							
April '77	Victoria	Human	0	12	12	12	12	9	9	9(2)
		Chimpanzee	1	16	16	12	12	11	7	
		Baboon	0	25	25	23	21	21	20	20

TABLE I.—*Continued.*

Date	Antigen	Primate Sera	Number of sera with HI titer (Cumulative numbers)							
			<10	≥10	≥20	≥40	≥80	≥160	≥320	>320
	New Jersey	Human	9	3	3	3	3(1)	2	3	2(1)
		Chimpanzee	17							
		Baboon	25							
May '77	Victoria	Human	1	50	45	37(7)	25(4)	12(1)	12	2(1)
		Chimpanzee				NOT	DONE			
		Baboon	0	61	61	61	61	59	59	59
	New Jersey	Human	34(1)	17(3)	4(1)	9(3)	5	5(2)	3	3(3)
		Chimpanzee				NOT	DONE			
		Baboon	58	1						
June '77	Victoria	Human	0	2	2	1(1)				
		Chimpanzee	0	16	11	8	6	4	1	1
		Baboon	0	22	20	17	14	10	5	5
	New Jersey	Human	0	1	1	1	1	1	1	1(1)
		Chimpanzee	16							
		Baboon	21	1						

[a] Number of individuals at indicated titer receiving vaccine.

employed throughout the study. Sera were pretreated with heat (56°, 30 min), trypsin, and periodate, according to procedures previously described (10). Appropriate controls and antigen "back-titrations" were included with each test.

Results. The survey was conducted over a 10-month period starting in September 1976, and ending in June 1977. Each month, 10–50 randomly collected serum samples were simultaneously tested, with the results given in Table I. The results indicate that influenza infection (principally by a strain related to A/Victoria) occurred in this area. All three primate species evidenced some level of antibody to the Victoria A antigen. Late winter testing suggested a possible localized outbreak evidenced by high titers to this antigen in all three species. Clinical evidence and virus isolation studies in the community confirmed these serologic findings. Similarly, lack of antibody (generally) to the newly isolated New Jersey strain, except in vaccinated individuals, as well as lack of isolation of virus from the community, indicated that this strain did not occur in the San Antonio area. No attempt was made to ascertain the reason for the few seropositives to the New Jersey strain that were recorded.

Discussion. Influenza, experimental and natural, has been reported (11) in various species of nonhuman primates. Very little is known about influenza in simians under natural conditions, but this is also true for other viruses (11). The data reported herein suggest that nonhuman primates, as reflected by chimpanzees and baboons, follow the serologic pattern to influenza virus developed in humans. A/Victoria virus was in the community, and the primate population reflected this. Similarly, there was no evidence for human infection with the A/New Jersey strain, and this, too, was supported by the serologic data. No attempt was made to determine any epidemiologic factors associated with the results, but two observations may have some relevance: (1) The animals are housed in "open" cages, permitting access to small wildlife and birds, and (b) exposure to staff, while minimized, does occur.

Periodically, we isolate influenza viruses from the colony of baboons (12). The source of these infections is unknown, but it has generally involved newly imported animals under surveillance in quarantine. The pattern of seroconversion noted at times suggests horizontal transmission from animal to animal. Horizontal transmission in baboons following experimental infection has been reported previously (6, 13). It has also been observed that the duration of virus excretion (approximately 20 days post inoculation) is somewhat longer than that generally observed in humans (13). These data do not suggest a poten-

tial reservoir but, more probably, a host reaction closely akin to that occurring in humans.

Summary. Nonhuman primate (chimpanzees and baboons) sera were compared with human sera for serological activity to influenza viruses A/Victoria A/3/75 (H3N2) and A/New Jersey 8/76 (Hsw_1N_1). The results obtained indicate that all three primates reacted similarly to the influenza virus that was present in this area (A/Victoria). The data suggested that the nonhuman primates are not a potential reservoir but react to infection as do humans.

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