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Transmission of Creutzfeldt-Jakob Disease to the Stumptail Macaque (*Macaca arctoides*) (38886)

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(Introduced by R. M. Chanock)

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A previous report reviewed the susceptible host range of Creutzfeldt-Jakob (C-J) disease in primates and other laboratory animals (1). A long incubation period was followed by a period in which clinical signs were observed for various periods of from 15 days to 12 mo in different species. In this report we describe the clinical disease and immunological and muscle enzyme studies performed in two stumptail macaques (*Macaca arctoides-speciosa*) which were inoculated, respectively, with a 10% suspension of brain from a human patient and from a chimpanzee with experimentally induced disease.

Experimental Methods. The stumptail macaques used in this investigation were born and raised at the California Primate Research Center and were 18 mo old at the time of inoculation. The inoculum consisted of 0.2 ml of a 10% suspension of brain in phosphate-buffered physiological saline, pH 7.4, which had been clarified by centrifugation at 1800 rpm for 20 min. The brain suspension inoculated into MSP 153 was obtained from C-J-infected chimpanzee (A54) brain in first chimpanzee passage (2), while inoculum from MSP 160 was from a C-J disease patient (A.T.), whose case history has been reported elsewhere (3). The chimpanzee brain inoculum has caused spongiform encephalopathy in chimpanzees and six other species of monkeys (squirrel, African green, cynomolgus, sooty mangabey, pigtail, and rhesus). The inoculum was injected into the left cerebral hemispheres of both monkeys on July 17, 1968.

Results and Discussion. Clinical disease in the form of occasional tremors and slight incoordination was first noted in both animals 60 mo after inoculation. The signs were more pronounced on the right side in MSP 160. Neurological signs were prominent for 2 wk and then slowly remitted and were no longer noted for 4 mo. In January 1974, both animals again demonstrated tremors and depression. In MSP 153, the incoordination and ataxia progressed rapidly over a 3-wk period to an advanced state in which the animal was prostrate and unable to feed itself. It was then killed. The clinical disease observed in MSP 160 progressed more slowly than in MSP 153 and after 5 mo there was pronounced ataxia, tremors in all limbs, spontaneous myoclonus, and excessive salivation. The animal maintained its strength and ability to eat. However, it was cautious, and tended to grasp the cage in order to stop the tremors. On July 18, 1974, 1 yr after the first onset of symptoms and in the sixth month of exacerbation, the animal was tranquilized for bleeding with chlorpromazine from which he was slow to recover. On the next day he was lethargic and eventually became prostrate. The animal was sacrified July 22, 1974, 72 mo after inoculation.

Microscopic examination of the nervous system of each animal revealed lesions of status spongiosus and astrogliosis of the cerebral cortical gray matter consistent with a diagnosis of experimental C-J disease. There was a loss of small and medium-sized neurons in the cortical gray matter. Many neurons had clear vacuolated cytoplasm which on occasion resulted in nuclear margination. Similar lesions were in the gray matter of the spinal cord. Promi-

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TABLE I. LYMPHOCYTE STIMULATION VALUES ON *Macaca arctoides* (NORMAL AND INOCULATED WITH CREUTZFELDT-JAKOB-INFECTED HUMAN BRAIN).

	Untreated		Phytohemagglutinin M		Concanavalin A		Mixed lymphocyte cultures	
Days	Normal	Infected	Normal	Infected	Normal	Infected	Normal	Infected
3	2,091[a]	2,452	75,394	27,792	11,317		Normal × infected = 72,862	
5	561	7,571	14,849	32,795	5,359	149,200	Normal[b] × infected = 61,637	
10		2,452		10,444			Normal × infected[b] = 29,173	

[a] Recorded as counts per million cells.
[b] Cells irradiated with 3000 rad.

nent vacuoles were present in the large motor neurons.

Lymphocytes obtained from the peripheral blood of MSP 160 by the Ficoll–Hypaque technique (4) were compared in cultures with lymphocytes similarly obtained from a control stumptail macaque (MSP 286). The cells were cultured for 3, 5, and 10 days and the uptake of ^{3}H-thymidine compared between the untreated cell cultures (5×10^6 cells/vial) and those treated with 2 mg PHA-M/vial or 50 μg Concanavalin A/vial. In addition, mixed lymphocyte cultures (5) were irradiated with 3000 rad to inactivate cells. The most apparent alteration was the unusually high counts observed on the fifth day in the untreated cultures (Table I). The high counts represent an average of four different samplings over a 2-mo period indicating an increased uptake of thymidine. This activity was not reflected in the phytomitogen cultures. The results of the mixed lymphocyte cultures indicate that the cells of the animal with C-J disease had a greater ability to respond than those obtained from the control animal.

Muscle biopsies were performed on the biceps brachii and quadriceps femoris shortly before the animal was killed. The muscles were evaluated on the basis of trichrome stains, DPNH, ATPase, and esterase and PAS-H activity. Trichrome stains revealed the presence of small numbers of angular fibers, many with randomly placed nuclei and questionable rods in four myofibrils. Type II myofibers comprised 90% of the biceps brachii and 60–70% of the quadriceps femoris. The changes were consistent with a mild neuropathy.

Summary. The successful transmission of Creutzfeldt-Jakob disease from both affected human and chimpanzee brain to stumptail macaques has been accomplished. The incubation period of 5 yr was the same for both animals; however, the course of the disease was longer in the animal receiving the human brain. In both cases, initial mild symptoms slowly remitted only to reappear some 4 mo later. Muscle biopsies revealed changes suggestive of a mild neuropathy. In addition, there appeared to be an increased ability to incorporate ^{3}H-thymidine in untreated cultures of lymphocytes from peripheral blood.

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