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Absence of Vertical Transmission of Subacute Spongiform Viral Encephalopathies in Experimental Primates (41092)

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Abstract. Vertical transmission of kuru, Creutzfeldt–Jakob disease, and scrapie has not been observed in 10 progeny of chimpanzees and monkeys born to parents which were either incubating or clinically ill with one of the diseases. Moreover, these 10 progeny have remained free of spongiform encephalopathy in spite of intensive postnatal contact with their affected parent(s). These data leave unanswered the mechanisms of viral transmission in the familial forms of Creutzfeldt–Jakob disease.

Extensive studies of the epidemiology of kuru have yielded no evidence for vertical transmission of the naturally occurring disease (1). With cessation of cannibalism in the kuru-affected villages of New Guinea, no one born in a given village, since the body of the last kuru victim was so disposed of, has developed kuru. Offspring of kuru-affected mothers, either those born before or those born while the mother was ill with kuru but after the cessation of cannibalism, have not developed kuru (1). However, patients with Creutzfeldt–Jakob disease appear in families with two or more such patients in 14% of the cases, and in such families it presents a pattern resembling autosomal dominance (2, 3). There are several studies showing at least indirect evidence of maternal transmission of scrapie (4). The importance of the sire in determining the eventual outcome of disease in the offspring has also been documented for scrapie (4, 5). These findings have led to speculations about vertical transmission of some of the subacute spongiform virus encephalopathies. However, genetic control of susceptilbility to scrapie has been well established (6). Although similar genetic mechanisms may be operative in Creutzfeldt-Jackob disease, the means of transmission of this rare virus to many members of one family remains to be explained.

Methods. During the course of 15 years of observations of monkeys and chimpanzees inoculated with the viruses of kuru, Creutzfeldt–Jakob disease, and scrapie, 10 infants have been born to parents which were either incubating or clinically ill with one of these diseases. None of these infants, summarized in the accompanying table, has gone on to develop a spongiform encephalopathy. All unaffected parents (not summarized in Table I) were long-term residents of our colony of experimentally inoculated primates and they had received inocula of CNS tissue from other as yet untransmitted diseases such as multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), and parkinsonism dementia (PD). They remain well to date. In cases 1, 3, and 10 (Table I) where the father was clinically affected, the mother had received inocula of brain tissue from human parkinsonism dementia (cases 1 and 3) and scrapie (case 10). Newborn chimpanzees and monkeys remained with their mothers for nursing for 2 years and 1 year, respectively. The still-healthy progeny of affected parents have had continuing close contact with their parents after their birth.

Results and Discussion. Histories of the 10 offspring are summarized in Table I, which illustrates the relationships between the time and type of inoculation to each parent and conception and birth of the various progeny. Conception data were calculated using the following gestational periods: 225 days for chimpanzees, 180 days for capuchins, 164 days for rhesus, 167 days for cynomolgus monkeys, and 175 days for squirrel monkeys. The species of primates

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TABLE I. ABSENCE OF EVIDENCE FOR VERTICAL TRANSMISSION OF KURU AND CREUTZFELDT–JAKOB DISEASE IN NONHUMAN PRIMATES BORN TO EXPERIMENTALLY INOCULATED PARENTS

Baby's ID	Species	Affected parent(s)	Inoculum of parent(s)	Time between parent's inoculation and conception	Time between parent's inoculation and birth	Time from conception to onset of clinical disease in parent	Time from birth to onset of clinical disease in parent	Present status of baby	Comments
1	Chimpanzee (male)	Father	Kuru	64 months	71½ months	18 months	10½ months	Alive and well 7 years 4 months after birth	
2	Chimpanzee (female)	Mother	Kuru	Inoculated 5½ months after baby was conceived	1 month	21 months	14½ months	Alive and well 4 years 4 months after birth	Inoculated with Alzheimer's disease 22 August 1978
3	Chimpanzee (female)	Father	CJD	8 months	Born ½ month after father died of kuru	6 months	Born 1½ months after onset of disease of father	Alive and well 9 years 9 months after birth	
4	Squirrel (female)	Mother	CJD	15½ months	21 months	12½ months	7 months	Alive and well 3 years 1 month after birth	Inoculated with schizophrenia 22 August 1978
5	Squirrel (female)	Mother	CJD	12 months	17½ months	6½ months	1 month	Alive and well 2 years 11 months after birth	Inoculated with Huntington's disease 22 August 1978
6	Capuchin (male)	Father Mother	Scrapie Scrapie	24 months 24 months	30 months 30 months	8 months 11½ months	2 months 5½ months	Alive and well 5 years 8 months after birth	
7	Rhesus (male)	Mother	Kuru	63½ months	69 months	38½ months	33 months	Died 1 year 9 months after birth Negative pathology	
8	Rhesus (male)	Mother	Kuru	48½ months	54 months	53½ months	48 months	Alive and well 11 years 11 months after birth	Inoculated with PML 17 December 1969
9	Rhesus (male)	Father Mother	CJD CJD	20 months 20 months	25½ months 25½ months	46 months 47 months	40½ months 41½ months	Alive and well 9 years 10 months after birth	Inoculated with MS 12 May 1971
10	Cynomolgus (female)	Father	Scrapie	51 months	56½ months	21 months	15½ months	Alive and well 7 years and 3 months old	

in the table are all susceptible to the subacute spongiform virus encephalopathies: chimpanzees and squirrel monkeys are highly sensitive (7).

Only one animal, a chimpanzee (No. 2), was actually *in utero* (5-½ months) before the mother was inoculated with kuru, and was delivered one month after the inoculation. Three progeny with an infected father, five with an infected mother, and two with both father and mother infected are represented. Five of the progeny in the table have never been used in later experiments; five others were later inoculated with nontransmissible neurologic diseases.

Although the type and time of exposure to infection varied somewhat, six of the progeny were exposed to maternal infection throughout the entire gestational period. In only one, the parent was suffering from clinical disease at the time of the birth of the offspring: the father of a chimpanzee (No. 3) developed clinical kuru 1-½ months before the baby's birth and died of kuru ½ month after her birth. Also, a capuchin (No. 6) nursed on his mother while she was clinically affected with scrapie. One offspring, a rhesus monkey (No. 7), died of other causes 1 year and 9 months after birth. Histopathology of its brain was negative for changes attributable to the subacute spongiform viral encephalopathies.

None of the progeny of infected parents has developed clinical disease characteristic of the subacute spongiform virus encephalopathies after periods ranging from 1 year 9 months to 11 years 10 months following birth in spite of continuing opportunity for horizontal infection from affected parents after that for vertical infection before birth. In our experimental colonies horizontal transmission of these diseases has not occurred in experimental primates even under the conditions of high exposure. These data are similar to the negative findings of Manuelidis using the experimental guinea pig as the host system (8), and leave unanswered the means of viral transmission in familial CJD (3).

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