for controls after 3 hours of avoidance stress. Significantly lowered values were observed for control monkeys on the 4th and 5th days after inoculation. Presumably these values reflect a response to the developing stress of infection which occurred earlier in controls.

These results contrast sharply with previous findings on reduced resistance to virus infection in mice subjected to shuttle box stress (*1, 2*). They also contrast with observations of increased susceptibility to poliovirus in hamsters and mice treated with cortisone before inoculation (*8, 9*). One factor which may be important in accounting for the directional difference in susceptibility is the schedule of exposure to stress. In experiments with mice an intermittent "chronic" stress schedule was used in which the animal was exposed for 6 hours daily with 18 hours of rest between exposures for a period of weeks, whereas, in the monkey, exposure was to a single "acute" 24-hour period of avoidance stress. A period of at least 14 days of intermittent exposure to stress was the minimum for producing decreased resistance to virus infection in the mouse in contrast to the 24-hour period which proved effective for increasing resistance in the monkey. In earlier work on the mouse (*10*) it was demonstrated that physiological changes, presumably related to pituitary adrenal function, occurred very early in exposure to intermittent stress, as did increased resistance to anaphylactic shock. Resistance decreased along with thymus and spleen involution only after 14 or more days of exposure to stress.

Seven of the 12 control monkeys received the original avoidance training because of the possibility that it and the stress associated with it might influence subsequent response to stress during the experiment. This did not prove to be true as all of the trained controls succumbed to polio while 7 of the 11 trained stressed animals did not. Similarly, the duration of the rest period (ranging from 9 to 480 days) between original training and the experiment did not affect results.

The effects of shock per se on resistance might be questioned since controls received no shocks. If shock was a crucial factor, some correlation between the number sustained by stressed animals and resistance to poliovirus might be expected. The total number of shocks sustained in the 24-hour period ranged from a minimum of 155 to 6042 in one animal. (The latter resulted from apparatus failure.) The four that died ranked fourth, sixth, eighth, and tenth among the 11 stressed monkeys in terms of the number of shocks. The number clustered about the mean for the group. Similarly there was no correlation between the number of shocks and the length of incubation period (see *11*).

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11. Supported in part by grant 2M-6415 from U.S. Public Health Service and research grant FD-GR-60-2 from the Army Chemical Corps. One of us (S.S.C.) had a grant from the International Cooperation Administration under the Visiting Research Scientists Program administered by the National Academy of Sciences.

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Tumors Induced in Primates by Chicken Sarcoma Virus

Abstract. *A suspension of a variant of Rous sarcoma was injected into four adult and eight newborn rhesus monkeys. Seven newborns developed tumors, three of which were diagnosed as fibrosarcomas, in 2 to 6 weeks; none of the adults have tumors after 11 weeks. Virus was demonstrated in two of the tumors by injecting a tumor-suspension preparation into the chick wing-web where tumors subsequently appeared. To the best of our knowledge this is the first time that sarcomas have developed in primates after a virus has been injected.*

A variant of Rous chicken sarcoma was injected into small laboratory animals. Newborn rats developed angiomas and conditioned rats developed fibrosarcomas (*1*), newborn and adolescent hamsters developed pleomorphic giant cell sarcomas, newborn guinea pigs developed fibromas, and adolescent mice developed fibrosarcomas (*2*). The strain of chicken sarcoma was obtained from L. A. Zilber of the Gamaleya Institute in Moscow (*3*). Another strain has been used successfully to induce tumors in hamsters, guinea pigs, and mice (see *4*).

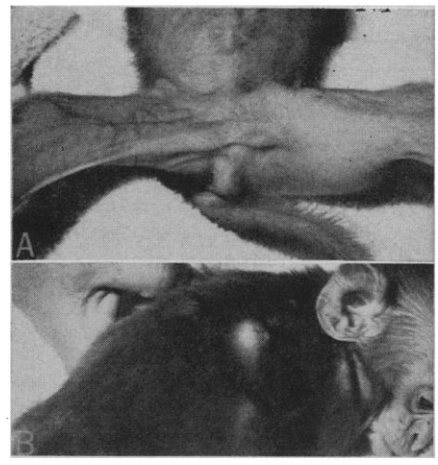

Fig. 1. Tumor in left thigh of monkey No. 403 (top) extending from pelvis to knee and causing a threefold increase in circumference as compared with right thigh. Recurring subcutaneous tumor in the back near the inferior angle of the scapula in monkey No. 397 (bottom). The scar over the lesion resulted from excision of a tumor of similar size at this site 3 weeks previously.

Fourteen monkeys (*Macaca mulatta*) were used in our study. Tissues of two newborn monkeys involved in fatal neonatal accidents were used as noninjected controls. The remaining 12 monkeys were injected with suspensions of chicken sarcoma. Four of these were 5- to 7-year-old adult monkeys; eight were newborn monkeys (*5*).

One of the newborn monkeys, No. 406, a premature, on the 6th day after injection died from what seemed to be a systemic illness with weakness, anorexia, weight loss, leukocytosis, and low-grade fever—all of which began on the day after virus injection. This generalized illness was also noted in most of the virus-injected monkeys, including the adults, within the first 10 days. Virus was demonstrated in the liver and at the site of injection (thigh) of monkey No. 406 by the chick wing-web technique (injection of a suspension of organs or tumor material into the wing web of chickens, 3 to 5 days old, which results in tumors).

All of the other newborn monkeys

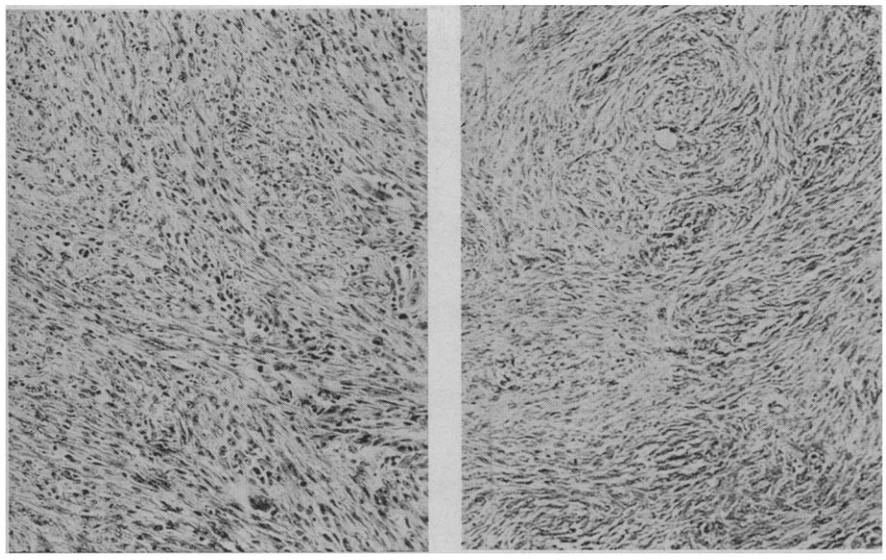

Fig. 2. Histological appearance of fibrosarcomas (left) from the thigh of monkey No. 407, and (right) the back of monkey No. 397. They consist of spindle-shaped cells in band and whorl formation.

developed subcutaneous tumors in 2 to 6 weeks after inoculation, and these tumors are continuing to grow (Fig. 1). No adults have developed tumors after 11 weeks of observation.

One tumor was excised from monkey No. 397 for histological diagnosis (fibrosarcoma, Fig. 2, bottom), and to try to recover virus (current).

Two monkeys, Nos. 404 and 407, developed generalized weakness, leukocytosis, and anorexia about 1 week after fast-developing tumors had appeared. They were killed on the 28th and 29th day after injection, lest they die. Tumors weighing 16 and 19.5 g respectively, were removed from the thighs; these, too, were fibrosarcomas (Fig. 2, top). The tumors and major organs of these two animals were used for electron-microscopical search for evidence of the sarcoma virus, and for chromosome counts (current). Virus was demonstrated in the tumors by the chick wing-web technique; and chromosome studies of these wing tumors show that the tumor consists of cells of the host.

Five newborn monkeys with progressively growing tumors are currently under observation (Table 1).

The occurrence of tumors in all seven of the newborn rhesus monkeys that were injected with chicken sarcoma and that lived more than a week is unique in our experience. The overall incidence of tumors out of injected newborn rats was 73 out of 162, newborn hamsters 57 out of 162, and newborn guinea pigs 7 out of 12; what is more, of 28 rat litters and 27 hamster litters there was no instance of a 100-percent take among the members of any litter of either species injected with the chicken sarcoma.

This study in newborn monkeys renews interest in ability of viruses generally, and oncogenic viruses in particular, to cross species barriers up or down the phylogenetic tree. In addition, its significance transcends the field of cancer and has implications in all areas of biology and medicine in which immunity problems are matters of concern.

To the best of our knowledge this is the first time that sarcomas have been reported to develop in primates after the injection of a virus.

Considering the fact that Peyton Rous initially found difficulty in passing the Rous sarcoma virus into noninbred strains of chickens (*6*), it is surprising that 50 years later a strain of chicken sarcoma virus should be shown to be so readily infective to primates.

Table 1. Chicken sarcoma in newborn monkeys. Inoculation into the thighs was intramuscular, in the back subcutaneous. No signs of tumor appeared in four adult monkeys, one 6 to 7 years old inoculated intramuscularly in the back and subcutaneously in the right thigh, and three 5 to 6 years old inoculated intramuscularly in the right thigh.

Animal number	Inoculation		Tumor				Histological diagnosis
	Age (days)	Site	Onset (days)	Site	Excision (days)	Presence of virus	
397	7	Back, Right thigh	50	Back	56*	Current	Fibrosarcoma
402	6	Left thigh	31	Left thigh	None		Not done
403	3	Left thigh	23	Left thigh	None		Not done
404	3	Left thigh	22	Left thigh	32 (killed)	+ (chick)	Fibrosarcoma
406	2	Left thigh	None		Died 8 days	+ thigh and liver	No tumor
407	2	Left thigh	19	Left thigh	29 (killed)	+ (chick)	Fibrosarcoma
414	1	Back	17	Back		Not done	Not done
415	1	Back	14	Back		Not done	Not done

* Tumor recurred in 14 days.

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5. The adult animals were studied at the Sloan Kettering Institute for Cancer Research in New York City where they had been maintained for over a year before they were injected; three are still being observed. The newborn monkeys were studied at the Laboratory of Perinatal Physiology, National Institute of Neurological Diseases and Blindness, National Institutes of Health in San Juan, Puerto Rico. We acknowledge cooperation of Dr. M. Diaz de Faro and Dr. R. Fleischman, assistance from the technical staff of the Laboratory of Perinatal Physiology and from D. Natham of the Sloan Kettering Institute for Cancer Research. We thank Dr. F. Shipkey for the electron microscopy, Dr. F. Stuart for advice in the histological diagnosis, and Dr. C. P. Miles for help in the chromosome studies. Supported by the grants from the New York City Health Research Council (U-1096 II C_3), and the National Cancer Institute, U.S. Public Health Service.
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