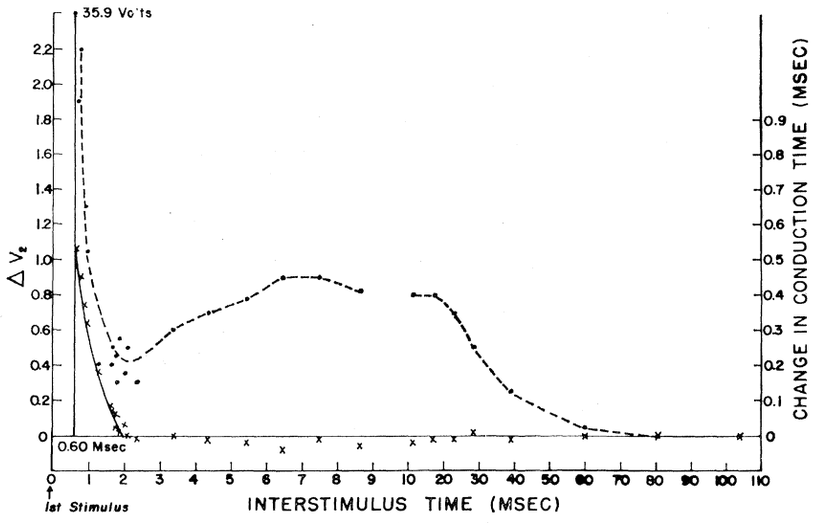

Fig. 3. Voltage threshold alterations for second stimulus after conditioning stimulus (•); change in conduction time of second evoked response (×).

dual electrical stimulation. In contrast to the latter, latency changes occurred beyond the relative refractory period, reflecting an increase in transduction time due to an elevated nerve fiber threshold close to the site of action potential initiation. A comparison of electrical and mechanical latencies showed a maximum mechanical transduction time of 1.3 msec and a minimum of 0.4 msec.

It appears that natural stimulation is capable of evoking firing frequencies that saturate the carrying capacity of the nerve fiber. The initial frequencies produced by sustained suprathreshold displacements (Fig. 2, middle) approach the maximum possible as determined by the absolute refractory period of the nerve and the recording site; the several spikes after the first are reduced in amplitude, indicative of the relative refractory period. Such high-frequency firing has also been observed from rapidly adapting hair receptors but stands in marked contrast to the lower frequencies naturally evoked by muscle receptors, the afferent fibers of which have equivalent or greater capacities (*5*).

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4. Typical threshold stimulation parameters: 0.8 volt (+); 0.3 ma; duration, 0.1 msec; skin contact area, approximately 3×10^{-2} cm².
5. Supported in part by the Defense Atomic Support Agency, contract No. DA-49-146-XZ-058.

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Sarcomas in Cotton Rats Inoculated with Rous Virus

Abstract. *When newborn cotton rats were inoculated with Carr's strain of the Rous sarcoma virus, 50 percent of the rats developed sarcomas. The significance of this finding is discussed in relation to the pathogenicity of various strains of this virus in other mammals.*

A peculiar cystic hemorrhagic disease has been described simultaneously and independently in this laboratory (*1*) and elsewhere (*2*). The disease was induced in albino rats by inoculating the Rous sarcoma virus during the embryonic or neonatal period. It was also shown that some rats developed sarcomas long after this virus was injected (*3*). These experiments were later confirmed and extended (*4–7*). We suggest that further studies of chronic infections of albino rats with Rous virus, in which there are relapses and remissions, and which develop first as a cystic hemorrhagic disease and then as a sarcoma, might contribute to our knowledge of the general mechanisms of the pathogenic action of viruses at the level of the organism.

In this report we describe the data obtained in a preliminary study of the pathogenicity of the Rous virus in cotton rats (*Sigmodon hispidus hispidus*). Carr's strain of Rous virus was used. Newborn cotton rats, within the first 12 hours of life, were inoculated subcutaneously with 0.1 to 0.15 ml of a 30 percent homogenate of chicken Rous sarcoma (4×10^6 chick sarcomagenic units per milliliter) prepared as previously described (*1, 8*). The growth of the inoculated cotton rats was significantly retarded in comparison with that of controls. Tumors developed in 12 out of 23 of the inoculated cotton rats surviving until the age of 2 to 3 months. Histological examinations of the tumors showed them to be sarcomas. Most of the sarcomas were polymorphic with a prevalence of spindle-shaped and round cells and a significant amount of mucoid substance. In general, the histologic pattern of these tumors was similar to that of the original chicken Rous sarcoma. Fluid exuded from them on cutting, and they showed a tendency to hemorrhage, and they became rapidly necrotic in the central parts. Some of the tumors, however, were more solid and monomorphic with spindle-shaped cells. The sarcomas in cotton rats usually attained diameters of approximately 4 to 6 cm. One of these sarcomas was successfully transplanted to normal adult cotton rats.

Antigens of the chicken Rous sarcoma were not detected in extracts of the sarcomas from cotton rats when they were tested against highly active rabbit antiserum in the ring precipitation test.

These data show that cotton rats, as well as albino rats (*1–8*), and rabbits (*9*), are susceptible to the Carr's strain of Rous virus, although the question still remains as to whether the sarcomas are caused directly by conversion of cotton rat cells to a malignant neoplastic state by the Rous virus. Although, in albino rats, the Rous virus was isolated from sarcomas induced by this virus (*5, 8*), it is quite possible that only some of the sarcomas (especially those which were polymorphic and contained a large amount of mucoid substance) were caused directly by the Rous virus, whereas others might have developed as a result of secondary effects of the virus-induced condition (cystic hemorrhagic disease). Since the walls of the cysts consist of parallel rows of fibroblasts distended by liquid, the conditions here may be similar to those involved in the induction

of sarcomas by the implantation of plastic plates (*10, 11*).

Inoculation of newborn cotton rats with Rous virus resulted in the appearance of sarcomas not preceded by visible cystic hemorrhagic disease. This difference is probably due to the higher rate of development of cotton rats compared with that of albino rats. It might be possible to induce some equivalent of the cystic hemorrhagic disease in cotton rats by inoculation of the embryos.

The induction of tumors by the Rous virus in mice and hamsters, as described by Kryukova and Morgunova (*12*), was unsuccessful in this laboratory, as were attempts to inoculate guinea pigs with the virus (*13*). Recently, Ahlström and Johsson (*6*) showed that the Schmidt-Ruppin strain of chicken sarcoma virus is pathogenic in newborn and adult hamsters, albino mice, rats, and adult guinea pigs (*14*). The Mill Hill strain of Rous virus, as well as the Bryan strain, were not pathogenic in mammals (*6, 7*). In mammals, therefore, there are apparent differences in the pathogenicity of various substrains of the Rous virus. It will be necessary to carry out a comparative genetic study of the various substrains and to study the pathogenic effects of avian leukemia viruses in mammals.

There is recent evidence (*15*) that even purified virus of the Rous sarcoma, Bryan strain, consists of two viruses. Hence, it appears very probable that the differences in pathogenicity of different strains of the chick sarcoma virus in mammals depends in some degree on the nature of the various viruses causing avian leukemia.

Important questions regarding the pathogenesis of mammalian diseases induced by Rous virus still remain unsettled. For example, What kinds of cells are affected in the lymphatic nodes of albino rats? What is the nature of the cells which are induced to undergo direct malignant transformation in some mammal species? Might the chronic relapsing course of the process in albino rats, and the comparatively long incubation period for tumor induction in various mammal species, be due to the fact that the Rous virus is adapted to the high temperature of the bird's body while in mammals the temperature is comparatively low?

The extremely wide range of hosts, from birds to mammals, in which the chicken sarcoma virus is pathogenic suggests that it may be possible to isolate from certain human tumors (regional lymph nodes or kidneys) the animal viruses causing them. In this connection the important problem arises, host systems which have accelerated viral tumorigenesis. Although detection of a host susceptible to a particular virus is a matter of chance, the rate of tumorigenesis may, to a certain degree, be dependent on the rate of ontogenesis of the animal species.

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Peromyscus leucopus: An Interesting Subject for Studies of Socially Induced Stress Responses

Abstract. *White-footed mice,* Peromyscus leucopus, *possess several characteristics which make them interesting subjects for the experimental study of social interactions and stress physiology: tolerance of very high cage densities among social congeners; marked behavioral intolerance among social strangers; exceptionally large adrenal glands; and adrenal and eosinophil responses sensitive to social disturbance.*

Experimental studies with rodents on behaviorally and socially induced stress responses have traditionally employed house mice, *Mus musculus* (*1*), Norway rats, *Rattus norvegicus* (*2*), meadow voles, *Microtus* spp. (*3*), or deer mice, *Peromyscus maniculatus* (*4*). The common white-footed mouse, *P. leucopus,* which is abundant in woodlands or brushlands east of the Rockies, has several characteristics not fully shown by those forms which make it an interesting species for further comparative study.

Table 1. Adrenal weights of adult *P. leucopus* in relation to population density and social climate. S.E., standard error.

Males				Females			
	Weights (± S.E.)				Weights (± S.E.)		
No.	Body (g)	Adrenal (mg)	Relative adrenal (mg/100 g)	No.	Body (g)	Adrenal (mg)	Relative adrenal (mg/100 g)
			Isolated controls				
24	18.8 ±0.4	13.1 ±0.7	70.2 ±3.8	24	18.0 ±0.6	10.9 ±0.4	61.6 ±2.9
			Low-density compatible*				
20	21.8 ±1.1	11.7 ±0.7	51.9 ±3.0	21	18.5 ±0.5	10.5 ±0.8	57.6 ±3.0
			High-density† compatible				
36	20.6 ±0.7	12.3 ±0.7	58.2 ±4.5	40	18.8 ±1.0	10.7 ±0.5	60.2 ±3.2
			Low-density incompatible				
			(*Dominant*)				
7	24.4 ±1.2	12.9 ±1.2	53.2 ±5.3	5	22.8 ±0.8	11.6 ±1.4	50.6 ±4.7
			(*Subordinate*)				
22	18.2 ±0.3	16.5 ±1.5	93.5 ±1.7	23	16.7 ±0.4	12.2 ±1.1	73.1 ±5.4

* Two to four adults per cage, 25 by 45 cm. † Ten to 20 adults per cage, 25 by 45 cm.