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.

The most pertinent qualities of *P. leucopus* for studies of this type are as follows. It adapts quickly to captivity and is easily handled in the laboratory. It maintains excellent health and breeds well under standard husbandry procedures. Individuals tolerate very high population densities (up to 16 adults per 0.1 m^2 of cage space) without disruption of their behavior or health if they have been caged together from weaning. Conversely, adults that have been caged separately and are social strangers are highly intolerant of each other; they fight severely and show marked disruption of normal behavior and health.

The adrenal glands of adult *P. leucopus* are exceptionally large, averaging 10.5 to 16.5 mg (50.6 to 93.5 mg/100 g) (Table 1). This is approximately three times as large as the adrenal weights reported for *P. maniculatus* (*4*) and for house mice or meadow voles. Mice and voles previously studied had mean paired adrenal weights in the range of 3 to 5 mg (15.0 to 45.0 mg/100 g) (*1, 3, 4*). Male *P. leucopus* have larger adrenals than females, whereas the reverse is true for all rodent species studied except the nutria (*5*). In rabbits and other lagomorphs the male usually has the larger adrenals (*6*). Further study is needed to evaluate the significance of differences in adrenal size between species and sexes, with qualitative and quantitative comparisons of hormonal outputs.

Adrenal weights of *P. leucopus* varied significantly in this study with social climate, but not with crowding or population density per se (*7*). Paired adrenals of isolated adult *P. leucopus,* 2 to 6 months old, which were born in the laboratory from wild-trapped parents averaged 13.1 mg (70.2 mg/100 g) for males and 10.9 mg (61.6 mg/100 g) for females (Table 1). Males from low-density compatible populations (two to four mice per cage, 25 by 45 cm) revealed significantly smaller relative adrenal weights than isolated males ($P < 0.05$). This suggests that isolation, in contrast to compatible social grouping, may be a stressful situation for male *P. leucopus.*

Increased population density (up to 20 adults per cage) did not produce enlarged adrenals if the populations were socially compatible (Table 1). If the individuals were socially incompatible, however, and fought or interacted agonistically, the adrenals of subordinate males were significantly larger than those of males from compatible populations ($P < 0.01$). There was considerable individual variation in adrenal weights of these subordinate males. Paired adrenal weights ranged from 8.2 mg to 36.4 mg, and the standard error of the mean (1.5) was approximately twice that of the control and compatible groups (Table 1). Welch and Klopfer (*8*) have emphasized the significance of increased endocrine variability in the adrenal stress response of house mice. The data in this report support their concept.

Low-density compatible populations of two or three mice were experimentally changed to incompatible populations by the introduction of one mouse which was a social stranger. Aggressive interactions, initially directed toward the strange mouse, often occurred between the resident individuals which had been completely compatible. Strangers were left in the cage for an experimental period of 1 week, during which there was considerable strife. Of 77 adult males introduced into compatible populations 60 percent were killed by the resident mice, and of 48 females 40 percent were killed. Increasing the amount of space and cover did not reduce this mortality. In colony pens (3.3 m^2) with abundant cover and only two resident mice mortality rates were actually higher than in cages (70 percent for introduced males and 50 percent for introduced females). At the end of 1 week, when surviving mice were autopsied, adrenals of subordinate males showed significant enlargement, but those of females and dominant males did not.

These observations support previous work on house mice which relates adrenal size to social status (*9*), but they are in disagreement with data which demonstrate adrenal enlargement with increased population density per se (*10*). Hence these results emphasize the importance of social climate, apart from crowding or high population density, in eliciting a stress response. Presumably crowding elicits an adrenal enlargement only when accompanied by increased strife. In many rodents high population density per se is not necessarily accompanied by increased social strife. These ideas are not new; several investigators have pointed to social interactions as more relevant variables in adrenal stress responses than to the population density (*9, 11*).

The eosinophil response of *P. leucopus* to behavioral and social disturbance follows the same pattern as in house mice (*12*). Males placed in empty colony pens (3.3 m^2) exhibited a 70 percent eosinophil decline within 4 hours, but by 72 hours counts returned to normal. Males placed in colony pens containing a resident pair exhibited a 92 percent decline, and the eosinophil count remained significantly depressed for 5 days (based on sample sizes of 20 experimental mice and 20 control mice).

This combination of behavioral, anatomical, and physiological traits suggests that *P. leucopus* would be an interesting laboratory rodent for studies of hormonal assay in relation to social interactions.

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