*tions of substances whose two component partial rotations are of opposite sign.*

P. A. LEVENE
ALEXANDRE ROTHEN
G. M. MEYER

THE ROCKEFELLER INSTITUTE
FOR MEDICAL RESEARCH
NEW YORK, N. Y.

## PSEUDORABIES AS A CONTAGIOUS DISEASE IN SWINE

PSEUDORABIES is recognized as an acute, infectious, highly fatal disease of cattle, cats and dogs. The causative virus is readily transmissible by inoculation to rabbits, guinea-pigs, rats and mice as well as to other animals less commonly used for experimental purposes. Pruritus and rapid death after a relatively short incubation period are salient features of the disease. Pseudorabies has not been found to be contagious among any of the common laboratory animals nor among cattle, cats or dogs, and its method of spread under natural conditions is unknown.

The susceptibility of domestic swine to pseudorabies was not extensively investigated by earlier workers; Schmiedhoffer[1] was unable to infect pigs experimentally. On the other hand, von Ratz[2] observed the disease occurring naturally in wild swine. The writer[3,4] has found that the virus administered subcutaneously produced in swine a mild disease in marked contrast to the uniformly fatal form which it produces in other species. The susceptibility of domestic swine to pseudorabies has since been observed by other workers[5,6,7] and the disease has been found to occur naturally in this species in Holland and Hungary as a rather mild ailment. The clinical features of swine pseudorabies induced by subcutaneous inoculation are malaise, decreased appetite and a 4 to 6 day febrile reaction; rarely, indefinite symptoms of central nervous system involvement were observed.

Further work has shown that the virus when administered intranasally produces a similar disease. In one instance intranasal inoculation was followed by a pneumonia. The mild disease described above may follow the repeated feeding of large amounts of virus or the intramuscular injection of small amounts. In the latter case a weakness or paresis of the inoculated leg may be detected. Injected intracerebrally under ether anesthesia into swine the virus produces marked central nervous system symptoms and death in from 36 to 96 hours.

In addition it has been observed that pseudorabies in swine is contagious. In a series of 9 experiments normal swine were placed in the same isolation pen with pigs experimentally infected either subcutaneously or intramuscularly with pseudorabies virus. In 8 of these experiments the exposed swine developed pseudorabies. In the single negative experiment it is believed, from what is known now, that the infected pig was removed before it had reached the stage at which the disease was communicable. Although the Hungarian virus was used in most of these experiments, the Iowa strain (mad itch) was also found capable of transferring from swine to swine by contact.

Pseudorabies in swine infected by pen exposure closely resembled the disease seen in pigs inoculated subcutaneously. None of the experimental animals died and none appeared dangerously ill. The nature of the illness contracted by exposure was proven in every case either by the demonstration of virus during the course of the disease or of specific virucidal antibodies in the blood serum following recovery. The latent period between the time of first exposure and the onset of symptoms varied from 4 to 11 days, probably depending upon the stage of the disease in the inoculated animal when the normal animal was placed in the pen.

In studying the mode of transmission of pseudorabies in swine it was found that hog lice played no rôle. Neither could virus be demonstrated in the urine, feces or salivary glands of infected pigs, indicating that the saliva and the excreta were unimportant as regards the transmission of the disease. Study of the distribution of the virus in swine killed early in an illness contracted by exposure finally suggested its portal of entrance. In such animals virus could be demonstrated only in the nasal washings. To test the possibility that virus spread from pig to pig by way of the nose, experiments were conducted in which the nasal passages of intramuscularly inoculated swine, as well as of those being exposed, were washed out daily with sterile physiological saline. By means of the inoculation of small amounts of these washings subcutaneously into rabbits it was found that virus was present in the nasal passages of inoculated swine on the sixth day, which is usually the last day of temperature elevation, and that it might persist for a day or two longer. It was not present

[1] J. Schmiedhoffer, *Z. Infektionskrankh., Haustiere,* 8: 383, 1910.
[2] S. von Ratz, *Z. Infektionskrankh., Haustiere,* 15: 99, 1914.
[3] R. E. Shope, *Jour. Exp. Med.,* 54: 233, 1931.
[4] R. E. Shope, *Proc. Soc. Exp. Biol. and Med.,* 30: 308, 1932.
[5] A. Burggraaf and L. F. D. E. Lourens, *Tijdschr. Diergeneesk.,* 59: 981, 1932.
[6] A. Braga and A. Faria, *Revista de Vet. e Zootech.,* 18: Nos. 3–4, 1932, referred to in *Bol. Instit. Vital Brazil,* No. 16, 1934.
[7] P. Remlinger and J. Bailly, *Bull. L'Acad. Vet. France,* 6: 169, 1933.

previous to the sixth day nor later than the eighth day following inoculation.

Virus was present in the nasal washings of swine infected by exposure on the day prior to the elevation of temperature above 40° C.; that is, on the last day of the period of incubation, and thereafter throughout the period of illness. The brain and viscera of one pig, killed after its nasal washings had contained virus of 4 consecutive days, were free of virus, while in another pig, killed after its nasal washings had contained virus for 6 consecutive days, virus was demonstrable in the lung and a mixture of spleen and liver but not in the blood, brain or other tissues tested. The nasal washings of one animal, under observation for 3 weeks, contained virus on the last day of the incubation period, on all the 6 days that the animal was ill, and on the first 4 days of convalescence.

The experiments just summarized indicate that in pseudorabies in swine the nose serves as the portal for the entrance and exit of the virus. They suggest that swine may be an important reservoir for the maintenance of pseudorabies infection because of the facts that the disease in swine is highly contagious, that it is not fatal for this species among all its hosts, and that it is of so mild and ill-defined a nature that it may escape notice, or, if it is noted, be incorrectly diagnosed. It is readily conceivable that the escape of this virus from its swine reservoir may be responsible for the sporadic and highly fatal cases of pseudorabies among cattle in the swine-raising states of the Middle West. Further evidence to support this possibility will be reported in detail later.

RICHARD E. SHOPE

THE ROCKEFELLER INSTITUTE
FOR MEDICAL RESEARCH
PRINCETON, N. J.

## CROSSOVERS IN MALE DROSOPHILA MELANOGASTER INDUCED BY HEAT*

THE long-known effect of heat in increasing the amount of crossing-over[1] in Drosophila females led the senior author some years ago to attempt to induce crossing-over in the male by use of the same agent. The undertaking failed. Perhaps others have essayed the same task without success. In view of the recent production of crossovers in the male through the agency of x-rays by Patterson and Suche[2] and by Friesen,[3] it seemed worth while to try once more the effect of heat. This time the effort has been successful.

The experiments began with a cross between wild-type flies and a multiple third-chromosome stock possessing the characters thread, scarlet, curled, stripe, sooty and claret, which we have been calling "theca," though it lacks the character rough eye contained by the stock originally called theca. The $F_1$ larvae from this cross were subjected, at ages ranging in different experiments from 0 to 6 days, to temperatures varying from 33° to 35° C., for periods of one to eight days. Males which survived this treatment were mated to theca females, one male and several females in each culture bottle. Non-crossover sperms from treated males would produce either wild-type or theca individuals among their offspring; crossover sperms would produce flies possessing some but not all of the mutant characters of the theca stock.

In the early experiments the flies were not classified with respect to thread or stripe. In one of these, 21 surviving $F_1$ males were back-crossed to theca females. One of these males gave rise, among a total progeny of 182 flies, to three crossover individuals, two of them scarlet curled sooty males, one a claret female. As a check upon the classification of these flies they were all mated back to theca individuals. The two scarlet curled sooty males gave only theca and scarlet curled sooty offspring by this cross, while the claret female yielded chiefly theca and claret classes with small numbers of crossovers in each of the delimited regions. Thus was the original classification of the crossover flies verified.

In a later series of similar experiments thread, but not stripe, was included in the classification. Of the many heat-treated cultures, one yielded 13 surviving males, three of which on being mated to theca females produced crossovers. Two of these three males produced one crossover each as follows: 1 curled sooty claret; 1 sooty claret.

The remaining one of the three is mentioned separately because it produced 32 crossover offspring, all thread scarlet, without any of the complementary class (curled sooty claret). This latter result is so unusual as to suggest contamination. No stock of thread scarlet is being maintained in this laboratory, so if contamination were the explanation it would have to come about in an indirect manner. Moreover, the conduct of the experiment seems to preclude that possibility. As in most of these experiments, the parents were transferred from bottle to bottle at frequent intervals, and the heat-treated male, after having been with one group of females for a number of days, was placed with a new group. The male which produced the 32 crossover offspring was thus introduced into two matings. Some of the crossovers appeared in two successive cultures from the first group of females, some in the first culture from the second group of females. If, therefore, contamination were the explanation of these 32 apparent crossovers, the same con-

* Contribution from the Zoological Laboratory of the University of Michigan.

1 H. H. Plough, *Jour. Exp. Zool.*, 24: 147–209, 1917.

2 *Genetics*, 19: 223–236, 1934.

3 SCIENCE, 78, 2031, 513–514, 1933.