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Serial Passage of the Human Influenza Virus in the European Hamster (*Cricetus cricetus*).

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The study of viruses pathogenic for man is largely dependent on having an animal host suitable for experimentation. So far in the study of human influenza, ferrets and mice have proved to be best suited to this purpose, although both animals are far from being ideal. A number of others such as the hedgehog,[1] white rat, guinea pig,[2] guinea pig foetus,[3] Chinese mink, and David's squirrel[4] have been shown to be susceptible only to varying degrees. However, search for additional suitable animals is being continued by most investigators engaged in the study of viruses, and the purpose of the present communication is to report briefly the results of the attempts to infect the European hamster *(Cricetus cricetus)*† with influenza virus.

The strain of virus employed in these experiments was obtained 4 months previously from a person suffering from a rather typical attack of influenza. This virus had been identified immunologically as belonging to the group of human influenza viruses. In ferrets it produced characteristic symptoms but no lung lesions.

The following procedure was adopted: In each passage 2 hamsters were inoculated intranasally with 0.5 cc of virus suspension while under ether anesthesia. One of the animals was sacrificed on the 4th day, and 20% suspensions in broth-saline solution of the turbinates and lungs were prepared separately for subinoculation to mice and for transfer to the 2 hamsters of the succeeding passage. The second

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1 Stuart-Harris, C. H., *Brit. J. Exp. Path.*, 1936, **17**, 324.

2 Stuart-Harris, C. H., *Brit. J. Exp. Path.*, 1937, **18**, 485.

3 Woolpert, O. C., Gallagher, F. W., Rubenstein, L., and Hudson, N. P., *J. Exp. Med.*, 1938, **68**, 313.

4 Tang, F. F., *Brit. J. Exp. Path.*, 1938, **19**, 179.

† The *Cricetus cricetus* belongs to the order Rodentia, tribe Muridæ, sub-family *Cricetinæ*, not to be confused with the smaller golden hamster, *Cricetus auratus*, found in the Near East. It occurs in large numbers in Hungary and other parts of Europe and can easily be captured. For identification of the animals used in these experiments we are indebted to Dr. J. Éhik, Hungarian National Museum of Budapest.

hamster in each passage series was held for determination of immunity response. Blood was drawn from the heart preceding, and 2 weeks following, inoculation, and the serum was tested quantitatively for neutralizing antibodies. Thus in each passage effort was made to determine the existence of infection by the recovery of the virus in mice and by a rise in the circulating antibodies.

In the first experiment a 10% mouse lung suspension of the above-indicated virus, which had been through 2 ferret and 21 mouse passages, was used for inoculating the primary pair of hamsters. Ten serial passages were made. During the first 6 passages a mixture of turbinate and lung suspension was used for transfer and in the other 4 passages turbinate suspension alone. The virus was recovered from the turbinates of each passage hamster, and the duplicate animal held for immunity response showed a definite development of circulating antibodies. Serum from the hamsters taken before inoculation showed no neutralizing properties, even when used undiluted, but specimens taken 2 weeks after inoculation gave complete neutralization in dilutions approximating 1/250.

While the virus was frequently recovered from the lungs, it was not possible to continue passage of the infection when transfers were made from the lungs alone.

The rather marked stimulation of antibodies is indicative of a constitutional reaction, yet the animals manifested no definite symptoms. Other than congestion and slight swelling of the turbinates, the autopsies revealed nothing remarkable.

Subsequently it was found possible to infect and pass serially in hamsters a virus strain from a ferret which had not been adapted to mice. No throat washings from persons ill with influenza were available at the time, and it remains to be determined whether or not the hamster may be infected directly from human beings.

It may be added that 3 unsuccessful attempts were made to pass the virus serially in the European souslik *(Citellus citellus)*. The virus could not be recovered beyond the first passage, nor was there any stimulation of neutralizing antibodies, except to a slight degree, in the souslik receiving the primary inoculum.