17160. The Golden Hamster (*Cricetus auratus*) as an Experimental Animal for Poliomyelitis Research.*

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Successful passage of the Lansing strain of poliomyelitis virus to the Syrian or golden hamster was reported by Armstrong and Packchanian,[1] Plotz, Reagan and Hamilton,[2] and Durand.[3] The purpose of this study was to investigate how the golden hamster (*Cricetus auratus*) compares to the white mouse and the cotton rat as a laboratory animal for experimental work with the Lansing strain virus.

Material and methods. Virus. Suspensions of spinal cords and medullae of infected animals were made up in buffered saline (pH 7.2-7.4). Hamster-passage, mouse-passage and cotton-rat-passage virus was used.

Hamsters. Two strains of golden hamsters were used, one bred at the Michigan Department of Health (designated here as MDH-hamsters), the other obtained from the Tumblebrook Farm, Brant Lake, N. Y. (referred to as TF-hamsters).

Comparative titrations and neutralization tests. Five 5-fold dilutions were used in the comparative titrations. The numbers of animals for each dilution were: 4 for cotton rats and hamsters, and 6 for mice. All the neutralization tests were carried out in mice using constant amounts of mouse-passage virus and decreasing amounts of serum. The animals were observed for a period of 30 days in all the experiments.

Titers and inocula. The LD_{50} titers of the virus preparations were calculated by the method of Reed and Muench[4] and expressed in terms of dilution of the original tissue material (in %).

Experimental. Serial passages. Serial passages were carried out in MDH-hamsters as well as in TF-hamsters. Mouse-passage virus was used for the initial passage, followed by hamster-to-hamster passages. All the passages were done by intracerebral inoculation of 10% suspensions of cords and medullae.

As shown in Table I, the outcome of hamster-to-hamster passages did not show considerable differences between the 2 strains of hamsters, either in the percentage of takes or in the average incubation period. In the sixth passage in the MDH-hamsters none of the animals developed any symptoms. No attempt was made to continue the passages in TF-hamsters beyond the sixth passage in view of the low percentage of takes.

Comparative virus titrations. The outcome of the titrations of mouse passage, cotton-rat passage and hamster passage virus in mice, cotton rats and hamsters is summarized in Table II. The data presented show that the mouse passage and the cotton-rat passage virus gave extremely low LD_{50} titers in MDH-hamsters (5% and more), while the same virus preparations gave high titers in cotton rats and mice (ranging from .028 to .0008% dilutions of virus). The MDH-hamster passage virus gave extremely low titers in MDH-hamsters (over 10%) as well as in cotton rats (5%) and mice (1.67%).

Considerably better results were obtained with TF-hamsters. Both mouse passage and cotton rat passage virus gave good titers in TF-hamsters (.015 and .09% respectively). The TF-hamster passage virus gave the lowest titer in TF-hamsters (.6%), but this titer was considerably higher than the corresponding titer obtained in MDH-hamsters (more than 10%). The general pattern was, however, the same with the 2 strains of hamsters: the use of the hamster as an experimental

* The data presented in this paper were used by the senior author for a thesis in partial fulfillment of the requirements for the Master of Science degree at the Michigan State College.

1 Armstrong, C., and Packchanian (unpublished data, see Vanderbilt Lectures, 1941).

2 Plotz, H., Reagan, R., and Hamilton, H. L., PROC. SOC. EXP. BIOL. AND MED., 1942, **51**, 124.

3 Durand, P., *Compt. Rend. Soc. Biol.*, 1943, **139**, 716.

4 Reed, L. J., and Muench, H., *Am. J. Hyg.*, 1938, **27**, 493.

TABLE I.
Serial Passages of Lansing Strain Virus in Hamsters.

Passage No.	No. of animals inoculated MDH	TF	No. of animals paralyzed MDH	TF	Incubation period in days MDH	TF
1	4	4	2	4	3, 4	2, 3, 3, 5
2	5	4	2	3	3, 11	3, 3, 18
3	5	4	1	2	3,	4, 4
4	5	4	4	1	4, 4, 8, 9	4
5	4	4	1	2	8	5, 16
6	5	4	0	1	—	6
					Avg 5.7	Avg 5.1

TABLE II.
Comparative Titrations.

Virus	Titrated in	LD_{50} (in %)
MDH-hamster passage virus	MDH-hamsters	>10.0
	Cotton rats	5.0
	Mice	1.67
TF-hamster passage virus	TF-hamsters	.6
	Cotton rats	.018
	Mice	.054
Mouse-passage virus	MDH-hamsters	5.0
	TF-hamsters	.015
	Cotton rats	.004-.0008
	Mice	.0016-.0008
Cotton rat passage virus	MDH-hamsters	>5.0
	TF-hamsters	.09
	Cotton rats	.029-.009
	Mice	.028-.0015

animal, or of hamster passage virus, resulted in lower titers than when mice or cotton rats were used, and the lowest titers were obtained when hamster passage virus was titrated in hamsters.

Attempts to increase the infectivity of the Lansing strain for the golden hamster. Attempts were made to enhance the infectivity of the Lansing strain virus for TF-hamsters by using as diluent saline buffered at a low pH (technique of Hammon and Izumi[5]). In one experiment (with cotton rat passage virus) the result was better at pH 4, while in 2 other experiments, for which mouse-passage virus was used, better results were obtained at pH 7.2.

In 2 other experiments with TF-hamsters the technic described by Milzer and Byrd[6] (autolyzed normal mouse brain tissue as adjuvant) was used. No enhancement of the infectivity was observed.

Immune response. It seemed interesting to investigate the immune response of the golden hamster to the Lansing strain virus. For this purpose, hamsters were immunized by intraperitoneal inoculations of .3 ml of a 10% suspension of live virus. MDH-hamsters were immunized with the mouse passage virus, while mouse passage, cotton rat passage and hamster passage virus were used for the immunization of 3 separate lots of TF-hamsters. The vaccinations were done twice weekly with a total of 7 vaccinations. In each lot, one group of animals was bled 2 weeks after the first vaccination, another group after 3 weeks, and still another group after 4 weeks (6 to 10 days after the last vaccination). The sera of each group were pooled and are referred to as 1st, 2nd and 3rd bleeding, respectively. The antibody content was determined by neutralization tests in mice.

TF-hamsters vaccinated with TF-hamster passage virus showed the weakest immune response with the maximum titer of 1:27. The titers of the sera of TF-hamsters vaccinated with mouse passage virus were 1:20 in the first bleeding, 1:47 in the second and 1:45 in the third bleeding. The vaccination of the MDH-hamsters with mouse passage virus gave a similar titer in the first bleeding (1:24) and a higher titer in the second bleeding (better than 1:96). There was a drop of the titer in the third bleeding.

The best results were obtained in TF-hamsters vaccinated with cotton rat passage virus. The titer was 1:17 in the first, better than 1:73 in the second, and better than 1:126 in the third bleeding.

[5] Hammon, W. McD., and Izumi, E. M., PROC. SOC. EXP. BIOL. AND MED., 1941, **48**, 579.

[6] Milzer, A., and Byrd, C. L., *Science*, 1947, **105**, 70.

Discussion. The two strains of golden hamsters used by the authors differ considerably in their susceptibility to the Lansing strain virus and in the titer of the hamster passage virus. One of the strains (MDH) is clearly not suitable for experimental research with the Lansing strain virus, and the other (TF) which gave considerably more favorable results, also is in every respect inferior to both the white mouse and the cotton rat.

The immunization of the hamster with active Lansing strain virus resulted in fairly good titers of neutralizing antibody, provided cotton-rat passage or mouse passage virus was used for immunization. In view of the small size of the hamster, use of this animal for serological work with the Lansing strain virus does not seem to present any particular advantage.

Summary and conclusions. Golden hamsters (*Cricetus auratus*) from two different sources were found to present marked differences in their susceptibility to the Lansing strain of poliomyelitis virus. Both strains were found to be markedly inferior to the white mouse and to the cotton rat as experimental animals for poliomyelitis research.

The adjustment of the inoculum at a low pH did not increase the titer of the hamster passage virus consistently. The use of the autolyzed normal mouse brain technic did not increase the infectivity of the virus for the hamster.

The intraperitoneal inoculations of mouse-passage and cotton-rat passage virus resulted in higher titers of neutralizing antibody in the golden hamster than when hamster passage virus was used.

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17161. Relation of Pregnancies to Induction of Ovarian Tumors by X-rays.

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Two forces are now postulated in the genesis of ovarian tumors: direct delayed x-ray effect and a hormonal "imbalance." Ova are highly sensitive to x-rays. Their destruction disrupts the normal development of the ovarian follicles. It is believed that new formation of ova occurs in young female mice, therefore, it can be assumed that the hormonal imbalance induced by x-rays in very young mice as well as that caused by small doses of x-rays is slight and under such conditions ovarian tumors are less likely to occur. These were the thoughts that led to the pilot experiments here described.

Irradiation of Mice at 1-3 Days of Age: Earlier experiments have shown that a single exposure to 87r or more at 5-10 weeks of age will produce tumors in most mice when they reach adult age.[1]

In the first experiment reported here, mice were irradiated with 150r at 1-3 days of age and were reared by their non-irradiated mothers and allowed to live until natural death or about 20 months of age. At about 4-6 weeks of age they were weaned and a few weeks later mated with normal males. When pregnant they were separated, allowed to nurse their babies after which they were returned to the mating cage. Table Ia indicates that about 30% of these mice became pregnant and some had as many as 4 pregnancies. Ovarian tumors developed in 76%. One-half of those that were pregnant remained free from ovarian tumors as compared to 8% of those that were completely sterilized by x-rays. However, even multiple pregnancies failed to prevent the development of ovarian tumors. The time of appearance of these neoplasms is not significantly shorter than that in mice irradiated at 4-6 weeks of age.[1]

[1] Furth, J., and Boon, M. C., *Cancer Research*, 1947, **7**, 241.