ADAPTATION OF THE AGENT OF SCRAPIE TO HAMSTERS

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The agent of scrapie (Compton strain) can be transmitted from mice to hamsters; the incubation period of the disease is 5-6 months. Passage of the agent of scrapie through suspensions of brain tissue was repeated 10 times. The scrapie agent was found in the spinal cord and spleen but it could not be found in the liver, kidneys, adrenals, and lungs of the infected animals in the last stage of the disease.

KEY WORDS: agent of scrapie; transmission to hamsters.

Slow infections of the CNS in man and animals with an inevitably lethal outcome have recently acquired particular importance (amyotrophic lateral sclerosis, Jakob–Creutzfeld disease, kuru, scrapie). Experimental transmission of scrapie to golden hamsters was described in 1963-1965 [5-7]. Subinoculation of the brain of infected hamsters into healthy animals caused the latter to develop the disease.

The object of this investigation was to study the possibility of reproducing scrapie in hamsters by means of the mouse-adapted agent of scrapie, to investigate the clinical picture of the disease, the duration of the incubation period, and the possibility of passage of the agent of scrapie through hamsters of different ages, and to study the distribution of the agent of scrapie in the organs of infected animals.

EXPERIMENTAL METHOD

The agent of scrapie (Compton strain) was obtained from Gajdusek and Gibbs (Bethesda, USA) in the form of a lyophilized suspension of the 3rd mouse passage in Swiss albino NIH mice. The agent was inoculated into BALB/c and C57BL mice, which developed scrapie 5 months after injection of a 10% suspension of the brain tissue of infected mice [1].*

Primary inoculation of the golden hamsters was carried out with the agent of scrapie adapted to mice, after three passages in these animals. The agent was inoculated into BALB/c mice, after which two passages were made in C57BL/10Sn mice.

Golden hamsters were used except in one case, when striped, hairy-footed hamsters were chosen. The animals were infected intracerebrally by injection of 0.03 ml of a 20% suspension of brain tissue from mice with scrapie. During inoculation and for the passages hamsters aged 3-5 days or older animals aged between 1.2-3 months and 1.5 years were used.

EXPERIMENTAL RESULTS

All the hamsters were susceptible to scrapie. In most animals no difference was found in the clinical picture of the disease. At the end of the fourth month all the inoculated hamsters showed the first symptoms of the disease; the clinical manifestations were similar to those observed in mice with scrapie. The hamsters were drowsy, and when awakened their gait was unsteady and their movements uncoordinated. Their eyes rolled, their back was arched, and their hind limbs were splayed. The sick animals died either very soon after the symptoms developed or after a period of complete prostration. Subinoculation of the brain

* Subsequently a 20% suspension of the brain tissue of infected animals was used.

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of the diseased hamsters into healthy animals led the latter to develop the disease after 5-6 months. No difference was found in the duration of the incubation period in animals of different ages.

Altogether 10 passages of brain tissue suspension of the diseased animals were carried out; a tissue suspension from the spinal cord and spleen of hamsters which developed scrapie was used at the same time. According to the observations of Eklund et al. [3], confirming that the agent of scrapie adapted to mice, 4 months after intracerebral inoculation the agent can be found in the spinal cord and spleen of the sick mice.

Altogether three passages of a tissue suspension of the spinal cord of hamsters with scrapie and four passages of a splenic tissue suspension were carried out. The clinical manifestations of the disease in animals inoculated intracerebrally with tissue suspensions of the brain and spleen were identical with those following injection of a tissue suspension of the spinal cord; just as in the last case, the incubation period was 5-6 months.

The experiments thus showed that hamsters develop a clinical picture of scrapie similar to that observed in mice and that the agent of scrapie can be transmitted from mice to hamsters. The clinical picture of scrapie was observed in all hamsters of whatever age studied and the incubation period was 5-6 months. The disease could be transmitted not only by tissue suspensions of the brain and spinal cord, but also by a tissue suspension of the spleen of the sick animals.

The presence of the agent of scrapie in the various organs of hamsters was then studied, in view of its importance in the study of the pathogenesis of the disease.

Hamsters were infected by the same method with a 20% suspension of the tissues of various organs of animals with scrapie. In each experiment the state of the animals was studied after receiving an injection of tissue suspension from the brain, spinal cord, liver, kidneys, adrenals, spleen, and lung of infected hamsters. Experiments were carried out at the sixth, seventh, eighth, and ninth passages through hamsters, when it could be considered that the agent of scrapie had become adapted to this species of animals. In each experiment animals of the same age were used and all the animals were killed in the period of agony.

The presence of the agent of scrapie in the tissues of the spinal cord, brain, and spleen of the infected hamsters has already been described above, together with the clinical picture of the disease, the incubation period, and the number of passages carried out. After infection of hamsters with a tissue suspension from the liver of animals with scrapie, in 2 of 3 experiments (in one experiment the animals died before the expected incubation period from intercurrent infections) none of the animals developed scrapie 8 and 10 months after infection. When mice of strain B10 · D2 were infected simultaneously with the same material, no case of the disease likewise was observed 1 year after intracerebral inoculation. The writer showed previously [1] that mice of all strains are susceptible to scrapie and that the disease can be reproduced in them in 100% of cases. After inoculation with a kidney tissue suspension in one experiment the hamsters did not develop the disease 1 year after inoculation, in another experiment they died earlier from intercurrent infections, and in the third experiment the picture observed after 8 months was uncertain; however, on subsequent infection of B10 · D2 mice, no animals developed the disease within 1 year after infection.

After inoculation of an adrenal tissue suspension the animals in two experiments died before the expected time and in a third experiment they died after 13 months; subsequent infection of C57BL/10Sn mice was not followed by death of any of the animals in the course of 1 year.

Finally, after intracerebral infection of hamsters with a tissue suspension of the lungs of animals with the disease, no animal developed the disease within 10 and 12 months in two experiments.

Hence, although some animals died before the expected time of observation, the impression was obtained that the agent of scrapie was not present in the liver, kidneys, adrenals, and lungs.

These data on adaptation of the agent of scrapie to hamsters agree with the observations of Zlotnik [5-7]. The author has found no report in the literature of a study of the presence of the agent of scrapie in the organs of hamsters with the disease.

It would be useful to compare the results obtained in mouse-adapted scrapie with those obtained in hamster-adapted scrapie. Data of this sort have been obtained by the study of the presence of the agent of scrapie in mouse organs. Pattison [4] found that if these animals were infected with various tissues from goats (liver, spleen, kidney, brain), suspensions of the spleen and brain contained the agent in about equal concentrations whereas its concentration was smaller in suspensions of the kidneys and liver.

Eklund et al., [2] did not find the agent of scrapie in the kidneys of infected mice, only a little of it

was present in the liver, and in the spleen and thymus it was also found only in small amounts.

The results of the present experiments agree with the observations of Eklund et al., [2] and of Pattison [4] and they confirm the impossibility of isolating the virus.

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