Interference between Bovine Parainfluenza 3 Virus and a Street Strain of Rabies Virus in Rabbits

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Summary
Rabbits proved to be protected against rabies (street virus) by the intravenous injection of bovine parainfluenza type 3 (BPI3) virus either 24 hours before or 10 minutes after the intradermal inoculation with a street strain of rabies virus. BPI3 virus given 24 hours after rabies infection had no effect upon the course of rabies infection.

In mice treated intraperitoneally with BPI3 virus and subcutaneously infected with a fixed strain of rabies virus no such protection could be observed.

It is considered that the protection of rabbits against rabies results from interference between BPI3 and rabies virus and is mediated by interferon.

1. Introduction
Vieuchange (1967) described interference between a neurotropic strain of vaccinia virus and rabies virus in rabbits when both viruses were inoculated intradermally. Later, Vieuchange and Fayaz (1969) reported the prevention of rabies in rabbits after intra-carotid injection of virus-free extracts of vaccinia infected skin which presumably contained interferon. Recently, Hermodsson (1964) and Rosenquist and Loan (1967) described the ability of bovine parainfluenza 3 virus (BPI3) to induce interferon in vitro.

In the present study, the ability of BPI3 virus to protect rabbits and mice against rabies due to an interference phenomenon was studied.

2. Materials and Methods
The “T1” strain of bovine parainfluenza 3 virus (Dawson, 1964) was used in this study. It was supplied in the form of a lyophilized calf kidney tissue culture suspension by J. H. Darbyshire, Central Veterinary Laboratory, Weybridge, England. The virus was serially passaged three times in BHK-21 cell cultures which were supplied by A. Hazrati, Razi Institute, Karadj, Iran. After cytological and serological confirmation of the virus as BPI3 virus in the harvested material from the third passage, it was used for intravenous and intraperitoneal inoculation of rabbits and mice, respectively. The virus suspension had a haemagglutinating titre of 128 HA units per millilitre.

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The street rabies virus strain was a suspension of human brain died of rabies, having a titre of $10^{4.5} \text{LD}_{50}$ in Swiss mice intracerebrally. The fixed rabies virus strain (CVS-27-NIH) was received from WHO, Geneva on 9 Nov., 1968 passaged twice in Swiss mice (i.c.) having a titre of $10^{3.2} \text{LD}_{50}$ in mice intracerebrally tested.

Groups of 5 and 15 adult rabbits each weighing 1300 to 1500 g were inoculated intradermally with 0.25 ml of a 1:20 dilution of the street strain of rabies virus.

Groups of 10 Swiss mice each weighing 16 to 20 g received 0.05 ml of a 1:100 dilution of the fixed strain of rabies virus (CVS-27-NIH) subcutaneously into the hind foot pad. The details of the experiments and the intervals between BPI3 virus and rabies virus inoculations are shown in Tables 1 and 2 for rabbits and mice, respectively. The rabbits and mice were kept until two and one months after infection, respectively, thus well beyond the incubation periods of rabies in these species. Sections of the brains of dead animals were examined by the fluorescent antibody technique for detection of rabies virus antigens.

### Table 1. Groups of Rabbits Inoculated Intravenously with Bovine Parainfluenza 3 Virus and/or with a Street Strain of Rabies Virus Intradermally

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Rabies Experimental data</th>
<th>Interval</th>
<th>2nd virus</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>15</td>
<td>Rabies¹</td>
<td>1</td>
<td>9</td>
<td>66.0</td>
</tr>
<tr>
<td>II</td>
<td>15</td>
<td>Parainfluenza² 24 hours</td>
<td>Rabies</td>
<td>1</td>
<td>6.0</td>
</tr>
<tr>
<td>III</td>
<td>5</td>
<td>Control³ 24 hours</td>
<td>Rabies</td>
<td>3</td>
<td>60.0</td>
</tr>
<tr>
<td>IV</td>
<td>5</td>
<td>Rabies 10 minutes</td>
<td>Parainfluenza</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>V</td>
<td>5</td>
<td>Rabies 24 hours</td>
<td>Parainfluenza</td>
<td>5</td>
<td>100.0</td>
</tr>
</tbody>
</table>

¹ Street strain.

² Bovine Parainfluenza type 3 (BPI3), strain T1.

³ Tissue culture fluid (1 ml) of non-infected BHK-21 cells.

### 3. Results

Table 1 summarizes the results obtained with rabbits. As shown, the percentage of rabies mortality among rabbits injected intravenously with bovine parainfluenza virus type 3 (BPI3) 24 hours before infection with rabies virus (group II) was tenfold lower than that recorded for rabbits inoculated only with rabies virus (group I) or with tissue culture fluid of non-infected BHK-21 cells (group III).

When parainfluenza virus was given after rabies virus infection a full protection was observed when the interval between these two infections was short — 10 minutes — (group IV), whereas the course of rabies infection could not be influenced by BPI3 virus injected 24 hours later (group V). No significant differences were found in the incubation periods of rabies among the different groups of rabbits. The clinical signs of rabies in rabbits were typical of the paralytic form of the disease in this species. All cases of rabies were confirmed by fluorescent antibody examination of brain sections.

The rates and percentage of mortality from rabies in infected mice are shown in Table 2. The intraperitoneal inoculation of BPI3 virus before or after rabies virus infection did not result in protection, and the difference in the mortality rates were not significant. Mice inoculated only with BPI3 virus remained healthy throughout the experiment (group VIII).