PREVENTIVE EFFECT OF 2, 4-DINITROPHENOL ON EXPERIMENTAL INFLUENZA

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Ackermann[1] *et al.* have demonstrated that 2, 4-dinitrophenol (DNP) has remarkable inhibitory effect on the propagation of influenza virus in tissue culture without showing virucidal effect. We have also ascertained the same effect[2] and have conducted experiments to find whether the inhibitory effect will be exerted on experimental influenza of mice in the same way as *in vitro*. The results are reported in this paper.

MATERIALS AND METHODS

Virus. The FM 1 strain of influenza type A′ virus was used. It had been passed in the chorioallantoic cavity of chicken embryonate egg.

Animal. Mice of 8–9 g body weight were used.

Administration of DNP. The solution of DNP of concentration 1 mg/ml was made. 0.1 ml of the solution was injected subcutaneously into mice two times a day. The injections were continued untill the 15th day after the inoculation when the mice did not die.

Challenge. Mice were inoculated intranasally with 0.015 ml of the viral suspension. The inoculum was prepared by making dilutions of infected allantoic fluid so that its 0.1 ml contained 30 hemagglutination titers with chicken erythrocytes. Observation was continued untill the 15th day after the challenge.

EXPERIMENTAL

Mice were divided into four groups. Each group contained four mice. Into the mice of the 1st group the injections of DNP were made from 24 hours before, into those of the 2nd from the same time, into those of the 3rd from 24 hours after the challenge and the 4th group acted as control and was not injected with DNP. The results are shown in Figure 1. The mice of the 1st and the 2nd groups survived longer than those of the 3rd and the 4th groups. The survival was most marked in the 1st group, half of which survived untill the 15th day after the challenge. All mice of the 3rd group except one died on the same day as those of the 4th group. In the lungs of all the mice which survived

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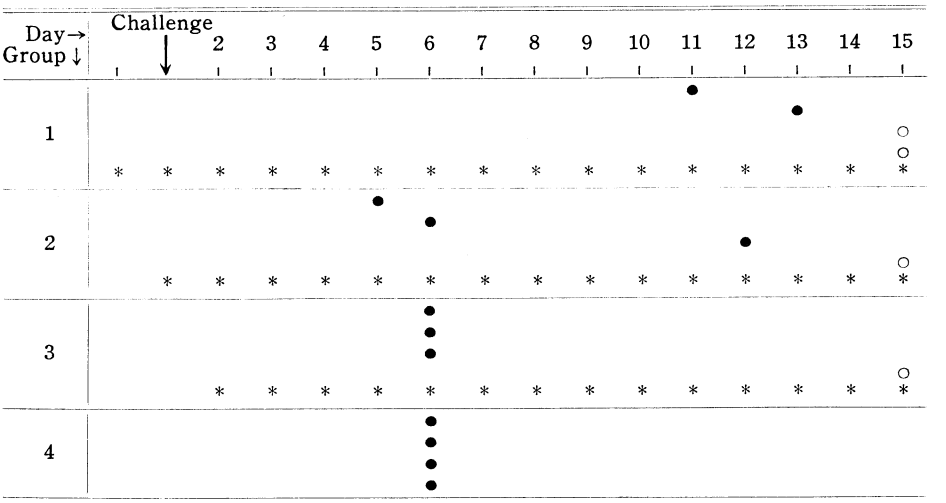

FIG. 1. The preventive effect of DNP on experimental influenza of mice.
Challenge dose: 30 hemagglutination titers.
Challenge virus: FM 1 strain.
● died.
○ survived.
* subcutaneous injection of 0.1 mg of DNP two times a day.

untill the 15th day after the challenge multiplication of the virus was not observed by hemagglutination titrations with chicken erythrocytes.

The injection of the described dose of DNP seemed to give no serious toxic effect on mice. But toxicity of DNP was very severe. The intravenous injection of 30 γ of DNP per g of body weight into mice brought about clonic convulsions of the legs within 10 minutes after the injection, followed by immediate death with rigidity of all muscles. Injected with the same dose into the peritoneal cavity, the mice died with the same symptoms within 60 minutes after the injection. Injected with 20 γ of DNP per g of body weight, they showed states of temporary unrest and survived.

DISCUSSION

From the experiments described here it is clear that DNP has some preventive effect on experimental influenza of mice. Ackermann *et al.* have concluded that the inhibitory effect of DNP on virus propagation in tissue culture depends on its blocking action on the oxidative phosphorylative activity of the host tissue from which the energy required for the viral synthesis is derived. It might be supposed that the host tissues *in vivo* receive also the same effect from the injection of DNP. Hence in tissue susceptible to influenza virus, bronchial epitheial cells, the energy supplying system for virus propagation might be inhibited. Next it may be said that the earlier the injection of DNP is begun, the more the preventive effect is shown.

The preventive effect of DNP on influenza may have no practical significance

because of its severe toxicity. It is interesting, however, that the inhibitory effect of DNP on the propagation of influenza virus observed ***in vitro*** was also shown ***in vivo***.

SUMMARY

DNP has some preventive effect on experimental influenza of mice. Its practical significance is not promising.

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