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Abstract

The effect of P³² in the experimental Japanese B Encephalitis infection was investigated. A remarkable delay of infection was observed, when a therapeutic dose of P³² was administered intraperitoneally to the mouse which had been inoculated intracerebrally with the virus suspension at the concentration of about LD₅₀. Almost equal results were obtained by intraperitoneal administrations to the mice when they had been inoculated intravenously or intraperitoneally.

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EFFECTS OF RADIOACTIVE P³² UPON JAPANESE B ENCEPHALITIS IN MICE

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Present paper deals with the investigation on the effects of p³² which was given in therapeutic dose to the mice infected with Japanese B Encephalitis.

Experimental

Materials and methods: The Japanese B Encephalitis virus, labeled "Okayama 52 B", was provided by Dr. Prof. K. Hiraki in 1952, and has since been maintained in our laboratory by intracerebral passage in mice.

Mice weighing 8—13 g. were obtained from commercial breeders. They were previously injected with the virus suspension intracerebrally, intravenously or intraperitoneally before the administration of P³².

Virus suspension was prepared as follows: Brains of mice with characteristic signs of advanced symptoms were immersed in 50% glycerol and stored at 5°C for 10 days as the stock virus. This was homogenized and diluted with Bouillon of pH 7.6 to the final concentration of one tenth.

The cell debris were centrifuged off and supernatant virus suspension was used as the virus preparation. This was further diluted to various concentration before application.

Radioactive P³² was delivered from U. S. A. in the form of phosphoric acid dissolved in dilute hydrochloric acid and diluted with 0.85% aqueous sodium chloride solution before use. Throughout this investigation P³² was administered intraperitoneally.

1) Experiment with intracerebrally inoculated mice. A certain numbers of mice were inoculated intracerebrally with each 0.03 ml. of virus suspension at various concentration. After 24 hours each of them was administered with each 20 μ c dose of P³². For three weeks thereafter the symptom were com-

pared with those of the control references which were likewise inoculated with the virus but with no P^{32} -administration.

2) Experiment with intravenously inoculated mice: 0.2 ml. virus suspension of various concentration was inoculated to each mice into the vein of the tail. 24 hours after this each 30 μ c. dose of P^{32} was administered to each mouse. The symptoms were examined for 3 weeks thereafter just as above.

3) Experiment with the intraperitoneally inoculated mice: Each 0.3 ml. of virus suspension was intraperitoneally inoculated. 48 hours after the virus inoculation every mouse was administered with 30 μ c. dose of P^{32} . The examination of the symptoms was continued for 3 weeks just as above.

All these results just obtained by the above experiments were further studied in comparison with the results obtained from another series of experiments in which the usual phosphoric acid (non-radioactive) was used in place of the radioactive phosphoric acid.

Results

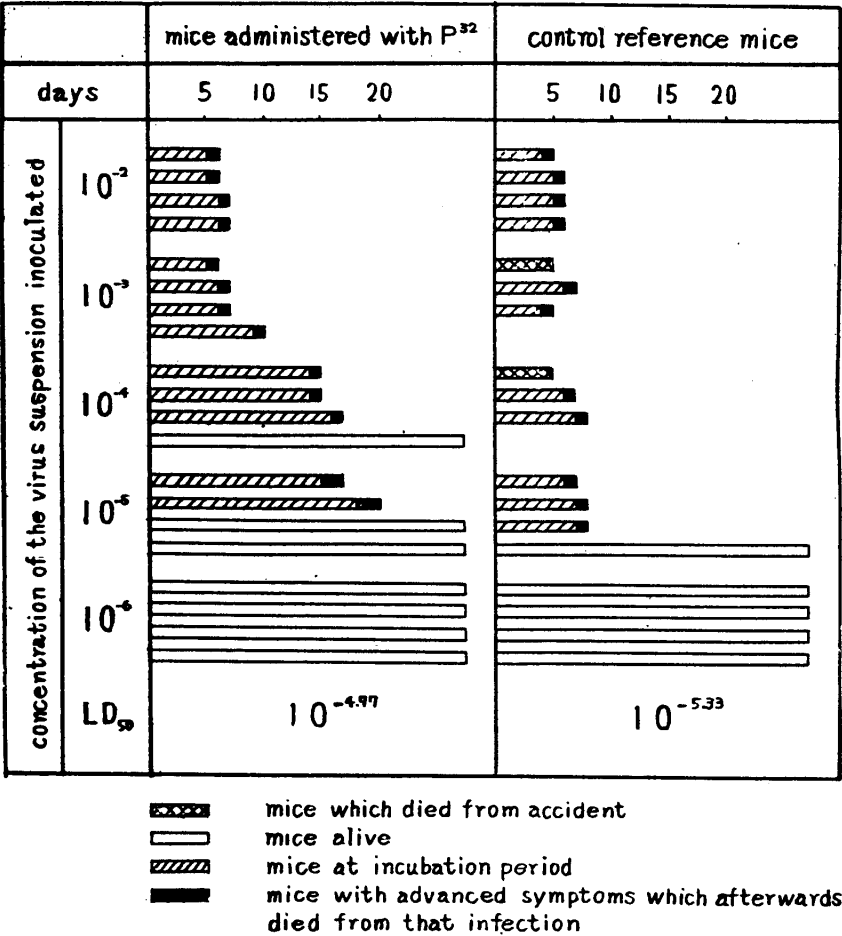
1) Intraperitoneal administration of P^{32} to the intracerebrally inoculated mice. (See Table 1.) LD_{50} (the 50 % end point) of the P^{32} -administered mice was obtained as $10^{-4.77}$ and, as compared with that of the control reference ($LD_{50}=10^{-5.33}$), there was no significant difference between these two values. But with regards to the P^{32} -administered mice, when the virus concentration had been 10^{-4} — 10^{-5} of the LD_{50} -value, the prolongation of survival time was observed.

That is, twice as long survival time with 10^{-4} of LD_{50} and thrice with 10^{-5} .

2) Intraperitoneal administration of P^{32} to the intravenously inoculated mice. (see Table 2.) There could be detected no difference between the LD_{50} -values of P^{32} -administered mice and control reference mice, the two LD_{50} -values equally being $10^{-4.5}$. Also in this case, at every concentration of virus suspension from 10^{-2} to 10^{-5} delayed infection was observed with the P^{32} -administered mice group.

3) Intraperitoneal administration of P^{32} to the intraperitoneally inoculated mice (Table 3). Even when the virus

Table 1. Intraperitoneal administration experiment of P³² to the intracerebrally inoculated mice.

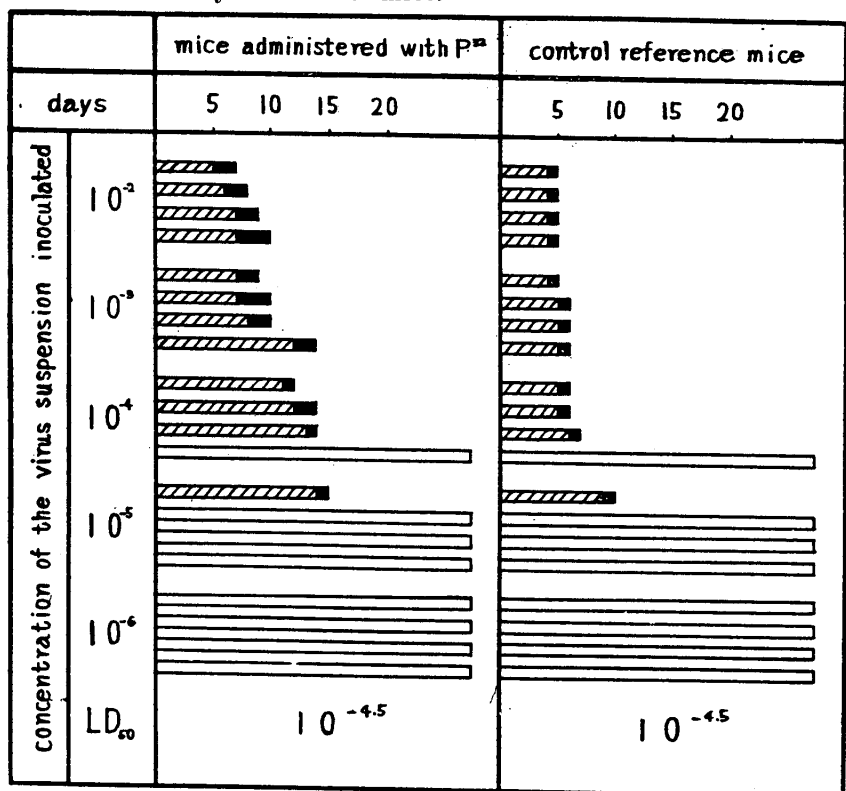


concentration was 10⁻¹, a considerable delay of infection was ascertained with the P³²-administration.

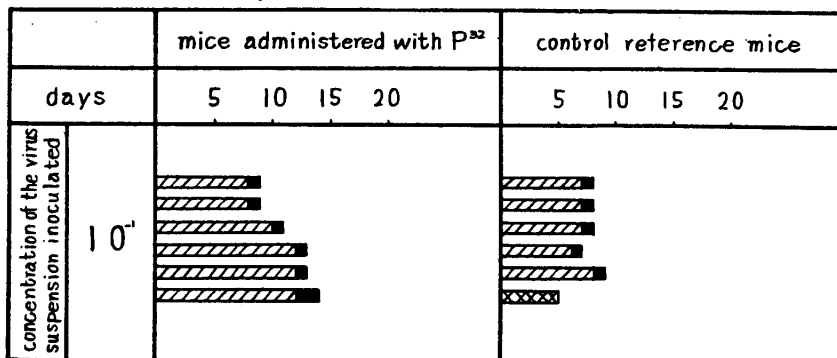
The control experiments with non-radioactive P showed no such delay of infection in contrast to the above experiments with radioactive P³².

Discussion

On the direct effects of radioactive isotopes to microbes several investigations had been reported. For instance, radioactive-iron (1) was studied in acute malarial infections in animals and polonium²¹⁰ or selenium⁷⁶ (2) in experimental Shistosoma

Effects of Radioactive P³² Upon Japanese B Encephalitis in Mice 9Table 2. Intraperitoneal administration experiment of P³² to the intravenously inoculated mice.

mice alive
 mice at incubation period
 mice with advanced symptoms which afterwards died from that infection

Table 3. Intraperitoneal administration experiment of P³² to the intraperitoneally inoculated mice.

mice which died from accident
 mice at incubation period
 mice with advanced symptoms which afterwards died from that infection

mansoni infections in mice.

But in all these experiments, no remarkable direct effect of radioactivity had been shown.

Recently, however, *Hershey et al.* (3) found an inhibitory effects to the activity of bacteriophage by the direct action of β -radiation of P^{32} .

In addition, they inform that this inactivation of bacteriophage can be achieved by the nuclear conversion ($P^{32} \rightarrow S^{32}$) which proceeds in the phage particle itself.

In the present investigation, the infectious activity of the virus Japanese B Encephalitis was shown to be inhibited by the direct effect of β -radiation of P^{32} or the nuclear conversion of P^{32} to S^{32} which would have proceeded in situ.

There are several special curatives for Japanese B Encephalitis infection.

Those are hyperimmune horse serum, sulfonamide, thiamine, phenosulfazole, sodium-3-phenyl-azonaphthionate and other antibiotics. However, few of them had been successful in experimental Japanese B Encephalitis infection.

The significant delay of infection caused by the use of P^{32} observed in the above experimental Japanese B Encephalitis infection seems to suggest some new curative method of this infection.

Summary

The effect of P^{32} in the experimental Japanese B Encephalitis infection was investigated.

A remarkable delay of infection was observed, when a therapeutic dose of P^{32} was administered intraperitoneally to the mouse which had been inoculated intracerebrally with the virus suspension at the concentration of about LD_{50} .

Almost equal results were obtained by intraperitoneal administrations to the mice when they had been inoculated intravenously or intraperitoneally.

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- ¹⁾ *Thompson, P. E., Mc Ginty, D. A., Bush, D. L. and Wilson, M. L.*: J. Inf. Dis., **83**, 23. 1948. — ²⁾ *Watts, N. P. and Mc Connell, K. P.*: Am. J. Hyg., **53**, 11, 1951. — ³⁾ *Hershey, A. D., Kamen, M. D., Kennedy, J. W. and Gest, H.*: J. Gen. Physiol., **34**, 305, 1951.