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Effect of Polychlorinated Biphenyl on Viral Infections in Mice

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Mice that were fed a diet containing 400, 200, or 100 μg of polychlorinated biphenyls (PCB) per g were significantly more susceptible to Herpes simplex virus than mice that were fed a PCB-free diet. The mortality of mice that were fed a diet containing 400 or 200 μg of PCB per g and infected with ectromelia virus was higher than that of normal control mice infected with virus. There was no significant difference in inducibility of interferon by polyinosinic acid-polycytidylic acid between PCB-fed mice and control mice.

Polychlorinated biphenyls (PCB) are potential environmental contaminants and cause many disturbances in the liver, skin, and other organs.

PCB have a tendency to accumulate chronically in the liver without excretion, so it is important to examine the synergism between PCB and microorganisms such as bacteria and viruses.

It has been proven that PCB suppresses humoral or cellular immunity or both in mice (6, 7), rabbits (4), and guinea pigs (8) and impairs host resistance to endotoxin, protozoa, and bacteria (5, 7) in mice. It has also been reported that PCB increases the mortality of ducks infected with hepatitis virus (1).

The purpose of this study is to examine the effect of PCB on herpes simplex virus (HSV) and ectromelia virus (EV) infection in mice, which can tolerate a relatively larger dose than can primates (7).

Four-week-old male ICR mice were purchased from Clea Japan, Osaka, Japan. They were fed a diet containing various concentrations of PCB. The PCB employed was Kanechlor 500. Mice were fed diets containing 400, 200, or 100 μg of PCB per g or a PCB-free diet for 21 days. After this, HSV or EV was inoculated into the mice, and PCB-containing or -free diets were given to the mice for another 10 days.

As a preliminary experiment, daily and total amounts of ingested PCB were measured. In the group which was fed the diet containing 400 μg of PCB per g, daily and total ingested amounts were 0.066 g/kg per day and 1.7 g/kg per 26 days on the average. In the 200-μg/g group they were 0.033 g/kg per day and 0.9 g/kg per 26 days on the average, and in the 100-μg/g group they were 0.018 g/kg per day and 0.5 g/kg per 26 days on the average. The body and organ weights were measured as mice were fed the diets. It was expected that the more PCB ingested, the more body weight and spleen weight would be reduced; but on the contrary, the weight of the liver increased with the increase of PCB concentration.

PCB accumulated in the liver for 21 days was quantified by electron-capture gas chromatography (Fig. 1). A 300-μg amount of PCB per g of liver was retained in the liver when the mice ingested the diet containing 400 or 200 μg of PCB per g, and 230 μg of PCB was retained when the mice ingested the diet containing 100 μg of PCB per g. This suggests that PCB tends to accumulate in liver.

A 0.7 50% lethal dose (LD_{50}) of Miyama strains of HSV, kindly supplied by S. Nii, Department of Virology, Okayama University Medical School, Okayama, Japan, and propagated in human FL cells, was intraperitoneally inoculated.

The mortality rate of HSV-infected mice that ingested the PCB-free diet was 30%, whereas the mortality rate was 80, 80, and 70% in the mice that ingested the diet containing 400, 200, or 100 μg of PCB per g, respectively (Fig. 2). The differences in mortality rate were significant between normal mice and mice that were fed the diet containing 400 or 200 μg of PCB per g ($P < 0.05$, $P < 0.05$).

However, there was no significant difference in the mean day of death (MDD) between the two groups. When mice that ingested the diet containing 400, 200, or 100 μg of PCB per g were not inoculated with HSV, they all survived (Table 1).

EV, kindly given by S. Kato, Research Institute for Microbial Diseases, Osaka University, Osaka, Japan, and propagated in L cells, was intraperitoneally inoculated at 0.7 LD_{50} into mice given diets with or without PCB. When the

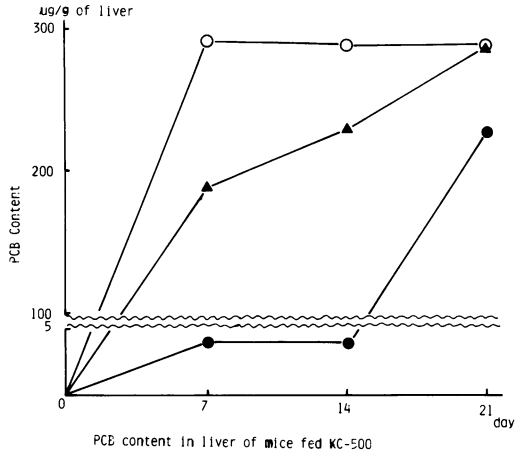

FIG. 1. *The quantity of PCB in the liver of mice fed the diet containing 400 (○), 200 (▲), or 100 (●) μg of PCB (KC-500) per g was measured by electron-capture gas chromatography.*

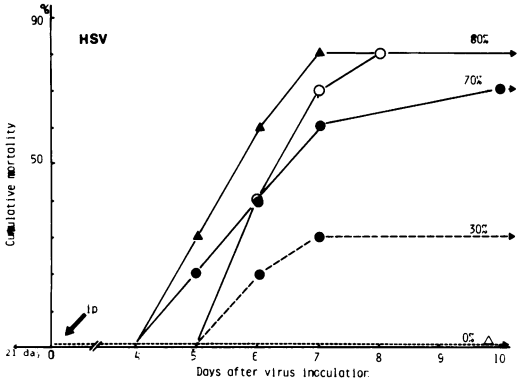

FIG. 2. *Effect of PCB ingestion on HSV infection in mice. Mice fed the diet containing 400, 200, 100, or 0 μg of PCB per g for 21 days were inoculated by HSV. P values were calculated by the Fisher exact test. P values among 400-, 200-, and 100- μg/g-fed mice and normal control mice infected with HSV were, respectively, <0.05, <0.05, and >0.05. Each experimental group consisted of 10 mice. ○——○, 400 μg/g; ▲——▲, 200 μg/g; ●——●, 100 μg/g; ●·····● virus control; △·····△, control. ip, Intraperitoneal inoculation.*

mice that were fed the PCB-free diet for 21 days were infected with EV, they all survived (Fig. 3). On the other hand, the mortality rate of EV-infected mice that were fed 400, 200, or 100 μg of PCB per g for 21 days was 50, 50, and 10%, respectively. The significant differences in mortality between mice given 400 or 200 μg of PCB per g and control mice were found by the Fisher exact test ($P < 0.05$) (Fig. 3).

However, there was no significant difference in the MDD between PCB-fed mice and control mice infected with EV by the Man-Whitney *U* test. When mice that ingested the diet containing 400, 200, or 100 μg of PCB per g were not inoculated with EV, they all survived (Table 1).

Thus, PCB ingestion increased the mortality rate of virus-infected mice. The mechanism of the decreased resistance to viral infection is not yet known. Some investigations show that PCB suppressed humoral immunity (4, 6, 7) and increased susceptibility to bacterial endotoxin (7). The authors examined the inducibility of interferon in mice given PCB to clarify the mechanism of decreased host resistance to viral infections and found that some heavy metals (2) and coal dust (3) depressed the inducibility.

We found that 100 μg of polyinosinic acid-polycytidylic acid induced about 500 IU of interferon per ml in the serum of control mice 3 h after administration, and the inducibility in mice fed PCB was not different from that of the

TABLE 1. *Effect of PCB ingestion on HSV and EV infection in mice*[a]

PCB (μg/g)	Cumulative mortality			
	HSV	Control	EV	Control
400	8/10	0/10	5/10	0/10
200	8/10	0/10	5/10	0/10
100	7/10	0/10	1/10	0/10
0	3/10	0/10	0/10	0/10

[a] Mice were fed the diet containing 400, 200, 100, or 0 μg of PCB per g for 21 days and inoculated with each virus.

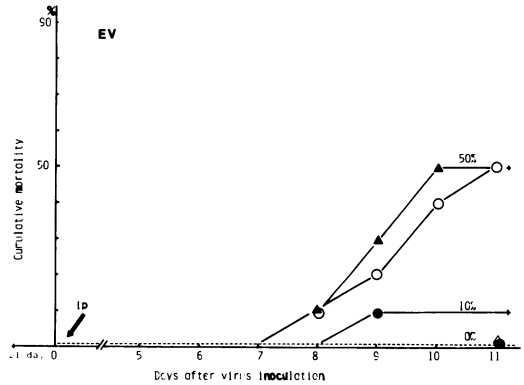

FIG. 3. *Effect of PCB ingestion on EV infection in mice. Mice were fed the diet containing 400, 200, 100, and 0 μg of PCB per g for 21 days and inoculated by EV. P values were calculated by the Fisher exact test. P values among mice given 400, 200, and 100 μg of PCB per g and normal control mice infected with EV were <0.05, <0.05, and >0.05, respectively. Each experimental group consisted of 10 mice. ○——○, 400 μg/g; ▲——▲ 200 μg/g; ●——● 100 μg/g; ●·····● virus control; △·····△ control. ip, Intraperitoneal inoculation.*

control mice.

At present, although the production and use of PCB is prohibited, it continues to remain in the world in the media of fishes and planktons, and humans are always in danger of being contaminated by it. It is important to examine the effect of PCB on host resistance to various infections and the mechanisms of response to PCB when it is habitually taken and accumulated in humans and animals.

We want to examine the effect of PCB on humoral and cellular immunity and on the functions of the reticuloendothelial system.

We are grateful to S. Nii, Department of Virology, Okayama University Medical School, Okayama, Japan, for supplying the herpes simplex virus and to S. Kato, Research Institute for Microbial Diseases, Osaka University, Osaka, Japan, for supplying the ectromelia virus used in this study.

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