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REDUCED RESISTANCE TO EXPERIMENTAL VIRAL AND BACTERIAL INFECTIONS OF MICE TREATED WITH POLYCHLORINATED BIPHENYL

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When mice given diet containing 100, 200 or 400 μ g of polychlorinated bipheynl (PCB) per g, or PCB-free diet for 21 days were inoculated intranasally with influenza virus, the mortality was higher in some groups given PCB than in the control group. When *Staphylococcus aureus* was inoculated intraperitoneally into mice given a diets with or without PCB, a significant difference was observed in the mortalities in the groups. Subcutaneous injection of *S. aureus* also caused a larger subcutaneous abscess in the mice given diets containing PCB than in those given control diet.

Thus, it is suggested that PCB ingestion reduces host resistance to systemic or local infection with viruses or bacteria.

Polychlorinated biphenyls (PCB) were widely used industrially for over 40 years. However, they are potent environmental pollutants, causing characteristic skin (Goto and Higuchi, 1969) and liver (Hirayama, Irisa and Yamamoto, 1969) diseases.

There are reports (Loose et al., 1977; Vos and van Driel-Grootenhuis, 1972; Thomas and Hinsdill, 1978) that PCB suppresses humoral and cellular immunity in various experimental animals and disturbs host resistance to viral, bacterial and protozoal infections (Loose et al., 1978; Friend and Trainer, 1970; Imanishi et al., 1980). Previously, we reported (Imanishi et al., 1980) that mice given diet containing PCB were significantly more sensitive than mice given PCB-free diet to Herpes simplex virus (HSV) and ectromelia virus (EV), which cause systemic infection and are

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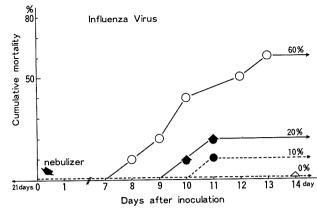


FIGURE 1. Effect of PCB on the mortality of mice infected with influenza virus. Mice were given diet containing 0, 100, 200, or 400 μ g of PCB per g for 21 days and then inoculated with influenza virus. The difference between the mortalities of the group given 400 μ g of PCB per g of diet and the control group was significant by Fisher's exact probability test (p<0.05: n=10). 0 μ g per g (virus-control) ($\bigcirc --- \bigcirc$), 0 μ g per g (dietcontrol) ($\bigcirc --- \bigcirc$), 100 μ g per g ($\bigcirc --- \bigcirc$), 200 μ g per g ($\bigtriangleup --- \bigstar$), 400 μ g per g ($\bigcirc --- \bigcirc$).

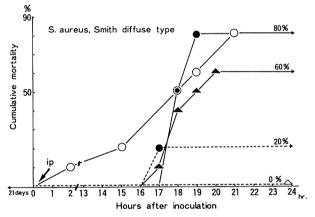


FIGURE 2. Effect of PCB on the mortality of mice infected with *Staphylococcus aureus*. Mice were given diets containing 0, 100, 200, or 400 μ g per g of PCB for 21 days and then inoculated with *S. sureus*. The differences between the mortalities of groups given diets containing 200 and 400 μ g of PCB per g and controls were significant by Fisher's exact probability test (p<0.05: n=10). 0 μ g per g (bacteria-control ($\bullet --- \bullet$), 0 μ g per g (diet-control) ($\Delta --- \Delta$), 100 μ g per g ($\bullet --- \bullet$), 200 μ g per g ($\Delta --- \Delta$), 400 μ g per g ($\bigcirc --- \circ$).

related mainly with cell-mediated immunity.

In the present study, we examined the effect of PCB on localized viral infection by influenza virus, which is related with IgAmediated local immunity, and bacterial systemic and local infections, which are related with humoral immunity and the function of polymorphonuclear leukocytes.

Influenza virus (AO/PR8, N0N1) was inoculated intranasally into 4-week-old ICR mice given a diet containing 100, 200 or 400 μ g of PCB (Kanechlor 500, Kanegafuchi Chemicals, Inc.) per g or PCB-free diet for 21 days. The mortality in the control group was 10%, while those in the groups given 100, 200 and 400 μ g PCG per g of diet were 10, 20 and 60%, respectively. The difference in the mortalities in the control group and the group given 400 μ g of PCB per g of diet was significant by Fisher's exact probability test (p< 0.05), but the differences between the mortalities in the other groups were not significant (Fig. 1). There was no significant difference in the mean survival times of mice given diets with and without PCB (data not shown). There was no death among the mice which were not inoculated with influenza virus, whether the diet contained PCB or not.

Next, Staphylococcus aureus (Smith strain, diffuse type) was inoculated intraperitoneally into mice given diets containing 100, 200 and 400 μ g of PCB per g and PCB-free diet for 21 days. Deaths occurred within 24 h with a peak at 16 to 18 h. The mortality of mice given PCB-free diet was 20%, while those of mice given diets containing 100, 200 and 400 μ g of PCB per g of diet were 80, 60 and 80%, respectively. The differences between the mortalities of mice on diets with and without PCB were significant (p<0.05) (Fig. 2).

The effect of PCB on local staphylococcal infection was then examined. *S. aureus* was inoculated subcutaneously into the mice given diets with and without PCB. An abscess formed at the site of injection within 48 h, and its size was measured by weighing the picture of the abscess projected onto paper. The sizes of the abscesses in mice on diets with and without PCB were significantly different (Fig. 3).

PCB is reported to suppress humoral and cell-mediated immunities (Thomas and Hinsdill, 1978; Vos and van Driel-Grootenhuis, 1972). However, little is known about whether PCB actually suppresses host resistance to various infections, although there are reports about its effects on systemic viral and bacterial infections in experimental animals (Thomas and Hinsdill, 1978; Friend and Trainer, 1970; Imanishi et al., 1980). In the present study, we confirmed that PCB also impairs host

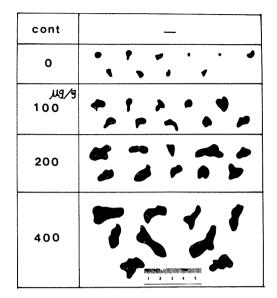


FIGURE 3. Effect of PCB on local staphylococcal infection in mice. *S. aureus* was inoculated subcutaneously into mice given diets with or without PCB. Abscesses formed at the site of injection were photographed and the projected pictures of the abscesses were drawn on tracing paper, cut out and weighed.

resistance to localized infections (both viral and bacterial) and systemic bacterial infection in mice. It is interesting that PCB promoted local viral and bacterial infections in mice, because this suggests that PCB influences various organs including the respiratory system and skin systemically. Furthermore, PCB may also impair various immune responses, including local immunity by secretory IgA and natural killer (NK) system, and nonspecific host resistance by macrophages and neutrophils, because protection against influenza virus is mediated mainly by IgA and NK cells, and that against staphylococcal infection is mediated mainly by neutrophils.

It is important to study the effect of PCB on host resistance to infections because PCB is still present in fish and shellfish although the production and use of PCB was prohibited 10 years ago. For this purpose, we are examining the the effect of PCB on the interferon system, NK activity, and humoral and cellular immunities, although previous studies showed that interferon induction by poly I: C in mice was not affected by diet containing PCB (Imanishi et al., 1980).

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