MONS 001361

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Myocarditis in Young Dogs due to Parvovirus

Sudden death in 25 of 31 puppies 4–6 weeks of age were reported. The pups were from five different litters and of various breeds and locations. Most puppies were found dead without previous signs of disease. Two pups experienced respiratory distress immediately prior to death.

Eleven of the 25 dead pups were necropsied. The lungs of the necropsied pups were edematous. Other gross lesions included pale hearts (9/11), right ventricular dilitation (8/11) and congested livers (4/11).

Histopathologically, all pups had a nonsuppurative myocarditis. The left ventricular wall and the ventricular septum were the most severely affected. Some myofibers contained large intranuclear inclusion bodies. These inclusion bodies were abundant in many of the pups but were difficult to find in others.

Electron microscopic studies revealed both low density and high density inclusion bodies which had fenestrae consistent with parvovirus particles. Fluorescent antibody test on one pup revealed specific labelling of myocardial nuclei in anti-canine parvovirus antiserum. Labeling frequency and patterns were consistent with the frequency of inclusions seen and with the distribution of particles within the nuclei.

Hoyer H A, Bemrick R G, Buhles L A: Sudden death in young dogs with myocarditis caused by parvovirus. *J Am Vet Med Assoc* 174: 1197 – 1200, 1979. Abstracted by L W Dixon.

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A Spontaneous Outbreak of Polychlorinated Biphenyl (PCB) Toxicity in Rhesus Monkeys (*Macaca mulatta*): Clinical Observations[1,2,3]

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Summary | A spontaneous, progressive disease occurred in a large domestic breeding colony of rhesus monkeys (*Macaca mulatta*). The disease was characterized by slow but continuous weight loss, alopecia, acne, facial edema, diarrhea and trauma from other monkeys. Breeding efficiency was impaired with a high incidence of abortions and stillbirths. Live offspring were small and unlikely survive, resulting in a high infant mortality rate. The cause of this disease was polychlorinated biphenyls (PCBs) which were present in the caulking material on the cage floors. Removing the caulked and resurfacing the floors alleviated the problem.

Key Words | Toxicology — Polychlorinated biphenyl — Signs and symptoms — *Macaca mulatta*

Polychlorinated biphenyls (PCBs) and other closely related chlorinated compounds have been in use in a variety of industrial processes since the 1930's. Polychlorinated biphenyls were recognized as major environmental contaminants in 1966 (1). Steps have been taken to restrict their usage to essentially closed systems such as transformers and hydraulic fluids. Polychlorinated biphenyls biodegrade poorly and are persistent in the environment (2). It is therefore essential to be aware of the signs associated with PCB toxicity since these signs are insidious and subtle, especially early in the disease.

This report describes the colony background and clinical course of an outbreak of PCB toxicity in a large breeding facility for rhesus monkeys (*Macaca mulatta*).

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the gastric lesions was not identified, and it was concluded that the changes were nonspecific and occurred spontaneously in most cases.

Most of the monkeys which had been used by IBFA were transferred to their new location. A group of 66 monkeys remained at Perrine, and an additional 100 rhesus monkey breeders from 1981 were added in 1980.

Clinical History

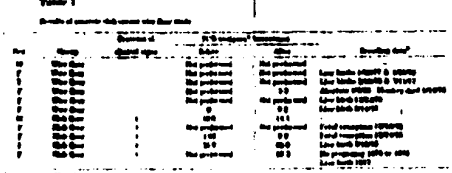
Remaining IBFA breeders. Since there was no reason to suspect an ongoing disease problem in the facility when IBFA operated control, the 66 remaining IBFA monkeys were assigned to breeding groups throughout the colony. At this time, all of the monkeys appeared clinically normal. Within 2 - 3 months after IBFA had emptied of the facility, many of these animals began to develop a variety of progressive clinical abnormalities including alopecia, photophobia, weight loss and intractable diarrhea. The monkeys seemed irritable and fought extensively. Within 6 months, 25 of the 66 monkeys died from diarrhea, pneumonia or trauma.

New IBFA breeders. Approximately 50% of the 100 rhesus monkey breeders from IBFA developed clinical signs resembling PCB toxicity (2) over the next 12 months. It was not possible to accurately determine the progression or sequential development of the clinical signs in these monkeys since the epidemic varied considerably in severity and time of onset from one building to the next. An additional diagnostic problem was that a major clinical sign was trauma. Since trauma was expected due to the establishment of new breeding groups, and the trauma made interpretation of the clinical picture more complex. An understanding of the clinical progression of the disease in the colony has been developed based on a retrospective analysis of the data and on experimental trial exposure of monkeys to one of the buildings.

Experimental Clinical Exposure

Based on an epidemiological analysis of affected monkeys, it was determined that several runs in one building were "hot" runs. That is, every monkey that had been in these runs developed severe clinical signs or had died. Since PCBs had commonly been added to concrete mixers in the 1920's, it was decided to test the hypothesis that the source of the contamination was the concrete floors. The following study was undertaken. In one of these runs (B-7), 25-cm pools of dishwashing water accumulated (5 cm above the concrete slab on floor) the monkeys could not contact the slab or reach liquids that fell through the wire. A new group of monkeys was obtained from the 1981 quarantine facility in Poolesville, Maryland. These monkeys never had been housed in any enclosures other than aluminum cages. A harem of three animals consisting of 1 male and 2 females was placed in this run in an adjacent run (B-8), all gutters were removed so that the monkeys had to sit on the concrete slab or all females from the same source was placed in this run. Adipose tissue biopsies (specimens were taken from selected animals before the study began and 3 months later. The results of this study, which are summarized in Table 1, indicated that the toxic substance was on the floor.

Table 1



Clinical Signs

Adults. The first clinical sign observed was a change in behavior. The monkeys became extremely irritable and aggressive. When the affected monkeys were approached by other monkeys they would scurry to the far recesses of the run. The most severely affected monkeys exhibited extreme apprehension of other monkeys but not human beings. This apprehension probably was the result of repeated attacks against these weak monkeys by the healthier ones. Recent studies have demonstrated a correlation between PCB burden and behavior in rhesus monkeys (4).

Photophobia developed in most affected monkeys, and it was accompanied by palpebral edema and crusty exudations at the margins of the eyelids. The combination of photophobia and palpebral edema caused the monkeys to squint, and the eyelids remained partially closed most of the time (Figure 1). The enlarged, lacrimose ducts of the Harderian gland visible upon eversion of the eyelids, were considered a classical sign of PCB intoxication in the colony. The edema was not limited to the eyelids and usually progressed to involve the entire face.

Figure 1
Severe palpebronasal edema, lacrimation in rhesus monkey. Observe swollen eyelids, closed eyes, alopecia of face, swollen earlobe and crusty exudation.



Alopecia was present in all affected monkeys. Beginning around the orbit and anterior part of the head, alopecia rapidly developed over the back, the lateral aspects of the legs and the ventral surface of the arms. Severely affected monkeys were almost hairless. Pruritus, which varied in intensity, usually was present in mild cases, the alopecia was not accompanied by other skin changes. As the disease progressed, the skin over the limbs and trunk became thinner and developed a cyanotic appearance. Facial skin developed severe acne especially around the eyes, mouth, cheeks and neck.

Dyschloric appeared especially around outer teeth, with resorption, inflammation and subsequent necrosis of the gums in a small number of monkeys. Teeth were easily removed in the more severely affected animals. The mandible appeared to be thickened, however, radiographic analysis showed this to be due to periosteum fibrous proliferation rather than osteodystrophy. Several animals developed a narrowing or constriction of the jaw.

Diarrhea developed in approximately 50% of affected monkeys in most cases it was transitory and responded to therapy. However, approximately 10% of these cases had recurrent bouts of diarrhea, many of which became intractable. The

MONS 001362

severely affected monkeys continued to lose weight and died despite vigorous symptomatic therapy. A unique feature of the disease was that the animals continued to eat normally. Even bald monkeys with severe diarrhea continued to eat until they were terminal.

A frequent and troublesome clinical problem was trauma. While some fighting was expected in breeding harems, the degree and severity of the trauma was excessive. It was not uncommon to find affected monkeys beaten to death by stronger cagemates.

The most frequent clinical signs observed during the *PCB outbreak in the colony* consisted of a change in behavioral characteristics: alopecia, photophobia, palpebral and facial edema, diarrhea, weight loss and trauma from the other monkeys. Other less frequent signs were gingivitis, osteomyelitis of the mandible, secondary pneumonia and encephalopathy.

Infants and neonates: Infants born to affected monkeys were generally weak and unthrifty. Many died soon after birth (Table 2). Those that survived developed clinical signs similar to those described for adults beginning at 10–14 days of age. It was assumed that the severity of the clinical signs varied depending on the mothers' PCB exposure. Milk levels of PCBs can be extremely high, and this was probably the major mode of PCB transfer to offspring (3). Many infants weighed less than 300 g at birth (normal = 450–500 g) and became hairless, stained, unthrifty animals. A small number of babies (approximately 4%) had "blond" hair.

Table 2

Breeding activity of the rhesus monkeys at the Primate Research Center*

	1976	1976	1977
Females of breeding age	751	630	683
Conceptions†	70	31	30
Pregnancy rate	9.3	4.9	4.4
Offspring born‡	60	30	9
		—	—

Breeding efficiency. Since the colony began with feral animals of unknown breeding background and the level of PCB exposure was not known for each animal, evaluation of the reproductive data is complicated.

pies. In evaluating trends over a 3-year period, the effects on reproduction were clear (Table 2). The cause of the disease outbreak (PCB) was not determined until late in 1975. Therefore, the breeding results for 1976 represent maximum colony exposure. The results for 1976 represent the carryover effect and those for 1977 a near normal control situation for the colony.

It became obvious from the data that PCBs usually did not affect male reproductive performance, breeding activity or conception rate. The effects were in abortions, stillbirths and neonatal deaths. The effect on reproduction was long term in the colony since PCBs are stored in adipose and other tissues and are excreted slowly by the body (3).

Source of the Contamination

An intensive search was conducted to determine the source of the PCBs after the results of the histopathology study became known. Analyses of the food, water and air were negative. Samples of the concrete slabs within several buildings were obtained and analyzed (8). Significant levels of PCBs (5280 mg PCB/g sample) were found in the "hot" runs where concrete sealant had been used. Since the PCBs were limited to the upper 0.78 mm of the concrete slabs, this layer was sandblasted off and each run was resurfaced with two coats of polyurethane sealant and one coat of epoxy sealant. This effectively removed the problem as evidenced by the lack of clinical signs and the reproductive performance in 1977.

Discussion

This is the first documented spontaneous outbreak of PCB toxicity in the rhesus monkey. The disease onset was insidious with vague clinical signs. The most common clinical signs (trauma, diarrhea and patchy hair loss) are commonly observed in large primate colonies. It was only the large number of cases, coupled with the high death rate and poor breeding efficiency which suggested toxicity as the source of the problem. The clinical features described in this outbreak have been experimentally reproduced (2,3,5,6). The chronological development of the clinical signs in the colony varied since the dose of PCBs and the exposure route were unknown. Based on the epidemiological and toxicological studies, the exposure to PCBs in our colony was probably through ingestion and percutaneous absorption. The practice of placing the feed on the concrete slab increased the risk of absorption into the feed and subsequent ingestion.

One of the buildings housed a breeding colony of 100 squirrel monkeys. While specific analyses for PCBs were not conducted in the squirrel monkey colony (1 out of 10 buildings), it was assumed that PCB residues also were present in that building. However, none of the squirrel monkeys developed clinical signs or pathological lesions associated with PCB toxicity. This observation is consistent with the previous report that a squirrel monkey which was given PCBs in the diet did not develop clinical disease or gastric hyperplasia (2). However, rhesus monkeys on similar regimen did develop toxicity. This points out the sensitivity of rhesus monkeys to PCBs.

This disease outbreak must also heighten an awareness of environmental factors and facility construction materials in animal housing areas. A suspected outbreak of PCB intoxication occurred in 1967 at the Oregon Regional Primate Center (7). The PCB outbreak in our facility and the other outbreak described above occurred in association with the construction of new facilities.

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Animal Model for Human Klebsiella Respiratory Infection

Because of the difficulty of clinical and biochemical studies in respiratory *Klebsiella pneumonia* infection in mice and rats, the squirrel monkey was selected as a model for study. Healthy juvenile male squirrel monkeys weighing from 0.5 to 1.0 kg were used. The organisms were administered intratracheally at a dose of 700 organisms per monkey. This dose was determined to be approximately one 50% lethal dose.

The clinical manifestations were fever, anorexia and coughing. Leukocytosis or leukopenia (with the latter more prominent in fatal infections), bacteremia and shedding of bacteria into the pharynx occurred. A lobar pneumonia developed by 24 hours. The mortality rate was 60% with the mean time of death 50.5 hours. The authors concluded that the squirrel monkey was a better model for human respiratory *Klebsiella pneumoniae* infection than rats or mice.

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MONS 001363