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Diagnosis and Physiologic Effects of Pentachlorophenols on Young Pigs. Part I. Effects of Purified Pentachlorophenol

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During the last few years an increasing number of cases of suspected pentachlorophenol (PCP) poisoning of farm animals have been brought to the attention of veterinarians and extension agents in the Mid-West. Diagnosis of PCP poisoning has been largely based on the statements of the farmers that the animals had been subjected to PCPs. Frequently the exposure was from buildings which had recently been treated with the wood preservative Penta. Later the animals had an unthrifty appearance, skin lesions and poor weight gains (THOMAS *et al.* 1977). Necropsy of these animals has not revealed signs that could be specifically attributed to the effects of PCPs. Analysis of plasma and tissues has not solved the diagnostic problem since it is not known what levels are associated with chronic effects. It is also known that commercial PCPs are contaminated with chlorodibenzo-p-dioxins and chlorodibenzofurans, some of which are more toxic than the PCPs (FIRESTONE *et al.* 1972, WOOLSON *et al.* 1972, SCHWETZ *et al.* 1973).

This study was initiated in hopes of finding clinical signs which could be correlated to overt signs of PCP poisoning. The first part of the study, with which this paper deals, was to determine the effects of purified PCPs on young pigs. The second part will compare the effects of purified and technical PCP and in the third part young pigs will be placed in pens treated with Penta wood preservative to determine if any clinical or overt signs of PCP poisoning occur.

METHODS AND MATERIALS

Twenty-four young pigs about 6 wk old were divided into 4 groups of 6 pigs each. Group 1, control, received a daily capsule of pure lactose. A pilot study with 4 young pigs indicated acute toxicosis at 30 mg/kg/day after 7 days so lower doses were used in this study. Groups 2, 3 and 4 received 5, 10 and 15 mg/kg body weight/day of purified PCP mixed with lactose for 30 days. Water and feed were given *ad libitum*. The animals were weighed and bled before the start of treatment and then weighed weekly and bled at the middle and end of the study. At necropsy liver, kidney, spleen, brain and muscle were removed for light microscopy examination.

All tissues and plasma were analyzed for PCPs using the method of HOBEN *et al.* (1976). Recovery studies of PCP in fortified tissues and plasma ranged from 93 - 100%. Analysis for contaminants in the purified PCP showed 4.7% of tetrachlorophenol and 3.2 ppm

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total of octachlorodibenzodioxins and furans. Method of analysis of dioxins and furans was that of BUSER (1975). Analysis of the same lot of PCP by Dow Chemical Co, Midland, Michigan gave 0.98% tetrachlorophenol and 0.4, 3.6 and 2.4 ppm, respectively, of combined hexa-, hepta- and octachlorodibenzodioxins and furans (personal communication). This laboratory was unable to analyze for the lower chlorinated dioxins and furans and Dow Chemical did not report the presence of the extemely toxic 2,3,7,8-tetrachlorodioxin or furan.

Methods of determination of blood chemistries are given in GREICHUS & HANNON (1973). Tissues for light microscopy were fixed in 10% buffered formalin, embedded in paraffin, sectioned at 6 µm and stained with hematoxylin and eosin or other appropriate stains.

All statistical analyses were performed employing a one way analysis of variance in conjunction with Dunnett's test.

RESULTS AND DISCUSSION

There were no significant differences between the PCP treated groups and the controls in total weight gains, kg of feed consumed per kg of weight gain or weight of kidneys in g/kg body weight (Table 1). The 10 and 15 mg/kg groups had significantly larger livers on a g/kg body weight basis than the controls ($p < .01$). KIMBROUGH & LINDER (1975) reported enlargement of livers in rats fed 1,000 ppm of pure PCP for 3 mo, with enlarged hepatocytes and inclusions in the cytoplasm of many cells.

TABLE 1

Total Weight Gains, Feed Consumed/Gain and Weight of Kidney and Liver per Kg Body Weight of PCP Treated and Control Pigs

Treatment	Total Weight Gain-Kg	Kg Feed Consumer per Kg Weight Gain	g Kidney per Kg Body Weight	g Liver per Kg Body Weight
Controls [a]				
Means	5.81	2.82	5.57	32.3
S.D.	±2.81		±0.43	± 0.90
5 mg/kg				
Means	6.98	2.38	5.05	31.8
S.D.	±1.16		±0.57	± 4.06
10 mg/kg				
Means	7.00	2.46	4.91	38.4 [b]
S.D.	±1.21		±0.23	± 1.95
15 mg/kg				
Means	5.70	2.48	5.69	38.0 [b]
S.D.	±2.11		±0.41	± 2.08

a - Six pigs per group.
b - Significantly different from control ($p < .01$).

Levels of PCPs in the blood, muscles, kidneys and livers did not appear to increase with increase of treatment (Table 2). The plateauing of PCP levels in the blood, muscle, kidneys and livers was unexpected. ZUMWALT *et al.* (1977) dosed 3 non-lactating dairy cows with capsules daily for 14 days and found average plasma levels for the three groups after 14 days of 69, 430 and 2,000 ppb, respectively. It appears that young pigs either more readily absorb or do not eliminate ingested PCP in the same manner as cows. Rats given a single oral dose of radioactive (^{14}C) PCP at 10 mg/kg eliminated 90+% of the radioactivity with a half-life of 17 h for males and 13 h for females. Elimination was primarily via the urine (BRAUN *et al.* 1975). In this study PCP levels increased only slightly in the plasma between the 15 day and the final 30 day bleeding (Table 2).

TABLE 2

PCP Values (ppm wet weight basis) in Blood and Tissues of Treated and Control Pigs

Treatment	15 Day Bleeding	30 Day Bleeding	Muscles	Kidneys	Livers
Controls [a]					
Means	0.53 [b]	0.74 [b]	0.19 [b]	0.21 [b]	0.54 [b]
S.D.	± 0.27	± 0.19	± 0.13	± 0.07	± 0.12
5 mg/kg					
Means	62.9	78.1	6.74	22.0	28.9
S.D.	± 8.81	± 5.28	± 0.98	± 3.16	±10.7
10 mg/kg					
Means	64.1	67.6	7.75	25.2	26.1
S.D.	± 6.14	±12.6	± 1.04	± 4.20	± 1.89
15 mg/kg					
Means	71.5	77.0	8.88	26.6	28.8
S.D.	± 3.92	±12.7	± 1.36	± 3.27	± 4.65

a - Six pigs per treatment group.
b - Significantly different from all PCP treated groups ($p < .01$).

Blood chemistry values for the 15 day and 30 day bleedings are given in Table 3 for the controls and PCP treated groups. No significant differences were found for either bleeding between the controls and treatment groups or between PCP treated groups for packed cell volume (PCV, %), hemoglobin (HG, g/%), serum protein (g %), serum glutamic oxalacetic transaminase (SGOT, International Units per Liter - IU/L), and lactic dehydrogenase (LDH, IU/L). The white blood cell (WBC) counts were lower in the 15 mg/kg group than the controls at the 15 day bleeding and lower for the 10 and 15 mg/kg groups than controls at the final bleeding. The normal range of WBC's for adult pigs is 11 - 32 $X10^3/mm^3$ (KANEKO 1973) so although significantly affected groups were still within the normal range, they were near the lower limits.

TABLE 3. Blood Chemistries of PCP-Treated and Control Pigs

Treatment	Day	Type of Analysis [a] PCV	HB	WBC	Serum Protein	SGOT	LDH	BUN
Control	15							
Means		33.0	13.3	17.6	4.61	60.0	64.6	10.3
S.D.		± 4.30	± 1.69	± 1.01	±0.39	±17.1	±25.4	± 2.37
5 mg/kg	15							
Means		31.6	13.0	13.4	4.26	70.3	76.6	10.8
S.D.		± 2.19	± 0.89	± 3.54	±0.35	±27.7	±38.1	± 1.43
10 mg/kg	15							
Means		29.7	13.3	12.4	4.41	55.7	58.3	17.5 [b]
S.D.		± 1.96	± 0.57	± 4.71	±0.43	±10.9	± 7.07	± 3.59
15 mg/kg	15							
Means		28.8	12.7	10.9 [c]	4.23	66.6	56.2	20.4 [b]
S.D.		± 2.63	± 1.02	± 2.25	±0.27	± 9.73	±14.6	± 4.66
Control	30							
Means		31.2	13.4	23.1	5.78	52.9	85.0	20.9
S.D.		± 4.30	± 3.30	± 5.79	±0.57	±20.0	±28.6	± 6.84
5 mg/kg	30							
Means		31.7	13.5	16.9	5.83	44.8	74.6	21.7
S.D.		± 1.90	± 1.81	± 2.61	±2.15	±12.3	±14.4	± 4.60
10 mg/kg	30							
Means		30.6	12.5	13.2 [b]	4.76	41.3	61.7	22.2
S.D.		± 2.10	± 0.92	± 1.90	±0.20	±18.4	±25.0	±11.4
15 mg/kg	30							
Means		31.2	12.5	13.3 [b]	5.03	31.5	65.4	32.1
S.D.		± 2.40	± 1.30	± 3.12	±0.23	± 4.88	± 8.78	± 9.23

a - Explanation of types of analysis and measurement units given in text.
b - Significantly different from controls ($p < .01$). c - Significantly different from controls ($p < .05$).

At the 15 day bleeding the blood urea nitrogen (BUN, mg%) values of the 10 and 15 mg/kg groups were significantly higher ($p < .01$) than the controls (Table 3). The 15 mg/kg group continued to show this trend at the final bleeding.

The only histopathologic finding observed in the PCP treated pigs was a nonspecific diffuse cloudy swelling of hepatocytes, characterized by enlarged cells which had a finely vacuolated cytoplasm. Sinusoids in some cases were decreased in size, presumably due to encroachment by enlarged hepatocytes.

It was concluded from this study that pigs treated with purified PCPs at 5, 10 and 15 mg/kg/day showed no overt signs of toxicosis. Clinical pathological signs of treated pigs at the 10 and 15 mg/kg level included significantly large livers, lower WBC and higher BUNs, than the controls. Levels of PCPs in the blood, muscles, kidneys and livers did not increase as treatment level was increased from the 5, 10 and 15 mg/kg. The enlargement of the liver may have been due to an enlargement of hepatocytes.

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