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ABSTRACT: PATHOBIOLOGICAL RESPONSES OF PRIMATES TO POLYCHLORINATED BIPHENYL EXPOSURE

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Male and female rhesus monkeys received varying levels of polychlorinated biphenyls (PCBs) and were evaluated for toxic effects, reproductive dysfunctions and metabolism of the compounds. Female rhesus monkeys exposed to PCBs (Aroclor 1248) at doses ranging from 25 to 300 ppm of the diet developed facial acne, erythema, subcutaneous edema, conjunctivitis and loss of eyelashes. Within 2 to 3 months, the majority of the animals had died or were moribund. Terminally, they developed anemia, anorexia, hyproteinemia, and hypolipidemia. Severe gastric mucosal hyperplasia and ulceration were present at autopsy. Surviving animals from the group that received 25 ppm for 2 months continued to have detectable levels of PCBs within their tissues, were devoid of eyelashes, and manifested facial erythema two years following the exposure period.

Female rhesus monkeys exposed to dietary levels of 2.5 and 5.0 ppm of PCB developed facial lesions within 2 months. Irregularities of the menstrual cycles were noted within 4 months. After 6 months exposure the animals were mated with control males. Six of the eight females on the 5.0 ppm diet conceived; the remaining two animals continued to cycle and were mated five times without conceiving. Five of the six animals that conceived aborted or experienced early fetal resorption. Eight out of eight females on the 2.5 ppm diet conceived; however, 3 of the 8 females did not carry their infants to term. The six infants born to the PCB-fed females were small (350 g vs. 475 g) and displayed areas of cutaneous hyperpigmentation. Skin biopsies obtained shortly after birth contained PCBs. As a result of exposure to PCBs through the lactating mothers, the PCB levels of the infant tissues increased rapidly. Within 2 months the infants developed conjunctivitis, periorbital edema, loss of eyelashes and acne. Three infants expired within 4 months following birth. The surviving 3 animals were weaned and showed decreased severity of symptoms after 4 months on a milk supplement diet free of PCBs.

In contrast to the severe effects of low PCB exposure experienced by female rhesus monkeys, male monkeys tolerated 5.0 ppm PCBs as a dietary additive for one year without showing signs of severe intoxication. In addition, these males demonstrated no reproductive abnormalities.

Dietary PCBs (Aroclor 1248) were absorbed from the gut and distributed in the body tissues of the rhesus monkeys with highest concentrations being in the adipose tissue and liver. The levels in the adipose tissue of males receiving 5 ppm and of females receiving 2.5 ppm continued to increase through 14 months of exposure. Levels in the adipose tissue of females receiving 5ppm reached a maximum level of 75 to 100 ug per g at 9 months. Following removal of the PCBs from the diet, the concentration of the material decreased from the adipose tissue with a half-life varying between three and four months. Gas chromatographic patterns of the adipose and hepatic tissues demonstrated the persistence of the more highly chlorinated PCB isomers and near absence of the lower chlorinated isomers.

Over 90% of an oral dose of a single PCB isomer labeled with tritium (^{3}H 2,5,2',5'-tetrachlorobiphenyl) administered to infant or juvenile rhesus

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monkeys was absorbed from the gastrointestinal tract and was most highly concentrated in the adipose and hepatic tissues. After one week, 12% of the dose given to a female juvenile monkey was excreted into the bile. Approximately 50% of the biliary material was reabsorbed by the gut as only 6% of the total dose was recovered from the feces during this period. The majority of the biliary material was in the form of a water soluble glucuronic acid conjugate. An additional 8% of the dose was recovered from the urine. Urinary metabolites consisted of monohydroxylated and dihydroxylated tetrachlorobiphenyls, trans-3,4-dihydro-3,4-dihydroxytetrachlorobiphenyl and hydroxy-3,4-dihydro-3,4-dihydroxy tetrachlorobiphenyl.

Single doses of tritiated 2,4,5,2',4',5'-hexachlorobiphenyl administered to juvenile monkeys were concentrated in adipose and hepatic tissues. The material was excreted at a much lower rate than that for the tetrachlorobiphenyl.

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ABSTRACT: TOXICOLOGY OF SELECTED SYMMETRICAL HEXACHLOROBIPHENYL ISOMERS: BIOLOGICAL RESPONSES IN CHICKS AND MICE

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One-day-old cockerels were fed: (I) 3,10,30,100, and 300 ppm of 3,4,5,3', 4',5'-hexachlorobiphenyl (HCB); (II) 400 ppm of 2,3,4,2', 3',4'-HCB; (III) 400 ppm of 2,4,5,2',4',5'-HCB; (IV) 400 ppm of 2,3,6,2',3',6'-HCB; and (V) 400 ppm of 2,4,6,2',4',6'-HCB. Surviving chicks were sacrificed at 21 days. Male mice were fed 10, 30, 100, and 300 ppm of three of the above isomers (I, III, V), and survivors were sacrificed at 28 days. HCB's levels in adipose tissue and livar were determined. There were variations among the isomers as to dose and pathologic effects. Isomer (I) showed the greatest effect of those studied on mortality, body weight gain, liver, thymus, and spleen; it also attained the highest tissue concentration. It was the only isomer which produced porphyrin accumulation; and, in the chicks, produced hydropericardium, ascites, and edema. The decreasing order of overall toxicity was I >> V > II, III, IV. A general similarity of response was observed in both chicks and mice.

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ABSTRACT: PRODUCTION AND USAGE OF PCBs IN THE UNITED STATES

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About 99 percent of the PCBs used in U.S. industry are produced by Monsanto in a single facility at Sauget, Illinois. These materials, termed Aroclors^{R}, are used in the production of capacitors (70 percent) and transformers (30 percent). Imported PCBs, comprising slightly over one percent of U.S. usage, are used in investment casting operations (80-90 percent; decachlorobiphenyl) and semi-closed heat transfer applications (10-20 percent). Capacitor and transformer production processes are similar in that process steps involving PCBs include filtration, flood or individual filling of the products, and removal of excess PCBs prior to sealing and individual testing of the products. Most losses occur from pump leaks to cooling water, spills, personal hygiene practice, and the like. Many of the discharges containing PCBs are to municipal sewers.

ABSTRACT: PCB CHLORINATION VERSUS PCB DISTRIBUTION AND EXCRETION

AUTHORS: M. Anderson and H. B. Matthews, Ph.D., National Institute of Environmental Health Sciences, Research Triangle Park, N. C.

The distribution and excretion of selected ^{14}C-labeled polychlorinated biphenyls (PCBs) were studied in the male rat. The distribution and excretion of each of the PCBs was studied after either i.v. or oral administration. Following administration, each of the PCBs was rapidly removed from the blood and stored in the liver and muscle. The rates of PCB redistribution from liver and muscle to skin and adipose tissue and/or elimination in urine was related to the degree of chlorination. The subsequent rates of PCB removal from skin and adipose tissue, excretion in urine and total excretion were related to the degree and position of chlorination of the biphenyl molecule. None of the PCBs studied were excreted to a significant extent prior to metabolism to more polar compounds. It appears as if the degree and position of chlorination controls the rate of metabolism. The limiting factor may be the facility of arene oxide formation as metabolic intermediates. The toxicologic implications of arene oxide formation versus PCB accumulation in animal tissues are discussed.

ABSTRACT: INPUTS AND DISTRIBUTIONS OF POLYCHLORINATED BIPHENYLS IN THE SOUTHERN CALIFORNIA MARINE ENVIRONMENT

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A number of potential anthropogenic sources of polychlorinated biphenyls (PCBs) were identified and their inputs quantified. Submarine discharge of municipal wastewater has been the dominant source of PCB to the marine environment off southern California. However, the level of input from this source has steadily decreased during the period 1972 (> 19,000 kg/yr) to 1975 (2,600 kg/yr). Dry aerial fallout also appears to be an important source, and if wastewater inputs continue to decrease, fallout will probably become the dominant input mode of the future. Surface runoff is of secondary importance, and inputs from direct industrial discharges and vessel antifouling paints are insignificant.

Despite the significant decrease in the municipal wastewater input, no significant decrease was observed over the 3 year period 1971-72 to 1974-75 in the level of PCB in muscle tissue of Dover sole, Microstomus pacificus, collected from throughout the Southern California Bight. In contrast, similar surveys of the intertidal mussel, Mytilus californianus, indicated that the PCB levels in this marine organism has significantly decreased over the same time period.

Bight-wide surveys of M. californianus and the yellow rock crab, Cancer anthonyi, indicate that PCB contamination of these marine animals is low but widespread. Levels of PCB in the harbor mussel, M. edulis, were highest in specimens collected from areas of intense vessel activity.

ABSTRACT: TOXICOLOGY OF SELECTED SYMMETRICAL HEXACHLOROBIPHENYL ISOMERS: CORRELATING BIOLOGICAL EFFECTS WITH CHEMICAL STRUCTURE

AUTHOR: James D. McKinney, Ph.D., National Institute of Environmental Health Science, Environmental Protection Agency, Research Triangle Park, N. C.

The symmetrical hexachlorobiphenyls (HCBs) represent model PCBs with high and constant chlorine content permitting unequivocal study of a given substitution pattern. These isomers show separate and distinct biological responses which can be related to chemical structure via effects on compound lipophilicity and metabolism. Compound purity must also be assured. Relative molecular polarizability can be correlated with lipophilicity and biological activity and is measurable by chromatographic and spectroscopic techniques. These parameters were highest in HCBs with planar symmetry and 4,4'-substitution. The rates of metabolism of these isomers are considered of lesser importance than the potentially highly toxic nature of some of the intermediary and terminal metabolites such as chlorinated dibenzofurans.

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ABSTRACT: TRANSPORT OF CHLORINATED HYDROCARBONS THROUGH THE UPPER CHESAPEAKE BAY

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Under contract to the Maryland State Department of Natural Resources, the staff of the Westinghouse Ocean Research laboratory (together with subcontractors at Johns Hopkins University and the University of Maryland) recently completed the Upper Bay Survey - a program having as the central task the study of the routes, rates, sources, sinks and reservoirs of chlorinated hydrocarbons (CHC's) in the upper Chesapeake Bay. Data from the field portion of this program will be presented; in particular, the levels of PCB's, chlordane and DDTR found in bottom sediments, suspended particulates, zooplankton, and shellfish will be summarized. The discussion will include the role of sediment deposits as traps for CHC's; suspended particulates as transport vehicles for CHC's; movement of CHC's from the suspended particulate reservoir into the biological system, particularly shellfish and zooplankton; and the sources of CHC's in the upper Chesapeake Bay.

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