The Effects of Paraquat on Neonatal Rat Lung: A Histological and Biochemical Study

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Abstract. The effects of paraquat on morphological, histological, and biochemical parameters in neonatal rat lung were studied. One-day-old rat pups were injected (IP) with 25 mg paraquat per kg body weight and sacrificed after 24 hr. At the end of the experimental period, the body weight in control and herbicide-treated animals slightly increased and decreased, respectively. The lung weight in the paraquat group was not significantly lower than those of the control. Histologically, the lungs from the paraquat group showed an increase in the thickness of the alveolar wall with much intra-alveolar infiltration of cells and cell debris. In the paraquat-treated group, while the total lung protein increased by about 18%, the enzyme phosphatidic acid phosphatase activity was reduced nearly 30%. These results indicate that paraquat induces both histological and biochemical changes in the neonatal rat lung.

Paraquat (1,1'-dimethyl-4,4' bipyridinium dichloride) is a general weed killer of the bipyridyl family of herbicides; it accumulates in greater concentration in the lung tissue (Rose and Smith 1977). Such an uptake by this tissue has been shown to be energy dependent. Other organs such as brain, kidney, liver, adrenal, muscle, and plasma accumulate paraquat to a lesser degree.

Toxicological studies with paraquat (see recent review, Haley 1979) after either accidental poisoning (Dasta 1978; Bullivant 1966; Duffy and O'Sullivan 1968; Masterson and Roche 1970; Almog and Tal 1967; Vijeyaratnum and Corin 1971; Heath and Smith 1977) or experimental administration of the chemical to rats (Greenberg et al. 1978; Malmquist et al. 1973; Fisher et al. 1973; Clements 1973) have shown that many of the histological and biochemical changes in the lung tissue were similar in nature.

Following is a brief summary of the observations reported by the investigators mentioned above. At the light microscopic level, 24 hr after paraquat administration, there was mild, acellular perivascular edema with little alveolar edema and no alveolar infiltration. On day 2 there was still little alveolar or...
interstitial edema, but some alveolar infiltration with macrophages and mononuclear cells was seen. Collagen, visualized by van Giesen's stain, exceeded the normal amount two or three days after injection. By day 6 however, there was much alveolar infiltration and heavy collagen staining.

Many biochemical changes have been observed after experimental treatment with paraquat, such as, reduction in total phospholipids specifically in anenoic lecithins in lung homogenates and alveolar washings, and increased collagen synthesis by lung slices in vitro. The first observation indicated that since lecithin is a major constituent of pulmonary surfactant, paraquat, in some way, interfered with the synthesis of this essential component of the lung tissue. Fisher et al. (1975) have reported that one day after the administration of 27 mg per kg to rats, lung surfactant showed a reduction.

Lung tissue has the ability for de novo lecithin synthesis (Farrell and Avery 1975). One of the most important precursors of lecithin and all glycerolipids is 1,2-diacylglycerol (diglyceride). This molecule is formed by the enzymatic hydrolysis of phosphatidic acid by phosphatidic acid phosphatase (PAPase). Because of its importance as a key intermediate for glycolipid synthesis, an adequate supply of diacylglycerides must be maintained. PAPase activity has been shown to increase significantly after birth in rats (Maniscalco et al. 1978). Since paraquat selectively disrupts the surfactant-secreting Type II epithelial cells, it was of interest to determine whether or not there are enzymatic changes in PAPase which are important for surfactant biosynthesis.

In view of the above, and as all of the studies have been carried out in adults, it was of interest to investigate morphological, histological, and biochemical changes in the lung tissues of neonatal rats treated with paraquat.

Materials and Methods

Animals

Sprague-Dawley rats were housed in clear plastic cages and given Wayne's laboratory food chow and water ad libitum. Pregnant rats were obtained by mating two females and one male in a single cage; the females were weighed every three or four days until a gradual increase in body weight was observed. Pregnant females were identified and were isolated in single cages. The animals were checked once in the early morning and once in the late afternoon for delivery of the pups. Shortly after birth, the pups were weighed and treated with either paraquat or with 0.9% saline.

Paraquat Experiment

Paraquat was purchased from Aldrich Chemical Co., as methyl viologen and dissolved in 0.9% saline at a concentration of 3 mg/ml. A dosage of 25 mg/kg body weight (in approximately 50 μl of medium) was administered intraperitoneally to each pup. The treated pups were returned to the mother’s cage to nurse for twenty-four hr, at which time they were weighed and sacrificed by cervical dislocation.

Tissue Preparation for Analysis

The animal’s chest was quickly opened, the trachea, heart, and thymus removed, and the lungs teased away from the connective tissue and diaphragm. Some lung tissue from each group was fixed in Bouin’s fixative and processed for light microscopy. Tissues for protein and enzyme