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Renal handling of Paraquat

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Paraquat (PQ) is a widely used herbicide, with the systematic name 1,1′-dimethyl-4,4′-dipyridylium dichloride. Experiments with animals have shown that it exists as the cation at physiological pH and that there is no appreciable degree of binding to plasma proteins (Daniel, personal communication).

We have been examining the renal handling of PQ, using adult male beagle dogs (Alderley Park strain) anaesthetized with pentobarbitone (30 mg/kg i.v.). In clearance studies, PQ was infused intravenously with inulin and *p*-aminohippurate (PAH) during water, saline or mannitol diuresis. Urine and plasma samples were analysed for PQ, inulin, PAH, urea, osmolality, sodium, potassium, calcium and magnesium, and the respective clearances calculated.

Initial experiments showed that there was net reabsorption of PQ in the kidney, the percentage reabsorption of filtered PQ varying from 35 to 65%. The PQ clearance was independent of plasma concentration over the range 10–150 μg/ml and, in most experiments, varied directly with urine flow. Ratios of the concentration of urine to plasma were never less than unity, but could approach this value at high urine flow rates, suggesting that passive diffusion was responsible for the reabsorption.

Further evidence against an active process for PQ reabsorption derives from experiments with diuretics (ethacrynic acid and mersalyl), where the increased clearance of PQ may be explained by postulating that the rate of diffusion of PQ may be decreased by other solutes, for example electrolytes (Giotti & Maynert, 1951). In two experiments, however, the substitution of *iso*-osmotic NaCl solutions for hypertonic mannitol infusions, which reduced urine flow and total solute output, unexpectedly increased the percentage excretion of PQ. These results are unexplained.

In an attempt to localize the site of PQ reabsorption, stop-flow experiments were carried out according to the technique of Malvin, Wilde & Sullivan (1958). The results indicated that PQ is reabsorbed in the proximal half of the nephron. There was no indication of any secretory component. The parallel rise in PQ concentration and urine osmolarity seen in distal samples suggests that this tubule segment is relatively impermeable to PQ.

Thus we conclude that PQ is reabsorbed in substantial quantities in the dog kidney, and this reabsorption probably occurs in the proximal tubules and that, while conclusive proof has not been presented to eliminate an active reabsorptive component, most results can be adequately explained by passive diffusion.

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