Removal of Blood Ammonia by Hemodialysis.* (22302)

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(Introduced by Matthew N. Levy.)

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In this communication we wish to report our experience with hemodialysis performed on dogs with raised blood ammonia values.

The use of portacaval shunts for portal hypertension and the use of cation exchange resins have presented problems in ammonia metabolism resulting in a considerable revival of interest in the metabolism of amino acids and ammonia in liver disease(1,2). Many patients in hepatic coma and acute liver failure have demonstrated an increase in the value for ammonia in the blood(3). Elevated blood ammonia values have been found and also induced in some patients with portacaval shunts (anastomosis of the portal vein to the vena cava)(1). It seemed of interest therefore to see whether the Kolff artificial kidney would reduce the values for blood ammonia in patients and in experimental animals.

Materials and methods. A number of dogs have been subjected to hemodialysis using a modified Kolff dialyzer. Mongrel dogs weighing from 10 to 20 kg were prepared by producing an end to side portacaval shunt. The "meat intoxication" syndrome was induced by feeding of meat and urea as described by Riddell(4). Eight dogs with an elevated blood ammonia level and "meat intoxication" manifested by lethargy, blindness, ataxia, catatonia, or convulsions were treated with the artificial kidney for 3 hours using a flow of 100 ml per minute and a dialyzing surface of about 12,000 cm^2. Blood ammonia, measured by the microdiffusion technic of Conway (5) utilizing a 10 minute diffusion time(6), was measured at the beginning of the cellophane loops used for dialysis and 2 minutes later at the end of these loops, the determinations were made intermittently during the period of dialysis for the purpose of evaluating the rapidity of removal of blood ammonia.

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Results. Percent removal of blood ammonia under these circumstances has been plotted against arterial concentration. (Fig. 1). It can be seen that blood ammonia concentration has been generally lowered by 50% during one passage through the artificial kidney with a tendency toward higher percentage removal with higher blood concentrations. The total amount of blood ammonia removed was estimated by multiplying the amount removed per milliliter of blood by the volume of blood dialyzed for successive twenty minute periods throughout the dialysis. This total amount removed was found to vary in 4 dialyses from 15,000 μg to 130,000 μg. When approximately 25,000 μg of blood ammonia had been removed, ammonia became detectable in the 100 liters of bath fluid used. No ammonia was ever detected in the bath fluid at the start of dialysis. The dif-

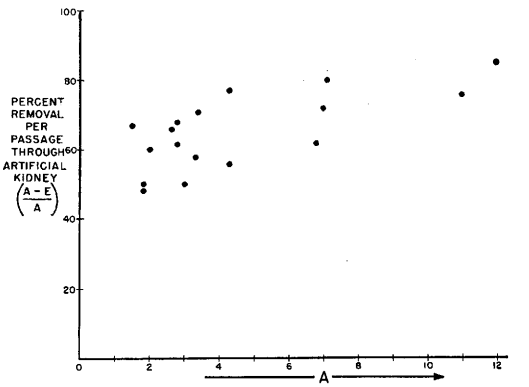

FIG. 1. Removal of ammonia from blood during one passage through a Kolff artificial kidney. Graph indicates % ammonia removed from blood of experimental animals with elevated values for blood ammonia. Note that the higher the value for blood ammonia the greater the extraction by dialysis. Normal value for blood ammonia in dogs is usually under 1 μg/ml. (Flow—100 ml/min.; dialyzing surface—approximately 12,000 cm^2.) (At a flow of 100 ml/min., clearance in ml/min. by the artificial kidney is numerically equal to percent removal.)

fusion of ammonia out of the bath fluid into the air however, may make erroneous an estimation of ammonia removal based on the amount of ammonia in the bath fluid. No fall in blood ammonia was noted on passage of blood through the artificial kidney if the cellophane loops were not immersed in the bath fluid. In fact a small but definite rise in blood ammonia was noted under these circumstances. Normal dogs without portacaval shunts when subjected to hemodialysis in the same manner as those with meat intoxication did not show any appreciable elevation of ammonia in the blood entering or leaving the kidney.

Comment. The invariable lowering of blood ammonia concentrations during passage through the artificial kidney and the appearance of ammonia in the bath water as dialysis proceeded indicated to us that hemodialysis removed blood ammonia in dogs with elevated blood ammonia levels.

We are presently using this method of removing blood ammonia to study certain aspects of liver disease. Whether hemodialysis may have any clinical value in the treatment of hepatic coma is also being investigated.

Summary. Blood ammonia, as measured by the microdiffusion technic of Conway, is removed efficiently from the blood of dogs with elevated blood ammonia levels by a Kolff type artificial kidney with a dialyzing surface of 12,000 cm^2. When flow through artificial kidney is 100 ml/minute the clearance of blood ammonia varies from about 50 ml/minute at lower arterial concentrations of blood ammonia to about 80 ml/minute at higher arterial concentrations.

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Hypothalamic Stimulation of ACTH Secretion. (22303)

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It has been shown that antidiuretic and oxytocic hormones of the hypothalamic-posthypophyseal system* may stimulate the anterior lobe of the pituitary gland to discharge ACTH. It has been demonstrated that these hormones produce, when injected into normal animals, significant fall of circulating eosinophils(2), adrenal ascorbic acid (3) and cholesterol(4); these actions which have not been observed in hypophysectomized animals(3,4), are apparently due to stimulation of the adenohypophysis. Release of ACTH occurs also in hypophysectomized rats bearing a hypophyseal graft in the anterior chamber of the eye after local injection of small amount of posterior pituitary hormones into the subconjunctival space(5). This observation rules out the possible participation of a "stress" reaction in the ACTH-releasing power of posterior pituitary hormones. These results are in agreement with the hypothesis(2-6) that hormones produced in the hypothalamic nuclei may act as neurohumoral agents in the hypothalamic control of the activity of the anterior lobe of the pituitary gland.

* There is much positive evidence to support the view that "posterior pituitary hormones" are produced by cells of the nuclei supraopticus and paraventricularis and pass along the axons of the tractus supraoptico-hypophyseus into the posterior lobe which serves as a storage-release center(1).