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Cadmium-induced changes in renal hemodynamics in the domestic fowl

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Summary. Low i. v. doses of cadmium chloride (15 µg Cd) given to pullets resulted in a significant reduction in urine flow (UF), glomerular filtration rate (GFR) and effective renal plasma flow (ERPF). However, in hens treated with the heavy metal chelate FeNa EDTA prior to cadmium treatment no oliguria or reduction in GFR or ERPF was observed.
It is suggested that the renal changes following the i. v. administration of cadmium to diuretic hens and alleviated in hens primed with the heavy metal chelate may result from changes in glomerular hemodynamics.
Key words. Glomerular filtration rate; effective renal plasma flow; FeNa EDTA chelate.

Long term exposure of humans and mammals to cadmium leads to profound changes in renal function[1]. In the present study we have investigated the short term effects of cadmium on renal homeostatis by monitoring glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) in pullets.

Twelve Rhode Island Red Cross Light Sussex hens of approximately the same age (14 weeks) and average weight (1.3 ± 0.2 kg) were used in this study. One group of birds was treated with cadmium and a second group was infused over the experimental period (1.5 h) with a heavy metal chelate, the ferric sodium salt of ethylene diamine tetra-acetic acid (FeNa EDTA), and then injected with cadmium.

The left brachial vein of each hen was cannulated for the continuous infusion (0.5 ml/min^{-1}) of isotonic saline solution (0.93% NaCl) containing an admixture of inulin (0.25%), para-amino hippuric acid (0.025%), and mannitol (10%). After establishing an adequate rate of urine flow local anesthetic (xylocaine) was applied around the cloaca prior to cannulation of the ureters of each hen.

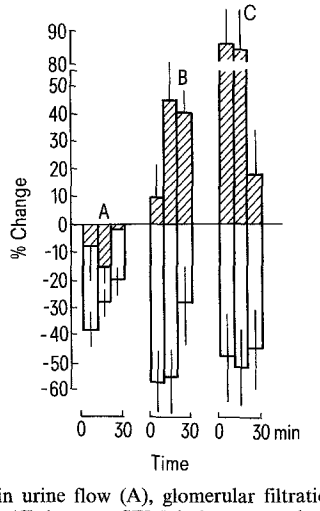
In the first group of birds (n = 7) six consecutive 10-min urine samples were obtained 1 h after the start of the saline infusion (control samples) and continued for 30 min after a single injection of 25 µg cadmium chloride (15.34 µg Cd). This procedure was repeated for the second group of pullets (n = 5) except that each bird was infused at a slow constant rate (0.1 ml/min^{-1}) with the heavy metal chelate (1% FeNa EDTA) 1 h before and 30 min after a single cadmium injection (15 µg Cd).

In both groups of hens blood samples (2 ml) were taken at the midpoint of each urine collection period.

Following cadmium treatment in group one pullets a significant reduction ($p < 0.05$) in urine flow (1.1 ± 0.12 to 0.77 ± 0.22 ml/min) was observed, reflecting an approximate 30% decline (fig.) from control values over the experimental period. In addition GFR was found to decrease significantly ($p < 0.02$) by about 50% compared with that observed before cadmium treatment (3.12 ± 0.4 to 1.67 ± 0.28 ml/min). Statistical analysis of these data revealed a positive significant correlation ($r = 0.59$; $n = 70$; $p < 0.002$) between urine flow and GFR. However, in group two pullets, pretreated with the heavy metal chelate and then cadmium, no pronounced oliguria was observed and this may be related to the 30% increase in GFR over the 30-min period of cadmium intoxication (fig.).

The renal clearance of PAH (ERPF) was shown to decline significantly (13.7 ± 2.06 to 6.9 ± 2.29 ml/min: $p < 0.02$) in poisoned hens indicating an overall decline of about 50%, 30 min after cadmium treatment. Based on the equation RBF = RPF · (1-hematocrit)$^{-1}$ [2] and assuming a cardiac output in similar sized hens of 430 ml/min[3] the fraction of cardiac output to the kidneys was calculated to be reduced by half in cadmium treated hens. Moreover, in pullets treated with FeNa EDTA and cadmium, ERPF increased significantly ($p < 0.02$) by about 60% above control values (fig.).

The changes observed following cadmium intoxication in both groups of birds were not attributable to the infusion of either isotonic saline solution or FeNa EDTA, since in separate experiments, when these constituents were infused continuously over a 3-h period, no marked differences were noted in urine flow, GFR or ERPF.



% change in urine flow (A), glomerular filtration rate (B), and renal plasma flow (C) (mean ± SEM) in hens treated with *a* 25 µg $CdCl_2$ (□) and *b* $CdCl_2$ + FeNa EDTA (□). 0% refers to controls for both groups before cadmium treatment. Each 0–30-min block represents results of consecutive 10-min sampling.

It is suggested that the reduction in filtration rate, urine flow and effective renal blood flow in poisoned pullets resulted either from a rapid redistribution of arterial blood away from the kidneys, or from renal arteriolar constriction which could result in a reduction in glomerular capillary pressure. However, the mechanisms by which the observed changes in renal homeostasis are effected in the poisoned birds and alleviated in the chelate-primed birds remain largely unresolved.

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Effect of bilateral nephrectomy on the recovery of blood pressure after acute hemorrhage in rats: role of renin-angiotensin system

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Summary. The effect of bilateral nephrectomy, and administration of an inhibitor of angiotensin converting enzyme, on the recovery of arterial blood pressure after hemorrhage (loss of 1% of b.wt), was studied in male Sprague-Dawley rats. Neither manœuver significantly affected the recovery of blood pressure within the first 10 min after hemorrhage. Thereafter, the recovery of the blood pressure was markedly suppressed. The study suggests that the initial recovery of blood pressure is unrelated to the kidneys, but the later one requires their presence and depends on the activity of the renin-angiotensin system.
Key words. Hemorrhage; blood pressure; renin-angiotensin system.

The fall in blood pressure following a loss of blood from the vascular system initiates rapid nervous and hormonal compensatory responses. Many investigators have described activation of the renin-angiotensin system in response to acute hemorrhage[1,2]. But the role of the kidney as a homeostatic organ for blood pressure maintenance during hemorrhage has not been fully described. The results of Regoli[3] suggest that nephrectomy exerts little influence on the time course of blood pressure response after hemorrhage. Sapirstein et al.[4] postulated that the renin-angiotensin system is the renal compensatory mechanism for maintenance of blood pressure in response to hemorrhagic hypotension. Zerbe et al.[5] showed that blockade of angiotensin II formation is accompanied by a blunted recovery of blood pressure after hemorrhage.

Earlier evidence[6,7], however, suggests that angiotensin may not be the pressor material released by the activation of the kidney, and in fact that renal factors other than the renin-angiotensin system may be involved in the compensatory response to hemorrhagic hypotension.

The present experiments were therefore designed to re-examine the role of the kidney in the recovery of blood pressure after hemorrhage in bilaterally nephrectomized rats and in rats that had a bolus injection of the converting-enzyme inhibitor, captopril, before the hemorrhage.

Material and methods. Male Sprague-Dawley rats weighing between 180 and 280 g were used. They were housed in the laboratory and allowed free access to standard laboratory rat pellets and water.

Experimental protocol. Anesthesia was induced with sodium pentobarbital (50 mg/kg, i.p.; Abbott Laboratories, Ill., USA). The animals were reweighed after the induction of anesthesia. Polyethylene catheters filled with heparin solution (100 units per 100 ml of saline) were inserted into the right carotid artery and the left external jugular vein. The rats were subsequently divided into four groups as shown in the table. Bilateral nephrectomy was performed through a midline incision. Non-nephrectomized rats were sham-operated.

The animals were allowed to equilibrate for 45 min, after which the mean blood pressure was recorded (pre-hemorrhage blood pressure) on a Gilson Polygraph Model 5/6H with a Stathem P23ID transducer via the carotid artery. Group 4 rats received a bolus injection of 1 mg/kg captopril (Squibb Inst., Princeton, NJ, USA) via the jugular vein after the equilibration period. 0.1 ml 5% dextrose was used to flush the jugular vein catheter after injection. In this group, the pre-hemorrhage blood pressure was recorded 10 min after the captopril injection and this was followed by the hemorrhage. Hemorrhage in all rats was carried out within 3–5 min via the carotid artery after the equilibration period of 45 min, and recording of the pre-hemorrhage blood pressure. The blood pressure was thereafter read at intervals of 5, 10, 20, 30, 40 and 60 min and recorded continuously for 60 min after hemorrhage.

Results are expressed as the mean±SEM and compared by Student's t-test or analysis of variance using a between and within design for repeated measures. A value of 0.05 or less was considered significant.

Results. The results are shown in the table and the figure.

a) Effect of nephrectomy. The blood pressure in nephrectomized

Baseline data on the role of the kidneys in the recovery of blood pressure after hemorrhage

Group	N	Weight (g)	Blood pressure before hemorrhage (mm Hg)	Volume of blood removed (ml)
1) Nephrectomy No hemorrhage	8	229 ± 5	98 ± 3	–
2) Nephrectomy Hemorrhage	7	233 ± 11	97 ± 3	2.4 ± 0.1
3) No nephrectomy Hemorrhage	7	239 ± 6	108 ± 5	2.5 ± 0.1
4) No nephrectomy Captopril, 1 mg/kg	7	229 ± 11	106 ± 6*	2.4 ± 0.2

*Blood pressure value 10 min after captopril injection. Values are means ± SEM.