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### EFFECTS OF ADRENALECTOMY ON HEMOCONCENTRATION AND BLOOD pH, UREA AND ELECTROLYTES IN THE MONGOLIAN GERBIL (MERIONES UNGUICULATUS)

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FOR THE DEGREE OF

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IN BIOLOGY

MAY 1984

bу

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## EFFECTS OF ADRENALECTOMY ON HEMOCONCENTRATION AND BLOOD pH, UREA AND ELECTROLYTES IN THE MONGOLIAN GERBIL (MERIONES UNGUICULATUS)

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### ABSTRACT

The effects of adrenalectomy on some blood profiles of the Mongolian gerbil, Meriones unguiculatus, were studied in order to clarify the possible causes of its short survival after adrenal ablation. Measurements of hematocrit, pH, urea and electrolytes were made 18, 24 and 30 hours after surgery. Results show the expected alterations: hemoconcentration, metabolic acidosis, high values of urea and disturbances in electrolytes. While hyponatremia was significant only after 24 hours, important hypochloremia was not present at any time. Hyperkalemia was the most significant alteration observed. It occurred as early as 18 hours after surgery, suggesting that it may be an important contributor to the failure of these rodents to survive after adrenalectomy.

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### INTRODUCTION

Meriones unguiculatus, a rodent of the family Cricetidae, subfamily Gerbillinae, whose natural habitats are the deserts of Mongolia and Northern China, has been described as critically adrenal-dependent. Death occurs 4-5 days following adrenalectomy (ADX), with or without saline drinking (Cullen and Scarborough, 1970). This in in sharp contrast to the much-studied white rat which survives ADX for many weeks with supplemental NaCl (Gaunt et al., 1935). The behavior of the golden hamster (Mesocricetus auratus) is similar to the Mongolian gerbil in that the hamster also fails to extend its survival time after ADX by drinking saline solution when it is offered together with tap water (Snyder and Wyman, 1951; Gaunt et al., 1971), though in both species it has been shown that under normal conditions they are able to drink highly concentrated NaCl solution (McManus, 1972; Freeman and Leftwich, 1981; Hagood, 1982; Salber and Zucker, 1974). This latter ability may be related to the similar habitats of these two species. Printz (1921, cited by Donaldson & Edwards, 1981) has described the semi-desert Mongolian/Siberian steppes as having highly saliniferous deposits of water together with soils that favor a vegetation of halophytic plants, some of them with high levels of electrolytes. Rats (non-desert rodents) live in mesophytic habitats (Wong, 1977). Mongolian gerbils and golden hamsters also share some adrenal histological characteristics (Kadioglu and Harrison, 1975). By contrast, gerbils and rats differ in habitat, behavior, adrenal anatomy and

histology, and adrenal-weight/body-weight ratios (Cullen <u>et al.</u>, 1971; Kadioglu and Harrison, 1975; Jones and Henderson, 1978).

Adrenalectomy causes serious problems in many biological systems in mammals in general. There are changes in ionic and fluid balance among tissues, blood and kidneys, producing changes in blood pressure and blood flow (Turner and Bagnara, 1976; Goldberger, 1980). ADX reduces renal activity of Na<sup>+</sup> -K<sup>+</sup> - ATPase impairing the transport of sodium and potassium across the renal tubules (Westenfelder et al., 1977). It also decreases renal permeability of  $K^+$  in the proximal and distal tubules (Jones and Henderson, 1978). These changes are reflected in blood profiles that show hemoconcentration, metabolic acidosis, hyponatremia and hyperkalemia. In most species, almost all these problems are related to the lack of adrenocorticoids rather than to the absence of adrenomedullar hormones (Jones and Henderson, 1978). Even in Mongolian gerbils, there is evidence that catecholamines do not increase survival time after ADX (Ussery, 1983). Rats (Bia et al., 1982), and hamsters (Snyder & Wyman, 1951; Gaunt et al., 1971) can be maintained for extended periods with replacement therapy of adrenocortical hormones. By contrast, hormonal replacement in Meriones unguiculatus, using aldosterone and cortisol at different doses and in various combinations, has given predictably variable results; some researchers report life maintenance of as much as 17 days (Cullen and Scarborough, 1970) while others report no significant increment in survival time (Baggia, 1983; Jefferson, 1983) and in no case have experiments in gerbils, designed on the

basis of rat or hamster data, revealed the critical adrenal components involved in gerbil survival. Little is known, in fact, regarding patterns of steroids, both qualitative and quantitative, produced by the gerbil adrenal cortex. There is some evidence that the ratio of glucocorticoid/aldosterone in Mongolian gerbils is lower than in white rats (Fenske, 1983), and that M. unguiculatus appears to be unique in secreting 19-OH-11-deoxicortisol as a primary corticosteroid, rather than corticosterone which is the main adrenocorticoid in most rodents (Oliver and Peron, 1964). It is important to note that this 19-steroid, although in high concentration, does not have effects on electrolyte and water regulation (Oliver and Peron, 1964). In addition to adrenal hormones, antidiuretic hormone (ADH) from the pituitary is also involved in water conservation acting on the distal tubule and collecting ducts of the nephron. While ADX enhances the release of ADH (Marchetti et al., 1978), it has been observed that this hormone is not essential for the correction of the acute water diuresis present after ADX, with adrenal corticoids alone being sufficient (Green et al., 1970).

Surprisingly, no studies of blood profiles after ADX, such as the numerous ones documented for other mammals, have been reported for M. unguiculatus. Therefore, it was the purpose of the present experiment to remedy this situation by investigating the effects of ADX on hemoconcentration and blood pH, urea and electrolytes in the Mongolian gerbil.

### MATERIALS AND METHODS

Seventy-five, 15 to 18 week old male <u>Meriones unguicu-latus</u>, with a body weight range of 65-90 g were obtained from Tumblebrook Farms, MA. The animals were housed individually in standard 8" x 8" x 10" wire cages, at an ambient temperature of 24°-26° and under a 14L:10D photoperiod. Each gerbil was supplied with tap water and Purina Lab Chow <u>ad libitum</u> (Ralson Purina Co.; composition in Appendix). All animals were acclimated to these conditions for seven days prior to surgery.

The gerbils were divided into three groups of twenty-five animals each. Each of these groups was subdivided as follows: ten adrenalectomized (ADX), ten sham-ADX, and five controls (no surgery). The adrenals were removed through bilateral dorsal incisions using sodium pentobarbital as the anesthetic (50 mg/kg). Body weight was recorded just prior to surgery and later at blood collection.

Surgery was performed at mid-morning (0930-1030) or mid-afternoon (1530-1630). Blood was collected from each group of twenty-five animals at 18, 24 and 30 hours after surgery. On a particular day two ADX, two sham-ADX and one control were bled. Blood was obtained by cutting the throat one side a time (Cloting time in these animals is very short and after several other attempts, this proved to be the best way to obtain the volume of blood needed.).

Blood was collected in several heparinized (ammonium heparinate) microcapillary tubes for hematocrit and plasma analysis,

and also in non-heparinized plastic test tubes to obtain serum. An average of four hematocrit measurements was obtained for each blood sample. pH and K<sup>+</sup> determinations were performed on plasma samples (Completely non-hemolyzed samples are required for K<sup>+</sup> determinations.). pH was measured immediately but K<sup>+</sup> concentrations were determined later from frozen plasma. Serum, for Na<sup>+</sup>, Cl<sup>-</sup> and urea determination, was obtained from the test tube after clot retraction and centrifugation.

pH was measured using a Model L-5 Sargent-Welch meter. The plasma was maintained at room temperature and the pH-meter calibrated at the same temperature. Later a correction of the measured pH was made for the gerbil's body temperature (Weisberg, 1977). Na<sup>+</sup> and K<sup>+</sup> concentrations were measured with a Coleman Flame Photometer (Perkin-Elmer Model 21). Working standards of sodium and potassium were used for calibration and water and NaCl solution were used, respectively, for dilution. Cl concentrations were measured with a Digital Chloridometer (Buchler) and NaCl working standard was used. Urea was measured colorimetrically as ammonia, following hydrolysis of serum urea with urease (Berthelot Method-Sigma Chemical Co. Kit). This method was chosen for color stability and reproducibility. Almost all determinations were done in duplicate, some in triplicate; the mean values are presented. A clinical Chemistry Control serum for urea, Na<sup>+</sup>, Cl<sup>-</sup>, and K<sup>+</sup> (Level 1 from Serachem-Fisher) was used to check methodology, mainly when the sample volume was too small to repeat each measurement.

All data are expressed as mean +SE. Studies were performed using the Statistical Package for the Social Sciences (SPSS). A preliminary study of the data was done by one-way ANOVA to look for significant differences among normal values obtained at different times (mid-morning and mid-afternoon). A two-way ANOVA was used to analyze the groups using time-aftersurgery as blocks and comparing the effects of ADX with those of sham-ADX on any parameter. Paired Student's t-tests were employed to specify the exact location of differences among means of the ADX groups and sham groups, and to verify ANOVA analysis. Also the t-test was used to compare the control group with both the ADX groups and the sham groups. Duncan's multiple-range test was employed to order means and groups means into similar groups after differences among them were determined. P values less than 0.05 were considered significant. Where the significance is greater than that, it is specified in the results.

### RESULTS

All adrenalectomized (ADX) animals lost weight after surgery. Although it was observed that none of them ate or drank water the first post-operative day, weight changes were not significantly different from sham-controls at 18 hours after the operation; however, ADX animals lost significant weight compared to sham groups at 24 and 30 hours (Fig. 1). No significant differences in weight changes were observed in gerbils after sham-operation, other than that attributable to any surgery.

Blood profiles of non-operated gerbils measured at midmorning and mid-afternoon (Table 1) did not differ significantly
and therefore, for statistical analysis, the two groups were
combined as a single control group (Table 2). Measurements made
on sham-operated animals in the two bleeding schedules also did
not differ (Table 3), and a mean of these sham groups was later
compared with its corresponding ADX group.

Figures 2 to 8 show variation of blood profiles of ADX animals and also compares them with unoperated control and sham-operated animals. Hematocrits were significantly higher in ADX gerbils when compared to control group at 18 hours (p<0.01) and at 24 and 30 hours (p<0.001) after surgery (Fig. 2). Similarly, hematocrits were significantly higher in ADX animals than in shams at the same intervals.

Following ADX, blood urea nitrogen (BUN) increased from 30.6 mg% at 18 hours to 36.7 mg% at 24 hours to 55.9 mg% at 30

hours (Fig. 3). The two latter values are significantly higher (p<0.001) than comparable values in control (28.9 mg%) and shamoperated gerbils. pH values were significantly lower (p<0.001) in ADX animals than in controls at any time (Fig. 4). Comparing ADX animals with their respective sham groups, no significant variation in pH was observed at 18 hours; however, at 24 and 30 hours the pH was found to be significantly lower.

Variation in chloride values after ADX was not different at any time or from control and sham-values (Fig. 5). Although statistically the sham group after 24 hours of surgery was different from the other two sham groups, it was not considered biologically significant as it could be attributed to an anomaly in one or two animals which had atypically high values. No significant variation in blood sodium was observed at 18 hours after ADX. However, at 24 and 30 hours, blood sodium was significantly higher in ADX animals (Fig. 6).

The most pronounced and earliest significant change in blood electrolytes induced by ADX occurred in  $K^+$ . Potassium levels increased from 7.9 mEq/L at 18 hours to 8.8 mEq/L at 24 hours to 10.9 mEq/L at 30 hours following surgery. These values were significantly higher (p < 0.001) than control values (6.5 mEq/L)(Fig. 7), and significantly higher than those of shamoperated animals at all times. The Na/K ratio decreased significantly following ADX compared to control and sham values (p < 0.001)(Fig. 8). The drop paralleled the increase in blood potassium of ADX gerbils. The change in blood  $K^+$ , manifested

early after adrenalectomy appeared to be the most striking effect of adrenal loss.

### DISCUSSION

Adrenalectomy in <u>Meriones unguiculatus</u> induced important blood changes within 30 hours after surgery (metabolic acidosis, and increases in hematocrits and urea concentration, with a decrease in sodium and a rise in potassium), findings which are similar to those in other adrenalectomized mammals. However, these changes were different in time of appearance and also in amplitude of the variation, the acute hyperkalemia being the most notable change and possibly the cause of the death of the animals due to myocardial arrest.

Blood profiles from normal animals obtained in this experiment appear to be consistent with those found in M. unguiculatus by other investigators (Mays, 1969; Mitteilung, 1979: Donaldson and Edwards, 1981), with slight differences which may be attributed to the fact that here, only males were studied. Sex-dependent differences in electrolyte values have been reported in Gerbillus gerbillus (Haggaad and El-Hussein, 1974) and in golden hamsters, Mesocricetus auratus (Snyder and Wyman, 1951; Reiter and Hoffman, 1968). Electrolyte values in the present experiment were generally higher than those reported for the white rat (Ringler and Dabich, 1979) but similar to those in the hamster (Reiter and Hoffman, 1968) which in general, shares more similarities with M. unguiculatus, both being desert rodents. values reported for the Mongolian gerbil were higher than those reported for the white rat (Ringler and Dabich, 1979), possibly attributable to a higher intake of proteins than normal for the

gerbil. Purina Lab Chow has twice as much protein as found in leaves and seeds eaten by wild gerbils (Edwards <u>et al.</u>, 1983). pH values from normal gerbils  $(7.59 \pm 0.03)$ , observed in the present experiment, were a little higher than those reported for normal albino rats  $(7.44 \pm 0.01)$  (Libermann, 1973), and mammals in general, perhaps a result of the different ways and conditions used to collect the blood.

The fact that the Na<sup>+</sup>, C1<sup>-</sup> and K<sup>+</sup> levels measured here did not differ at mid-morning and mid-afternoon in unoperated control gerbils is in contrast to findings in other rodents. For example, the highest blood concentrations of Na<sup>+</sup> and Cl<sup>-</sup> in white rats (nocturnal rodents) are found at 0700 hours while blood K level is highest at 2300 hours (Altman and Dittmer, 1973). Circadian rhythms of K<sup>+</sup> excretion in white rats have been observed to be controlled by the rhythmic secretion of adrenocortical hormones. Although Na+ excretion appears not to be directly related to the function of the adrenal cortex (Hilfenhaus and Hertig, 1979), adrenal rhythms are important for regulation of those ions. Meriones unguiculatus is difficult to categorize as diurnal or nocturnal. Their thermoregulatory ability suggests them to be diurnal (Robinson, 1959; Luebbert et al., 1979), but at nesting sites, underground burrows, they are active on the surface both at night and day. Also they do not hibernate or aestivate (Winkelmann and Getz, 1962).

After adrenalectomy (ADX) a linear increment in hematocrit was observed. This hemoconcentration is probably the result of

at least two factors: first, an important diuresis with accompanying low sodium reabsorption caused by lack of aldosterone (Turner and Bagnara, 1976) (M. unguiculatus has a low water requirement, Arrington and Ammerman, 1969 and excretes only small quantities of urine, Rich, 1968); second, a shifting of water into the cells as a result of plasma hypotonicity which may be partly the result of a reduction of the glomerular filtration rate due to the lack of glucocorticoids (Cortney, 1969). It is well known that blood viscosity leads to changes in renal function. In the present experiment, 30 hours after ADX, when the renal problem was apparent as indicated the rise of BUN, the hematocrit increased 6.7% over the control value. Friedman et al. (1962) reported an increase in hematocrit, in white rats, of 7.7% but this increase was not recorded until 12 days after ADX.

A rise in blood urea in the present experiment became apparent as early as 24 hours after surgery. Westenfelder et al. (1977) found in adrenalectomized rats a two fold increment, but not until 14 days post-operation. An increase of this magnitude was observed in the present work in only 30 hours. Edwards et al. (1983) worked with M. unguiculatus and observed that normal animals having a high protein intake and salt in their water were easily able to excrete large amounts of urea and NaCl at the same time. The Mongolian gerbils (Edwards et al., 1983), as do many desert mammals (Schmidt-Nielsen, 1958), produce hypertonic urine mainly due to the urea concentration. Therefore, the elevation of BUN values after ADX observed in

gerbils in the present experiment probably is due to a failure in the ability of the animals to concentrate urea in the urine, much as observed in adrenal ctomized <u>G</u>. <u>gerbillus</u> (Burns, 1956), a species closely related to <u>M</u>. <u>unguiculatus</u>. Measurements of urinary urea will be necessary to test this hypothesis.

The decrease of pH was apparent as early as 18 hours after ADX. Classic acidosis often involves increased excretion of bicarbonate ions with an increase of  $\operatorname{H}^+$  ions in the blood; the high concentration of H<sup>+</sup> ions in the extracellular water allowing K+ ions to move out of the cells (Goldberger, 1980). Within 24 hours, however, in this experiment, the pH began to rise again. A compensatory mechanism (ventilatory response), which may have taken 24 hours or more to develop, probably occurred after initial acidosis. (Carbonic acid is excreted by the lungs as CO2 and bicarbonate ions are retained by the kidneys; the  $pCO_2$  falls and the pH rises toward normal (Howorth, 1977; Goldberger, 1980)). The drop in blood pH, which reoccurred by 30 hours, was probably due to the reimpairment of bicarbonate excre-The slightly lower pH observed in the sham gerbils compared to unanesthetized controls could be due solely to the anesthetic (Libermann et al., 1973).

In the present experiment a decrease of blood Na<sup>+</sup> was observed 24 hours after ADX and was not accompanied by Cl<sup>-</sup> loss.

Usually sodium deficit is accompanied by a chloride decrease.

Loss of Cl<sup>-</sup> can be compensated by an increase of bicarbonate ions when the loss of sodium is small (Weisberg, 1962). An increase in the pH values at 24 hours was observed here, suggesting that

the bicarbonate level might have been higher for a while, which could explain the normal values of Cl observed after ADX.

In the present work, the sodium decrease of 6.1% from the control value 24 hours after ADX, was greater than the decrease of 2.3% observed in golden hamsters at a similar interval (Snyder and Wyman, 1951). Later, 30 hours after ADX, gerbils had a decrease in sodium of 8.18%, which appeared to be only slightly greater than earlier. Hamsters, 43 hours after ADX, exhibit a decrease of 17.0% and, after 72 hours, a decrease of 30.3% followed by an increase that reaches normal levels just before death at 6-7 days after ADX (Snyder and Wyman, 1951; Gaunt et al., 1971). In contrast to these studies, most investigations of the effects of ADX on electrolytes in rats are started several days after surgery; to be sure that animals are truly depleted of mineralocorticoids and mainly because rats survive that period after ADX and do not show changes until then. French and Manery (1964) reported a decrease of sodium of 9.2% on the 5th day after surgery while Friedman et al. (1962) reported a decrease of 7.8%, 12 days after ADX. In adrenal insufficiency, Na<sup>+</sup> is lost in the urine mostly from the extracellular fluid, but also from the intracellular space, largely as a result of a shift in water distribution (Friedman et al., 1962).

Cullen and Scarborough (1970) found that the hyponatremia produced by ADX does not induce the Mongolian gerbil to drink NaCl solutions to improve its deficit. However, Mongolian gerbils do exhibit sodium appetite when sodium depletion is induced by drugs such as Aldactazide (a diuretic) or high dose of DOCA

(Wong and Jones, 1978). Besides, Stark (1980) reported that M. unguiculatus was able to live with few apparent side effects for 28 days without access to sodium, suggesting a high capacity to retain this ion. In the same way, Kutschen (1969) observed that during a food-restriction experiment, M. unguiculatus was able to conserve sodium in spite of the polyuria produced by the polydipsia induced by food deprivation. It is possible that in these situations these gerbils recycled Na<sup>+</sup> rather than excreted it, in the same way they conserve water (Donaldson and Edwards, 1981; Edwards et al., 1983). These abilities are probably related to the gerbil kidney's adaptation for desert existence (long loops of Henle and pronounced development of the renal pelvis) (Edwards et al., 1983). It may be that the hyponatremia observed after ADX is not important to these animals and, perhaps, after a first period of low sodium, the blood levels of Na+ return to normal and remain so until death occurs, as in hamsters.

Potassium values in gerbils in the present work, 24 hours after ADX had increased 26.0% over the control and 6 hours later, 40.3%. Snyder and Wyman (1951) reported, in hamsters, 24 hours after ADX, an increment of 17.4%, of 29.1% after 48 hours and of 52.7% after 72 hours. In rats, an increment of 38.9% was reported 5 days after ADX (French and Manery, 1964), which is quite similar to the increment observed in gerbils in the present experiment after only 24 hours. Friedman et al. (1962) found, in white rats, an increment of K<sup>+</sup> of 50.9% that occurred 12 days after ADX.

Thus, while hyperkalemia in rats proceeds slowly, in gerbils and hamsters it appears very rapidly. Hamsters before death exhibit a rise of potassium over 100% (Snyder and Wyman, 1951). Rats on the other hand show only a 50% increase. These authors, quoted above, studied electrolyte excretion and found a concominant decrease in urinary potassium. Therefore, they suggested that the hyperkalemia was due to renal failure.

Hyperkalemia is caused by many factors simultaneously present. It has been reported that lack of aldosterone lowers K<sup>+</sup> excretion (Cortney, 1969), which in turn produces hyperkalemia. Williamson et al. (1961) found (in rats) an increased reabsorption of K<sup>+</sup> in the proximal tubule, which occurred shortly after removal of the adrenal gland and remained unchanged until death. The high blood K<sup>+</sup> characteristic of corticoadrenal insufficiency may also be caused by liberation of K+ from the cells, interchanging it for Na+ and H+. Usually 3 K+ ions are lost from the cell from the uptake of 2Na<sup>+</sup> ions, the excess being replaced by H+ ions (Kerman, 1965). Friedman et al. (1962) directly measured the increase of extracellular  $K^+$  and found that it was partly due to movement of extracellular water into the cell and partly to K+ excreted from the cells. In addition, French and Manery (1964) studied electrolytes in the blood of adrenalectomized rats maintained on different diets. They pointed out that potassium values after ADX may vary significantly with dietary NaCl content.

Hyperkalemia, observed in many adrenalectomized animals, regardless of origin, may be corrected in most mammals with mineralocorticoids, by inducing a significant kaliuresis and

concominantly correcting the hyponatremia by inducing reabsorption of sodium (Turner and Bagnara, 1976; Horisberger and Diazi, 1983). However, a relative resistance of adrenal ectomized animals to the kaliuretic effect of aldosterone has also been re-(Bia et al., 1982). That correction appears to occur through different mechanisms. Some studies provide evidence that aldosterone stimulation of Na transport requires RNA synthesis, while those stimulating K<sup>+</sup> or H<sup>+</sup> transport use another pathway not involving such synthesis (Fanestil and Park, 1981). Claire et al. (1981) found that aldosterone binds to two different kidney receptors: type I with mineralocorticoid activity producing antinatriuretic response; and type II with glucocorticoid activity, involved in kaliuretic response. Dexamethasone, a potent glucocorticoid, is fixed in binding site II, and competes with aldosterone. Recently, Bia and co-workers (1983) found that this steroid increases potassium excretion in adrenalectomized rats, normalizing the values in plasma. Aldosterone secretion is regulated by the renin-angiotensin system, ACTH, plasma concentration of potassium and less importantly by sodium concentration (Kotchen and Guthrie, 1980). Studies in rats demonstrated that chronically high potassium intake caused more profound stimulation of aldosterone secretion than chronically lowsodium intake (Boyd et al., 1971; Douglas et al., 1978). These effects of potassium on the stimulation of aldosterone secretion are not mediated by the alteration of plasma renin, as occurs with low-sodium mediation (Sealey et al., 1970). Kotchen and

Guthrie (1980) suggested that because aldosterone is an important regulator of potassium balance, the effect of potassium on aldosterone secretion might be a protective mechanism. Therefore, it would be important to quantify in Mongolian gerbils the effectiveness of the aldosterone feedback system controlled by potassium.

The toxic effects of high K+ such as those described in corticoadrenal insufficiency may be reproduced in normal animals when the serum potassium level is increased by infusion or diets. Muscle weakness is usually the first manifestation of hyperkalemia; in adrenalectomized animals caused by loss of K+ from skeletal muscle, with muscle paralysis developing later (Katz, 1977). Many physiological changes are observed in the heart when extracellular K+ values are too high: the cardiac cell is partially depolarized during diastole, impairing the entry of Na<sup>+</sup> to the cell. Besides, K<sup>+</sup> ions reduce myocardial contractility by accelerating repolarization of the action potential. Ventricular fibrillation and cardiac arrest occur. The heart at death is reported to be found in diastole (Katz, 1977; Goldberger, 1980). Wyman et al. (1953) observed in adrenalectomized golden hamsters that alteration of electrolytes, mainly high K<sup>+</sup>, was accompanied by changes in the ECG, with a depressed T wave and an increase QT interval. In hamsters, bradycardia was observed in dying animals. Hyperkalemia also affects peripheral nerves (Goldberger, 1980). When intracellular K+ is altered, mitochondrial respiration, glycogen metabolism, amino-acid

distribution, and protein and fat metabolism appear to be impaired. Some of these effects are produced indirectly because of impaired phosphate metabolism; others occur because K<sup>+</sup> ions are needed for the activation of a great number of enzyme systems (Kerman, 1965).

It is thus obvious that changes in  $K^+$ , both extracellular and intracellular, produce major problems in the body, the cardiac effects being life-threatening. It would appear, from the present work, that a major component contributing to early death after ADX in Mongolian gerbils is dysfunction of adrenal-mediated  $K^+$  balance.

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Table 1. Blood profiles of the Mongolian gerbil (unoperated) at mid-morning and mid-afternoon. (Mean  $\stackrel{+}{-}$  SE)

	Mid-morning	Mid-afternoon
Hematocrit (%)	45.86 + 0.91	46.17 + 0.57
pH	7.57 + 0.05	7.61 ± 0.02
BUN (mg/100 m1)	29.56 + 1.68	28.14 + 1.21
C1 (mEq/L)	110.80 + 1.56	111.14 + 2.71
Na <sup>+</sup> (mEq/L)	160.25 ± 2.39	162.57 + 3.74
K <sup>+</sup> (mEq/L)	$6.27 \pm 0.36$	$6.78 \pm 0.79$
Na/K	26.15 + 1.59	24.20 + 1.05

Table 2. Blood profiles of the Mongolian gerbil  $(unoperated \ controls) \qquad N \ = \ 15$ 

	Mean + SE	Range
Hematocrit (%)	46.00 + 0.54	43.0 - 49.0
pH	7.59 + 0.03	7.4 - 7.8
BUN (mg/100 ml)	28.9 ± 1.04	22.0 - 35.0
C1 (mEq/L)	110.0 ± 1.45	102.0 - 121.0
Na <sup>+</sup> (mEq/L)	161.3 + 2.10	150.0 - 176.0
K <sup>+</sup> (mEq/L)	6.51 ± 0.43	4.8 - 8.0
Na/K	25.24 + 0.98	20.7 - 34.4
Weight (g)	76.67 ± 1.52	

Table 3. Blood profiles of sham-operated Mongolian gerbils at mid-morning and mid-afternoon.  $(\text{Mean} \buildrel - \text{SE})$ 

	Mid-morning	Mid-afternoon
Hematocrit (%)	45.50 ± 0.56	44.15 + 0.83
pН	7.46 + 0.04	7.51 + 0.09
BUN (mg/100 m1)	27.56 <sup>+</sup> 1.27	25.71 <sup>±</sup> 1.13
Cl (mEq/L)	112.71 <sup>+</sup> 1.06	113.40 ± 1.01
Na <sup>+</sup> (mEq/L)	161.80 + 2.00	164.26 + 2.23
K <sup>+</sup> (mEq/L)	6.64 + 0.14	7.03 + 0.17
Na/K	24.49 + 0.47	23.52 + 0.59

Fig. 1. The effects of adrenalectomy on body weight (g) of

Meriones unguiculatus, 18, 24 and 30 hours after

surgery. Weight change is expressed as the difference

of Initial and Final weight.

Mean  $\frac{+}{x}$  SE. =  $\frac{-}{x}$ 

S = sham-operated N = 10

A = adrenalectomy N = 10

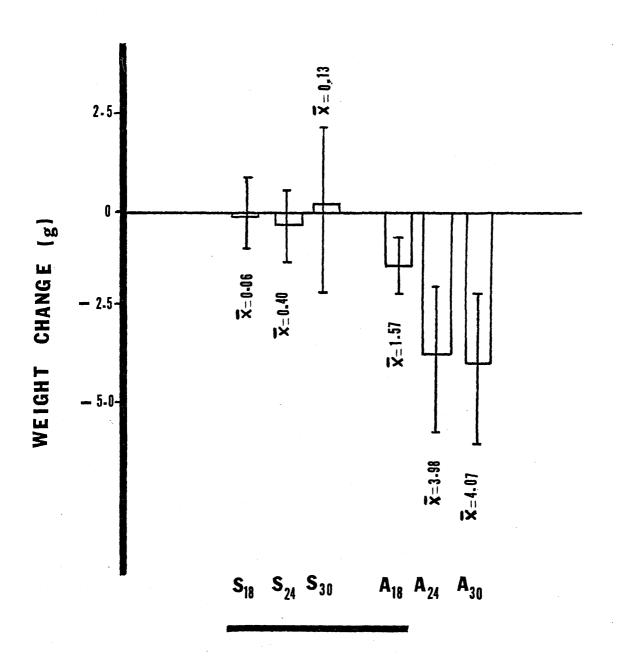


Fig. 2. The effects of adrenalectomy on hematocrit (%) of <u>Meriones unguiculatus</u>, 18, 24 and 30 hours after surgery. Mean  $\pm$  SE. =  $\frac{1}{x}$ 

S = sham-operated N = 1

UC = unoperated control N = 15

A = adrenalectomy N = 10

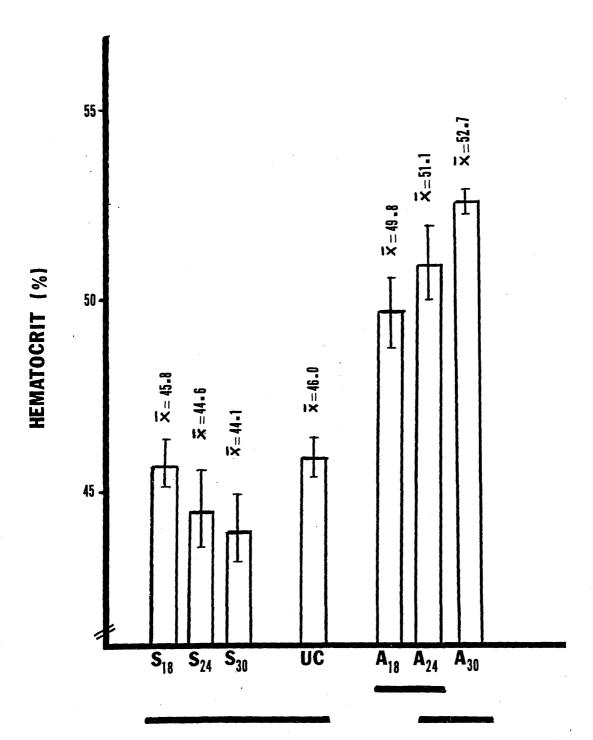


Fig. 3. The effects of adrenalectomy on BUN (mg/100 ml) of Meriones unguiculatus, 18, 24 and 30 hours after surgery. Mean  $\frac{+}{2}$  SE. =  $\frac{-}{x}$ 

S = sham-operated

N = 10

UC = unoperated control

N = 15

A = adrenalectomy

N = 10

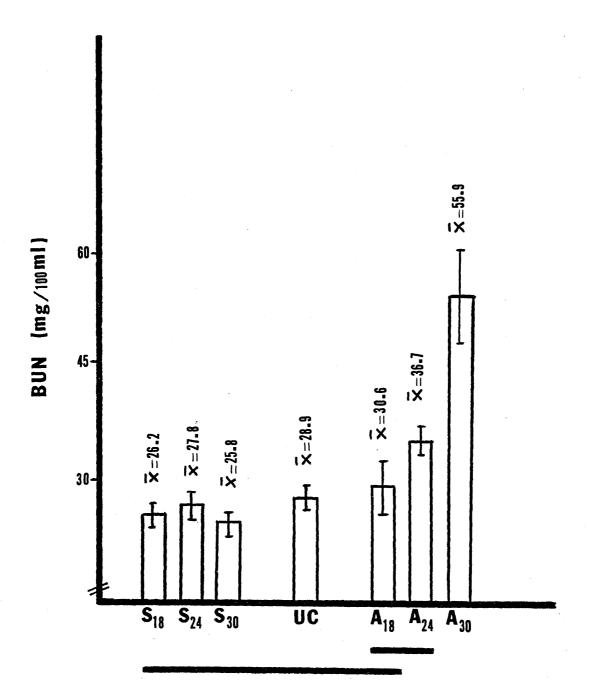


Fig. 4. The effects of adrenalectomy on blood pH of Meriones unguiculatus, 18, 24 and 30 hours after surgery. Mean  $\pm$  SE. =  $\frac{1}{x}$ 

UC = unoperated control N = 15

S = sham-operated

N = 9

A = adrenalectomy

N = 10

Means underscored by the same line do not differ significantly at p = 0.05

\* also not significantly different (S  $_{18}$  &  $\mathrm{A}_{18}\mathrm{)}$ 

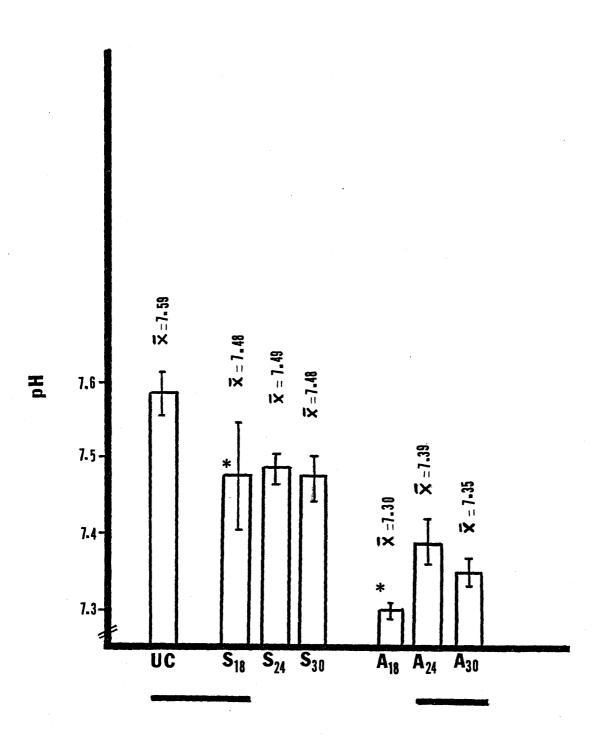


Fig. 5. The effects of adrenalectomy on blood C1<sup>-</sup> (mEq/L) of Meriones unguiculatus, 18, 24 and 30 hrs.

after surgery. Mean + SE. = x

S = sham-operated N = 10

UC = unoperated control N = 15

A = adrenalectomy N = 9

\* differs significantly at p = 0.05

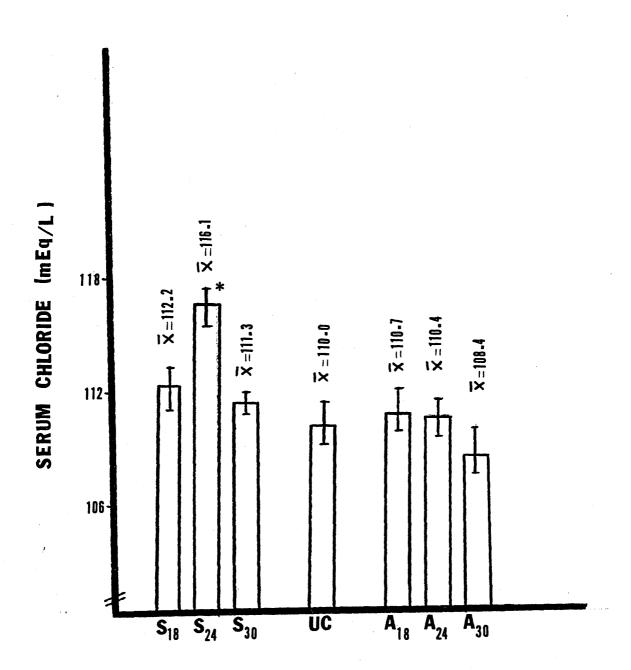


Fig. 6. The effects of adrenalectomy on blood Na<sup>+</sup> (mEq/L) of Meriones unguiculatus, 18, 24 and 30 hours after surgery. Mean  $\frac{+}{-}$  SE. =  $\overline{x}$ S = sham-operated N = 10

UC = unoperated control N = 15

A = adrenalectomy N = 10

Means underscored by the same line do not differ significantly at p = 0.05

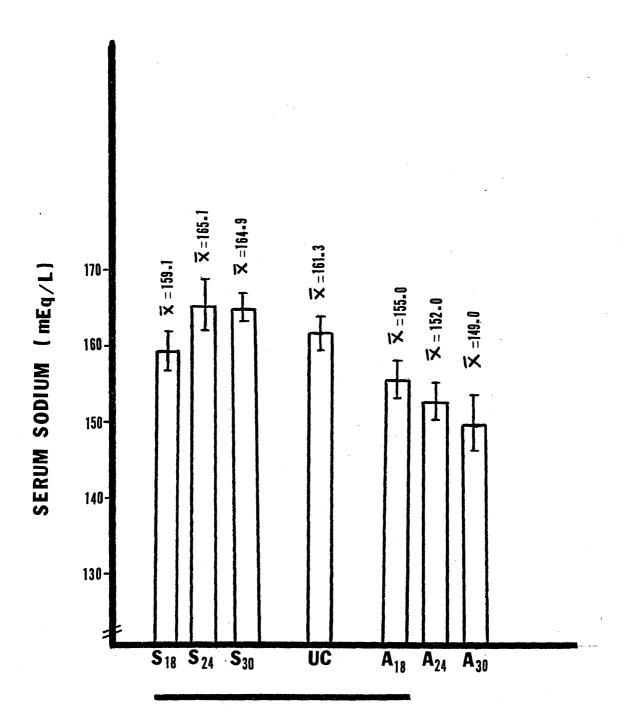


Fig. 7. The effects of adrenalectomy on blood K<sup>+</sup> (mEq/L) of Meriones unguiculatus, 18, 24 and 30 hrs. after surgery. Mean  $\pm$  SE. =  $\frac{1}{x}$ 

S = sham-operated N = 10

UC = unoperated control N = 15

A = adrenalectomy N = 10

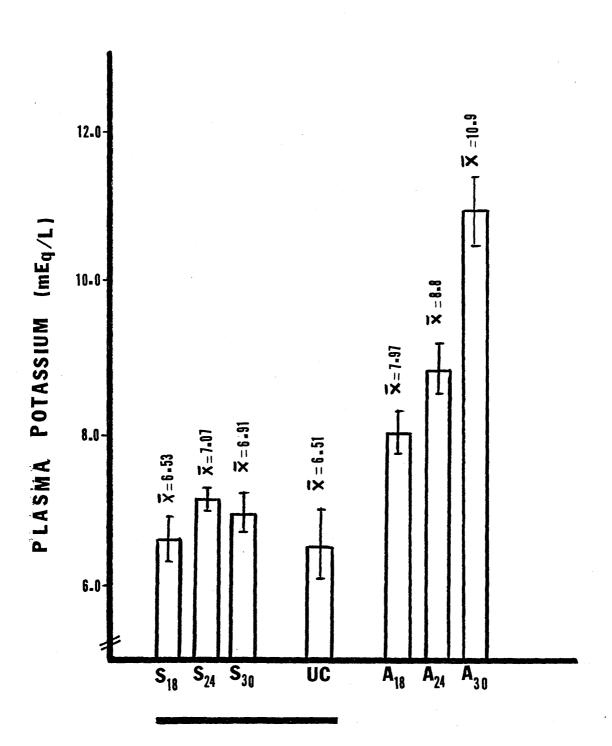
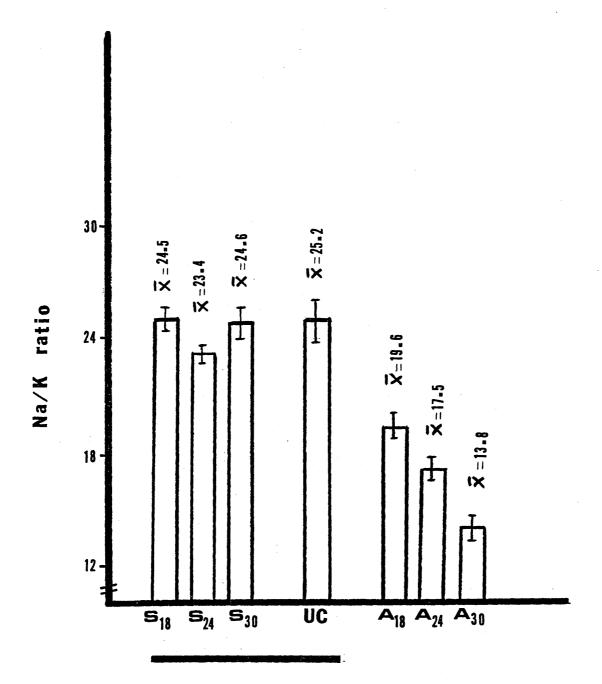


Fig. 8. The effects of adrenalectomy on blood Na/K ratio of Meriones unguiculatus, 18, 24 and 30 hrs. after surgery. Mean  $\pm$  SE. =  $\bar{x}$ 

S = sham-operated N = 10

UC = unoperated control N = 15

A = adrenalectomy N = 10



## APPENDIX

## Purina Lab Chow 5001

Sodium0	. 40%
Potassium 1.	.10%
Chloride 0.	.50%
Calcium 1.	. 20%
Phosphorus 0.	.80%
Magnesium 0.	. 21%
Proteins23.	.00%

## VITA

Magally Aellos de Cova was born October 4, 1946 in Caracas, Venezuela. She received her primary education at Cecilio Acosta School and her secondary education at Pedro E. Coll High School in Caracas. She attended Central University of Venezuela and received the title of <u>Bioanalista</u> in 1966.

From 1966 to 1973 she worked as <u>Bioanalista</u> II at the Laboratory of Clinical Research of the University Hospital of Caracas (Central University of Venezuela), and from 1972 to 1973 was employed by the Medical Institute "Ia Floresta," Caracas.

She then continued her studies at the Central University of Venezuela and received her degree of <u>Licenciado en Bio-analisis</u>, in 1975. From 1974 until 1981 she was working at the Medical School, University of Oriente, Ciudad Bolivar as Docent Assistant at the Hematology Department, and as <u>Bio-analista</u> II at the University Hospital "Ruiz y Paez," Ciudad Bolivar. She obtained a fellowship from the University of Oriente for postgraduate studies in the United States in 1981. She received the degree of Master of Science in Biology from the University of Richmond in May, 1984. In July 1984 she will continue her work at the University of Oriente in Ciudad Bolivar, Venezuela.