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HARMFUL EFFECTS OF SEA WATER ADMINISTRATION ON KIDNEY STRUCTURE AND FUNCTION

By

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التغيرات التركيبية والفسيولوجية للكلية المترتبة على عملية انسداد الحالب بربطه

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لقد أجريت هذه التجارب على ذكور الأرانب البالغة ، حيث خدرت حيوانات التجارب وتم عملية ربط الحالب الأيمن فقط بالقرب من اتصاله بالكلية اليمنى واستمرت عملية الربط لمدة ٨ أسابيع ولقد أسفرت هذه الدراسة على حدوث عدة تغيرات بالكلية المربوطة الحالب بالمقارنة بالكلية الأخرى . وتشمل هذه التغيرات ما يأتي : امتلاء الكلية بالبول كنتيجة لعملية الربط ، زيادة وزن الكلية زيادة ملحوظة مع ارتفاع محتواها المائي كنتيجة لحدوث عملية استسقاء كلوي ، حدوث تهتك شديد بالنسيج الكلوي سواء بالقشرة أو النخاع ، حيث كان النخاع أكثر تأثراً بعملية الربط ، زيادة المحتوى الايوني للصوديوم ونقص كل من المحتوي الايوني للبوتاسيوم واليوريا في البول المؤخوذ من الكلية المربوطة الحالب مع نقص ملحوظ في المحتوى الأيوني للصوديوم والبوتاسيوم واليوريا في مختلف مناطق النسيج الكلوي ، نقص نشاط إنزيم Na-K-ATPase نقصا واضحا مع زيادة نشاط إنزيم AC في النسيج الكلوي .

Key Words: Sea water, Kidney structure, function.

ABSTRACT

Rattus rattus received oral infusion of 3 ml of sea water for 5 consecutive days. Certain blood parameters and kidney structure and function were studied 24 hours and one week later. Hematocrit, plasma osmolality, sodium, potassium, urea and creatinine increased 24 hours and one week following the final infusion of sea water respectively. On the other hand, plasma calcium and magnesium decreased. Urine volume and osmolality and urea, potassium and creatinine excretion decreased. In contrast, urine sodium, calcium and magnesium excretion increased 24 hours and one week following sea water administration. Renal angiotensin-1-converting enzyme significantly decreased 24 hours following the administration but increased significantly one week later comparing to control. Renal tissue of these animals showed marked evidence of extensive cell destruction of the renal tubules.

INTRODUCTION

Drowning is considered as one of the major causes of child mortality as reported by Giammona and Modell, (1967) and Baker *et al.*, (1988). In wet drowning, water enters the lungs and the death caused due to asphyxiation following submersion in water (Miles, 1968). In dry drowning (Rivers *et al*, 1970) water enters the alimentary canal because of a reflex closing of the glottis (Miles, 1968 and Oren *et al*, 1982). In such case, diarrhoea, relative dehydration (Lockwood, 1963), nausea, vomiting, shivering and shortness of breath (Grausz *et al*, 1971) may occur. Also, Infusion of sea water into the alimentary canal causes flow of water from blood to the intestines, thereby leading to reduced renal function and may result in acute renal failure in albino rats (Oren *et al*, 1982). Therefore, the present research was initiated to evaluate the effects of sea water ingestion on *Rattus rattus* kidney structure and function.

MATERIALS AND METHODS

1. Animals used

Three groups, each of 10 adult albino rats, *Rattus rattus*, weighing 200-230g each, were used. Three ml of sea water (the composition of which is given in Table 1), was given orally to each rat in two groups via a gasteric tube for consecutive five days. The third group was used as control and was given 3 ml of tap water for the same period.

2. Metabolic study

The animals were maintained in metabolic cages with free

access to food and drinking water. Urine volume was recorded 24 hours and one week following the last gastric infusion of sea water. Urine samples were collected and stored at -20°C till analysis. At the end of each metabolic study (24 hr. and one week following the final infusion of sea water), ten experimental and five control animals were sacrificed using a sharp razor blade. Blood was collected into heparinized tubes, then centrifuged to separate plasma for electrolyte analysis. Right kidneys of treated and control rats were excised immediately and used for the angiotensin-1-converting enzyme assay as described by (El Gohary, 1986). While left kidneys were fixed in an aqueous Bouin's solution. After dehydration in an ascending alcohol series and clearing in terpeniol, the tissues were embedded in paraffin wax sectioned at 6 μm mounted sections were stained with Harris' hematoxyline and eosin.

Table 1
Electrolytes concentrations of sea water and normal tap water

	Sea water	Tap water
Sodium (mmol/L)	530	6.1
Potassium (mmol/L)	13.3	0.3
Calcium (mg%)	38	87
Magnesium (mg%)	187	39

3. Plasma and urine osmolalities

Osmolalities of plasma and urine were computed by the equation where osmolality =urea concentration (mmol/L) +2 (sodium and potassium concentrations) as stated by (Trimble, 1970).

4. Renal concentrating ability

Concentrating ability of the kidney was determined by the ratio U/P, where U =urine osmolality and P =plasma osmolality.

5. Plasma and urine electrolyte analysis

An atomic absorption spectrophotometer was used for determination of sodium, potassium, calcium and magnesium concentrations in both plasma and urine. Urea concentration was determined by the method of Foster and Hochholzer, (1970) and creatinine concentration was determined by using a commercial kits.

RESULTS

1. Blood and plasma investigations

Twenty-four hours following the last infusion of sea water, there was a significant increase in hematocrit (49+/−1.2, $P < 0.001$), plasma osmolality (321+/−1.3, $P < 0.001$), urea (41+/−0.8, $P < 0.02$), creatinine (0.8+/− $P < 0.001$), sodium (149+/−3.2, $P < 0.01$), and potassium (8.1+/−1.1, $P < 0.01$) concentration (Table 2). In contrast, there was a significant decreased in calcium (5.9+/−1.1, $P < 0.001$), and magnesium (1.6+/−0.09, $P < 0.001$) concentrations as well as in the Na/K ratio (18.4+/−1.4, $P < 0.001$) comparing to respective control values as given in (Table 2).

Table 2
Blood Hematocrit (Hem), plasma osmolality (Osm, mOsm/L), urea (mg%), sodium (Na, mmol/L), potassium (K, mmol/L), Na/K ratio (Na:K), calcium (Ca, mg%), magnesium (Mg, mg%) and creatinine (Creat, mg%) concentrations 24 hours and one week following sea water ingestion. All data are presented as means+/−SE. N presented the number of animals for each group.

	Contr. (N) 10	24 hours (N) 10	One week (N) 10
Hem.	40+/−1.9	49+/−1.2	46+/−0.5
Osm.	293+/−5.7	321+/−1.3	332.6+/−4.6
Na con.	139+/−3.9	149+/−3.2	155+/−2.8
K con.	4.5+/−0.6	8.1+/−1.1	7.2+/−0.9
Na/K ratio	30.9+/−2.1	18.4+/−1.4	21.5+/−1.9
Mag con.	2+/−0.03	1.6+/−0.09	1.1+/−0.02
Ca con.	13.3+/−1.3	5.9+/−1.1	6.8+/−1.02
Creat con.	0.6+/−0.01	0.8+/−0.002	0.9+/−0.003
Urea con.	36+/−1.7	41+/−0.8	49+/−0.9

One week after the final infusion of sea water, hematocrit (46+/−0.5, $P < 0.001$), plasma osmolality (332.6+/−4.6, $P < 0.001$), urea (49+/−0.9, $P < 0.001$), creatinine (0.9+/−0.003, $P < 0.001$), sodium (155+/−2.8, $P < 0.001$) and potassium (7.2+/−0.9, $P < 0.01$) were also significantly greater than respective values in the control. On the other hand, calcium (6.8+/−1.02, $P < 0.001$), magnesium concentration (1.1+/−0.02, $P < 0.001$) as well as Na/K ratio (21.5+/−1.9, $P < 0.01$) were greatly reduced when compared with the control (Table 2).

2. Urine investigations

The respective values 24 hours and one week after sea water administration for urine volume (3.4+/−0.02, $P < 0.001$ and 4.1+/−0.3, $P < 0.002$ respectively), potassium (0.83+/−0.02, $P < 0.01$ and 0.5+/−0.04, $P < 0.001$ respectively), urea (135+/−3.2, $P < 0.001$ and 160+/−1.5, $P < 0.001$ respectively) and creatinine excretions (4.8+/−0.6, $P < 0.002$ and 5.8+/−:.8, $P < 0.02$ respectively) of treated rats were significantly lower than the corresponding ones in the controls. On the other hand, urine osmolality (1796.9+/−102, $P < 0.01$ and 1577+/−95, $P < 0.01$ respectively), sodium (1.1+/−0.02, $P < 0.001$ and 1.4+/−0.05, $P < 0.001$ respectively) calcium excretion (0.8+/−0.01 $P < 0.001$ and 1.3+/−0.03, $P < 0.001$ respectively and magneisum excretions (2.3+/−0.3, $P < 0.05$ and 3.6+/−0.01, $P < 0.001$ respectively) were markedly increased in treated animals comparing to controls (Table 3).

3. Renal angiotensin-1-converting enzyme activity

Twenty-four hours following sea water infusion, the activity of renal angiotensin-1-converting enzyme (2.1+/−0.4) was significantly lower ($P < 0.001$) than that in the control (5.7+/−0.02). In contrast, the enzyme activity (9.5+/−0.8) was significantly higher than the control ($P < 0.001$) one week later (Table 3).

Table 3

Urine volume (U.V., ml), osmolality (Osmol, mOsmol/L), urea excretion (U. Exc., mg%), creatinine excretion (Crea. Exc., mg%), sodium excretion (Na. Exc., mEq), potassium excretion (K. Exc. mEq), excreted Na:K ratio, calcium excretion (Ca. Exc., mg%) and magnesium excretion (Mg. Exc., mg%) as well as renal angiotensen-1-converting enzyme activity (AC) (U mol hippuric acid/mg protein/min) and renal concentrating ability (R.C.A.) in rats 24 hours and one week following sea water infusion into the stomach. All data are presented as means+/−SE. N the number of animals for each group.

	Cont. (N) 10	24 hours (N) 10	One week (N) 10
U.V.	8.3+/−1.1	3.4+/−0.02	4.1+/−0.3
Osmol.	1361+/−106	1796.9+/−102	1577+/−95
U. Exc.	366+/−5.3	135+/−3.2	160+/−1.5
Crea. Exc.	9.3+/−1.2	4.8+/−0.6	5.8+/−0.8
Na. Exc.	0.8+/−0.01	1.1+/−0.02	1.4+/−0.05
K. Exc.	1.8+/−0.01	0.83+/−0.02	0.5+/−0.04
Exc. Na/K	0.4+/−0.02	1.3+/−0.01	2.8+/−0.2
Ca. Exc.	0.4+/−0.01	0.8+/−0.01	1.3+/−0.03
Mg. Exc.	1.5+/−0.2	2.3+/−0.3	3.6+/−0.01
AC	5.7+/−0.02	2.1+/−0.4	9.5+/−0.8
R.C.A.	4.6+/−0.4	5.6+/−0.6	4.7+/−0.3

4. Renal histopathological changes

There was no mortality among the experimental animals. The normal appearance of the renal tissue has given in (Figs. 1 and 2). Twenty-four hours following the final administration of sea water, kidney of treated rats did not exhibit an obvious change in the nephric units (Fig. 3). However, one week later the kidney showed marked evidence of extensive cell destruction of the proximal, distal and collecting tubules. Nuclear chromatolysis and pyknosis and cytoplasmic vaculation in the renal tubule lining cells were evident (Fig. 4-6). In addition, some of the renal tubules were more dilated as compared with those of the control kidney.

DISCUSSION

Inspite of the great importance of the biological effects of dry drowning, only very few reports are available in this respect.

Spontaneous introduction of sea water into human stomach causes abnormal electrolyte absorption which leads to metabolic disorders that could be fatal (Yagil *et al*, 1982), and may be attributed to water flowing from the blood stream to the intestine (Oren *et al*, 1982). In the present study the drop in plasma magnesium strongly suggests that electrolyte and water flux is from blood to intestine. Also, increased hematocrit may be attributed to attraction of water from blood to the stomach consequence to sea water infusion. Support of this view comes from the study of Lockwood, (1963) who demonstrated attraction of water from blood to intestine as a result of ingestion of hyperosmotic solution.

In the present study, the demonstrated hypocalcemia is probably due to the high intraluminary magnesium content

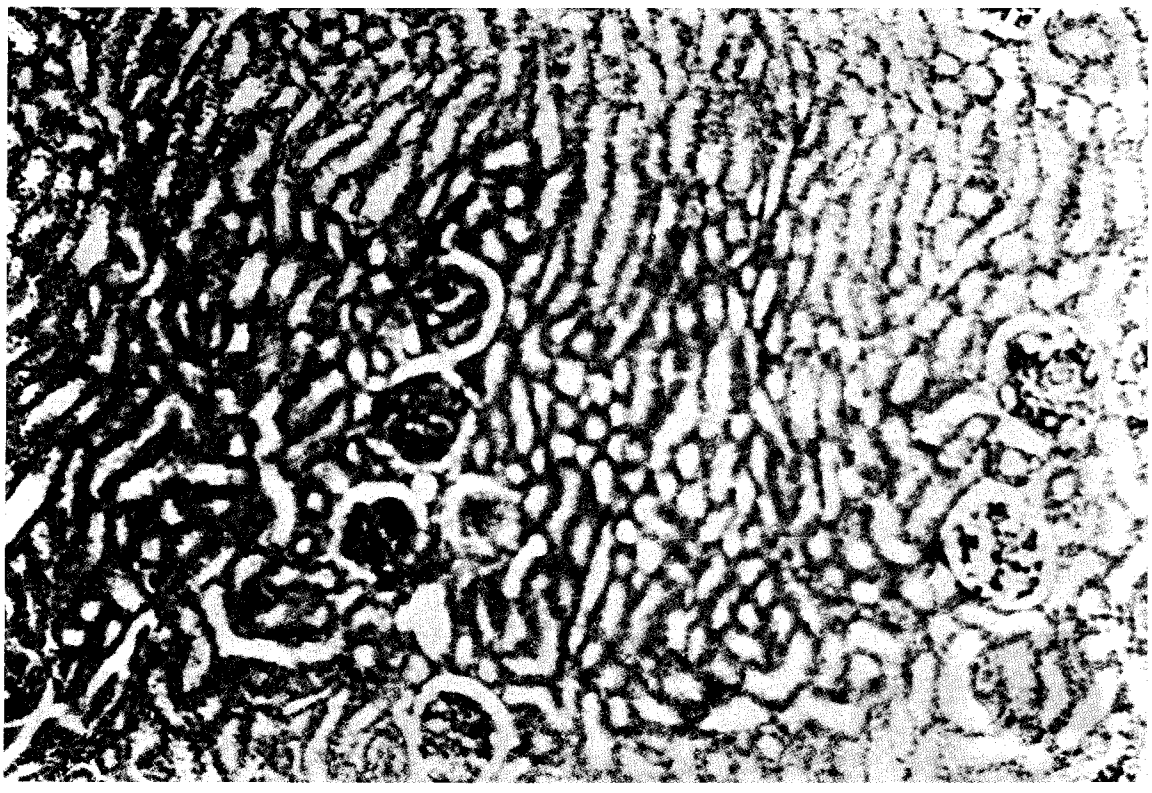

Fig. 1: Cross section of the control rat kidney shows the normal appearance of the glomeruli and the renal tubules. E & H × 100

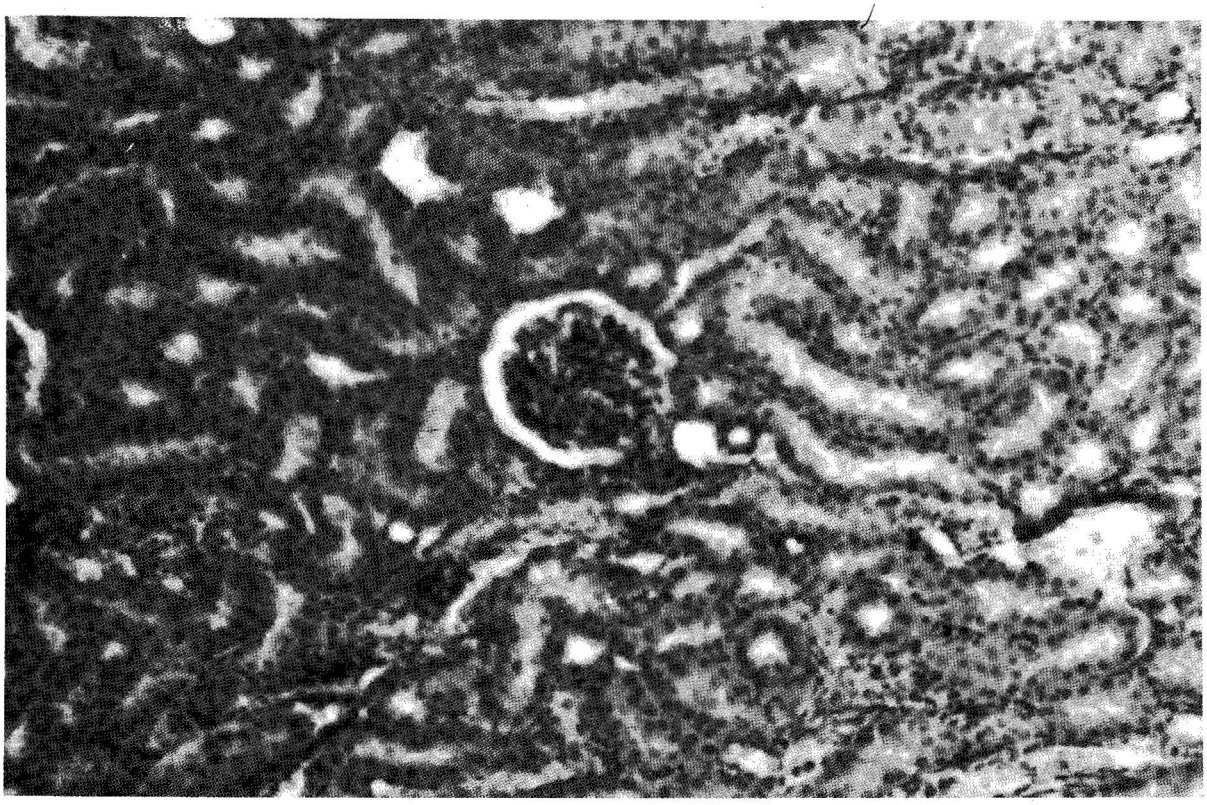

Fig. 2: Cross section of the control rat kidney shows the normal magnified glomerulus and renal tubules. E & H × 200

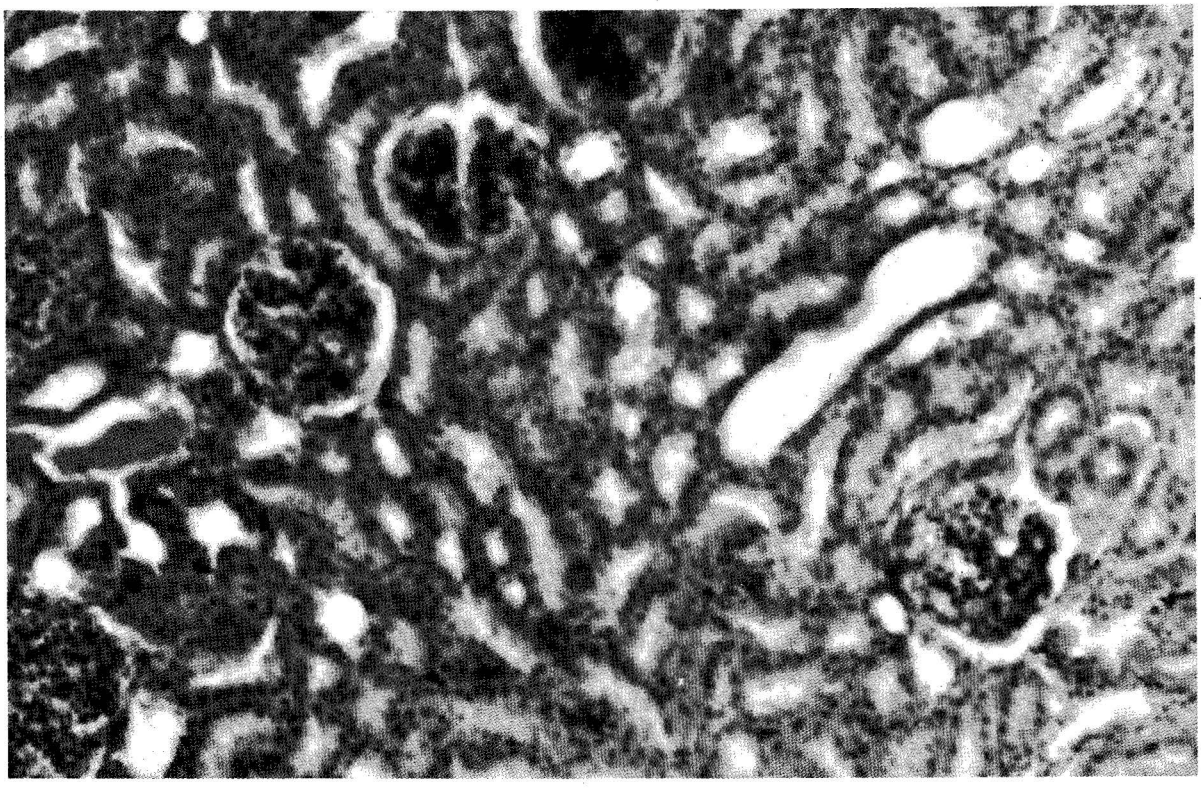

Fig. 3: Cross section of the treated rat 24 hours following the final administration of sea water. It shows nearly normal appearance of renal structure. E & H × 200

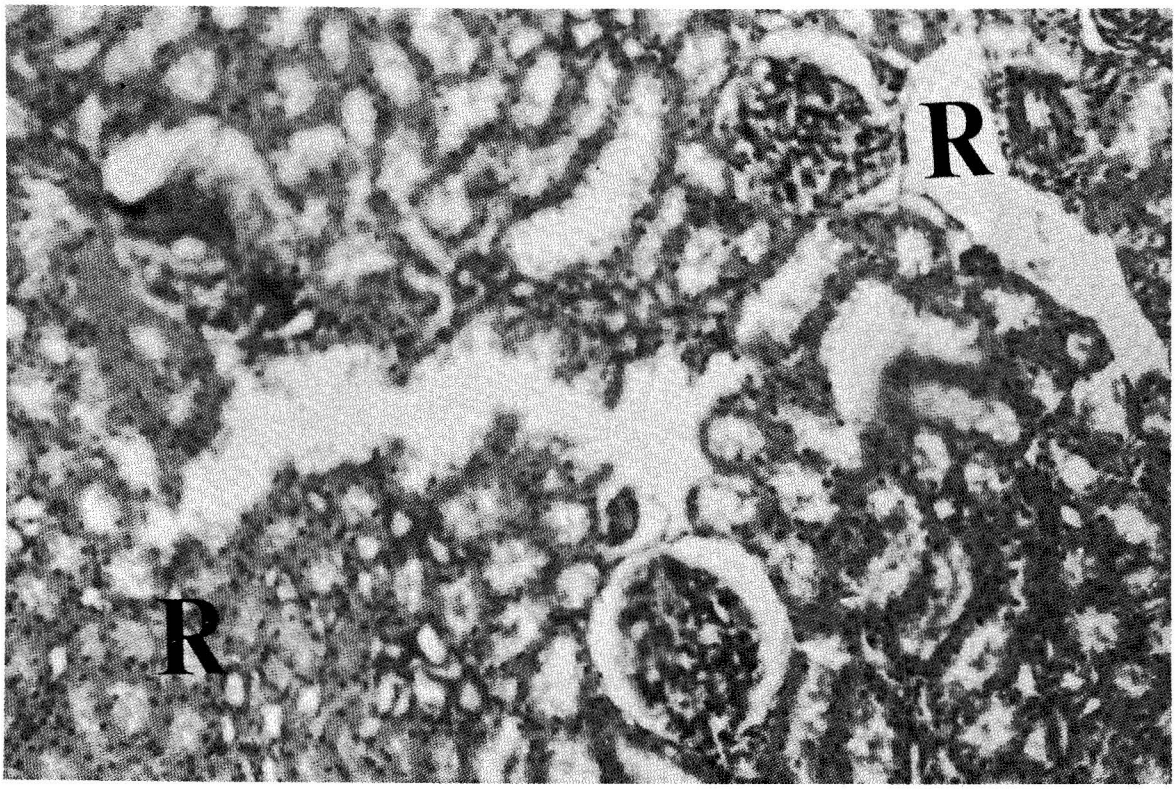

Fig. 4: Cross section of the treated rat kidney one week following the final administration of sea water. It shows marked signs of renal degenerations (R) including vacuolated tubular cytoplasm with compact small darkly stained nuclei. E & H × 200

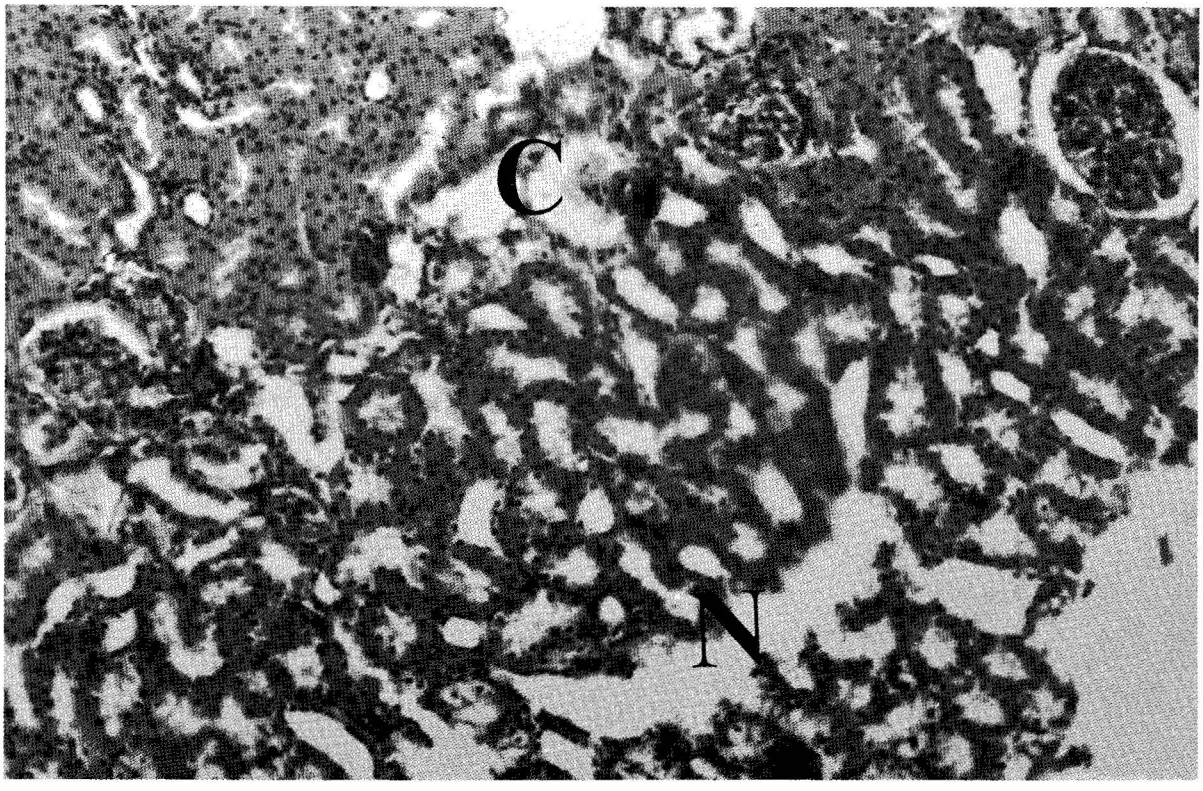

Fig. 5: Cross section of treated rat kidney one week following the final administration of sea water. It shows severe nectrotic patches (N) with com pacted glomeruli (C). E & H × 200

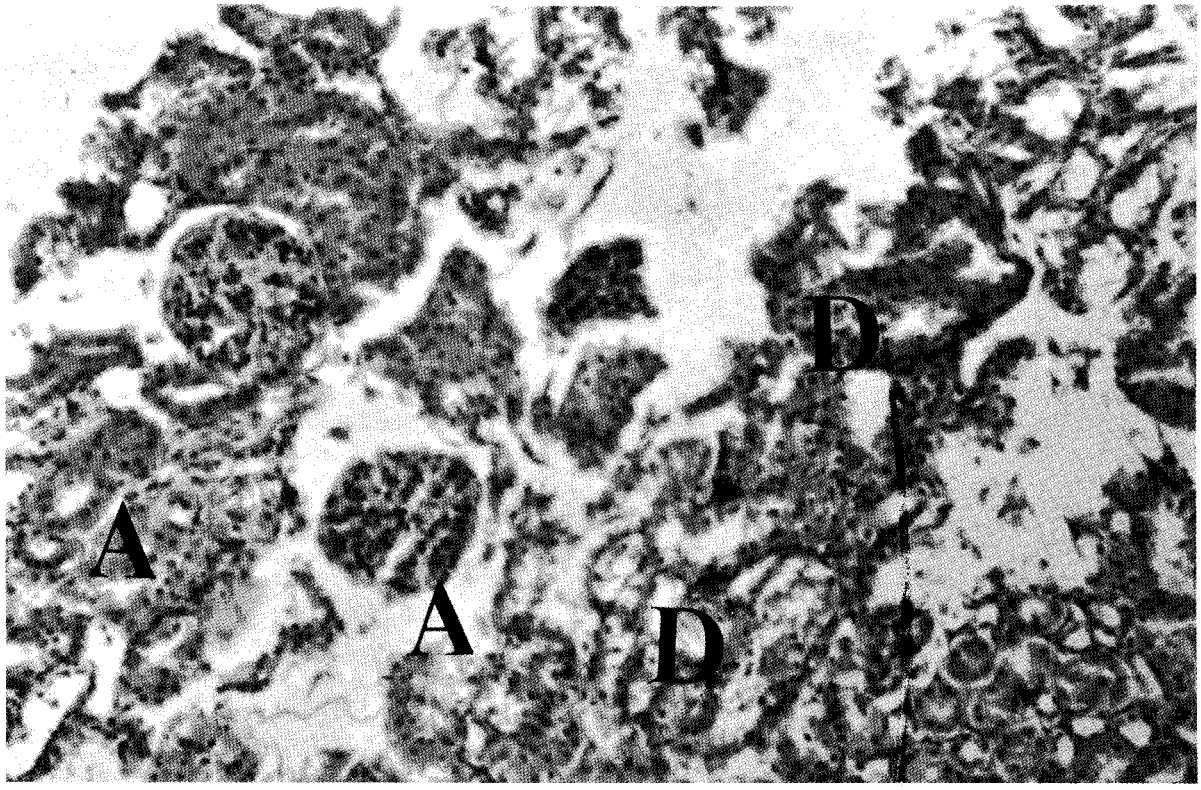

Fig. 6: Cross section of treated rat kidney one week following the final administration of sea water. It shows that some of the renal tubular cells are deattached and appeared within the lumen of the tubules (D). Also, the lumina of many tubules contained many darkly stained particles which may be the nuclear and cytoplasmic debris of destructed cells (A). E & H × 200

which depresses clacium absorption (Brannan *et al*, 1976) as well as absorption of water and other electrolytes (Di-Bona and Sawin, 1976). In agreement with these results is the study of Grausz *et al*, (1971) and Oren *et al*, (1982) who reported hypocalcemia in near-drowning human conditions and in rats drinking sea water respectively. Also the present results are in line with the study of Coburn *et al*, (1969) who reported hypocalcemia as a common disorder in cases of human chronic renal failure.

The detected hypernatremia and increased urinary sodium excretion in the present study are similar to those reported by De Boer *et al*, (1970) in human. Such results may be attributed to the combined effects of ADH and aldosterone on absorption and reabsorption of water from the colon and kidneys (Yagil and Etzion 1979). The need for water caused by the flux of water from blood to the intestine (De Boer *et al*, 1970) and the depressed water absorption (Massry and Seelig, 1977) initiates ADH secretion which, thereby, initiates aldosterone secretion (Hilton, 1960) despite of the hypernatremia. Such changes allow for augmented sodium and water absorption from the colon (Efstratopoulus *et al*, 1974). In the nephron, the hypernatremia depresses sodium reabsorption and ADH causes urea and water reabsorption in the collecting ducts (Ganong, 1979). The present data on plasma Na/K ratios also strongly suggest a higher plasma aldosterone content.

In the present study the increased urinary sodium may be due to a fall in both absolute and proportional tubular sodium reabsorption as a result of hematocrit changes (Knox *et al*, 1973). This view is in line with the results of Brenner *et al*, (1971) who reported a reduction in plasma protein concentration and sodium reabsorption in the proximal renal tubules in rats given large loads of saline intravenously.

Many circulating substances may alter urinary sodium excretion (Klahr and Rodriguez, 1975 and De Wardener, 1977). Aldosterone is closely linked to the sodium balance and probably exerts the most important antinatriuretic controlling influence. The demonstrated uremia may represent, in part, a physiological mechanism for balancing water requirements. Crenation of erythrocytes caused potassium escape which inturn may account for the hyperkalemia observed in the present study.

Angiotensin has been suggested to be involved in sodium metabolism, and it has been proposed that the increase in sodium chloride delivered to the macula densa increases angiotensin productivity and, consequently, constriction of the afferent arteriole. It has been also inferred that raised sodium chloride supply to the macula densa increases the ouput of renin (Morgan and Gillies, 1977). However, although Blendstrup *et al*, (1975) and Baumbach *et al*, (1976), using superfused glomeruli *in vitro*, found that a sustained high sodium chloride concentration around the glomeruli increases renin production, they reported that a sudden rise in sodium chloride concentration reduces its production.

The present results of the reduced renal angiotensin-1-converting enzyme activity 24 hours following sea water inges-

tion are in accordance with the results of Blendstrup *et al*, (1975) and Baumbach *et al*, (1976). However, in the present study, the prolonged change in salt concentration resulted in an elevated enzyme activity.

In the present study renal failure in the experimental animals was represented by the severe decline in urine volume, hypocalcemia and uremia. Acute tubular necrosis may account for such renal failure (Grausz *et al*, 1971). These results are in fit with the study of Grausz *et al*, (1971) who described two cases of acute renal failure following submersion in sea water. The renal histopathological lesions may be attributed to the high trace heavy metal content of sea water.

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