Acta vet. scand. 1964, *5*, 99—114.

From the Department of Surgery and Department of Clinical Biochemistry, Royal Veterinary College, Stockholm, Sweden.

# RENAL FUNCTION IN DOGS WITH PYOMETRA

## 6. SODIUM EXCRETION DURING OSMOTIC DIURESIS AND ITS RELATION TO THE RENAL DYSFUNCTION

By

*Åke Åsheim*

The poor concentrating ability of the kidneys in bitches with pyometra (chronic purulent endometritis) results mainly from a reduced capacity for resorption of free water from the collecting tubules (*Åsheim* 1964 a). The reduced resorption capacity in turn seems to depend mainly upon a drop in the sodium content of the renal medulla (*Åsheim* 1964 b). According to current concepts, the normal kidney is characterized by a steady increase in the sodium content of the medullá towards the papillary tip — the sodium gradient. Sodium is resorbed mainly from the fluid in the ascending portion of Henle's loop and partly from the fluid in the collecting tubules (*Hilger et al.* 1958, *Gottschalk & Mylle* 1959). If sodium resorption is interfered with, a normal sodium gradient cannot be established. There are two conceivable ways in which this dysfunction can arise — either the capacity of the loops of Henle and the collecting tubules for sodium resorption is depressed or else, a reduced amount of sodium is available for resorption. The latter state can result from greater than normal resorption of sodium from the filtrate in the proximal tubules to leave less sodium in the fluid than is usually the case for establishment of the sodium gradient (*Levinsky et al.* 1959).

The ability of the kidneys to resorb sodium can be tested by inducing osmotic diuresis. The presence of a non-resorbable solute will reduce the passive rediffusion of water in the proximal tubules and thus reduce the relative concentration of sodium in

the tubular fluid and consequently resorption of the ion in the proximal tubules (*Wesson Jr. & Anslow Jr.* 1948, *Ullrich et al.* 1963). If sodium resorption in the proximal tubules is reduced, greater amounts of sodium will pass through the nephron and out in the urine to give a natriuretic diuresis.

For normal animals, sodium excretion during osmotic loading is a nearly linear function of Cosm (*Goldsmith et al.* 1962). If sodium resorption increases in relation to the amount of sodium in the filtrate — as can happen in such states as prolonged hyponatraemia (*Goldsmith et al.* 1962) or a lowered GFR (*Levinsky et al.* 1959, *Goldsmith et al.* 1961) — the natriuretic response to osmotic loading will be considerably reduced in relation to the normal value for the corresponding Cosm. The concentrating ability is reduced in hyponatraemia (*Goldsmith* et al. 1961) and after reduction of GFR to less than 70 per cent of the normal value (*Levinsky et al.* 1959, *Abbrecht & Malvin* 1960).

The studies described in this paper were undertaken to find out whether there is an increased tubular resorption of sodium during osmotic diuresis and if this is the case, whether this increase in sodium resorption is a possible cause of the reduced concentrating ability which characterizes the renal dysfunction of pyometra.

## MATERIALS AND METHODS

The studies were carried out on eight normal bitches and twelve bitches with pyometra. Experimental techniques have been described in detail in a previous paper dealing with inulin clearance ($C_{In}$) and maximum resorption capacity ($T^cm_{H_2O}$) of the collecting tubules (*Åsheim* 1964 a). The bitches were dehydrated and osmotic diuresis established by giving 5 or 10 per cent mannitol solution containing 100 mEq NaCl per litre. The studies covered determinations of glomerular filtration rate (GFR) and $T^cm_{H_2O}$ (the values obtained are given in another context) and determination of sodium and potassium excretion during steadily increasing osmotic diuresis.

Seven of the twelve pyometra bitches were re-examined once or several times at intervals after the first examination and the immediately following ovariohysterectomy. On all occasions the experimental technique was identical for the particular animals.

## RESULTS

The relation between osmolar clearance (Cosm) and sodium excretion in the normal bitches is illustrated in Fig. 1. The osmotic diuresis was accompanied by increased sodium excretion and — in agreement with the results of *Goldsmith* et al. (1962)

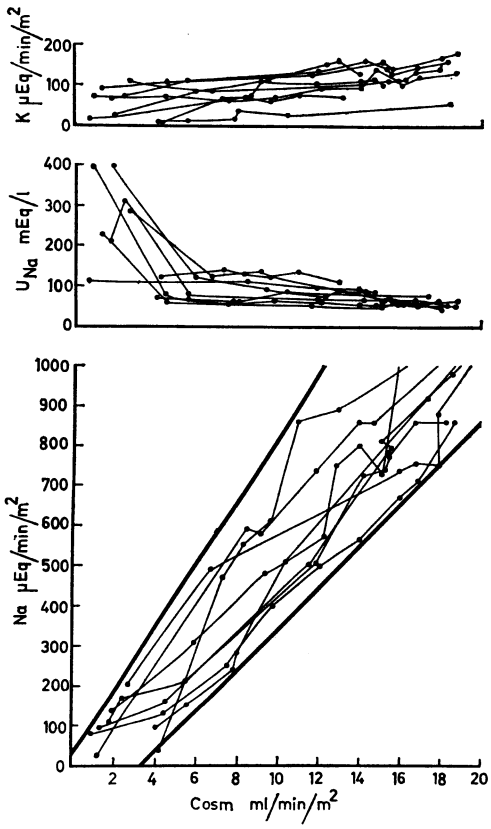



Fig. 1. Sodium and potassium excretion and urine sodium ($U_{Na}$) in normal bitches during mannitol-induced osmotic diuresis.

— sodium excretion was a practically linear function of Cosm. As can also be seen from Fig. 1, as the solute excretion rate increased, the sodium content of the urine ($U_{Na}$) decreased although never to less than 50 mEq/l.*) With a rise in Cosm,

*) Cosm values up to 20 ml/min/m² are included in this paper. For two normal bitches the osmotic load was so great that Cosm exceeded 40 and 50 ml/min/m² without the sodium content dropping below 50 mEq/l.

potassium excretion increased much less than sodium excretion and, for the Cosm values obtained, apparently did not exceed 200 mEq/min/m².

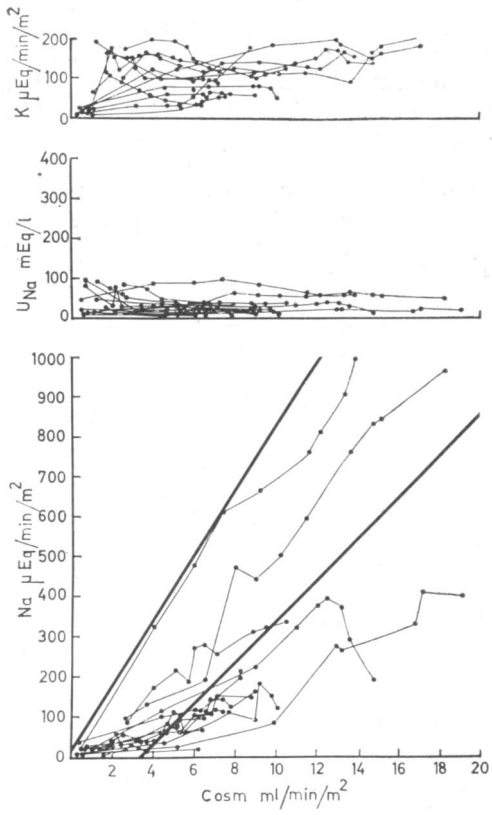
Table 1. $C_{In}$, $T^cm_{H_2O}$, plasma sodium and plasma potassium in normal bitches determined during the experiments shown in Fig. 1. Plasma sodium and potassium values were determined before the beginning of the dehydration period.

| Normal bitches no. | $C_{In}$ ml/min. per m² | $T^cm_{H_2O}$ ml/min. /m² | $T^cm_{H_2O}$ ml/min. /100 GFR | Plasma sodium mEq/l | Plasma potassium mEq/l |
|---|---|---|---|---|---|
| P 5 | 97 | 3.8 | 4.5 | 150 | 3.9 |
| P 9 | 97 | 6.1 | 6.3 | 154 | 4.3 |
| P 15 | 67 | 5.9 | 7.7 | 153 | 4.3 |
| P 18 | 87 | 5.5 | 6.3 | 153 | 5.3 |
| F 8 | 88 | 6.3 | 7.2 | 152 | 4.5 |
| F 12 | 83 | 4.8 | 5.8 | 147 | 4.1 |
| F 22 | 93 | 7.7 | 8.2 | 152 | 4.1 |
| F 95 | 62 | 4.3 | 6.8 | 142 | 4.5 |
| Mean | 84 | 5.6 | 6.6 | 150 | 4.4 |
| S.D. | ± 13 | ± 1.2 | ± 1.2 | ± 4 | ± 0.4 |

The values for $C_{In}$ and $T^cm_{H_2O}$, obtained at the same time as sodium and potassium excretion was determined, are listed in Table 1. The values given for $C_{In}$ represent the mean $C_{In}$ for the test periods. Plasma sodium and potassium levels were determined in blood samples taken before the beginning of the period of dehydration.

For ten of the twelve pyometra bitches sodium excretion was reduced in comparison with that of normal bitches at the same solute excretion rates (Fig. 2). The sodium content in the urine of these ten bitches was reduced to less than 35 mEq/l and in one of them, no. 40, the sodium content at a Cosm of 6.0 ml/min./m² was as low as 3 mEq/l. For the other two pyometra bitches, nos. 10 and 30, the values for sodium excretion were within normal limits and did not drop lower than 50 mEq/l.

Potassium excretion by the pyometra bitches was of much the same magnitude as that of the normal bitches with increase in the solute excretion rate (Fig. 2).




**F i g. 2.** Sodium and potassium excretion and urine sodium in pyometra bitches during mannitol-induced osmotic diuresis. The normal range — see Fig. 1 — is represented by the two heavy lines.

$C_{In}$ and $T^c m_{H_2O}$ during osmotic loading of pyometra bitches are listed in Table 2. $T^c m_{H_2O}$ was greatly reduced in all pyometra bitches ($P < 0.001$) and $C_{In}$, a measure of the glomerular filtration rate, varied for the different pyometra bitches from normal to greatly reduced values. The plasma sodium and potassium levels, also listed in Table 2, can be compared with the normal values given in Table 1. Sodium plasma levels fell within the same limits but the potassium levels for the pyometra bitches were lower ($0.01 > P > 0.001$).

To ascertain whether or not there was a relation between the reduction in the glomerular filtration rate and the reduction in sodium excretion, the bitches have been ranked in Table 3 according to the magnitude of the $C_{In}$ value and for each animal

Table 2. $C_{In}$, $T^cm_{H_2O}$, plasma sodium and plasma potassium in pyometra bitches before ovariohysterectomy. $C_{In}$ and $T^cm_{H_2O}$ were determined during the experiments shown in Fig. 2. Plasma sodium and potassium were determined before the beginning of the dehydration period. The results have been compared statistically with the normal values in Table 1.

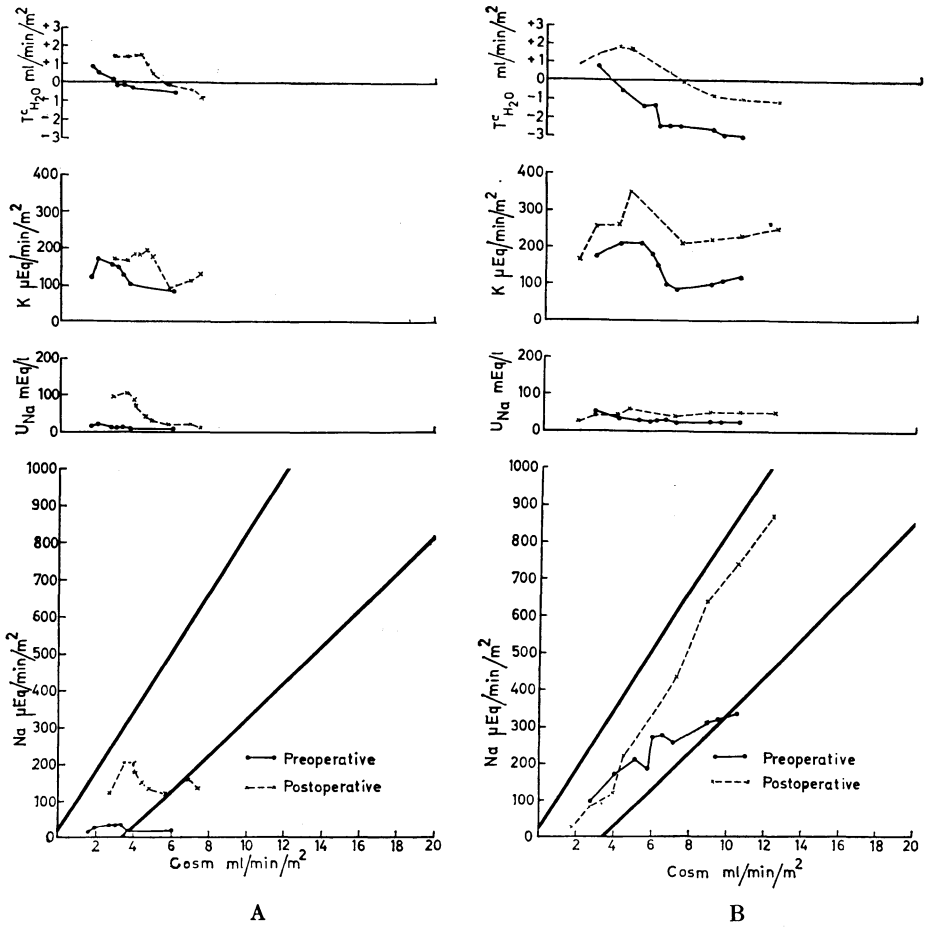
| Pyometra bitches no. | $C_{In}$ ml/min. per $m^2$ | $T^cm_{H_2O}$ ml/min. /$m^2$ | $T^cm_{H_2O}$ ml/min. /100 GFR | Plasma sodium mEq/l | Plasma potassium mEq/l |
|---|---|---|---|---|---|
| 10 | 86 | 1.3 | 1.5 | 149 | 3.6 |
| 12 | 79 | 0.8 | 1.0 | 149 | 4.1 |
| 13 | 61 | 1.3 | 2.1 | 144 | 3.6 |
| 16 | 61 | 1.5 | 2.5 | 144 | 3.5 |
| 29 | 35 | 0.4 | 1.1 | 147 | 3.0 |
| 30 | 92 | 2.0 | 2.1 | 143 | 3.8 |
| 31 | 74 | 1.6 | 2.2 | 147 | 4.1 |
| 32 | 80 | 1.6 | 2.0 | 157 | 4.1 |
| 39 | 41 | 1.0 | 2.4 | 139 | 3.6 |
| 40 | 62 | 0.8 | 1.3 | 147 | 4.1 |
| 46 | 27 | 0.6 | 2.2 | 145 | 4.0 |
| 52 | 58 | 0.1 | 0.1 | 152 | 4.1 |
| Mean | 63 | 1.1 | 1.7 | 147 | 3.8 |
| S.D. | ± 20 | ± 0.5 | ± 0.8 | ± 4 | ± 0.3 |
| P-value | | | $P < 0.001$ | $P > 0.05$ | $0.01 > P > 0.001$ |

the value for sodium excretion is given for Cosm at two levels, 6 and 9 ml/min/$m^2$. Cosm at 6 ml has been chosen since it was the highest value at which sodium excretion was determined for any animal. Cosm at 9 ml has been taken as the other reference since the natriuretic effect is more pronounced at this degree of osmotic loading. The values of sodium excretion are given graphically on the basis of the curves in Fig. 2. As can be seen from Table 3, there is a tendency towards a correlation between sodium excretion and GFR at the *lower* Cosm value. For the *higher* Cosm value the tendency is even more obvious. The sodium excretion could be calculated for eight of the twelve pyometra bitches. In the case of the two bitches (nos. 10 and 30) with normal sodium excretion, the values for GFR are similar to or greater than the normal values. For the other six, both sodium excretion and GFR are reduced. It also appears from Table 3 that there is no correlation between sodium excretion and $T^cm_{H_2O}$.

Table 3. $C_{In}$, sodium excretion, and $T^cm_{H_2O}$ during osmotic loading of pyometra bitches before ovariohysterectomy. Sodium excretion has been calculated graphically for two values of Cosm:
I = 6 ml/min/m²
II = 9 ml/min/m²

| Pyometra bitches no. | $C_{In}$ ml/min. per m² | Sodium excretion μEq/min./m² | | $T^cm_{H_2O}$ ml/min. | |
|---|---|---|---|---|---|
| | | I | II | /m² | /100 GFR |
| 30 | 92 | 152 | 445 | 2.0 | 2.1 |
| 10 | 86 | 477 | 682 | 1.3 | 1.5 |
| 32 | 80 | 151 | 223 | 1.6 | 2.0 |
| 12 | 79 | 268 | 312 | 0.8 | 1.0 |
| 31 | 74 | 102 | 150 | 1.6 | 2.2 |
| 40 | 62 | 20 | — | 0.8 | 1.3 |
| 16 | 61 | 65 | — | 1.5 | 2.5 |
| 13 | 61 | 108 | — | 1.3 | 2.1 |
| 52 | 58 | 88 | 163 | 0.1 | 0.1 |
| 39 | 41 | 44 | 113 | 1.0 | 2.4 |
| 29 | 35 | 71 | 91 | 0.4 | 1.1 |
| 46 | 27 | 92 | — | 0.6 | 2.2 |
| Mean values for normal bitches (n = 8) | 84 ± 13 | 278 ± 99 | 458 ± 107 | | |

At different intervals after the first examination and in conjunction with it ovariohysterectomy, renal function for seven of the twelve pyometra bitches was re-examined. Among these seven animals were the two, nos. 10 and 30, which had a normal sodium excretion when first examined. Table 4 contains results for all seven bitches, and more details are given for four of the seven in Figs. 3 and 4. Fig. 3 illustrates sodium and potassium excretion and resorption capacity of the collecting tubules for free water ($T^c_{H_2O}$) for three of the bitches with reduced sodium excretion at the time of the first examination. The results for bitch 40 are given in Fig. 3 A. At the time of the first examination, sodium excretion and the sodium content of the urine were greatly reduced and $T^c_{H_2O}$ was much below the normal level. By the time of the second examination sodium excretion and the sodium content of the urine had increased somewhat but had not attained normal values. The resorption capacity of the col-




lecting tubules had also increased somewhat. These improvements occurred in spite of the GFR remaining practically unchanged.

When bitch 12 (Fig. 3 B) was re-examined, sodium excretion had risen to a normal level and the sodium content of the urine increased to a value greater than the lower normal limit (50 mEq/l) while GFR was almost unchanged. Although sodium excretion had become normal by the time of the second examination, $T^c_{H_2O}$ was still much lower than normal.

The results for the pre-operative and three post-operative examinations of bitch 46 are given in Fig. 3 C (see also Table 4). On the last two occasions the animal was examined, the sodium content of the final urine had become normal to exceed 50 mEq/l

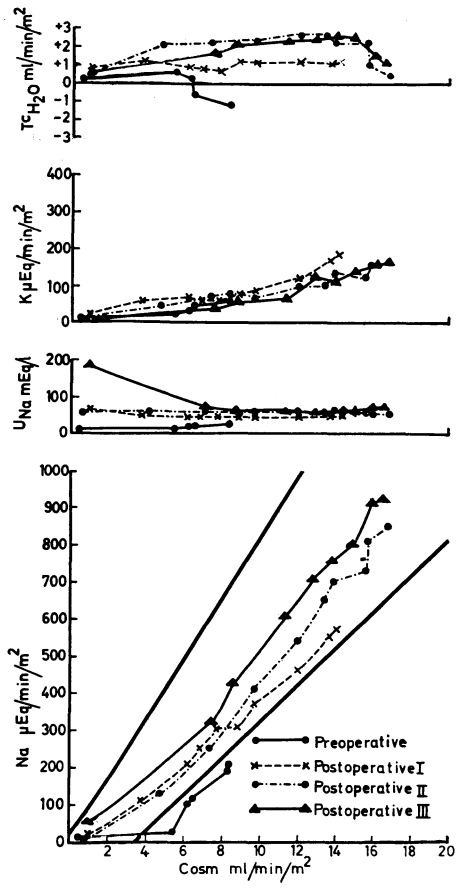



Fig. 3 A—C. Pre-operative and post-operative values for $T^c_{H_2O}$, sodium excretion, potassium excretion and urine sodium during mannitol-induced osmotic diuresis in three pyometra bitches showing reduced sodium excretion pre-operatively. Normal values — see Fig. 1 — are represented by the two heavy lines.

and sodium excretion appeared to be normal. $T^c_{H_2O}$ steadily improved but the GFR was persistently greatly reduced.

Fig. 4 contains the results for bitch 10 which had normal sodium excretion and a greatly reduced $T^c_{H_2O}$ at the time of the first examination. The post-operative examination demonstrated a vast improvement in $T^c_{H_2O}$ and maintenance of sodium excretion within normal limits.

Potassium excretion for four of the five bitches with low pre-operative sodium excretion was increased after ovariohysterectomy. In the two bitches with normal sodium excretion, the values for potassium excretion were unchanged after operation.

Table 4. $C_{In}$, $T^cm_{H_2O}$, plasma sodium, plasma potassium, and sodium excretion in pyometra bitches before and after ovariohysterectomy. Compare the column headings with those in Tables 2 and 3.

| Pyometra bitches no. | No. of days post-op. | $C_{In}$ ml/min. per $m^2$ | $T^cm_{H_2O}$ ml/min. | | Plasma sodium mEq/l | Plasma potassium mEq/l | Sodium excretion $\mu$Eq/min./$m^2$ | |
|---|---|---|---|---|---|---|---|---|
| | | | /$m^2$ | /100 GFR | | | I | II |
| 10 | pre-op. | 86 | 1.3 | 1.5 | 149 | 3.6 | 477 | 682 |
| | 12 | 100 | 4.4 | 4.4 | 152 | 3.8 | 497 | 514 |
| 12 | pre-op. | 79 | 0.8 | 1.0 | 149 | 4.1 | 268 | 312 |
| | 14 | 77 | 1.8 | 1.8 | 154 | 4.6 | 334 | 646 |
| 29 | pre-op. | 35 | 0.4 | 1.1 | 147 | 3.0 | 71 | 91 |
| | 35 | 53 | 2.3 | 4.3 | 150 | 3.8 | 234 | 548 |
| 30 | pre-op. | 92 | 2.0 | 2.1 | 143 | 3.8 | 152 | 445 |
| | 44 | 65 | 1.8 | 2.3 | 139 | 3.7 | 141 | 468 |
| 31 | pre-op. | 74 | 1.6 | 2.2 | 147 | 4.1 | 102 | 150 |
| | 13 | 74 | 5.3 | 7.7 | 147 | 4.8 | 142 | 478 |
| 40 | pre-op. | 62 | 0.8 | 1.3 | 147 | 4.1 | 20 | — |
| | 12 | 64 | 1.6 | 2.6 | 149 | 4.0 | 132 | — |
| 46 | pre-op. | 27 | 0.6 | 2.2 | 145 | 4.0 | 92 | — |
| | 12 | 42 | 1.2 | 3.1 | 153 | 4.1 | 213 | 330 |
| | 27 | 47 | 2.6 | 6.3 | 154 | 4.1 | 191 | 369 |
| | 65 | 39 | 2.8 | 7.0 | 157 | 3.9 | 262 | 457 |

## DISCUSSION

Osmotic loading with mannitol of bitches with polyuria in association with pyometra can give a greatly reduced natriuretic effect. This observation gives rise to several questions.

I. What is the cause of the reduction in sodium excretion and where in the nephron is the site of the functions or dysfunctions which are responsible for the disorder in sodium metabolism?

II. What is the significance of the reduction in sodium excretion for the reduced concentrating ability in bitches with pyometra?

As a background to the first question, it can be pointed out that sodium excretion by the pyometra bitches and the normal bitches is compared at the same rates of solute excretion. A reduction in sodium excretion means that the amount of sodium excreted is reduced in relation to the other solutes excreted. The reduction could depend upon the glomerular filtrate containing less sodium than is normally the case, i. e. in hyponatraemia. For the pyometra bitches this possibility must be excluded since the plasma sodium levels were normal. The demonstrated re-

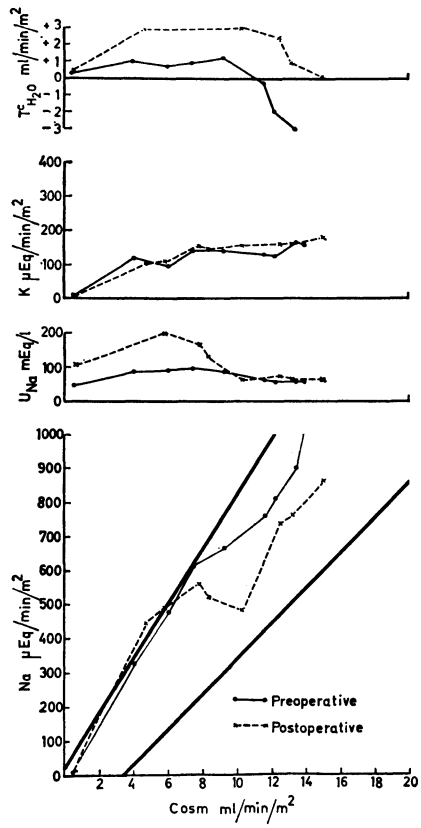



Fig. 4. Pre-operative and post-operative values for $T^c_{H_2O}$, sodium excretion, potassium excretion and urine sodium content during mannitol-induced osmotic diuresis in a pyometra bitch with normal pre-operative sodium excretion. Normal values — see Fig. 1 — are represented by the two heavy lines.

duction in sodium excretion, then, must instead depend upon proportionally greater resorption of sodium in some part of the nephron than is normally the case. Resorption of an abnormally great part of the sodium in the glomerular filtrate, as mentioned in the introduction, has been shown to occur a) in long-standing hyponatraemia and b) with a reduced glomerular filtration rate.

Pyometra bitches with the most distinct reduction in sodium excretion had the greatest reduction in GFR. It seems likely that a reduction in GFR is a major factor for the reduced sodium excretion during osmotic loading in pyometra bitches. Normalization of sodium excretion after hysterectomy in spite of a

persistent reduction in GFR is still compatible with this assumption since the possibility of successive adaptation of remaining functioning nephron has to be taken into account (*Bricker et al.* 1960).

There are several aspects to be considered in attempting to locate just where in the nephron the absolute or relative increase in sodium resorption takes place to explain the reduced excretion of sodium.

Sodium is normally resorbed at all levels of the nephron but most (some 80 to 85 per cent) is resorbed together with an equivalent amount of water in the *proximal tubules* (*Ullrich et al.* 1963). There do not appear to be any clinical means of ascertaining the magnitude of the sodium resorption in that region. Sodium resorption in Henle's loops is a prerequisite for the establishment of the sodium gradient in the medulla. But since the sodium content in the medulla is in fact reduced in bitches with pyometra (*Åsheim* 1964 b), an increase in sodium resorption here is unlikely. Sodium resorption in the distal tubules is governed mainly by the adrenal mineralocorticoids and can be considered as the "fine adjustment" of sodium metabolism. At this level sodium resorption represents an exchange of $Na^+$ for $K^+$ and $H^+$ (*Davidson et al.* 1958). Since the greater part of the potassium in the glomerular filtrate is resorbed proximally in the nephron the amount of potassium excreted mainly reflects this ion exchange (*Sullivan et al.* 1960). Potassium excretion can accordingly be taken as an approximate measure of sodium resorption in the distal tubules (*Goldsmith et al.* 1962). The reduced potassium excretion by pyometra bitches before ovariohysterectomy scarcely suggests that an increase in sodium resorption by the distal tubules is the cause of the reduced sodium excretion. On the other hand, this hypothesis presupposes a normal relation between $K^+$ and $H^+$ in the body. If the balance between these two ions is tipped in favour of $H^+$ as in acidosis or potassium deficit, the exchange between $Na^+$ and $K^+$ will be reduced (*Berliner et al.* 1951, *Welt et al.* 1960). Under such circumstances potassium excretion will no longer be a reliable measure of sodium resorption in the distal tubules. Since both acidosis (*Åsheim* 1964 c) and hypopotassiemia (see Table 2) can occur in bitches with pyometra, the conclusion that sodium resorption in the distal tubules is not increased must be accepted with a degree of reservation.

As for the remaining possibility, increased sodium resorption in the collecting tubules, the reduced sodium gradient in the medulla, just as was the case for sodium resorption in Henle's loops, is scarcely compatible with dysfunction here.

To sum up this survey of possibilities, it seems most likely that the assumed absolute or relative increase in sodium resorption takes place in the proximal tubules. It must be admitted that this hypothesis is based upon indirect evidence.

In reply to the second question, it is conceivable that the increased sodium resorption — which, it seems, most likely takes place in the proximal tubules — can affect the concentrating ability through the fluid reaching Henle's loops containing so little sodium that a normal sodium level in the medulla cannot be established. If sodium excretion is considered in relation to the values obtained for $T^cm_{H_2O}$, however, it appears that

1. the $T^cm_{H_2O}$ can be greatly reduced pre-operatively in spite of a normal sodium excretion, and that
2. a post-operative normalization of a pre-operatively reduced sodium excretion is not always accompanied by normalization of $T^cm_{H_2O}$.

There is, then, no obvious correlation between concentrating ability and sodium excretion during osmotic loading.

The results of these studies on bitches with pyometra show that sodium excretion during osmotic diuresis is reduced, apparently in association with a reduction of GFR. From consideration af various possibilities, it appears that the reduction in sodium excretion is probably caused by an increased sodium resorption in the proximal tubules. Such an increase in sodium resorption can, theoretically at least, affect the concentrating ability by reducing the amount of sodium available for establishing the medullary sodium gradient by resorption in the ascending portion of Henle's loop. But since the concentrating ability can be impaired in spite of a normal sodium excretion, it appears that the renal dysfunction which is manifested by reduced sodium excretion during osmotic loading is not the major factor in the pathogenesis of the reduced concentrating ability displayed by bitches with pyometra.

## REFERENCES

*Abbrecht, P. H.* and *Malvin, R. L.:* Flow rate of urine as a determinant of renal countercurrent multiplier system. Amer. J. Physiol. 1960, *199*, 919—922.

*Åsheim, Å.:* Renal function in dogs with pyometra. 4. Maximum concentrating capacity during osmotic diuresis. Acta vet. scand. 1964 a, *5*, 74—87.

*Åsheim, Å.:* Renal function in dogs with pyometra. 5. Sodium content of the renal medulla in relation to concentrating ability. Acta vet. scand. 1964 b, *5*, 88—98.

*Åsheim, Å.:* Comparative pathophysiological aspects of the glomerulonephritis associated with pyometra in dogs. Acta vet. scand. 1964 c, *5*, 188—207.

*Berliner, R. W., Kennedy, Jr. T. J.* and *Orloff, J.:* Relationship between acidification of the urine and potassium metabolism. Amer. J. Med. 1951, *11*, 274—282.

*Bricker, N. S., Morrin, A. F.* and *Kime, S. W.:* The pathologic physiology of chronic Bright's disease. Amer. J. Med. 1960, *28*, 77—98.

*Davidson, D. G., Levinsky, N. G.* and *Berliner, R. W.:* Maintenance of potassium excretion despite reduction of glomerular filtration during sodium excretion. J. clin. Invest. 1958, *37*, 548—555.

*Goldsmith, C., Beasley, H. K., Whalley, P. J., Rector, F. C.* and *Seldin, D. W.:* The effect of salt deprivation on the urinary concentrating mechanism in the dog. J. clin. Invest. 1961, *40*, 2043—2052.

*Goldsmith, C., Rector, F. C.* and *Seldin, D. W.:* Evidence for a direct effect of serum sodium concentration on sodium reabsorption. J. clin. Invest. 1962, *41*, 850—859.

*Gottschalk, C. W.* and *Mylle, M.:* Micropuncture study of the mammalian urinary concentrating mechanism: evidence for the countercurrent hypothesis. Amer. J. Physiol. 1959, *196*, 927—936.

*Hilger, H. H., Klümper, J. D.* and *Ullrich, K. J.:* Wasserrückresorption und Ionentransport durch die Sammelrohrzellen der Säugetierniere. Pflüg. Arch. ges. Physiol. 1958, *267*, 218—237.

*Levinsky, N. G., Davidson, D. G.* and *Berliner, R. W.:* Effects of reduced glomerular filtration on urine concentration in the presence of antidiuretic hormone. J. clin. Invest. 1959, *38*, 730—740.

*Sullivan, L. P., Wilde, W. S.* and *Malvin, R. L.:* Renal transport sites for K, H and $NH_3$. Effect of impermeant anions on their transport. Amer. J. Physiol. 1960, *198*, 244—254.

*Ullrich, K. J., Schmidt-Nielsen, B., O'Dell, R., Pehling, G., Gottschalk, C. W., Lassiter, W. E.* and *Mylle, M.:* Micropuncture study of composition of proximal and distal tubular fluid in rat kidney. Amer. J. Physiol. 1963, *204*, 527—531.

*Welt, L. G., Hollander Jr., T. J.* and *Blythe, W. B.:* The consequences of potassium depletion. J. chron. Dis. 1960, *11*, 213—254.

*Wesson Jr., L. G.* and *Anslow Jr., W. P.:* Excretion of sodium and water during osmotic diuresis in the dog. Amer. J. Physiol. 1948, *153*, 465—474.

SUMMARY

Excretion of sodium during osmotic loading has been followed in normal bitches and in bitches with polyuria in association with pyometra. The values obtained for sodium excretion have been considered in relation to the values obtained at the same time for plasma sodium, glomerular filtration rate (GFR), and resorption of free water in the collecting tubules ($T^cm_{H_2O}$).

Sodium excretion was reduced in ten of the twelve pyometra bitches. The most likely explanation for the reduction in the natriuretic effect in pyometra bitches exposed to mannitol loading appears to be increased sodium resorption in the proximal tubules. The increased sodium resorption in the proximal tubules seems in turn to be associated with a reduction in GFR. Only the two pyometra bitches which had the highest values for GFR maintained a sodium excretion within normal limits.

It is conceivable that the reduced sodium excretion can affect renal concentrating ability through reducing the amount of sodium in the fluid reaching the loops of Henle which are mainly responsible for establishing the sodium gradient in the medulla and indirectly the ability of the collecting tubules to resorb free water. But since there is no obvious correlation between the reduction in sodium excretion and $T^cm_{H_2O}$, it is not likely that the reduced sodium excretion during osmotic loading is a major component in the pathogenesis of the reduction in the renal concentrating ability which is associated with pyometra.

ZUSAMMENFASSUNG

*Die Nierenfunktion bei Hunden mit Pyometra.*

6. *Die Natriumausscheidung bei osmotischer Diurese und ihr Zusammenhang zu Störungen der Nierenfunktion.*

Die Na-Ausscheidung bei osmotischer Belastung durch Mannitol nach Dehydrierung, wurde bei normalen Hunden sowie bei Hunden mit Polyurie infolge einer Pyometra bestimmt. Die erhaltene Werte der Na-Ausscheidung wurden mit dem Na-Plasmagehalt, Glomerulifiltration (GFR) und mit der Resorption vom freien Wasser im Sammelrohr ($T^cm_{H_2O}$) verglichen, welche Funktionen wurden gleichzeitig untersucht.

Der Verfasser fand eine Verminderung der Na-Ausscheidung bei zehn von zwölf untersuchten Pyometra-Hunden. Die Ursache einer Verminderung des natriuretischen Effektes unter Mannitolbelastung bei Pyometratieren ist am wahrscheinlichsten eine Steigerung der Na-Resorption in proximalen Tubuli. Die gesteigerte Na-Resorption steht wahrscheinlich im Zusammenhang mit der Reduktion der

Glomerulifiltration. Nur zwei Pyometra-Hunden, mit höchsten Werten für GFR, hatten eine Na-Ausscheidung die innerhalb normalen Grenzen lag.

Der Verfasser bespricht die Möglichkeit, dass die reduzierte Na-Ausscheidung könnte auf die Konzentrationsfähigkeit der Nieren auf diese Weise einwirken, dass man der Henleschen Schleife, die hauptsächlich verantwortlich ist für den Aufbau des Na-Gradientes im Mark (und somit ist indirekt das Sammelrohr imstande das freie Wasser zurückzuresorbieren), zuführt eine Flüssigkeit mit mangelndem Na-Gehalt. Da keine bedeutende Korrelation zwischen der Na-Ausscheidung und $T^cm_{H_2O}$ besteht, betrachtet der Verfasser als unwahrscheinlich, dass die Funktionsstörung die sich unter osmotischer Belastung in einer reduzierten Na-Ausscheidung manifestiert, könnte eine überragende pathogenetische Bedeutung haben für das Entstehen einer Reduktion der Konzentrationsfähigkeit, welche die Nierenfunktion bei Pyometra charakterisiert.

## SAMMANFATTNING

*Njurfunktionen hos hundar med pyometra.*

6. *Sodiumexkretionen under osmotisk diures och dess relation till störningarna i njurfunktionen.*

Utsöndringen av Na under osmotisk belastning med mannitol efter dehydrering har bestämts på normala hundar och på hundar med polyuri i samband med pyometra. De erhållna värdena på Na-utsöndringen ha ställts i relation till plasmahalten Na, glomerulifiltrationen (GFR) och återresorptionen av fritt $H_2O$ i samlingsrören ($T^cm_{H_2O}$), vilka funktioner studerats samtidigt.

Förf. finner en reduktion av Na-utsöndringen hos tio av de tolv undersökta pyometrahundarna. Den troligaste orsaken till minskningen av den natriuretiska effekten på pyometradjuren av mannitolbelastning synes vara en ökad Na-resorption i proximala tubuli. Denna ökade Na-resorption synes stå i samband med en reduktion i glomerulifiltrationen. Endast de två pyometrahundarna, som hade de högsta värdena på GFR, hade en sodiumexkretion som låg inom gränserna för normalvärdena.

Förf. diskuterar möjligheten av att den reducerade Na-utsöndringen kan påverka njurens koncentrationsförmåga sålunda att Henle's slynga, som är huvudansvarig för uppbyggandet av märgens Na-gradient (och därmed indirekt samlingsrörens förmåga att återresorbera fritt $H_2O$) tillföres en vätska med otillräckligt Na-innehåll. Då det emellertid ej föreligger någon tydlig korrelation mellan Na-utsöndringen och $T^cm_{H_2O}$ finner förf. det osannolikt, att den funktionsstörning som manifesterar sig i en reducerad Na-utsöndring under osmotisk belastning kan ha någon dominerande patogenetisk betydelse för uppkomsten av den reduktion av koncentrationsförmågan som karakteriserar njurfunktionen vid pyometra.

*(Received August 1. 1963).*