Urine-concentrating Mechanism in Man

Although many extensive investigations in animals[1–3] have demonstrated the existence of renal medullary hyperosmolality suggestive of a counter-current mechanism of urine concentration, direct evidence of medullary hyperosmolality in man has never been obtained hitherto. We have examined the tissue concentrations of sodium, potassium, urea and ammonia in human kidneys removed at operation or shortly after death, using standard techniques[4].

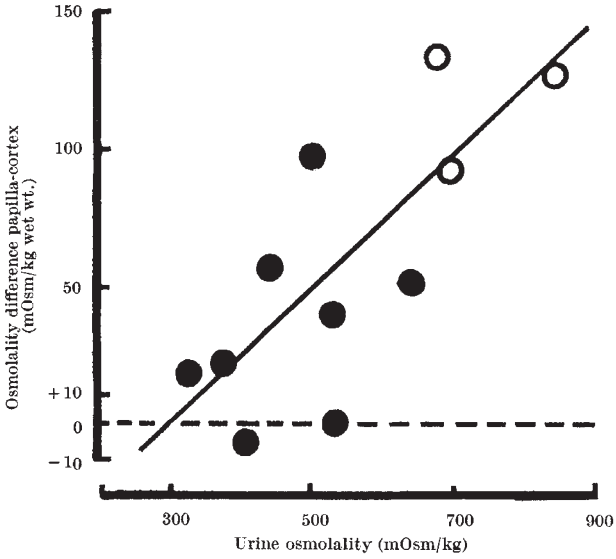

Fig. 1. Relationship of cortico-papillary tissue osmolality gradient to urine osmolality. ○, Nephrectomy specimens; ●, post-mortem specimens. Calculated regression line formula is $y = 0{\cdot}228\,x - 66{\cdot}8$; $r = 0{\cdot}76$; $0{\cdot}01 > P > 0{\cdot}001$

The results in Table 1 show that there is a rise in sodium and urea tissue concentrations from cortex to papilla in persons producing hypertonic urine; potassium and ammonia concentrations show little change. A more detailed report, including an investigation of renal solute concentration changes after death, will appear elsewhere[5]. The relationship between urinary osmolality and the cortico-papillary tissue osmolality gradient is highly significant, $r = 0{\cdot}76$; $0{\cdot}01 > P > 0{\cdot}001$, the calculated regression line formula being $y = 0{\cdot}228x - 66{\cdot}8$. The regression line reaches urinary isotonicity with plasma at a tissue osmolality gradient of zero; this differs from the findings in dogs in which there is a persistent cortico-papillary tissue osmolality gradient even in extreme water diuresis[6], but we have not had the opportunity of examining human kidney tissue under conditions of urinary hypotonicity.

The importance of sodium and urea in producing an increase in tissue osmolality in the human papilla is similar to that found in dogs[2] although the absolute values are lower; this correlates well with man's inferior maximal urinary concentrating ability when compared with the dog.

The increasing cortico-papillary tissue osmolality gradient with increasing urine concentration supports the hypothesis that urine concentration in man is carried out by a counter-current mechanism.

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Micro-injection of Trypsin into Axons of Squid

Recent work appears to show that phospholipids play a fundamental part in membrane physiology[1,2]. The participation of protein has been thought by some to be more doubtful since external application of proteases seems not to interfere with electrical function of squid, lobster or frog axons[3–5]. However, it should be recalled that externally applied protease does produce injury potentials in muscle[4]. Attempts to demonstrate that protease had entered squid axons without producing changes in electrophysiological properties may have been in error even though the controls at the time seemed appropriate[3].

This communication presents, without further interpretation, the results of five experiments which indicate that nerve proteins do play an important part in impulse generation.

Pieces of giant axons (1,000–1,500μ in diameter and 5 cm long) from the large squid *Homastrephes gigas* were used in these experiments. A micropipette (100–200μ tip diameter) was introduced longitudinally into the axon from one end. This pipette was connected to a syringe filled with mineral oil to which pressure could be applied. The pipette was also connected by means of a T tube and an agar sea-water bridge to a calomel electrode. Another calomel electrode was in contact through an agar sea-water bridge with the external medium (natural sea-water). In this way, the micropipette was used both to inject solutions into the axon and to measure resting and action potentials. Stimulation was effected with two external platinum-electrodes.

Resting potentials were within the range of 40–45 mV. Overshoots were between 20 and 35 mV. After measuring resting and action potentials, approximately 10^{-3} c.c. of

Table 1. Papilla-cortex Concentration Gradient

Patient No.	Nephrectomy or post-mortem	Disease	Hours *post mortem*	Sodium (m.equiv./kg wet wt.)	Potassium (m.equiv./kg wet wt.)	Ammonia (mM/kg wet wt.)	Urea (mM/kg wet wt.)	Tissue osmolality (mOsm./kg wet wet)	Urine osmolality (mOsm./kg)
1	N.	Renal artery stenosis	—	+ 44·8	− 1·3	− 3·0	+ 8·2	+ 89·2	694
2	N.	Renal stones	—	+ 52·1	− 1·6	+ 2·7	+ 15·9	+ 122·5	848
3	N.	Polar hypernephroma	—	+ 48·8	− 6·0	+ 1·0	+ 45·6	+ 133·2	680
4	P.M.	Cerebral hæmorrhage	2½	+ 34·9	− 11·4	− 1·1	+ 52·8	+ 97·6	505
5	P.M.	Carcinoma bronchus	6	+ 15·7	− 22·0	− 0·6	+ 9·3	− 4·2	407
6	P.M.	Mitral stenosis	9	+ 14·7	+ 4·4	− 0·1	+ 7·2	+ 45·2	637
7	P.M.	Carcinoma bronchus	8	+ 13·2	− 15·4	− 0·1	+ 5·3	+ 0·7	531
8	P.M.	Steatorrhœa	8	+ 25·7	− 5·0	+ 0·1	+ 2·6	+ 44·2	530
9	P.M.	Diabetic coma	1	+ 32·0	− 19·8	+ 3·6	+ 25·5	+ 57·1	446
10	P.M.	Empyema. Broncho-pneumonia. Recovering from acute glomerulonephritis	8	+ 6·8	− 2·2	+ 4·7	− 1·0	+ 17·6	328
11	P.M.	Syphilitic aortitis	2½	+ 7·0	− 0·3	+ 1·6	+ 5·6	+ 22·4	374
12	P.M.	Pneumonia	15	+ 73·2	+ 25·5	− 3·6	− 1·3	+ 189·0	Urine not available

Tissue concentration gradients obtained by subtracting cortical concentrations from papillary concentrations. All figures expressed in terms of wet weight of tissue.