out equal to the SCC, suggesting the absence of HCO_3 nsport.

(4) The s-to-m unidirectional Cl flux was only about e-fourth of the s-to-m Na flux, indicating a greater rmeability to cations than to anions. The permselecti-y of the "tight" junction for cations may in fact be derestimated by the ratio of s-to-m unidirectional fluxes ce a portion of the Cl flux may not be due to extra-llular diffusion. Replacement of Na with a less rmeant cation (choline) increased Cl permeability.

(5) Reduction of the HCO_3 concentration of the dium to 5 mM reduced net Cl absorption from 5.5 to and SCC from -3.2 to -1.2 μEq/h cm^2. This is in eping with the observation of Oide (*Comp. Biochem. siol.* 46A, 639, 1973) that fluid absorption by eel estine is greatly enhanced by increasing luminal pH m 7.2 to 9.0.

(6) Replacement of all Na in the medium with ine reduced net Cl flux and SCC to zero. Replace-nt of all Cl with SO_4 and Mannitol reduced net Na flux SCC to zero. Thus Na and Cl transport processes are sely coupled. Huang and Chen (*Am. J. Physiol.* 220, 34, 1971) previously reported the apparent absence of ch coupling in flounder intestine. Their choline-Ringer ntained 25 mM Na, however, and their SO_4-Ringer ntained 5 mM Cl. Furthermore, they added glucose to r SO_4-Ringer to maintin constant osmolality and thus y may have specifically stimulated co-transport of cose and Na.

(7) Addition of cAMP and theophylline (table 2) ought the SCC closer to zero ($p<.001$) and reduced ntly the net absorptive fluxes of Na and Cl, although ther change was significant statistically. The ratio of t Cl to net Na fluxes remained at 2.7. Dibutyryl cAMP d a similar effect although the change in SCC was less ng.

(8) Addition of cAMP and theophylline or of dibutyryl AMP doubled the s-to-m Cl flux but had no effect on Na xes. Thus cAMP appears to selectively increase the ssive Cl conductance of the tissue.

The apparent absence of cAMP-mediated Cl cretion in flounder intestine (Cholera toxin also failed to cit secretion - see Rout et al. *Fed. Proc.* 32, 424Abs, 73) provides circumstantial evidence for the crypt cell gin of secretion in mammalian intestine. The absence either crypts or immature cells in flounder intestine was nfirmed histologically (We are indebted to William B. nter and his associates for these examinations).

The apparent coupling of "active" Na and Cl fluxes ust be reconciled with the large difference in their gnitudes. It is possible that NaCl is pumped by the thelial cell into the lateral space and that the nsmural PD is largely a diffusion potential across the ht junction, which appears to be highly cation-selective e the explanation of Machen and Diamond, *J. Membr. l.* 1, 194, 1969) for the small negative PD across gall adder epithelium). This view implies that under ort-circuit conditions most of the Na entering the lateral ace returns to the luminal solution via the "tight" nction whereas most of the Cl enters the serosal solu-n. For this to be the case, about two-thirds of the resistance to transmural Na diffusion must reside in the lateral space beyond the junctional complex.

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Selective Adaptation of Secretory Function in the Flounder Nephron

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An important function of the kidney of a marine teleost appears to be the secretion of magnesium and sulphate enabling the fish to maintain plasma concentrations of these ions at least fifty times lower than those of the surrounding seawater. (*Can. J. Zool. 46*: 439, 1968). Urine to plasma concentration ratios for magnesium of 100-300 are achieved almost entirely by tubular secretion, glomerular filtration accounting for less than 3% of the magnesium excreted. Other routes of excretion, such as the gills, do not participate in the homeostasis of these ions and, although some processing of ingested seawater does occur in the bowel (*Can. J. Zool. 46*: 457, 1968), the large amounts of both magnesium and sulphate that are added to the body fluids daily require a powerful control system.

A second, extensively studied, tubular transport system governs the excretion of a wide variety of organic anions such as diodrast, p-ammohippurate (PAH) and dyes of the phenol red class (*Am. J. Physiol., 211*: 1152, 1966). Despite the widespread interest in this secretory system, its physiological significance remains obscure with no information available as to the normal metabolites handled by this system or to its importance in overall homeostasis.

The present studies examined the response of the remaining nephrons of the flounder kidney to the removal of approximately half of the total renal mass in order to establish the relative importance of the two secretory systems in overall regulation of body fluid composition.

The teased flounder tubule preparation described by Forster (*Science, 108*: 65, 1948) was used to examine the ability of the tubules to concentrate substanced within their lumina. The in-vitro properties of this system have been shown to correlate closely with the in-vivo behaviour of the kidney (*Bull. MDIBL, 9*: 29, 1969).

Winter flounder (*pseudopleuronectes americanus*) 150-400 g in weight were anesthetized with intravenous sodium pentobarbital (0.2 g/kg body weight) and the single fused kidney lying in apposition to the spinal column exposed via a small incision. The renal tissue was cauterized along its whole length using a red hot wire or a heated tungsten filament. Approximately 50% of renal tissue was destroyed by this means without obvious damage to the large vessels running through the center of the kidney. Control flounder were sham-operated using the identical procedure apart from the removal of renal tissue, and the fish returned to tanks of running seawater. On the sixth postoperative day the fish were removed from the tanks, a venous blood sample drawn, and all viable renal tissue removed and weighed.

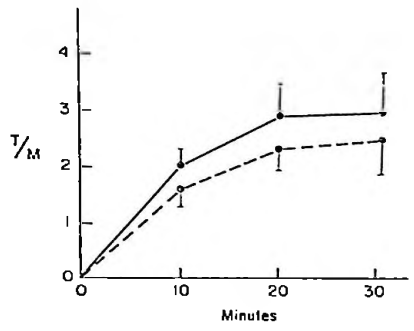
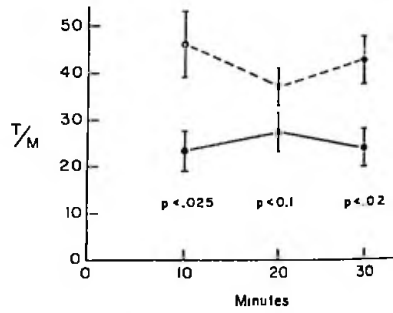


Figure 1 (left) Uptake of p-aminohippurate PAH by teased flounder tubules from six sham-operated (o—o) and six partially nephrectomized (o·····o) flounder. Medium concentration of PAH was 1 x 10^{-4}M. Each point represents the mean ± SE. Uptake is expressed as tissue:medium ratio (T/M). There is no significant difference between the two groups at any stage of uptake.

Figure 2 (right) Uptake of magnesium by teased flounder tubules from six sham-operated (o—o) and six partially nephrectomized (o---o) flounder. Medium concentration of magnesium was 1 mM/1. Each point represents the mean ± SE. Uptake is expressed as tissue:medium ratio (T/M). P refers to the significance of the difference between the two groups.



The total wet kidney weight of sham-operated fish was 2.69 ± 0.2 g/kg body weight. In the partially nephrectomized fish it was 1.65 ± 0.17 g/kg body weight ($p<.001$). This represents a 40% reduction in functioning renal tissue. For the measurement of tubular uptake of PAH and magnesium, pieces of tissue approximately 3x3x3 were cut with a razor blade and placed in a dish containing ice-cooled Forster's saline medium. Each piece of tissue was gently teased into an open colourless meshwork with fine needles, and replaced into the cooled medium for up to 10 minutes. Three pieces of tissue were then transferred to each of three flasks containing 4 ml of Forster's saline medium (total of 9 pieces for each fish). This incubation medium contained ^{3}H PAH (specific activity 141.3 mCi/mMol) at a concentration of 1x10^{-4}M and ^{14}C inulin (50 μCi/ml), the latter serving as an extracellular marker. Flasks were incubated in a bath of running seawater for 10, 20, and 30 minutes, respectively, and were agitated continuously.

Each tissue section was then weighed, homogenized and extracted in 1 ml of 4% trichloroacetic acid for 24 hours and centrifuged. 50 μl of the supernatant was pipetted into counting vials and simultaneously counted for ^{3}H and ^{14}C in a Packard Tricarb liquid scintillation counter. Duplicate aliquots of the supernatant were also analyzed for magnesium concentration, using a Perkin Elmer Atomic Absorption Spectrophotometer. Magnesium concentration of the incubation medium was 1 mM/1.

Results are expressed as tissue:medium (T/M) ratios where tissue content of ^{3}H PAH and magnesium are expressed in Mols/g wet weight and medium content as Mols/g water. Inulin (extracellular) space is expressed as the percentage of wet weight.

Inulin space, as measured at 30 minutes incubation, was 25.9 ± 3.9% of wet weight in the sham-operated group and 28.0 ± 3.2% in the partially nephrectomized group. Since these values are not significantly different from each other, comparisons of tissue uptake in which T/M values are uncorrected for extracellular space, appear to be valid.

The results of tabular uptake of PAH, expressed as the tissue:medium ration (T/M) are depicted graphically in Fig. 1. Tissue uptake reached a steady state in both sham-operated normals and in the partially nephrectomized fish by 20 minutes. No significant differences emerged between the two experimental groups for any of the experimental periods. Mean T/M at 30 minutes w 3.15 ± 0.75 in sham-operated group and 2.62 ± .68 the partially nephrectomized group.

In Fig. 2, T/M ratios for magnesium uptake are cc pared in the two experimental groups. Since tabular ma nesium was not determined at zero time, uptake cur were not constructed. After 10, 20, and 30 minutes inc bation T/M ratios for the sham-operated group we 23.3 ± 4.3, 27.4 ± 3.1 and 23.1 ± 4.09, respectively. the partially nephrectomized group these values we 45.9 ± 7.1, ($p<.025$) 37.5 ± 4.1 ($p<0.1$) and 42.8 ($p<.02$), respectively. Mean serum magnesium concent tion was 0.70 ± 0.5 mM/1 in the sham-operated fish a 0.71 ± .03 mM/1 in the partially nephrectomized fish.

In order to evaluate whether structural hypertrop occurred in the remaining nephrons of the partially nep rectomized fish, studies were performed on four expe mental and four sham-operated fish. 150-250 μg pieces renal tissue were removed, placed on a glass slide, a the tubules teased under a dissecting microscope so th minimal over-lapping of tubules. The preparation w covered with a coverslip and photographed under a mic scope at a magnification of x37.5. The tissue was th transferred to a piece of aluminum foil, dried in an ov for 12 hours at 100°C and weighed to obtain the d weight. The total length of the tubules in the sample w measured directly from the photograph and results e pressed as dry weight per mm length. Dry weight in t sham-operated fish was 2.3 ± 0.1 μg/mm length and the surviving nephrons of the partially nephrectomiz fish 2.4 ± 0.4 μg/mm length.

The adaptation of the renal tubular magnesium tran port system in response to a reduction in renal mass w the maintenance of a normal magnesium concentration the extracellular fluid attests to a powerful and homeos tically important control system for magnesium in t flounder. The absence of a parallel change in organic a ion transport suggests either that this system is unimp tant homeostatically or that it is normally highly unsat ated, requiring a minimal adaptive change in order maintain external balance. Failure of the surviving nep rons to undergo structural hypertrophy within the o week period of observation probably reflects the slo overall metabolic rate of the marine environment.

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