proximal holding pipet. This maneuver improved the electrical seal as is indicated by the increase of R_T and V_T^{oc}, and the agreement between D_e and D_o, respectively the lumen diameter measured electrically (cable analysis) and optically (ocular micrometer). At 35 minutes the tubule began its rhythmical constrictions near the collection (distal holding) pipet (Fig. 1). From this moment on, V_T^{oc} drifted towards zero mV, R_T and R_c increased, and I_{sc} decreased (Fig. 3).

DISCUSSION

In the present study we incubated kidney slices of the winter flounder in chlorphenol red in order to identify proximal tubules which are known to accumulate this dye in their lumen. However, chlorphenol red appeared in the lumen of tubules with lumen-negative and lumen-positive voltages, with low and high transepithelial resistances, and tubules of the collecting system. These observations reveal that chlorphenol red cannot be used as a selective marker for proximal tubules.

The vast majority of perfused tubules had lumen-negative transepithelial voltages when flounder Ringers was present on both sides of the epithelium. The ion dependence of this potential is unknown. However, the generation and the maintenance of the transepithelial potential appears to be dependent on perfusion flow through the tubule lumen. When the perfusion pressure is lowered to halt perfusion, the transepithelial voltage soon declines towards zero mV. The transepithelial voltage also declines when the tubules spontaneously constrict. This constriction can be expected to narrow the tubule lumen thereby 1) increasing the core resistance R_c (Fig. 3), and 2) increasing the hydraulic resistance to axial flow, and 3) reducing perfusion flow. Reduction of perfusion flow would lower transepithelial voltages and short-circuit currents, and increase transepithelial resistances if the luminal concentration of a transported species now become the rate-limiting factor of transepithelial transport (Figs. 1, 3).

The transepithelial resistance of the lumen-negative tubules is low, 3,400 Ωcm tubule length. Converted to resistance per cm^2 luminal surface (tubule inner diameter, 21 μm) the resistance is 22.3 Ωcm^2; on the basis of the peritubular surface area (tubule outer diameter, 50 μm) R_T is 53.0 Ωcm^2. These values are not as low as those measured in rat proximal tubules, 5 Ωcm^2 (Hegel et al., Pflügers Arch. 294: 274, 1967). In contrast the two tubules with lumen-positive potentials had significantly higher transepithelial resistances than those with lumen-negative potentials. They measured 71.0 Ωcm^2 and 169.8 Ωcm^2 on the basis of luminal and peritubular surface areas respectively.

The function of the muscular layer partially or completely covering the renal tubule of the flounder is unknown. The present study showed that the tubule wall is capable of spontaneous invaginations. Presumably these derive from the thin muscular layer that is thought to exist in winter flounder renal tubules (Kinter, 1966; Maack and Kinter, Am. J. Physiol. 216: 1034, 1969; Renfro, Am. J. Physiol. 234: F522, 1978). In Fig. 1 the single constriction was sufficient to reduce the average electrical diameter of the lumen from 38 μm to 30 μm and to decrease luminal perfusion flow. In other tubules as many as 10 such radial constrictions could be observed in a segment less than 1 mm long. In vivo, where the hydrostatic pressure for fluid flow through the tubule lumen might be low, these radial constrictions may serve to advance tubular fluid along the length of the nephron. Supported by a grant from the Whitehall Foundation to A. K., Cornell University start-up funds to K.W.B., and NIH 2 SO7 RR 05764-06 to MDIBL.

THE VOLTAGE-CLAMPED DOGFISH GASTRIC MUCOSA: DEPRESSION OF NET H^+ SECRETION, CONDUCTANCE CHANGE AND ANOMALOUS "BASE" SECRETION

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It is asserted that proton transport across the apical border of the oxyntic cell is electrogenic because hydrogen

ion secretion is modified by displacing the transmucosal potential difference, PD. For the canine gastric wall perfused in situ and the isolated frog gastric mucosa, hyperpolarization rendering the mucosal face more negative with respect to the serosal surface enhances hydrogen ion secretion and depolarization inhibits secretion: the "Rehm" effect. Earlier study failed to elicit a Rehm-effect from the isolated gastric mucosa of the dogfish (Hogben, Bull. Mt. Desert Island Biol. Lab. 15: 45, 1975 and Sharks, Skates and Rays. Editors, P.W. Gilbert R.F. Mathewson and D.P. Rall. Johns Hopkins Press Baltimore, Maryland, pp. 299-315, 1967). The electrical transient of the dogfish mucosa had not displayed slow components, $t_{1/2}$ of several seconds to minutes, (Hogben, Acta Physiol. Scand., Special Suppl. 1978, pp. 111-130). Such slow transients imply that voltage-clamping perturbs the intracellular ionic milieu and provide an alternate basis for the Rehm-effect. With a pO_2 of 1 atm, Kidder altered the secretory rate by voltage-clamping the dogfish mucosa but did not establish an unqualified Rehm-effect (Bull. Mt. Desert Island Biol. Lab. 17: 25, 1977). The response to voltage displacement was delayed by thirty minutes and hyperpolarization did not consistently enhance secretion. From the present study it is apparent that the consequences of voltage-clamping are highly time-dependent and are associated with a delayed conductance change. An anomalous "base" secretion was encountered sporadically.

METHODS

Dogfish caught in Frenchman Bay were held in a live car 1-3 days, but for Series I the sojourn was not recorded. Gastric mucosa was separated from the muscle coat by dissection and mounted in a flux chamber providing for study of 2 adjacent segments, each 3 cm^2, bathed on either side by 30 ml of saline. To promote heat exchange with the flux chamber, whose general features have been depicted elsewhere (Invest. Opthalmol. 6: 340, 1967), the bases were aluminum plates separated from the bathing solutions by thin Teflon sheet. Placement of pins about the apertures defining the exposed areas of mucosa allowed stretching of the mucosa just short of tearing. The wet weight of stretched mucosa was 107 $\pm$ 28 (SD) $mg.cm^{-2}$, n=28. The interval from removal of the fish from the live-car to mounting in the flux chamber and being bathed by gassed saline was 20 $\pm$ 3 (SD) minutes. The elasmobranch saline, (E_s), at the serosal surface was Na^+ 252, K^+ 10, Ca^{2+} 10, Mg^{2+} 4, Cl^- 240, HCO_3^- 30, PO_4 2, SO_4^{2} 4 mEq/l with 28 mM glucose and gassed normobarically with 5% CO_2, 95% O_2. At the mucosal face the saline was similar but an additional 32 mEq/l of Cl^- replaced HCO_3^- and PO_4. It was gassed by 100% O_2. A second serosal solution, (E_{TES}), was bicarbonate free but buffered by 30 mM by TES (commonly known as N-tris-(hydroxy methyl) methyl-2-aminoethane sulfonic acid) adjusted to pH 7.5 at 15° and gassed by 100% O_2. The solutions in the chamber were held at 15 $\pm$ 0.5° by a heat exchanger. At 15 and 30 minutes the bathing solutions were replaced twice for a total of 4 changes. Carbachol was added to the serosal solutions at 31 minutes, final concentration 5 μM. For mucosae to be titrated to pH 4.5, 50-200 μl of 9 mM HCl in 275 mM NaCl were added to the mucosal solution to reduce the pH to about 4.5. The mucosal solutions were "stat" titrated to either pH 4.5 or pH 7.0 employing a straight syringe pump delivering 73 mM NaOH in 275 mM NaCl at 7 μl/min and controlled by a signal from the pH meter, Radiometer PHM-62, via a trip relay, pH being measured with a combination glass-calomel electrode, Radiometer GK 2321 C. Rates of acid secretion were derived from the elapsed time of pump operation. In actual operation the ON to OFF running times were for pH 4.5, 35 $\pm$ 27 (SD) and pH 7.0, 71 $\pm$ 41 seconds. The first hourly period commenced 21 $\pm$ 3 (SD) minutes after addition of carbachol. For each hourly period, delivery of NaOH was recorded at 15, 35 and 60 minutes. pH was standardized with both combination electrode and reference buffer at 25°. However, for an experiment of several hours, while the tip of the combination electrode was in the mucosal solution at 15°, the electrode head (calomel cell) was at ambient temperature which on occasion rose from 20 to 35°. When "base"

secretion occurred, the mucosal solution was titrated by hand with a graduated 0.25 ml syringe delivering 9 mM HCl in 275 mM saline.

Two protocols were followed. For Series I the sequence of 5 hourly periods was: 1. open circuit, 2. voltage-clamp at +60 mV or -60 mV, 3. open circuit, 4. voltage-clamp at -60 mV or +60 mV and 5. open circuit. Voltage-clamping was instituted 30 seconds prior to the start of the period and discontinued 30" before the end. the voltage-clamp current was recorded at 2 and 58 minutes. The spontaneous (open-circuit) PD was recorded at 2, 58, 122, 178, 242, and 278 minutes. Conductance was computed from the ratio of the voltage clamp current to open-circuit PD. The sequence of hourly periods for Series II was: 1. open circuit, 2. voltage-clamp at +45 mV, -45 mV or control open-circuit, 3. open-circuit. At 3, 13, 30 and 50 minutes the voltage-clamp current was turned on or interrupted for 10-15 seconds. For a given mucosal segment, the polarity of the clamping current was consistent throughout three hours. The PD was recorded with a pair of matched calomel cells, Radiometer GK 2026 C, and meter PHM -62. The junction between the calomel cell and 275 mM NaCl-3% agar bridge was a 1 M KCl solution, (Invest. Ophthalmol. 6: 340, 1967). The asymmetry PD was less than $\pm$ 1 mV and stable. An interbridge resistance of 7.4 ± 0.8(SD) $\Omega.cm^2$ was ignored. The voltage-clamp current from a battery and variable resistor was periodically adjusted by hand and delivered to a pair of carbon electrodes in saline-agar wells separated from the bathing solutions by a diffusion barrier (Invest. Ophthalmol. 6: 340, 1967).

Carbachol has been observed to increase mucosal conductance and establish a modest positively oriented PD of about +5 mV (Comp. Biochem. Physiol. 42A: 153, 1972). However, the earliest conductance for stretched mucosae is 2.6 times that previously recorded, perhaps because inter-tubular diffusion is favored allowing carbachol to attain a higher effective concentration earlier.

RESULTS

In the experiments of Series I, the mucosal solution bathing one segment was "stat" titrated at pH 4.5 and for the adjacent segment at pH 7.0. Mucosae from 6 fish were first voltage-clamped at +60 mV and after an hour of recovery then clamped at -60 mV, mucosal surface negative to ECF or serosal surface. The sequence was reversed for 5 other fish. During the second hour both hypo- and hyper-polarization progressively reduced the H^+ ion secretory rate, Table 1. Recovery during the third hour was incomplete and not sustained. While a comparable pattern obtains for subsequent voltage-clamping, hour 4, and recovery, hour 5, one cannot exclude a bias from the antecedent episode of voltage clamping.

During voltage clamping, one might anticipate from random error that the pattern of the successive secretory rates of 15, 20 and 25 minutes could be one of progressive enhancement for some individual mucosal segments. Such a pattern was encountered 4 times among 44 mucosal-segment hours of clamping but these were confined to hyper-polarization at hour 4 and in each case similar results were achieved in both segments from the same fish. The random chance for such pairing is less than 1:64.

The limited scrutiny of conductance only revealed an appreciable increase evoked by hyperpolarization. The PD changes were negligible.

In series II voltage-clamping was confined to a single one-hour period. Nine mucosal segments serving as controls were operated continuously for 3 hours at their spontaneous PD except for 12 brief, 10-15 second pulses required for conductance determination. Even though polarization was less, 45 mV, again both hypo- and hyperpolarization progressively reduced H^+ secretion, Table 2a. The reduction was more pronounced for hyperpolarization and followed by a more striking recovery. Removal of exogenous HCO_3^- and CO_2 by the use of the TES, 100% O_2 serosal solution, E_{TES}, did not qualitatively modify the response to polarization.

TABLE 1. Series I: Ordinary elasmobranch saline, ($\bar{x}$±SE).

	Q_{H^+}					G				PD			
	μ Eq.cm^{-2}hr^{-1}					mS.cm^{-2}				mV			
Titrate pH	4.5	7.0	4.5	7.0		4.5	7.0	4.5	7.0	4.5	7.0	4.5	7.0
Minutes					Minutes								
	Spontaneous PD					Spontaneous PD				Spontaneous PD			
0-15	2.8±.6	3.2±.4	3.4±0.8	4.1±0.7	2					2.2±.5	2.2±.5	3.0±0.8	2.8±0.4
15-35	2.8±.5	3.0±.4	3.2±0.8	4.0±0.7									
35-60	2.7±.6	2.6±.3	4.5±1.5	3.5±0.7	58					-0.3±.4	0.2±.4	0.0±1.7	0.0±1.3
Clamp	+60mV		-60mV			+60mV		-60mV		+60mV		-60mV	
60-75	2.0±.5	2.0±.3	2.8±0.7	2.4±0.5	62	3.1±.3	3.7±.3	4.5±.6	5.2±0.6				
75-95	1.5±.6	1.8±.3	2.1±0.7	1.8±0.7									
95-120	1.1±.4	1.3±.1	1.8±0.7	1.6±0.6	118	3.4±.2	3.5±.3	8.0±.6	8.4±1.2				
	Spontaneous PD					Spontaneous PD				Spontaneous PD			
120-135	1.4±.4	1.5±.2	2.1±1.0	3.0±0.6	122					-2.3±.7	-0.8±.8	-1.8±0.8	-1.8±0.7
135-155	2.4±.6	2.1±.3	2.0±0.9	2.8±0.9									
155-180	1.8±.3	1.8±.2	1.9±1.0	2.4±0.7	178					-2.0±.7	-0.2±.8	-0.6±1.0	-0.6±0.8
Clamp	-60mV		+60mV			-60mV		+60mV		-60mV		+60mV	
180-195	1.7±.4	1.8±.2	1.7±0.9	2.5±1.2	182	4.1±.3	3.9±.4	3.5±0.3	4.4±0.6				
195-215	1.5±.5	1.3±.3	1.6±0.9	2.5±1.2									
215-240	1.3±.5	1.5±.5	1.4±0.9	2.3±0.7	238	7.0±.4	6.4±.7	3.5±0.4	4.6±0.8				
	Spontaneous PD					Spontaneous PD				Spontaneous PD			
240-255	1.5±.4	1.4±.2	1.5±0.8	2.6±0.7	242					-1.7±.2	-0.7±.4	0.6±0.9	0.6±1.1
255-275	1.2±.4	1.5±.3	2.1±0.7	2.7±0.7									
275-300	1.5±.5	1.5±.4	2.1±0.8	2.4±1.0	298					-1.7±.3	-0.7±.5	-0.2±1.0	0.6±0.8
n	6	6	5	5									

TABLE 2a. Series II: Rate of H^+ Ion Secretion, ($\bar{x}$±SE).

Minute	Q_{H^+} μ Eq.hr^{-1}cm^{-2}				
	Ordinary Saline			TES, 100% O_2	
	Spontaneous PD				
0-15	4.1±.3	3.8±.2	4.3±.3*	3.6±.1	4.1±.5
15-35	4.6±.2	4.4±.2	4.8±.3	3.6±.4	4.2±.3
35-60	4.4±.2	4.5±.2	4.5±.3	3.4±.4	3.9±.3
Clamp	--	+45mV	-45mV	+45mV	-45mV
60-75	4.2±.2	4.2±.2	3.3±.3	3.3±.4	3.0±.5
75-95	4.2±.2	3.9±.2	2.6±.4	3.2±.4	1.8±.5
95-120	4.0±.2	3.2±.3	2.6±.2	2.8±.3	1.9±.3
	Spontaneous PD				
120-135	3.9±.2	3.4±.3	3.9±.4	2.6±.3	3.4±.5
135-155	4.0±.2	3.8±.3	4.0±.3	2.7±.2	3.4±.4
155-180	3.8±.2	3.6±.3	3.8±.2	2.6±.3	3.3±.5
n	9	12	7*	4	4

*Omitting Experiments 17B and 18B, see TABLE 3.

Unexpectedly 3 mucosal segments "stat" titrated at pH 4.5 escaped from stat control, when hyperpolarized, the pH of the mucosal solution rising above 8. On the first occasion, the unexpected development disrupted the protocol. The two subsequent episodes are presented individually, Table 3. While from the log it is noteworthy that these two

TABLE 2b. Series II: Electrical Parameters ($\bar{x}$±SE)

Min-utes	G mS.cm^{-2}					PD mV				
	Ordinary saline (E_s)			TES,100%O_2 (E_{TES})		E_s			E_{TES}	
	Spontaneous PD					Spontaneous PD				
3	7.4±.8	7.4±.6	7.5±.8*	6.7±1.0	6.3±0.4	5±1.1	3±.3	5±.6	3±1.2	4.0±1.2
13	7.2±.8	7.2±.5	7.6±.7	6.6±1.0	5.6±0.4	6±0.8	4±.3	6±.6	4±1.5	4.3±1.1
30	6.4±.7	6.2±.4	6.9±.6	5.8±0.9	5.1±0.4	5±0.6	4±.3	5±.6	4±1.7	3.0±1.1
58	5.2±.6	5.2±.3	5.8±.4	4.8±0.7	4.4±0.4	5±0.4	3±.4	4±.6	2±1.3	2.3±0.6
Clamp	--	+45mV	-45mV	+45mV	-45mV	--	+45mV	-45mV	+45mV	-45mV
63	4.9±.5	5.2±.3	5.7±.4	4.7±0.7	4.9±0.7	5±0.6	5±.5	3±.7	5±2.0	0.5±0.3
73	4.7±.4	5.1±.4	5.7±.4	4.6±0.6	6.2±1.3	5±0.5	6±.4	2±.6	6±1.6	0.3±0.3
90	4.4±.4	5.0±.4	6.5±.4	4.4±0.6	7.5±1.8	4±0.4	6±.6	2±.6	6±1.8	0.0±0.4
118	4.1±.3	4.8±.4	7.2±.4	4.5±0.5	8.7±2.1	4±0.4	5±.6	1±.6	5±1.4	-0.3±0.5
	Spontaneous PD					Spontaneous PD				
123	4.0±.3	4.9±.4	5.5±.3	4.5±0.6	6.0±1.4	4±0.5	3±.7	2±.6	3±1.6	0.0±0.4
133	3.9±.3	4.8±.4	5.0±.2	4.6±0.7	4.5±0.7	4±0.3	2±.8	2±.5	1±1.9	0.3±0.3
150	3.8±.3	4.8±.4	4.9±.2	4.8±0.9	4.2±0.5	4±0.3	2±.8	2±.5	1±1.8	0.5±0.3
178	3.8±.3	4.7±.4	5.0±.2	5.2±1.2	4.0±0.4	4±0.4	3±.6	3±.4	2±1.5	1.0±0.0
n	12	9	7*	4	4					

*Omitting Experiments 17B and 18B, see TABLE 3.

TABLE 3. Two mucosae that developed anamalous "base" secretion, (ordinary saline).

Minutes	Q_{H^+} μ Eq.cm^{-2}hr^{-1}		Min-utes	G mS.cm^{-2}		PD mV	
	17B	18B		17B	18B	17B	18B
			Spontaneous PD				
			3	2.8	7.6	3	5
0-15	4.7	5.5	13	3.0	7.8	3	4
15-35	4.3	5.8	30	2.7	7.9	2	4
35-60	4.4	6.0	58	2.4	7.0	0	2
			Clamped at -45mV				
			63	2.4	7.9	-3	1
60-75	2.2	0.05	73	4.2	8.1	-2	1
75-95	0.2	-2.4	90	6.1	8.3	-2	1
95-120	-12.3	-30.2	118	6.4	9.0	-3	0
			Spontaneous PD				
			123	3.4	6.4	-2	1
120-135	0.9	-1.7	133	3.2	6.1	-2	1
135-155	3.0	0.9	150	2.8	6.0	-2	1
155-180	2.8	4.0	178	2.6	6.0	-1	1

"Base" secretion expressed as negative Q_{H^+}.

(Paired controls 17A and 18A included in TABLE 2)

experiments were conducted in an exceptionally smooth manner, the rudimentary provision for back-titration by hand does not allow assigning the recorded rates of "base" secretion precisely to the specified intervals. Most conservatively, the minimum rates of "base" secretion can be computed to embrace the preceding and subsequent intervals, for 17B, $-4.8\ \mu Eq.cm^{-2}hr^{-1}$ over 1.0 hour and 18B, -8.5 over 1.6 hours, with the voltage-clamp current being 2.9 and $8.2\ \mu Eq.cm^{-2}hr^{-1}$, respectively. Though for 18B the difference between the minimum rate of "base" secretion and the clamp current is small it is manifestly real. Note that there was a substantial restoration of the H^+ ion secretory rate during recovery. The expected increase of conductance induced by hyperpolarization was not exceptional. The absence of a significant change in the open-circuit PD is remarkable. The adjacent segments, 17A and 18A, which were not polarized, followed the normal course depicted in Table 2a.

Thus a significant and high rate of "base" secretion was encountered in 3 episodes of hyperpolarization and "stat" titration to pH 4.5 out of 10 such episodes in Series II. Though not an infrequent event, these are the first observed episodes of "base" secretion encountered in 24 years of studying the dogfish gastric mucosa. In Series II, there was a fourth episode of "base" secretion 33A, asceetained 10 minutes after addition of carbachol while the PD was +5 mV (open-circuit) and 17 minutes before "stat" titration capture. The minimum rate was $3.6\ \mu Eq.cm^{-2}hr^{-1}$ and of course a zero voltage-clamp current. Retrospectively for Series I. there were 2 episodes when no net secretion of H^+ ion was recorded for 1.0 hour, the last 45 minutes of hour 4 and the first 15 minutes of hour 5, when the mucosal solutions were being "stat" titrated to pH 4.5, one each for hypo- and hyperpolarization. It was not recognized whether or not there had been escape from "stat" control. Among the 22 mucosal segments were 4 isolated intervals of 20 or 25 minutes of 0 acid secretion recorded. A zero rate of acid secretion was not encountered when the mucosal solutions were titrated to pH 7.0.

The conductance changes induced by and following polarization are presented in Table 2b, the corresponding secretory rates having been portrayed in Table 2a. Paralleling the effect on secretion, the conductance response to hypopolarization was modest. Strictly speaking it is relative. Whereas control mucosae displayed a continued decline of conductance during hour 2, -21%, during hypopolarization G decreased by only -8%. The +24% conductance increase during hyperpolarization of -45 mV is unambiguous. Again the change is delayed. Examined as a "very-slow transient", the perturbation of G during the hour of hypopolarization would escape detection and not be evident until 30 minutes of hyperpolarization. Again recovery is more dramatic after hyperpolarization. The status quo ante was not restored by the end of 1 hour of recovery after either hypo- or hyperpolarization. Experience with solution E_{TES} was qualitatively similar. While the concomitant changes of the open-circuit PD are trivial, because they are so small they require documentation. The delayed responses of induction and recovery are considered more incisively by contrasting the 95% confidence limits of the last 25 minutes of each hour. Both hypo- and hyperpolarization reduced the rate of proton secretion, though recovery was not established for hyperpolarization to -60 mV, Table 4. Within the context of conventional perception (cf. The Significance Controversy Eds. Morrison, DE & Henkel RE, Aldine Publishing Co., Chicago, 1970), it could be said that for hypopolarization by +45 mV, a conductance increase has not been established, Table 5. The events of hour 4 and 5 of Series I do not qualify for singular comment other than noting that they are undoubtedly biased by prior intervention.

DISCUSSION

For the record it is necessary to comment on prior study of a putative Rehm-effect displayed by the isolated dogfish gastric mucosa, though the issue may be somewhat academic in the light of hitherto unrecognized con-

TABLE 4. Mean differences ± 95% confidence limits for H^+ secretory rates, $\mu Eq.cm^{-2}hr^{-1}$, of the third 25 intervals; from Tables 1 and 2.

Minutes / Clamp	(95-120)-(35-60)	(155-180)-(95-120)	(215-240)-(155-180)	(275-300)-(215-240)	n
		Series II			
CONTROL	-0.33± .25	-0.28±.18			9
+45mV	-1.25± .45	+0.42±.50			12
-45mV	-1.87± .61	+1.12±.39			7
		Series I			
+60mV; -60mV	-1.45± .30	+0.64±.41	-0.41±.65	+0.08±.41	12
-60mV; +60mV	-2.32±1.36	+0.43±.64	-0.32±.43	+0.42±.50	10

Underlined values are outside the 95% confidence limits of the control.
For series I, combined values obtained by titrating to pH 4.5 and 7.0.
*Omitting experiments 17B and 18B.

TABLE 5. Mean differences ± 95% confidence limits for conductance, mS. cm^{-2}; from Tables 1 and 2.

Clamp	CLAMP	RECOVERY	CLAMP
	Series II		
Minute	118'-58'	178'-118'	
CONTROL	-1.18± .64	-0.23± .49	
+45mV	-0.39± .33	-0.11± .37	
-45mV*	+1.48±1.04	-2.27±1.06	
		Series I	
Minute	118'-62'	182'-118'	238'-182'
+60mV; -60mV	+0.02± .27	+0.56± .52	+2.70± .89
-60mV; +60mV	+3.33± .82	-4.24±1.08	+0.10± .24

Footnote and n see Table 4.

ductance changes. In the first study (Bull. Mt. Desert Island Biol. Lab. 15: 45, 1975), the mucosal solutions, removed every 45 minutes, were titrated outside the flux chamber precluding scrutiny of delayed effects. The electrical parameters were not measured. Less reasonably, the statistical consolidation of 4 staggered "recovery" periods introduced bias. Though not then considered to be "statistically significant" polarization would have appeared to enhance acid secretion. In retrospect, the subsequent claim (Bull. Mt. Desert Island Biol. Lab. 17: 25, 1977), that the dogfish gastric mucosa develops a Rehm-effect in the absence of a slow electrical transient would appear to be premature. The studies differ in several important respects: protocol as they relate to decay and incomplete recovery, temperature at 18°, "stat" titration at pH 4.5, and a carbachol concentration of 250 vs 5 μM. It is not enlightening to single out a further difference, a pO_2 of 1.9 vs 0.9 atm, as a sufficient explanation for the disparity between the two studies.

While the inflection points in the I/V plot of an epithelium have been variously interpreted (Biochem. J. 43: 336, 1948; Am. J. Physiol. 229: 947, 1975), it is prudent to regard voltage-clamping beyond the inflection point

as operating in a different domain. Kidder determined for the dogfish gastric mucosa that there is a hypopolarization inflection point at +24 mV and a possible hyperpolarization inflection point about -50 mV (Bull. Mt. Desert Island Biol. Lab. 18: 6, 1978).

Though the present study was not designed to advance understanding of anomalous "base" secretion, a few comments are in order. Conditions for evoking "base" secretion by the isolated fundic mucosa have been established by Flemström (Am. J. Physiol. 233: E1, 1977) and by Rehm (Am. J. Physiol., in press, 1981). However the rates reported to date for amphibia have been modest, about 0.4 μEq.cm^{-2}hr^{-1}, and an order of magnitude less than that of the dogfish fundic mucosa. It is not known whether the exceptional rate would be maintained. Clearly study of "base" secretion by the isolated fundic mucosa is intrinsically important, but to use a pejorative adjective it is by no means certain it is "physiological" and can be extrapolated to the mammal in vivo. To date "base" secretion has been accompanied by a deteriorated conductance. Whether sporadically or consistently, it has only been elicited by adverse circumstances, e.g., excessive voltage-clamping, anoxia or inhibition (Sanders SS personal communication). "Stat" titration at pH 4.5 deemed meritorious by some should be regarded as an adverse circumstance for the isolated gastric mucosa. The implicit and at times explicit inference that "base" secretion represents bicarbonate secretion is so far without foundation. It is noteworthy as noted here as well as by others that the open-circuit PD does not change importantly with the onset of base-secretion. Thus the net change of transmucosal ionic currents is at best small. The overall process is one of ion exchange. That the exchange is passive is remote. Though the nature of the exchange is unknown a forced H^+:Na^+ exchange (Transport Mechanisms in Epithelia. Alfred Benzon Symposium V. Editors, H.H. Ussing and N.A. Thorn, Academic Press, New York and London, pp. 236-253, 1973) should not be considered remote

Though it may be regrettable to close on an editorial note, it should be acknowledged that we may be at the end of an era. Much if not all of the world literature on the isolated gastric mucosa of the last 45 years must now be re-evaluated.

ACTIVE POTASSIUM SECRETION BY FLOUNDER URINARY BLADDER: ROLE OF A BASOLATERAL NA-K PUMP AND APICAL POTASSIUM CHANNEL

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We reported previously (Dawson and Andrew, Bull. MDIBL, 19: 46, 1979) that the urinary bladder of the winter flounder exhibited a short circuit current (I_{sc}) which was consistent with the flow of positive charge from serosa to mucosa. Although I_{sc} was abolished by ouabain the current was not directly related to NaCl absorption. Bladders with no detectable I_{sc} nevertheless absorbed NaCl. Furthermore, I_{sc} could be abolished with either lidocaine or the calcium ionophore, A23187, while NaCl absorption was unaffected.

In this paper we present evidence that I_{sc} in the flounder bladder is attributable to active potassium secretion. The results are consistent with a simple model (Fig. 3) in which potassium is actively accumulated by the epithelial cell via a basolateral Na-K ATPase and then leaves the cell, down a favorable electrochemical potential gradient, through a barium-sensitive potassium channel in the apical membrane.

METHODS

Urinary bladders were removed from flounder which had been maintained for several days to a week in flowing sea water and mounted in Ussing chambers (Area = 1.25 cm^2) as previously described (Dawson and Andrew, loc cit).