Res, 60, 45-53, 1970) and x irradiation (Rieck, unpublished data). To further evaluate this relationship, fertilized embryos were incubated in 3 μg/ml camptothecin at 3, 15, 30, 40, 50 minutes following fertilization. In those incubated in camptothecin between 3 - 40 minutes following fertilization cleavage occurred at 145 minutes while in the control and 50 minute sample cleavage occurred at 100 minutes. It thus appears that camptothecin is acting during the initial S period. To corroborate this hypothesis samples of treated embryos were preserved for later histological study.

Thus, camptothecin may be acting like cytosine arabinoside, necessitating repair before cleavage can occur; further studies are necessary to substantiate this hypothesis. Rifamycin SV and gallium nitrate have no significant effect on sand dollar embryos in the concentrations examined.

1971 #17

FURTHER OBSERVATIONS ON THE RESPONSE OF THE DOGFISH GASTRIC MUCOSA TO CATION SUBSTITUTION

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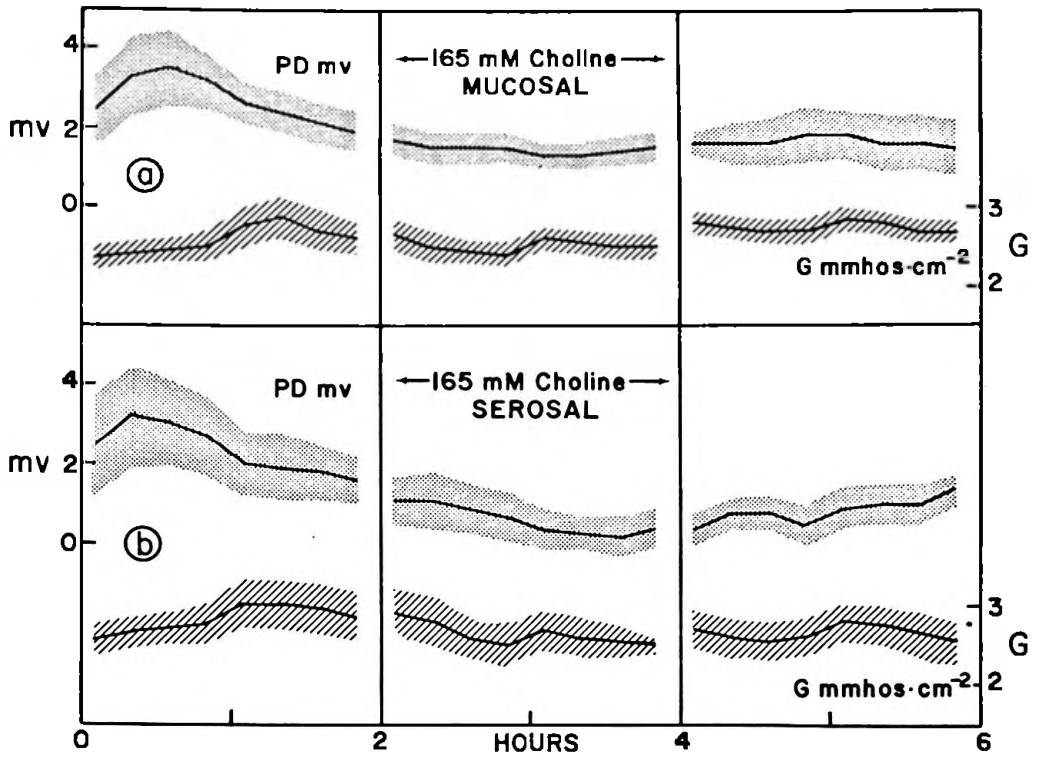
Exposure of the isolated dogfish gastric mucosa to a high extracellular [K^+] partially inhibits the active transport of Cl^-, dissociating it from the active transport of H^+ (Hogben et al., Comp. Biochem. and Physiol. [in press]). Both active transport of Cl^- and H^+ continue when almost all extracellular Na^+ is replaced by choline. The following experiments extend these observations.

In the first of three series of experiments, one surface of the mucosa was exposed to a saline in which [Na^+] was reduced to 87 mEq/L by the substitution of 165 mEq/L of choline$^+$. The other surface was bathed by the customary saline resembling dogfish plasma; [Na^+] 252 and [K^+] 10 mEq/L. Every 15 minutes the transmural potential difference (PD) and conductance (G) were recorded and short-circuit current (Isc) calculated as the product. The liquid junction potential difference due to the asymmetrical cation composition of the bathing solutions was ignored since measurement through 3 M KCl bridges established that it was less than 0.5 mv. In a second series of experiments, the customary saline was replaced at both surfaces by one having 175 mEq/L K^+ and 87 mEq/L Na^+. Before further measurements were obtained the solutions were removed and replaced 5, 15 and 30 minutes later. The H^+ ion secretory rate was determined at hourly intervals. The last series was conducted in a similar manner with both surfaces bathed by a Na^+ free saline in which Na^+ had been replaced by 252 mEq/L of choline. In other respects the experimental methods were those described in the report cited above.

In a previous study, the effects of unilateral exposure of the dogfish gastric mucosa to an elevated [K^+] were ascribed to the increased [K^+] though there was a concomitant reduction of extracellular [Na^+]. The electrical variables, PD and G, are graphed in Figure 1 for before, during and after exposure of one surface to a low Na^+ saline. Reduction of extracellular Na^+ at either surface did not materially change PD, G or Isc. Thus insofar as choline$^+$ can be considered an indifferent ion, the earlier conclusion has been validated.

The consequences of exposing both surfaces simultaneously to a high extracellular [K^+] have been summarized in Table 1. After an interval of 30 minutes from the time solutions were changed,



The time course of PD and G of the isolated dogfish gastric mucosa before, during exposure of one surface to a low Na^+ saline, and after. Before and after both surfaces were exposed to normal dogfish saline, 252 mEq Na^+. From 2 - 4 hours the mucosal surface was exposed to a saline having 87 mEq Na^+ and 165 mM choline$^+$, panel "a", or the serosal surface, panel "b".

a decidedly positive PD was sustained for 2 hours. Since G increased somewhat, the altered PD was induced by a marked increase of Isc. Acid secretion continued although at a somewhat reduced rate. In the control state Δ, the difference between Isc and H^+, is essentially the rate of active secretion of Cl^-. The high extracellular $[K^+]$ drastically reduced the value of Δ indicating a profound in-inhibition of active transport of Cl^- without a parallel inhibition of H^+ transport. Since the solutions bathing the mucosa were symmetrical, the inhibition of Cl^- transport is evident without requiring correction for net K^+ and Na^+ movement. The inhibition of Cl^- transport is greater with an elevated $[K^+]$ at both surfaces than at one surface.

Successive replacement of the Na^+ free saline over a 30 minute interval was undertaken to insure that residual Na^+, derived chiefly from the mucosa, would be reduced to less than 1 mEq. Even after the reduction of the extracellular Na^+ to a trace, H^+ secretion was maintained though at a somewhat slower rate for 2 hours, Table 1. The inconsequential change in the small value of Isc indicates that the dogfish gastric mucosa continued to actively transport Cl^- when extracellular Na^+ is essentially eliminated.

TABLE 1. ELECTRICAL VALUES AND H ION SECRETION FOR DOGFISH GASTRIC MUCOSA FOLLOWING CATION SUBSTITUTION.

HOUR	E mv	G mmhos.cm^{-2}	Isc μEq.cm^{-2}hr^{-1}	H^+ μEq.cm^{-2}hr^{-1}	A μEq.cm^{-2}hr^{-1}
Control					
1	+ 2.2 ±.7	1.9 ±.1	+0.16 ±.05	+2.64 ±.14	-2.49 ±.18
2	+ 3.3 ±.7	2.3 ±.1	+0.28 ±.06	+3.07 ±.19	-2.79 ±.18
Both surfaces bathed by 175 mEq K^+					
3	+14.9 ±.7	2.9 ±.2	+1.60 ±.10	+2.01 ±.13	-0.41 ±.16
4	+11.9 ±.8	2.7 ±.1	+1.21 ±.11	+1.76 ±.14	-0.54 ±.15
Control					
1	+ 1.7 ±.8	1.8 ±.1	+0.14 ±.06	+2.89 ±.16	-2.75 ±.19
2	+ 2.8 ±.3	2.2 ±.1	+0.24 ±.04	+3.19 ±.17	-2.94 ±.17
Both surfaces bathed by 252 mEq choline$^+$					
3	+ 3.7 ±.3	2.2 ±.1	+0.30 ±.03	+2.08 ±.15	-1.77 ±.17
4	+ 4.0 ±.3	2.5 ±.1	+0.37 ±.03	+2.01 ±.12	-1.64 ±.12

$\bar{x}$ ± SE, n = 10. A = algebraic sum of all unidentified net ionic currents in short-circuit state. Isc obtained from the product E·G. High potassium solution obtained by replacing 165 mEq of Na^+ by 165 mEq of K^+. Extracellular solution having no sodium obtained by replacing 252 mEq of Na^+ by 252 mEq of choline$^+$.

1971 #18

PERMEABILITY OF THE DOGFISH AND BULLFROG GASTRIC MUCOSAE TO UREA AND THIOUREA

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Among the functional attributes which set the elasmobranchs apart from other vertebrates is the fact that although they copiously secrete hydrochloric acid, their isolated gastric mucosae, unlike the mucosae from other vertebrates, do not develop the typical transepithelial potential differences (*Sharks, Skates and Rays*, pp. 299-315, ed. Gilbert, Mathewson and Rall, Johns Hopkins Press, 1964). One explanation advanced for the origin of the usual electrical potential difference is that it is a bicarbonate diffusion potential (Hogben, C.A.M.: Gastric anion exchange: Its relation to the immediate mechanism of hydrochloric acid secretion. Proc. Natl. Acad. Sci. 38:13-18, 1952). Reasoning that the elasmobranchs may have acquired plasma membranes that are uniquely impermeable to urea in order to conserve urea, it was thought that this transformation might also modify the selective permeability to other small solutes such as the common ions.

Gastric mucosae of *Squalus acanthius* and *Rana catesbiana* were separated from their serosal muscle coats. Each, when mounted in a flux chamber, was bathed by a saline solution having a composition approximating the plasma of the appropriate species. The solutions were gassed with 95% O_2, 5% CO_2 and glucose was provided as a substrate. Experiments on the dogfish were conducted at ca. 15 C and on the bullfrog at ca. 25 C. In most experiments the solution on either side of the