epithelium morphologically similar to that of the collecting ducts covers the inner medulla (F. J. Silverblatt, Kidney Internat., 5:214-220, 1974).

Our studies have shown that: (1) each major tissue zone of the hamster kidney (cortex, outer stripe, inner stripe and inner medulla) is exposed to the urinary space of the pelvis; (2) four morphologically distinct types of epithelia line the pelvis; (3) each type of epithelium covers a particular kidney zone. These morphologically different epithelia and their relationship to specific kidney zones may suggest differences in permeability to urea.

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BRAIN EDEMA IN *Squalus acanthias*

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Brain edema is a pathological condition characterized by a marked increase in brain water. Current therapeutic regimens for treatment of brain edema, caused by such events as head trauma, brain tumor, and stroke, are rather disappointing. Although not totally ineffective, the treatment of brain edema by steroids, osmotherapy, craniectomy, and debridement is cumbersome or has significant risk. It might be argued that the greatest challenge to neurosurgical research lies in the search for precise pathogenesis and specific therapy of brain edema.

Most vertebrates will develop brain edema if the brain is frozen, lacerated, squeezed, pinched, seared or otherwise traumatized. It seemed a curious, perhaps heuristic, discovery when Klatzo reported (Acta Neuropath., 5:161, 1965) that several lemon and nurse sharks subjected to freezing, searing, and detergent brain lesions did not develop histological evidence of inflammation nor did Evans blue-albumin complex suffuse the necrotic tissue, as it would in a mammal similarly injured. Hoping that the explanation of this unique resistance to brain edema might direct a new clinical therapeutic approach, a study in *Squalus acanthias* was undertaken to confirm Klatzo's earlier observation; water content and brain capillary permeability to sodium and albumin were the measured parameters.

Method. Dogfish sharks of varying size and sex were used in this study. A trephine hole, 1.5 cm in diameter, was made in the cartilagenous skull in an area over the olfactory lobes which was devoid of large blood vessels. For cold lesions, a small piece of dry ice was placed in contact with both telencephalic (cerebral) hemispheres and allowed to sublime. The hole was plugged with a rubber stopper, and the fish were returned to a live car. The stopper gave physical protection from trauma but did not prevent the leakage of some sea water into the extradural space which surrounds the brain and cranial meninges. For heat lesions, the right telenecephalic hemisphere was seared through the trephine hole with a red hot rod. Following this the hole was plugged, and the animal returned to the water. Animals which resumed swimming within an hour of the operation were found to survive for many days without any apparent after effects. Those animals which did not promptly resume normal swimming behavior died within one day of the injury.

After one or more days the animals were killed by decapitation; the brains were removed, and the telencephalon and medulla were assayed for water content by drying the sample for 18 hours at 105°C. The water content was calculated as: [1-(dry weight/wet weight)] X 100.

In a second set of dogfish, tracer sodium (^{22}Na, given intramuscularly) and serum albumin (^{125}I-RISA, given intravenously) were simultaneously injected three days after producing a telencephalic cold lesion. Thirty minutes after the injections of the isotopes, these animals were killed, and samples of telencephalon, medulla, and plasma were obtained and analyzed for radioactivity by liquid scintillation spectroscopy. From these data, tissue:plasma ratios were calculated.

Results. Table 1 presents the water content for the various animal groups. Statistical analysis (analysis of variance) was carried out on these results. It was found that there was no difference in water content between the telencephalon of normal fish and the unseared left telencephalon from heat-treated dogfish; however, there were statistically significant differences in the telencephalic water contents between both the normal ($.01 < p < .02$) and unseared ($.02 < p < .05$) groups and the seared (heat lesion, right hemisphere) group. Similar analysis of the telencephalic data from cold-lesioned animals showed statistically significant increases in water content for only the two- and three-day fish ($p < .01$ for both).

TABLE 1

WATER CONTENT (%) OF TWO BRAIN REGIONS IN NORMAL AND BRAIN-LESIONED DOGFISH SHARKS

CONDITION	PROCEDURE	NUMBER	PER CENT WATER* TELENCEPHALON	MEDULLA
Normal		20	83.09 ± .22	73.54 ± .29
Heat Lesion (1 day delay)	Unseared left hemisphere	10	83.32 ± .31	73.02 ± .46
	Seared right hemisphere	9	84.18 ± .34	
Cold Lesion	1 day delay	7	83.29 ± .31	73.87 ± .63
	2 day delay	5	85.84 ± .81	76.36 ± .65
	3 day delay	12	84.96 ± .38	74.12 ± .27

*Values are the mean ± SE

Regarding the medulla, the water contents of the normal, heat-lesioned, and one- and three-day cold-lesioned animals were similar. A significant difference ($p < .01$) was found, however, between normal and 2-day animals.

The tracer data from cold-lesioned fish, 3 days after injury, are presented in Table 2. There are no significant differences between the normal and cold-lesion ratios, with the possible exception of the RISA ratios for the telencephalon ($.02 < p < .05$).

Discussion. Among the various changes which occur as part of brain edema are increases in tissue water, albumin, and sodium content and in brain capillary permeability. These were the parameters measured in the present study.

TABLE 2

TISSUE:PLASMA RATIOS FOR TRACER SODIUM AND ALBUMIN

30 MINUTES AFTER INJECTION

REGION	CONDITION	RATIO* ^{22}Na	RISA	EXTRAVASCULAR ^{22}Na**
Telencephalan	Normal†	.052 ± .004 (5)	.012 ± .002 (17)	.040 ± .004 (5)
	Cold Lesion (3 day)	.063 ± .015 (6)	.021 ± .004 (6)	.042 ± .011 (6)
Medulla	Normal†	.030 ± .003 (5)	.009 ± .001 (17)	.021 ± .003 (5)
	Cold Lesion (3 day)	.034 ± .002 (6)	.011 ± .003 (6)	.023 ± .002 (6)

* Values are mean ± SE, with N given in parentheses.

† Normal values taken from Fenstermacher and Patlak, Am. J. Physiol (in press).

** Extravascular ^{22}Na was calculated by subtracting the RISA ratio from the ^{22}Na ratio.

Although some statistically significant differences in the telencephalic water data between the controls and the various experimental groups were found, the magnitude of these changes were not very large in terms of "clinical meaningfulness." In mammals such lesions as used in this work produce an increase in beain water of 10% or more, but in these sharks the differences were only on the order of 1-2%. Furthermore, the fact that the water content in the medulla, a brain region quite far from the site of the lesion, appeared to be somewhat higher in those same groups which showed "cerebral edema" suggests that some other factor, such as hemorrhage and subsequent clot formation along the entire neuraxis, may have caused an apparent or spurious elevation of brain water content.

The RISA data indicates that no detectable changes in brain plasma volume or capillary permeability to albumin occurred in the cold-injured region of the brain. In contrast to the mammalian situation, no increase in ^{22}Na uptake by the brain were induced in these animals by this type of lesion.

On the basis of the similarity between the control, unseared hemisphere, and 1-day cold-lesion data, we conclude that the trephining and plugging procedure plus the leakage of sea water into the extradural space did not affect brain water for at least a period of one day. The remainder of our data suggests that sharks do not suffer much edema formation in response to lesions which would cause marked edema in mammals and provides partial support for Klatzo's observations with nurse and lemon sharks.

In his earlier work, Klatzo suggested that factors such as low body temperature, low systemic blood pressure, and unusual capillary-glial relations might account for the resistance to brain edema formation in elasmobranchs. To this list of untested hypothesis, we would like to add unique plasma and tissue protein composition, high urea and salt concentrations in plasma and cerebral fluids, and differences in vesicular transport capab ilities. These hypotheses deserve testing in hopes of revealing clues to the basic mechanism(s) of brain edema formation in mammals which would yield more effective therapeutic schemes.