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Postmortem Biochemical Changes in Canine Cerebrospinal Fluid

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ABSTRACT: Time and temperature effects on postmortem cerebrospinal fluid samples from 60 adult mongrel dogs were studied. After death the dogs were held at 4, 20, or 37°C for intervals of 3, 6, 12, 24, or 48 h. Antemortem and postmortem cerebrospinal fluid was evaluated for sodium, chloride, potassium, urea nitrogen, glucose, creatinine, calcium, phosphorus, and carbon dioxide. Sodium and urea nitrogen values remained stable. Chloride levels decreased. Potassium and phosphorus levels increased with postmortem interval and may be of forensic science value. Low levels of postmortem calcium might indicate antemortem hypocalcemia; high levels of postmortem glucose may indicate antemortem hyperglycemia. Calcium and creatinine levels increased slightly but continually after death; carbon dioxide values dropped.

KEY WORDS: pathology and biology, postmortem examinations, cerebrospinal fluid

Testing postmortem cerebrospinal fluid can be a diagnostic aid, especially when lack of consent or advanced postmortem autolysis prohibits a necropsy. It has been used to evaluate uremia, renal failure, and diabetes mellitus [*1*] in man. Potassium [*2–4*] and inositol [*5*] levels in cerebrospinal fluid reportedly increase with postmortem interval.

Unlike blood, cerebrospinal fluid is free from hemolysis and liver glycogenolysis. It is more difficult to obtain, however, and is commonly contaminated with blood. Also, it is difficult to interpret postmortem values from reports of studies on postmortem cerebrospinal fluid because in those studies, mostly on humans, time and temperature were seldom controlled.

This report is based on a study to determine the postmortem values for urea nitrogen, glucose, creatinine, sodium, potassium, chloride, calcium, phosphorus, and carbon dioxide in dogs killed and held in an environmental chamber.

Materials and Methods

Experimental dogs and procedures were described previously [*6*].

Antemortem cerebrospinal fluid was removed from the foramen magnum with a 21-gauge, 38-mm (1.5-in.) needle attached to a 6-cm^3 syringe. Postmortem cerebrospinal

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fluid was aspirated ventrally from the foramen magnum by penetrating the ventral atlantooccipital membrane after skin, muscles, esophagus, and trachea had been removed.

Chloride levels were obtained with a Buchler-Cotlove chloridometer (Scientific Products, N. Kansas City, Mo.). Other values were determined with a Micro SMA/12-60 sequential multiple analyzer (Technicon Instruments, Inc., Tarrytown, N.Y.).

Results

Antemortem chemical values of canine cerebrospinal fluid—along with means, ranges, standard deviations, and sample sizes—are given in Table 1. For clarity, the postmortem values are divided into three groups: (1) chemistries remaining stable after death; (2) chemistries decreasing after death; and (3) chemistries increasing after death.

Stable Values

Sodium and urea nitrogen remained stable after death. Postmortem sodium values ranged from a mean of 131.25 to 144.5 meq/litre; they were not statistically different (Table 2). The postmortem value dropped an average of 15.6 meq/litre from the antemortem value. Urea nitrogen values ranged from a mean of 11.25 to 25.725 mg/dl

TABLE 1—*Antemortem chemistries of canine cerebrospinal fluid.*

Constituent	Sample Size	Mean	Range	Standard Deviation
Sodium, meq/litre	60	152.47	109-172	7.66
Urea nitrogen, mg/dl	60	16.68	6-38	6.13
Chloride, meq/litre	60	131.17	90-142	6.17
Glucose, mg/dl	60	71.1	52-120	11.1
Carbon dioxide, meq/litre	58	28.66	22-32	2
Potassium, meq/litre	60	3.05	2-3.7	0.24
Phosphorus, mg/dl	58	1.51	1.1-2.2	0.18
Calcium, mg/dl	60	4.77	3.5-6	0.38
Creatinine, mg/dl	60	0.52	0.1-0.8	0.13

TABLE 2—*Postmortem means (upper number), difference means (lower number) between postmortem and antemortem means, and sample size for sodium (meq/litre) in canine cerebrospinal fluid.*

	Postmortem Hours				
Temperature	3	6	12	24	48
4°C	144.5^{a*}	141.6_a	135^a	131.25^a	143.25^a
	$n = 4$	$n = 3$	$n = 4$	$n = 4$	$n = 4$
	-5^{z**}	-20^{xyz}	-20.25^{xy}	-25.75^{x}	-12^{xyz}
20°C	140.25^a	135^a	132.3^a	134.6^a	...
	$n = 4$	$n = 2$	$n = 3$	$n = 3$	...
	-10.25^{yz}	-15^{xyz}	-20^{xyz}	-22.3^{xy}	...
37°C	141^a	138^a	133.5^a	...	...
	$n = 4$	$n = 4$	$n = 4$	...	...
	-9.75^{yz}	-15.25^{xyz}	-15^{xyz}	...	...

*Postmortem means with different superscripts are significantly different ($P < 0.05$).
**Difference means with different superscripts are significantly different ($P < 0.05$).

(Table 3). The antemortem-postmortem difference fluctuated from a rise of 6.675 to a drop of 5.475 mg/dl.

Decreasing Values

Chloride, glucose, and carbon dioxide levels dropped after death. Chloride values were influenced by both time and temperature (Table 4). As indicated, levels dropped with time for each temperature group. Chloride values decreased with temperature when time was held constant. That change was not apparent under 12 h, but thereafter chloride levels dropped by larger amounts with each temperature increase.

Postmortem glucose levels ranged from 0 to 73 mg/dl (Table 5). There was no apparent correlation with time or temperature. For dogs in the 20°C group for 12 h, the postmortem values rose by 2 mg/dl over antemortem values; values dropped for all other groups by 14.5 to 80.5 mg/dl.

Except for the group held at 37°C for 12 h, the postmortem carbon dioxide values were

TABLE 3—*Postmortem means (upper number), difference means (lower number) between postmortem and antemortem means, and sample size for urea nitrogen (mg/dl) in canine cerebrospinal fluid.*

	Postmortem Hours				
Temperature	3	6	12	24	48
4°C	11.25^{c*}	24.375^{ab}	18.875^{abc}	11.25^{c}	23.925^{ab}
	$n = 4$	$n = 4$	$n = 4$	$n = 4$	$n = 4$
	0.25^{uv**}	1.375^{uv}	3.125^{vw}	0.5^{uv}	6.675^{x}
20°C	14^{c}	15.76^{bc}	17.6^{abc}	19.3^{abc}	...
	$n = 4$	$n = 3$	$n = 3$	$n = 3$	...
	-0.25^{uv}	2.76^{vw}	-2^{u}	2.3^{vw}	...
37°C	17.175^{abc}	19.5^{abc}	25.725^{a}	...	...
	$n = 4$	$n = 4$	$n = 4$	...	...
	1.175^{uv}	0.75^{uv}	5.475^{wx}	...	...

*Postmortem means with different superscripts are significantly different ($P < 0.05$).
**Difference means with different superscripts are significantly different ($P < 0.05$).

TABLE 4—*Postmortem means (upper number), difference means (lower number) between postmortem and antemortem means, and sample size for chloride (meq/litre) in canine cerebrospinal fluid.*

	Postmortem Hours				
Temperature	3	6	12	24	36
4°C	131^{a*}	128^{ab}	122.75^{b}	113.5^{c}	101.75^{d}
	$n = 4$	$n = 4$	$n = 4$	$n = 4$	$n = 4$
	-0.5^{z**}	-6.25^{yz}	-10.75^{xy}	-17.5^{wx}	-32.25^{u}
20°C	129^{ab}	128^{ab}	112.6^{c}	112^{c}	...
	$n = 4$	$n = 1$	$n = 3$	$n = 3$	...
	-2.5^{z}	-2^{z}	-19.6^{vw}	-22.6^{vw}	...
37°C	126^{ab}	120.5^{bc}	101.5^{d}	...	...
	$n = 4$	$n = 2$	$n = 4$	...	...
	-3.5^{yz}	-8.5^{yz}	-27.75^{uv}	...	...

*Postmortem means with different superscripts are significantly different ($P < 0.05$).
**Difference means with different superscripts are significantly different ($P < 0.05$).

not statistically different (Table 6). Values for the remaining groups ranged from 10.5 to 19 meq/litre. The postmortem value dropped an average of 12.9 meq/litre from the antemortem value.

Increasing Values

Potassium and phosphorus increased greatly after death; creatinine and calcium increased slightly but continuously. Potassium increased with time; phosphorus increased with time and temperature (Tables 7 and 8).

Postmortem calcium groups (Table 9) were not statistically different. However, the postmortem means indicated that there was a small but consistent rise in calcium with time. Creatinine (Table 10) increased similarly. In addition, when time was held constant, creatinine increased as temperature increased.

TABLE 5—*Postmortem means (upper number), difference means (lower number) between postmortem and antemortem means, and sample size for glucose (mg/dl) in canine cerebrospinal fluid.*

	Postmortem Hours				
Temperature	3	6	12	24	36
4°C	3^{a*}	2.6^{a}	0.5^{a}	37.25^{a}	11^{a}
	$n = 4$	$n = 3$	$n = 4$	$n = 4$	$n = 3$
	-73.5^{xy**}	-75.6^{xy}	-75^{xy}	-37.75^{xy}	-57^{xy}
20°C	56.25^{a}	6.3^{a}	73^{a}	25^{a}	...
	$n = 4$	$n = 3$	$n = 3$	$n = 3$	...
	-14.5^{xy}	-63.6^{xy}	2^{y}	-46^{xy}	...
37°C	0.75^{a}	0^{a}	24.5^{a}	...	...
	$n = 4$	$n = 4$	$n = 4$	...	...
	-63.75^{xy}	-80.5^{x}	-35^{xy}	...	...

*Postmortem means with different superscripts are significantly different ($P < 0.05$).
**Difference means with different superscripts are significantly different ($P < 0.05$).

TABLE 6—*Postmortem means (upper number), difference means (lower number) between postmortem and antemortem means, and sample size for carbon dioxide (meq/litre) in canine cerebrospinal fluid.*

	Postmortem Hours				
Temperature	3	6	12	24	36
4°C	16.25^{a*}	19^{a}	17.6^{a}	16.25^{a}	19^{a}
	$n = 4$	$n = 1$	$n = 2$	$n = 4$	$n = 1$
	-13^{x**}	-13^{x}	-12^{x}	-10.5^{x}	-8.5^{x}
20°C	18^{a}	...	10.5^{ab}	14^{ab}	...
	$n = 4$	...	$n = 2$	$n = 3$	...
	-11.5^{x}	...	-21.5^{y}	-13^{x}	...
37°C	18.6^{a}	18.5^{a}	8.6^{b}	...	...
	$n = 3$	$n = 4$	$n = 3$	...	...
	-9^{x}	-10.75^{x}	-20.3^{y}	...	...

*Postmortem means with different superscripts are significantly different ($P < 0.05$).
**Difference means with different superscripts are significantly different ($P < 0.05$).

TABLE 7—*Postmortem means (upper number), difference means (lower number) between postmortem and antemortem means, and sample size for potassium (meq/litre) in canine cerebrospinal fluid.*

	Postmortem Hours				
Temperature	3	6	12	24	36
4°C	18.45^{de}*	34^{bc}	31.25^{bc}	22.4^{cde}	46.5^{a}
	$n = 4$	$n = 2$	$n = 4$	$n = 4$	$n = 4$
	15.425^{uv}**	30.55^{wx}	28.125^{wx}	19.15^{uvw}	43.375^{y}
20°C	17.575^{de}	25^{bcde}	27.3^{bcd}	35.6^{b}	...
	$n = 4$	$n = 2$	$n = 3$	$n = 3$	...
	14.725^{uv}	22.05^{uvwx}	24.3^{vwx}	32.7^{x}	...
37°C	16.1^{e}	29^{bc}	35.25^{b}	...	...
	$n = 4$	$n = 4$	$n = 4$	...	...
	13.025^{u}	26.025^{wx}	32.125^{x}	...	...

*Postmortem means with different superscripts are significantly different ($P < 0.05$).
**Difference means with different superscripts are significantly different ($P < 0.05$).

TABLE 8—*Postmortem means (upper number), difference means (lower number) between postmortem and antemortem means, and sample size for phosphorus (mg/dl) in canine cerebrospinal fluid.*

	Postmortem Hours				
Temperature	3	6	12	24	36
4°C	4.1^{d}*	7.3^{cd}	10.16^{cd}	16.925^{b}	24.3^{a}
	$n = 1$	$n = 1$	$n = 2$	$n = 4$	$n = 1$
	2.7^{u}**	6.1^{uv}	7.95^{uv}	15.4^{w}	22.9^{x}
20°C	6.725^{d}	...	12.86^{bc}	23.03^{a}	...
	$n = 4$	...	$n = 3$	$n = 3$	...
	5.25^{u}	...	11.53^{vw}	21.53^{x}	...
37°C	6.3^{d}	10.525^{cd}	24.03^{a}	...	...
	$n = 3$	$n = 4$	$n = 3$	...	...
	4.7^{u}	8.925^{uv}	22.3^{x}	...	...

*Postmortem means with different superscripts are significantly different ($P < 0.05$).
**Difference means with different superscripts are significantly different ($P < 0.05$).

TABLE 9—*Postmortem means (upper number), difference means (lower number) between postmortem and antemortem means, and sample size for calcium (mg/dl) in canine cerebrospinal fluid.*

	Postmortem Hours				
Temperature	3	6	12	24	36
4°C	4.9^{b}*	5.4^{ab}	5.4^{ab}	6.05^{ab}	6.1^{ab}
	$n = 2$	$n = 1$	$n = 3$	$n = 4$	$n = 1$
	0.25^{x}**	0.6^{x}	0.73^{x}	1.05^{x}	1.8^{x}
20°C	6.325^{ab}	...	6.45^{ab}	7.13^{a}	...
	$n = 4$	...	$n = 2$	$n = 3$	...
	1.675^{x}	...	1.65^{x}	2.1^{x}	...
37°C	5.2^{b}	5.9^{ab}	5.6^{ab}	...	...
	$n = 3$	$n = 4$	$n = 2$	...	...
	0.36^{x}	0.825^{x}	0.95^{x}	...	...

*Postmortem means with different superscripts are significantly different ($P < 0.05$).
**Difference means with different superscripts are significantly different ($P < 0.05$).

TABLE 10—*Postmortem means (upper number), difference means (lower number) between postmortem and antemortem means, and sample size for creatinine (mg/dl) in canine cerebrospinal fluid.*

	Postmortem Hours				
Temperature	3	6	12	24	36
4°C	0.45^{d*}	0.5^{cd}	0.73^{bcd}	0.8^{bcd}	0.8^{bcd}
	$n = 2$	$n = 1$	$n = 3$	$n = 4$	$n = 1$
	0^{u**}	0^{uv}	0.26^{uvw}	0.55^{wx}	0.2^{uxw}
20°C	0.7^{bcd}	...	0.95^{bc}	1.3^{a}	...
	$n = 4$	...	$n = 2$	$n = 3$	...
	0.1^{uv}	...	0.45^{vwx}	0.66^{x}	...
37°C	0.63^{cd}	0.95^{b}	1.23^{a}	...	...
	$n = 3$	$n = 4$	$n = 3$	...	...
	0.2^{uvw}	0.35^{vw}	0.76^{x}	...	...

* Postmortem means with different superscripts are significantly different ($P < 0.05$).
** Difference means with different superscripts are significantly different ($P < 0.05$).

Discussion

Sodium in postmortem fluid has been reported to decrease [*7,8*] and to be comparable with amounts in antemortem fluid [*2*]. Our work supports both statements: postmortem sodium levels were lower but uniformly so. They were not influenced by time or temperature; differences reflected antemortem variation, not postmortem change.

Urea nitrogen values were also stable; postmortem fluctuations were related to antemortem variations. Several workers [*1,9–11*] reported the possible diagnosis of uremia in postmortem fluid. High urea nitrogen values in postmortem fluid would support that diagnosis, especially if the fluid were analyzed soon after death.

As the time interval increased, chloride dropped consistently and apparently as uniformly as potassium increased. Therefore, chloride is possibly as reliable an indicator of postmortem interval as potassium. Other researchers [*7,12*] have noticed a decrease but did not suggest its forensic science use. In contrast, Paulson and Stickney [*8*] recorded a slight increase.

Postmortem glucose levels [*1,8,9,11,12*] could possibly aid in diagnosing diabetes mellitus. Authors agree that levels drop, but whether the glucose level is time-dependent and of diagnostic value is questionable. In our study we recorded an invariable drop not related to time; elevated postmortem cerebrospinal glucose values might indicate antemortem hyperglycemia, thus supporting a diagnosis of diabetes.

Carbon dioxide values dropped greatly, an average of 12.9 meq/litre. However, the drop was not influenced by time or temperature. Low carbon dioxide values also have been reported by others [*8,13*]. Possibly a high antemortem carbon dioxide value (metabolic alkalosis) could be diagnosed in an animal after its death.

Potassium [*2–4*] and inositol [*5*] have been discussed as to their usefulness in determining postmortem interval. In our study potassium rose with time and phosphorus increased with time and temperature. The postmortem interval might be estimated more nearly accurately if several constituents—such as potassium, phosphorus, and chloride—were considered instead of one electrolyte.

Naumann [*13*] noted that in man creatinine increased in the cerebrospinal fluid up to 10 h postmortem. Naumann [*7*] and Fraschini et al [*2*] reported that calcium levels were stable. Our work confirms their findings. Both creatinine and calcium increased with postmortem interval but only slightly. Therefore, depending on one's interpretation, they could be considered stable. Because calcium increased in cerebrospinal fluid after death,

levels below 4 mg/dl suggest a calcium deficiency. High levels should be interpreted cautiously, and only with prior knowledge of the time of death. High creatinine levels may have diagnostic potential, but only if the time of death and environmental temperature are known.

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