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Sudden Infant Death: Chemical Analysis of Vitreous Humor

The syndrome of sudden and unexpected infant death ("crib death") has long been the subject of investigation. Most reports indicate that a cause of death can be demonstrated at autopsy in one-half to two-thirds of the cases. New diagnostic approaches have been attempted for the remainder; but microbiologic, hematologic, toxicologic, and other studies have been helpful in only a few instances.

An analysis of the postmortem vitreous humor has been shown to reflect the terminal chemical state of the body. This technique has not previously been used in exploring the pathogenesis of sudden infant death. We examined a series of such deaths in this manner hoping that the results might explain one or more of the underlying mechanisms.

Materials and Methods

Specimens of vitreous humor from 67 infants, up to one year of age, most of whom died suddenly and unexpectedly, were obtained. A 12-cc disposable plastic hypodermic syringe with attached #20 needle was inserted in the lateral scleral angle of each eye. The total amount of fluid withdrawn approximated 2 cc and was similar in clarity and consistency to adult samples. Each specimen was refrigerated in a rubber-stoppered tube until the analyses were performed. Osmolality was initially determined, using the Cryomatic Osmometer, Model 31 CM.[2] Following this nondestructive procedure, the entire sample was available for analysis employing either the 2- or 4-channel Auto Analyzer.[3] Sodium, chloride, potassium, calcium, urea nitrogen, and glucose concentrations were measured.

Results

The cases were divided into three groups. There were twelve asphyxial deaths, and they are shown in Table 1. The 33 cases that demonstrated other pathology sufficient to cause death are shown in Table 2. There were 22 undetermined causes of death in the series, and they are shown in Tables 3A and 3B. Since vitreous humor specimens were occasionally of insufficient volume to perform all of the desired tests, some were not performed (. . .), whereas a few could not be reanalyzed following initial measurements (> = greater than; < = less than).

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TABLE 1—*Deaths from asphyxia.*

Case Number	Age	Race	Sex	Postmortem Interval, h	Mechanism of Death	Findings	mOsm/l Osm	mEq/l Na^+	mEq/l K^+	mEq/l Cl^-	mg% VUN	mg% Glu	Ca
1093	1 mo	W	M	>8	Compression by sibling	Neck hemorrhage	289	138	>8.0	122	8	29	...
971	1 mo	N	F	>5	Wedged	Contusions	298	138	11.1	120	14	44	...
641	2 mo	W	M	>3	Wedged	Abrasions	...	136	9.1	116	15	32	...
737	3 mo	W	M	1	Smoke inhalation	Burns	312	128	>8.0	116	21	...	...
645	3 mo	W	F	2	Suffocation	Aspiration	...	139	7.0	...	6	50	...
226	5 mo	W	M	4	Smothered	Bronchiolitis	297	138	9.0	122	14	35	...
413	5 mo	W	F	17	Plastic bag	Otitis	...	139	>8.0	124	17	23	...
556	6 mo	N	F	1	Wedged	Patterned lividity	...	137	6.4	...	16	75	6.2
651	7 mo	W	M	16	Drowning	Atelectasis	293	141	11.0	121	22	< 25	...
883	8 mo	W	F	3	Plastic bag	Pulmonary edema	...	141	7.0	...	19	62	6.3
453	8 mo	W	M	>4	Hanging	Abrasions	...	143	9.5	...	13	15	...
705	8 mo	N	F	>2	Drowning	Scald burns	...	139	7.5	...	13	51	5.9

TABLE 2—*Other recognized causes of death.*

Case Number	Age	Race	Sex	Postmortem Interval, h	Findings	History	mOsm/l Osm.	mEq/l Na^+	mEq/l K^+	mEq/l Cl^-	mg% VUN	mg% Glu	Ca
118	3 wk	W	F	9	Pneumonitis	None	...	133	10.0	113	15	<25	...
681	1 mo	W	M	5	Congenital heart disease	Antibiotic given	309	142	>8.0	>124	15	31	...
041	6 wk	W	F	4	Congenital heart disease	None	300	144	...	124	11	...	7.0
933	2 mo	W	F	17	Bronchiolitis	"Diarrhea"	299	141	>8.0	125	10	28	...
724	2 mo	N	F	8	Malnutrition and dehydration	Twin; diarrhea	334	150	>8.0	>124	24	76	...
709	2 mo	W	M	17	Pneumonitis	None	317	135	>8.0	81	...	<25	...
434	2 mo	W	F	13	Bronchitis and pneumonitis	3 days in hospital	340	146	>8.0	118	...	...	...
092	2 mo	N	F	6	Malnutrition and dehydration; lacerated esophagus	None	...	147	>8.0	>124	105	...	...
397	10 wk	N	M	2	Bronchitis and pneumonitis	Unknown	311	142	>8.0	110	...	17	8.0
096	10 wk	W	F	4	Dehydration; diarrhea	None	327	148	9.4	137	33	40	...
613	3 mo	N	M	12	Endocardial fibroelastosis	Fever and vomiting	327	150	>8.0	>124	35	26	...
040	3 mo	W	M	7	Hemorrhagic pneumonitis	"Difficult breathing"	328	149	12.5	131	...	...	6.8
353	3 mo	N	F	18	Bronchitis	"Cold"	353	144	13.0	125	18	<25	7.5
069	14 wk	N	M	8	Aspiration pneumonitis; slept with mother	None	304	135	11.5	119	15	33	7.1
1086	4 mo	N	F	19	Bronchiolitis	None	299	132	14.5	123	12	<25	...

432	4 mo	N	F	5	Bronchitis and pneumonitis	Respiratory Infection	304	142	>8.0	124	...	58	7.2
313	4 mo	N	M	2	Bronchiolitis	None	302	143	8.5	123	19	35	...
145	4 mo	N	M	2	Malnutrition; pneumonitis	Diarrhea	354	146	6.7	175	91	148	...
216	18 wk	W	M	4	Malnutrition; pneumonitis	Birth injury	304	141	9.0	106	44	...	...
1084	5 mo	W	F	11	Aspiration pneumonitis	None	323	146	13.0	124	32	57	...
1817	5 mo	W	F	3	Auto accident; multiple injuries	None	...	138	6.8	...	24	118	6.3
025	6 mo	W	M	4	Dehydration from diarrhea	Diarrhea; home enema	327	146	>8.0	131	54	88	7.2
351	6 mo	W	F	4	Acute alveolitis with "Intestitial pneumonitis"	None	...	142	15.5	123	...	90	...
440	7 mo	N	M	12	Malnutrition; dehydration	Diarrhea	342	151	>8.0	>124	66	112	...
395	7 mo	N	M	18	Malnutrition; thromboses	Hb S–A	...	144	>10.0	...	73	150	6.7
354	8 mo	W	F	8	Mongolism	None	...	153	12.5	125	42	990	...
869	9 mo	N	M	4	Bronchitis	Respiratory infection	...	...	9.4	...	22	50	6.6
1003	12 mo	W	F	4	Dehydration; terminal thromboses	Fever and diarrhea	272	126	6.9	110	100	32	...
441	12 mo	W	M	11	Subdural hemorrhage	Craniotomy	312	136	>8.0	113	12	32	6.8
108	12 mo	W	M	10	Enteritis (Staph)	Vomiting, diarrhea and shots	...	141	8.0	123	40	60	...
342	12 mo	W	M	18	Status Epilepticus	Seizures	...	137	>10.0	...	28	15	6.6
380	12 mo	N	M	8	Myocarditis	Fever	...	145	8.8	...	11	20	5.9
091	12 mo	W	M	14	"Battered child"	None	...	140	8.5	...	15	50	6.5

TABLE 3A—*Undetermined causes of death, normal electrolytes.*

Case Number	Age	Race	Sex	Postmortem Interval, h	Circumstances	History	mOsm/l Osm.	mEq/l Na^+	mEq/l K^+	mEq/l Cl^-	mg% VUN	mg% Glu	Ca
635	1 mo	W	M	8	Found in own crib	"Cold"; premie	. . .	. . .	. . .	118	26	27	7.2
875	2 mo	N	F	2	Slept with mother (2nd baby death)	None	289	136	>8.0	123	18	22	. . .
809	2 mo	N	F	8	Hb S–A–F	"Cold"	285	136	8.8	121	7	37	. . .
593	2 mo	N	F	3	Small pancreas	Twin; hypoglycemia	304	140	>8.0	120	11	99	. . .
891	2 mo	W	M	4	Crib liner on face	None	291	135	9.6	118	17	<25	. . .
184	2 mo	N	M	4	Increased head size; patent foramen ovale	Premie; fever; heart murmur	291	137	10.5	120	13	25	. . .
492	2 mo	W	F	2	Slept with parents	Fever	303	136	>8.0	123	21	. . .	. . .
143	2 mo	W	M	14	Aspiration	None	312	136	>8.0	116	11	36	. . .
325	10 wk	W	M	2	Face down in playpen	None	. . .	. . .	7.2	. . .	10	70	6.4
1120	3 mo	N	M	4	Tonsillitis	"Cold"	305	140	8.6	124	16	118	. . .
722	4 mo	W	M	4	In adult bed; calcified carotid artery	"Cold"	. . .	. . .	9.4	. . .	24	40	6.6
609	5 mo	N	M	5	Slept with sister (16)	None	297	135	10.1	124	9	28	. . .
137	5 mo	N	M	2	Slept with parents; chronic infection	Maternal syphilis and preeclampsia	299	139	9.3	. . .	12	50	6.4
848	6 mo	W	M	14	Aspiration; pylorus normal	Vomiting since birth	. . .	144	9.4	. . .	17	29	6.4
443	6 mo	N	F	12	DOA at hospital	diarrhea 1 month prior	. . .	137	9.5	. . .	9	19	6.0
344	10 mo	W	M	6	Blanched face; on floor	Premie; R.D.S.	. . .	138	8.9	. . .	13	50	6.2

TABLE 3B—*Undetermined causes of death, abnormal electrolytes.*

Case Number	Age	Race	Sex	Postmortem Interval, h	Circumstances	History	mOsm/l Osm	mEq/l Na^+	mEq/l K^+	mEq/l Cl^-	mg% VUN	mg% Glu	Ca
513	2 wk	W	F	10	Cold bath; gastric ulcers	Fever	317	136	>8.0	112	16	...	...
133	6 wk	N	F	2	Slept with mother; empty GI tract	None	306	134	11.3	112	21	48	...
647	6 wk	N	M	4	Slept with parents	Maternal asthma and renal failure	...	138	3.9	115	7	40	...
256	2 mo	W	M	3	Aspiration; terminal	None	...	133	9.3	...	12	50	6.4
101	10 wk	N	M	17	Slept with father	Diarrhea for 2 days	297	140	11.0	104	9	<25	...
472	3 mo	N	F	6	Found in own crib	"Cold"	...	130	...	111	11	<25	...

NORMAL RANGES OF VITREOUS CHEMISTRIES

	Serum (Hosp)	Vitreous (Coe)	Vitreous (S.U.D.)
Na+	135-145 mEq/L.	(143) 135-151 (4.0)	135-145
Cl^-	95-105 mEq/L.		
Cl^- (CSF)	120-130 mEq/L.	(121) 108-132 (5.9)	115-125
K+	3.2-4.5 mEq/L.	(5.6) 4.2-7.2 (0.7	4.0 +
Urea	8-22 mg%	(17) 6 - 40 (7.6)	5-25
Glucose	70-110 mg%		
Glucose(CSF)	40-70 mg%	(84) 37-180 (40)	<25-100
Calcium	8.8-10.5 mg%		
Calcium (ionized)	5.3-6.3 mg%	(6.7) 6.0 - 8.0 (0.4)	6.0-8.0

Discussion

A range of normal adult values for osmolality in vitreous humor has been established [*1*], and chemical values of vitreous humor in normal adults over varying postmortem intervals have been recorded by Coe [*2*]. He concluded that all sodium and chloride levels and elevated urea and glucose values accurately reflect the antemortem state. The concentrations of other substances required a more careful interpretation when assessing the terminal chemical status. Values for vitreous humor in infants and adults are presumed to be similar if not identical. Normal ranges of electrolytes in this series were set at 135–145 mEq/l for sodium and 115–125 mEq/l for chloride. Urea nitrogen was considered elevated when greater than 25 mg percent. A potassium level of less than 5 mEq/l could indicate hypokalemia (see below). Erratic decreases of glucose, known to occur over the postmortem interval, precluded exact interpretation of these concentrations. These ranges of values were more narrow than those established by Coe in normal adults.

The twelve deaths from asphyxia had no alteration of chemical substances with the exception of the case of smoke inhalation, which revealed a decrease in sodium concentration. In addition, none of these infants demonstrated petechial hemorrhages of the thoracic organs, probably indicating that a rapid terminal anoxic episode had taken place.

In the category of other recognized causes of death, marked changes in sodium, chloride, and urea nitrogen were observed in cases of malnutrition and dehydration, in those having vomiting and diarrhea, in some instances of respiratory infection, and in a few hereditary and traumatic conditions. Marshall [*3*] has described elevations of postmortem blood urea nitrogen in sick infants and in some apparently in good health. Twenty of these 33 cases revealed one or more abnormal chemical concentrations. Fourteen of the cases were analyzed for calcium and all revealed levels considered within normal limits for vitreous humor [*4*]. As expected, osmolality levels generally reflected the concentration of sodium. Five glucose levels over 100 mg percent were noted, including a marked elevation in the case of mongolism.

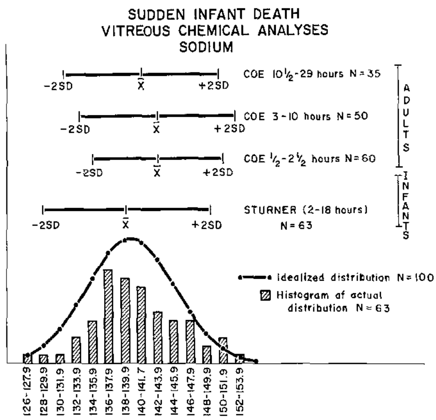
In the 22 infants who had undetermined causes of death, six instances of abnormal electrolytes were noted (see Table 3B). This was manifested by an individual or combined decrease in sodium, chloride, and potassium. In the case showing hypokalemia (3.9 mEq/l), this substance was presumed to be depressed at the time of death because of the constant rise in potassium that takes place during the postmortem interval, in this case four hours [*5*]. The potential for electrolyte imbalance existed in four of these infants when the history and/or the autopsy findings were considered. All six infants were three month of age or younger. The remaining 16 cases (Table 3A) revealed a mild decrease in chloride in three instances, a high glucose in two others, and a slightly elevated urea nitrogen in one infant; but normal findings existed in the remainder. The seven instances in which calcium was measured showed no abnormal values.

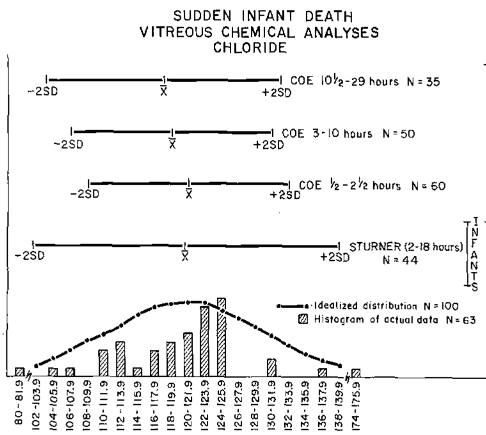
It appears that most infants dying from asphyxia (anoxia) have a rapid terminal episode and so do not undergo a chemical imbalance. In instances of certain protracted illness substantiated by autopsy findings, the supporting evidence of severe chemical alterations can be obtained. More significantly, some sudden infant deaths with insufficient pathology to cause death may reveal an unsuspected electrolyte imbalance, thus affording a "chemical diagnosis" and a probable mechanism of death.

Summary

Sixty-seven cases of sudden infant death were examined and placed in three groups relative to the cause of death; vitreous humor chemical analyses were performed in each case. Asphyxial deaths showed no significant variations from normal concentrations.

Cases with confirmed causes of death had chemical alterations in many instances which were in keeping with the history and autopsy results. In the twenty-two undetermined deaths, there were six instances of electrolyte imbalance which indicated the probable mechanism of death.





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