

Changes in Blood Gases and $A-aDO_2$ during Near-drowning

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The effects of aspirating distilled water, chlorinated distilled water, and sea water on blood gases and intrapulmonary shunting were studied for 72 hours in dogs. A severe persistent arterial hypoxemia followed aspiration of sublethal quantities of all fluids tested. This hypoxemia was associated with intrapulmonary shunting. Hypoxia and shunting were more severe with sea water than with fresh water. Addition of chlorine to distilled water did not change blood gas values. Periodic hyperinflation of the lungs significantly affected blood gas values after aspiration of fresh water, but not after aspiration of sea water. The primary mechanism proposed for the non-ventilation of alveoli after aspiration of fresh water is alteration of the normal properties of pulmonary surfactant with the collapse of alveoli. After aspiration of sea water the presence of fluid in the alveoli prevents ventilation. Whereas the shunt after aspiration of sea water seems to be due almost entirely to perfusion of non-ventilated alveoli, uneven ventilation-perfusion ratios owing to hypoventilation of overperfused alveoli or diffusion abnormalities may contribute to the hypoxia seen after aspiration of fresh water.

EXPERIMENTAL STUDIES of animals following near-drowning indicate that the major abnormality after aspiration of either fresh or sea water is acute asphyxia with persistent arterial hypoxemia. The duration of hypoxemia is unknown, because blood gas changes have

not been followed beyond the first few hours post-aspiration.¹⁻⁶ Recent observations of nine human near-drowning victims show that, in some cases, hypoxia may persist for days.⁷ Measurements of alveolar-arterial oxygen gradients were made in four of these patients during breathing of 100 per cent oxygen. The findings suggested that the initial lesion in near-drowning is perfusion of non-ventilated alveoli, i.e., an intrapulmonary shunt.⁷

The cause of the pulmonary lesion is not clear. Three explanations have been proposed: the presence of fluid interferes with ventilation of alveoli; reflex closure of the terminal airways results; and aspirated fluid alters the properties of pulmonary surfactant. The present experiments were designed to study the natural history and etiology of the aspiration lesion.

Methods

This study was conducted in three parts. In the first, the natural history of the pulmonary lesion was studied in untreated animals after aspiration of sublethal volumes of various fluids. Second, the effect of periodic hyperinflation of the lungs after aspiration of fresh or distilled water or sea water was investigated ("sigh"-treated animals). Third, the effect of continuous mechanical ventilation following aspiration was studied (respirator-treated animals). The latter study also incorporated the effect of a potent bronchodilator.

UNTREATED ANIMALS

Fifteen mongrel dogs weighing from 13.0 to 22.7 kg. (mean 16.2 kg.), were divided according to a table of random numbers into three equal groups, lightly anesthetized with sodium pentobarbital (24 mg./kg. intravenously), and their tracheas intubated with a

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This paper was presented at the Annual Meeting of The American Society of Anesthesiologists, Las Vegas, Nevada, October 2, 1967.

Received from the Department of Anesthesiology, University of Miami School of Medicine and Jackson Memorial Hospital, Miami, Florida. Accepted for publication November 21, 1967. Supported by a Public Health Service Research Career Development Award, 1-K3-GM33840, from the National Institutes of Health, and a grant from the U. S. Public Health Service, 5-R01-CM12154.

cuffed endotracheal tube. With the animals in the supine position, a siliconized polyethylene catheter (I.D. 0.066") was threaded via the femoral artery into the abdominal aorta. The distal end of the catheter was implanted subcutaneously in the thigh to facilitate sampling for 72 hours.

Heparinized arterial blood was drawn anaerobically and analyzed for pH, P_{O_2} and P_{CO_2} within five minutes by direct-reading electrodes in the IL 113-S1 micro apparatus* at 37° C. All electrodes were calibrated immediately prior to drawing each blood sample. Hemoglobin was measured by the cyanmethemoglobin method, and hematocrit with the Guest Weichselbaum microcapillary centrifuge.

The animals then breathed 100 per cent oxygen via a non-rebreathing valve and reservoir bag. Nitrogen washout was assumed to be complete after 15–20 minutes, and a second blood sample was drawn and analyzed for P_{aO_2} , P_{aCO_2} and pH. The alveolar oxygen tension (P_{AO_2}) was calculated from the modified alveolar gas equation:

$$P_{AO_2} = P_B - P_{H_2O} - P_{ACO_2} \quad (10)$$

where P_B = barometric pressure, P_{H_2O} = water vapor tension at 37° C., and P_{ACO_2} = alveolar carbon dioxide tension. The P_{ACO_2} was assumed equal to the P_{aCO_2} . The alveolar-arterial oxygen gradient ($A-aDO_2$) then was calculated. The portion of cardiac output representing shunt was calculated from alveolar and arterial oxygen tensions, hemoglobin concentrations and pH using the shunt equation:

$$\dot{Q}_s/\dot{Q}_t = \frac{C_{CO_2} - C_{aO_2}}{C_{CO_2} - C^{*}O_2} \quad (11)$$

Pulmonary capillary (C_{CO_2}) and arterial (C_{aO_2}) oxygen contents were calculated by a programmed computer method.¹² The program assumed that no alveolar end-capillary diffusion gradient exists; the form of the oxygen dissociation curve was not abnormal; one gram of hemoglobin fully saturated combines with 1.34 ml. oxygen; the solubility of oxygen in whole blood is 0.0031 volumes per cent per mm. Hg P_{O_2} ; and arterial-mixed venous oxy-

gen content difference is 5 volumes per cent.¹³ Since venous oxygen content ($C_{\bar{v}O_2}$) was not measured directly, the values reported indicate approximate magnitude of shunt rather than precise values. Shunt calculations also were performed when the animals breathed room air. For these calculations, the alveolar oxygen tension was calculated from the equation:

$$P_{AO_2} = F_{IO_2} [P_B - P_{H_2O}] - P_{ACO_2} \left[F_{IO_2} + \frac{1 - F_{IO_2}}{R} \right] \quad (14)$$

The respiratory exchange ratio (R) was assumed = 1.

After baseline studies were completed the endotracheal tube was connected via a Y-adaptor to a water reservoir and breathing bypass described previously.¹ At zero time the bypass was occluded and the animals aspirated 11 ml. of fluid per kilogram of body weight (equal to the approximate tidal volume).¹ Group 1, aspirated distilled water (DW); Group 2, chlorinated distilled water (CDW)†; and Group 3, sea water (SW). Three minutes after aspiration, the trachea was suctioned and the volume of fluid obtained measured. All studies were repeated one, four, 24, 48 and 72 hours after aspiration.

After four hours the dogs were allowed to awaken, extubated and returned to their cages. For subsequent studies, the animals were lightly anesthetized with 50 mg. increments of sodium thiopental until active movement ceased (lid reflex and respiration remained active, however). The tracheas were re-intubated, the arterial catheters exposed and studies performed as described previously.

Post-aspiration results were compared to pre-aspiration values in order that each animal might serve as its own control. The results were keypunched on data cards and analyzed for statistical significance with the aid of a digital computer, according to Student's *t* test.¹⁵

"SIGH"-TREATED ANIMALS

Ten dogs, average weight 16.7 ± 3.9 kg., were divided into two groups and prepared

* Instrumentation Laboratories Inc., Boston, Massachusetts.

† Five parts trichloro-s-triazinetriene added per million parts distilled water.

TABLE 1. Mean Change and Standard Deviation in P_{aO_2} Between Pre- and Post-aspiration Values (Reported as ΔP_{aO_2} for untreated animals. All measurements were made with the animals breathing room air. P values for statistical significance between the pre- and post-aspiration values are based on Student's t test.)

Group	Number of Animals	Hours Post-aspiration									
		1		4		24		48		72	
		ΔP_{aO_2} mm. Hg	P	ΔP_{aO_2} mm. Hg	P	ΔP_{aO_2} mm. Hg	P	ΔP_{aO_2} mm. Hg	P	ΔP_{aO_2} mm. Hg	P
DW	5	-56±15	**	-51±10	*	-26±1	*	-21±8	**	-20±7	**
CDW	5	-61±13	*	-54±23	**	-34±20	†	-28±18	††	-19±13	††
SW	5	-63±13	*	-66±15	*	-37±14	**	-27±9	**	-25±10	**

* 0.001 > P .** 0.01 > P > 0.001.† 0.05 > P > 0.01.†† 0.1 > P > 0.05.

exactly as the untreated animals. The animals in one group were subjected to aspiration of unchlorinated distilled water, 11 ml./kg., and those in the other to an equal volume of sea water.

Seventy-five minutes post-aspiration these animals were given a forced deep breath by means of a four-liter reservoir bag connected to a Y-adaptor and pressure manometer. Compressed air was delivered into the tail of the bag, and when the manometer registered 30 cm. of water the bag was connected to the endotracheal tube. The animal breathed through this system until the pressure reached 35 cm. of water. The procedure took 5 to 15 seconds to perform and was repeated at 15-minute intervals from 1½ to 3¾ hours post-aspiration. The data from these two groups of animals were compared with those from untreated animals which aspirated unchlorinated fresh water, (DW) and sea water, (SW).

RESPIRATOR-TREATED ANIMALS

Ten animals, average weight 18.7 ± 4.9 kg., were subjected to aspiration of 11 ml./kg. of distilled water (five dogs) or sea water (five dogs). Seventy-five minutes post-aspiration, these animals were connected to a volume-limited respirator* modified to deliver 100 per cent oxygen. Their lungs were ventilated at a tidal volume of 44 ml./kg. (four times normal) and a rate of 10 per minute. Blood gases were analyzed and $A\text{-}a\text{D}O_2$ and shunts

* Emerson Post-Operative Ventilator, J. H. Emerson Co., Cambridge, Massachusetts.

were calculated at 15-minute intervals for four hours post-aspiration. During mechanical ventilation, if spontaneous ventilatory efforts appeared, succinylcholine was administered intravenously in 10-mg. increments to produce apnea. The fact that hyperventilation was achieved in all animals was confirmed by the low P_{aCO_2} values found (20–38 mm. Hg). No attempt was made to hyperinflate the lungs periodically during the course of ventilator therapy, other than the constant ventilation at high tidal volumes.

The effect of a bronchodilator on the aspiration lesion was studied as follows. Four additional animals (two DW, two SW) were prepared as above. Five minutes post-aspiration, however, these animals were allowed to breathe 100 per cent oxygen via a non-rebreathing system. Arterial blood gases were determined and $A\text{-}a\text{D}O_2$ and shunt calculated 30 minutes post-aspiration and at five-minute intervals thereafter. After the 30-minute blood sample was drawn, mechanical ventilation was instituted as above. Fifty minutes post-aspiration an intravenous infusion of isoproterenol was started via a Harvard infusion pump at a rate of 0.0033 mg./kg. per minute for 40 minutes. Mechanical ventilation was continued until the experiment was terminated 150 minutes post-aspiration.

During preparation of the animals which were to be either periodically hyperinflated or mechanically ventilated, three dogs failed to show a large $A\text{-}a\text{D}O_2$ after aspiration of distilled water. Since it was not possible to evalu-

TABLE 2. Mean Change and Standard Deviation in A-aDO₂ While Breathing 100 Per Cent Oxygen Between Pre- and Post-aspiration Values (Reported as ΔA-aDO₂ for untreated animals. *P* values for statistical significance between the pre- and post-aspiration values are based on Student's *t* test.)

Group	Number of Animals	Hours Post-aspiration									
		1:15		4:15		24		48		72	
		ΔA-aDO ₂ mm. Hg	<i>P</i>	ΔA-aDO ₂ mm. Hg	<i>P</i>	ΔA-aDO ₂ mm. Hg	<i>P</i>	ΔA-aDO ₂ mm. Hg	<i>P</i>	ΔA-aDO ₂ mm. Hg	<i>P</i>
DW	5	437 ± 75	*	454 ± 145	**	234 ± 191	††	244 ± 214	††	186 ± 156	††
CDW	5	486 ± 104	*	448 ± 206	**	283 ± 224	†	161 ± 139		81 ± 34	†
SW	5	531 ± 44	*	540 ± 55	*	190 ± 87	**	74 ± 96		91 ± 89	††

* 0.001 > *P*.
** 0.01 > *P* > 0.001.

† 0.05 > *P* > 0.01.
†† 0.10 > *P* > 0.05.

ate the effects of "sigh" or respirator therapy unless a gradient was present prior to therapy, animals with an A-aDO₂ of less than 400 mm. Hg 75 minutes after near-drowning were eliminated from this part of the study. The data from these animals were included, however, in the results dealing with all animals in which blood gases and A-aDO₂ measurements were taken 75 minutes after aspiration.

ALL DW AND SW ANIMALS PRE-ASPIRATION VS. 75 MINUTES POST-ASPIRATION

To define the relationship between acute aspiration of equal quantities of fresh water and sea water more clearly, the data from all animals that aspirated DW or SW and were untreated for at least 75 minutes post-aspiration were combined for analysis; 18 animals in the DW group and 15 in the SW group. In 14 of the animals (six SW and eight DW) a second catheter, threaded via the femoral vein into the pulmonary artery, was connected to a pressure transducer, and mean pulmonary artery pressure was recorded on a direct-writing recorder (confirmation of the site of the catheter was determined by the configuration of the pressure tracing).

Results

UNTREATED ANIMALS

Fourteen of the 15 animals survived the experiment. One died 24 hours after CDW aspiration. Pre-aspiration baseline values for the 15 animals were pHa, 7.41 ± 0.06; PaCO₂, 31.6 ± 6.3 mm. Hg; PaO₂, 92.5 ± 11.2 mm. Hg;

A-aDO₂ during breathing of 100 per cent oxygen, 97 ± 39 mm. Hg; and shunt (Q_s/Q_t), 6.0 ± 3.3 per cent while breathing room air and 5.5 ± 1.8 per cent while breathing 100 per cent oxygen. This degree of shunt, although seemingly high for unanesthetized animals, is within normal limits for anesthetized dogs.¹⁶

Three minutes post-aspiration, no water could be suctioned from the tracheas of animals who aspirated DW or CDW. After SW aspiration, however, 12.7 ± 3.9 ml/kg., 115 per cent of the volume aspirated was obtained by tracheal suction.

One hour post-aspiration, the pHa decreased in 13 of the 15 animals, mean ΔpH, -0.08 ± 0.08 (*P* < 0.01); and the PaCO₂ increased in 12, mean ΔPaCO₂, +7.0 ± 12.1 mm. Hg (*P* < 0.05). After four hours, however, neither the pHa nor PaCO₂ were significantly different from pre-aspiration levels.

The PaO₂ decreased immediately after aspiration and remained below the control value for the full 72 hours in all animals (table 1). There were no significant differences in PaO₂ among the three groups.

The ΔA-aDO₂ 75 minutes post-aspiration exceeded 300 mm. Hg in all animals. The increase in A-aDO₂ was significant in all groups 75 minutes and 4:15 hours post-aspiration, but by 48 hours significant changes were no longer detected in any group (table 2).

There was a six- to 12-fold increase in shunt one and four hours post-aspiration in all animals (*P* < 0.05) (table 3). Although the shunt was slightly less during oxygen breath-

TABLE 3. Percentage of Cardiac Output Representing Shunt (\bar{Q}_s/\bar{Q}_t) During Breathing of Room Air and 100 Per Cent Oxygen (Calculated as described in the text. Mean value and standard deviation of each group is listed. There was no significant difference between room air and oxygen shunts at any time period in any group. Each group consisted of five animals.)

	Group	Hours Post-aspiration					
		0	1:15	4:15	24	48	72
Breathing Room Air	DW	6.8±5.0	56.7±10.5*	50.3±13.5*	21.0±15.2†	17.9±13.5†	16.7±14.5
	CDW	6.3±3.0	59.3±11.6*	52.1±16.0**	29.4±21.7	10.0±10.1	9.4±4.6
	SW	4.9±1.6	60.2±6.5*	63.5±12.4*	26.6±12.7†	16.2±6.7†	13.9±7.0†
Breathing 100 Per cent Oxygen	DW	5.2±2.3	39.0±18.8**	42.0±17.6**	19.6±15.8	17.0±14.2	15.0±11.1
	CDW	5.2±1.5	45.5±20.0†	40.6±22.2†	19.6±12.1	13.0±7.0	8.7±0.9
	SW	6.0±1.9	55.2±8.2*	63.8±15.4*	15.2±5.8†	9.6±4.0	10.2±4.6

The change from pre-aspiration levels was analyzed for significant difference.

* 0.001 > P.

** 0.01 > P > 0.001.

† 0.05 > P > 0.01.

TABLE 4. Mean and Standard Deviation of P_{aO_2} During Breathing of Room Air and A-aDO₂ After 15-20 Minutes of Breathing of 100 Per Cent Oxygen for Animals who Aspirated 11 ml./kg. Distilled Water or Sea Water (All animals were untreated until after the one-hour postaspiration samples were drawn. They were then "sighed" as described in the text from 1½ to 3¼ hours postaspiration. Percentage of cardiac output representing shunt was calculated during both room-air and 100 per cent oxygen breathing.)

		0		1 Hour*		4 Hours		24 Hours		48 hours		72 Hours	
		Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Distilled Water—"Sigh" (5 Animals)	P_{aO_2} mm. Hg	91	11	39	11	54†	8	63	15	73	5	77	8
	A-aDO ₂ mm. Hg	102	22	580	29	461	133	206	32	178	52	147	42
	Per Cent Shunt (Air)	6.1	5.4	50.9	13.7	34.4†	10.9	22.8	13.3	15.2	2.2	10.6	3.0
	Per Cent Shunt (Oxygen)	5.3	1.5	35.1	8.7	26.5	11.9	11.0	1.3	9.1	2.0	8.1	1.9
Sea Water—"Sigh" (5 Animals)	P_{aO_2} mm. Hg	91	6	27	6	34	4	68	9	77	11	75	8
	A-aDO ₂ mm. Hg	103	43	621	16	693	22	270	190	165	73	144	18
	Per Cent Shunt (Air)	5.3	1.5	65.2	6.9	57.1	6.1	25.4	23.9	10.8	5.5	12.0	8.1
	Per Cent Shunt (Oxygen)	5.9	2.5	53.5	14.3	42.3	10.9	14.2	10.1	8.7	2.7	7.4	1.2

* One hour for data during air breathing; 75 minutes for data during oxygen breathing.

† Post-sigh sample (4 hours) significantly different from pre-sigh sample (1 hour) ($P < 0.05$).

ing than during air breathing, the difference was not significant in the three groups ($P > 0.1$).

"SIGH"-TREATED ANIMALS

All ten animals survived the study. Periodic hyperinflation after aspiration of sea water had no significant effect on the P_{aO_2} , A-aDO₂, or shunt ($P > 0.2$) (table 4).

On the other hand, the P_{aO_2} increased at least 12 mm. Hg from the one-hour sample to the four-hour sample in all animals that were "sighed" after DW aspiration ($P < 0.05$) (table 4). Only one untreated animal showed a comparable change. Three of the five dogs showed a decrease in A-aDO₂ of at least 150

mm. Hg after hyperinflation. Whereas the shunt did not change appreciably in the untreated group from one to four hours post-aspiration (table 3), the shunt decreased in all animals who were "sighed" (table 4).

RESPIRATOR-TREATED ANIMALS

Within 15 minutes of instituting mechanical ventilation, four of the five DW animals showed a decrease in A-aDO₂ and shunt ($P < 0.05$) (fig. 1). Although there were slight increases in these measurements from two to four hours, both were still significantly less at the termination of the experiment than before mechanical ventilation ($P < 0.05$).

Four of the five SW animals also exhibited a decrease in A-aDO₂ with mechanical ventilation (fig. 2). Improvement was only temporary, however, and at the termination of the experiment the mean A-aDO₂ and shunt values were not significantly different from the values prior to therapy ($P > 0.3$).

The Δ A-aDO₂ values for the four animals given isoproterenol and mechanical ventilation are shown in figure 3. An increase in A-aDO₂ was seen 30 minutes after aspiration, but within five to ten minutes of starting mechanical ventilation, Δ A-aDO₂ decreased to less than 100 mm. Hg in all animals. The Δ A-aDO₂ began to increase again almost immediately, being more marked in the SW than the DW animals. The Δ A-aDO₂ decreased further when isoproterenol infusion was started. The decrease was only transient, however, and despite continued infusion and mechanical ventilation, a constantly increasing Δ A-aDO₂ was observed in all animals.

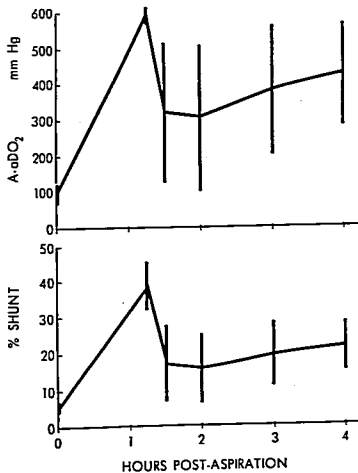


FIG. 1. The mean and standard deviation for A-aDO₂ and shunt calculated during breathing of 100 per cent oxygen are plotted against time. All five animals were ventilated mechanically from 1:15 to 4 hours after aspiration of distilled water.

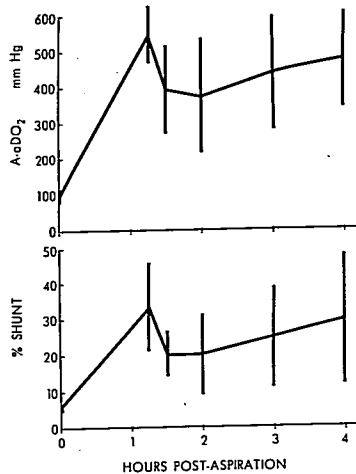


FIG. 2. The mean and standard deviation for A-aDO₂ and shunt calculated during breathing of 100 per cent oxygen are plotted against time. All five animals were ventilated mechanically from 1:15 to 4 hours after aspiration of sea water.

ALL DW AND SW ANIMALS PRE-ASPIRATION
VS. 75 MINUTES POST-ASPIRATION

Prior to aspiration there were no differences in mean values between the fresh water and sea water groups (table 5). The volume of water suctioned from the trachea after DW aspiration was negligible, whereas 13.9 ± 4.3 ml/kg. was suctioned from the SW animals.

The pH_a decreased in both groups ($P < 0.05$), but no difference was observed between them ($P > 0.6$). The Pa_{o₂} decreased in all 33 animals ($P < 0.0001$). The difference between the mean Pa_{o₂} one hour after aspiration of sea water (36 mm. Hg) and distilled water (43 mm. Hg) was of borderline significance ($P < 0.08$).

The A-aDO₂ increased after aspiration in all but one animal (DW). The A-aDO₂ was significantly higher 75 minutes following SW (602 ± 57 mm. Hg) than after DW aspiration (505 ± 161 mm. Hg) ($P < 0.05$).

The shunt during breathing of oxygen was significantly greater in the SW group than in

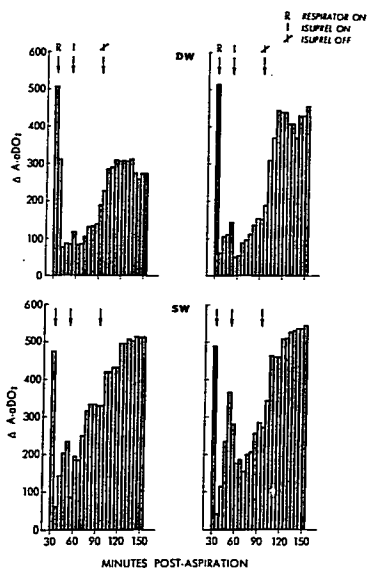


FIG. 3. Thirty to 150 minutes after DW or SW aspiration, the $A-aDO_2$ during breathing of 100 per cent oxygen was compared to the pre-aspiration value at 5-minute intervals. The change is reported as $\Delta A-aDO_2$. Mechanical ventilation of all four animals was begun 30 minutes post-aspiration and continued throughout the experiment. Isoproterenol infusion (0.0033 mg./kg./minute) was administered intravenously from 50 to 90 minutes post-aspiration.

the DW group ($P < 0.01$). The shunt on room air was also higher in the SW group ($0.1 > P > 0.05$). When the shunts measured in room air were compared with those measured in oxygen, they were significantly less during breathing of oxygen after DW aspiration ($P < 0.05$), but not after SW aspiration ($P > 0.05$).

Changes in mean pulmonary artery pressure five minutes following aspiration did not show a consistent pattern. Of the six SW animals, four showed a slight decrease in pressure (from 1 to 4 mm. Hg) and two showed no change. Of the eight animals who had mean pulmonary artery pressure monitored during aspiration of fresh water, there were increases

in pressure in three (2, 5 and 17 mm. Hg), decreases of 2 mm. Hg in two, and three animals showed no change.

Discussion

This study quantitates the acute asphyxia that occurs during near-drowning in chlorinated or unchlorinated distilled water, or sea water. The acidosis and hypercarbia which developed within the first hour of aspiration were transient and were no longer present four hours post-aspiration. The arterial hypoxemia, however, was both severe and persistent.

The large $A-aDO_2$ and calculated shunt found during breathing of 100 per cent oxygen one and four hours post-aspiration suggest that the hypoxia was due predominately to absolute intrapulmonary shunting; i.e., perfusion of non-ventilated alveoli.¹¹ When all animals that aspirated either DW or SW were compared, the total shunt measured during breathing of air was significantly greater than that measured in 100 per cent oxygen one hour after DW, but not after SW, aspiration. It appears, therefore, that in addition to absolute shunt, relative shunt due to ventilation-perfusion imbalance or diffusion abnormalities plays a small role in the hypoxia seen after DW aspiration.

During recovery from aspiration of either fluid, significant hypoxia was present during breathing of room air even after $A-aDO_2$ while breathing oxygen had returned to normal. Similar findings have been observed in humans recovering from near-drowning.⁷ These findings suggest that ventilation-perfusion imbalance or diffusion problems persist even after absolute shunt no longer can be demonstrated.

Periodic hyperinflation of the lungs after aspiration of distilled water produced a significant increase in Pa_{O_2} and a decrease in shunt. After aspiration of sea water, however, "sighing" had no significant effect on these parameters. Colebatch and Halmagyi⁵ reported similar results after smaller volumes of aspirated fluid in sheep. Although the end result (i.e., hypoxia) was the same after aspiration of either fluid, the causes may have been different. Further evidence for this is that when all the animals that had aspirated distilled water were compared with those that had aspi-

rated sea water, mean Pa_{O_2} was lower and $A-aDO_2$ and percentage shunt higher one hour after aspiration of sea water.

Three possible explanations for the shunting and hypoxia seen immediately after near-drowning are: 1) the aspirated fluid alters the surface-tension properties of the surfactant lining the alveoli,^{4,9} 2) presence of the fluid interferes with ventilation of alveoli,^{2,7,8} and 3) reflex closure of the terminal airways results.⁶

Recent experiments in our laboratory have shown that although total immersion of the lungs in sea water or physiologic saline solution can wash out normal pulmonary surfactant, it does not alter its surface tension characteristics. Sufficient quantities of surfactant remained after drowning so that material extracted from the lung still had normal properties. On the other hand, both chlorinated and unchlorinated distilled water altered the characteristics of pulmonary surfactant, elevating the minimum surface tension readings on compression.⁹ Similar changes may occur in alveoli that come in contact with the aspirated fluid during near-drowning. Thus, although distilled water is removed from the alveoli rapidly,^{2,8} its persistent effect may be the result of alveolar instability owing to alteration of pulmonary surfactant. This could account for the decrease in lung compliance and abnormal pressure-volume curves reported after aspiration of fresh water.⁵ If this is the case, periodic "sighing" should temporarily decrease

shunting and elevate Pa_{O_2} . Unless the surface active material was regenerated, however, uneven ventilation and recurrent collapse of alveoli would occur. This also explains why animals which were ventilated continuously with large tidal volumes showed a smaller $A-aDO_2$ and less shunting after four hours than those that were "sighed" intermittently. Even with continued mechanical ventilation, however, unless the surface active material were regenerated, uneven ventilation-perfusion ratios and alveolar collapse would be expected.

Although distilled water is removed from the lung very rapidly after aspiration, sea water has been shown to remain longer.⁸ Because of its hypertonicity, it also draws plasma into the lung.^{3,8} The acute effect of this fluid transfer on blood volume has been reported previously.³ Hypovolemia still can be demonstrated 48 hours after aspiration of sea water in untreated animals (unpublished data). If the alveoli are filled with fluid this would prevent their ventilation, thus explaining the non-ventilation of perfused alveoli which occurs after aspiration of sea water. Manual hyperinflation of the lung every 15 minutes had no effect on this group of animals. Although continuous hyperinflation after sea water initially decreased $A-aDO_2$ and size of absolute shunt, this was only temporary. Similar findings have been reported after aspiration of 1-3 ml/kg. of sea water in sheep,⁵ wherein it was proposed that inflation of the lung further dis-

TABLE 5. All Animals Which Aspirated Distilled Water or Sea Water and Were Not Treated for at Least 75 Minutes (Mean and standard deviation of pH_a , Pa_{CO_2} , Pa_{O_2} and per cent shunt during room-air breathing, and $A-aDO_2$ and per cent shunt during 100 per cent oxygen breathing, are listed prior to and one hour after aspiration. The data one hour post-aspiration are compared to the pre-aspiration data for statistical significance.)

	Time	pH_a	Pa_{CO_2} mm. Hg	Pa_{O_2} mm. Hg	$A-aDO_2$ mm. Hg	Per Cent Shunt (Air)	Per Cent Shunt (100% O_2)
Distilled Water (18 Animals)	0	7.39±0.07	30±8	93±11	105±33	6.6± 4.4	5.6± 1.8
	1 hour†	7.34±0.08**	37±12**	43±13*	505±161*	47.0±15.9*	33.0±15.1*
Sea Water (15 Animals)	0	7.39±0.07	33±4	92±6	101±36	5.8± 2.1	5.8± 1.9
	1 hour†	7.32±0.08*	33±9	36±12*	602±57*	56.6±13.2*	47.5±15.0*

† 1 hour for data during air breathing; 75 minutes for data during oxygen breathing.

* Significantly different from "0" time, $P < 0.0001$.

** Significantly different from "0" time, $P < 0.05$.

tributed the fluid which had accumulated, thereby interfering with alveolar ventilation.⁵

Reflex airway closure which responds to isoproterenol has been reported to play a major role in the shunting found after aspiration of small quantities of water.⁶ After an initial decrease, the A-aDO₂ progressively increased in spite of continuous isoproterenol infusion in this study. It is unlikely, therefore, that this mechanism accounts for a major contribution to shunting after aspiration of 11 ml./kg. of either fresh or sea water.

Reflex pulmonary hypertension is reported to occur in sheep following aspiration of small quantities of fresh water. The increase in pressure was not related causally to the accompanying fall in arterial oxygen saturation.¹⁷ In the present experiments, aspiration of sea water did not elevate mean pulmonary artery pressure, and following aspiration of fresh water the changes varied considerably from animal to animal.

The rapidity with which changes in A-aDO₂ can occur is stressed by results in animals which were ventilated mechanically 30 minutes post-aspiration. The wide and rapid changes in A-aDO₂ recorded emphasize the necessity of frequent evaluation of arterial oxygen tension when treating for aspiration.

Conclusions

These studies indicate that severe, persistent arterial hypoxemia follows aspiration of sublethal quantities of distilled water, chlorinated distilled water and sea water. The initial cause of hypoxemia is shunting of blood through perfused, but non-ventilated, alveoli. The underlying mechanism for non-ventilation of alveoli after aspiration of fresh water is an alteration of the normal surface tension properties of pulmonary surfactant with collapse of the alveoli. These alveoli are prone to hypoventilation and recollapse even after reinflation. After aspiration of sea water, fluid in the alveoli prevents ventilation. The degree of hypoxia and shunting is more severe with sea water than with fresh water. Whereas the intrapulmonary shunt after aspiration of sea water is due almost entirely to perfusion of non-ventilated alveoli, uneven ventilation-perfusion ratios due to hypoventilation of over-

perfused alveoli or a diffusion abnormality also may contribute to the hypoxia seen after aspiration of fresh water. The addition of chlorine to distilled water did not change the observed blood gas and A-aDO₂ values. Further study is necessary before conclusions can be drawn as to whether the continued hypoxia seen 48 and 72 hours after aspiration is due to ventilation-perfusion imbalance or to interference with diffusion of oxygen. This study also confirmed that mechanical ventilation with oxygen initially can decrease the alveolar-arterial oxygen gradient and shunting sufficiently to provide adequate PaO₂ for full saturation of hemoglobin. The effect is temporary, however, especially after aspiration of sea water.

The technical assistance of April V. Showers, R.N., Earlene J. Newby and Bruce C. Ruiz is gratefully acknowledged.

The assistance of Richard Sandifer in the statistical analysis of the data, and the suggestions for preparation of the manuscript by Drs. Leon Farhi and Lawrence Saidman, are gratefully acknowledged.

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Anesthesia

PORPOISE ANESTHESIA Anesthesia was induced by injecting thiopental 10 mg./kg. into the tail fluke veins of the porpoise. The trachea was then intubated without the use of succinylcholine because of the reported absence of plasma cholinesterase in these animals. Following thiopental, no more than 2 per cent halothane vaporized with a Mark 2 vaporizer was necessary for induction. Swimming movements of the free tail flukes were found to be a most reliable indicator of depth of anesthesia. During induction, swimming movements disappeared after loss of strong corneal and eyelid reflexes. When these movements disappeared, the animal was sufficiently anesthetized for surgery to begin. A Bird Mark 9 respirator was used for ventilation. The use of nitrous oxide was discontinued after three trials, because it was not reliable as an anesthetic agent and when pushed to high concentrations was associated with cyanosis. The halothane technique was used satisfactorily in 18 porpoises. (Ridgway, S. H., and McCormick, J. G.: *Anesthetization of Porpoise for Major Surgery*, *Science* 158: 510 (Oct.) 1967.)

FULMINANT HYPERTHERMIA Rapid, progressive hyperpyrexia is becoming a cause for concern. It occurred in 12 patients, ten of whom did not survive the acute episode. Conventional anesthetic drugs, including thiopental sodium, succinylcholine chloride, nitrous oxide, and halothane, were employed in most of the patients. No specific signs or symptoms heralded the onset of the hyperthermia. Usually the first observation was that the skin of the patient felt very hot; cardiovascular collapse developed shortly thereafter. At the moment, the primary treatment is prophylactic: continual monitoring of body temperature will detect the beginning of increases in body heat and permit therapy before the condition becomes irreversible. When the syndrome develops, drastic measures must be instituted at once to reduce body temperature, provide high concentrations of oxygen with hyperventilation, and combat metabolic acidosis. (Stephen, C. R.: *Fulminant Hyperthermia during Anesthesia and Surgery*, *J.A.M.A.* 202: 178 (Oct.) 1967.)