

An Evaluation of Steroid Therapy in Aspiration Pneumonitis

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Endotracheal instillation of 0.1 N HCl in 19 anesthetized dogs caused a severe pulmonary reaction that resulted in hypoxia, hypercarbia, metabolic acidosis, hemoconcentration and death in 80 per cent of the animals. The resultant pulmonary damage was not altered morphologically or physiologically by high (30 mg/kg), low (0.3 mg/kg), or multiple (30 mg/kg every 8 hours for three days) doses of methylprednisolone administered intravenously. (Key words: Lung; aspiration; Hormones; steroid; aspiration.)

ASPIRATION of acidic gastric contents results in a high mortality rate, regardless of the therapy instituted.¹⁻³ Recommended treatment includes parenteral steroids, prophylactic antibiotics, and oxygen administration.²⁻⁵ The optimum steroid dose and regimen have not been established. This study was designed to evaluate the effects of high- and low-dose steroid therapy after aspiration of hydrochloric acid.

Materials and Methods

Nineteen mongrel dogs ranging in weight from 13.0 to 17.5 kg had blood drawn anaerobically from their femoral arteries for determinations of pH_a , PaO_2 , $PaCO_2$,§ complete blood cell counts (CBC), and hematocrit. Their respiratory and heart rates were recorded

and they were anesthetized with sodium pentobarbital (25 mg/kg, iv). The trachea of each dog was intubated with a cuffed endotracheal tube, an esophageal thermistor probe was inserted to the level of the heart, and a 20-g Teflon catheter was inserted percutaneously into the femoral artery. After inhalation of 100 per cent oxygen through a reservoir bag and nonbreathing valve for 20 minutes, Hct, pH_a , PaO_2 , and $PaCO_2$ were determined again. Five ml of 0.9 per cent NaCl were instilled through the endotracheal tube, and a tracheal aspirate was obtained for culture on blood agar. An anterior-posterior chest x-ray was taken. The dogs again breathed room air for 15 minutes and a third blood sample was analyzed for Hct, pH_a , PaO_2 and $PaCO_2$ to ensure return of preanesthetic respiratory function. All blood-gas tensions were corrected for the animals' temperatures.

Then, 0.1 N hydrochloric acid, pH 1.0 to 1.1, 2 ml/kg body weight, was instilled through the endotracheal tube. Animals were assigned randomly to four groups and treated 21 minutes after aspiration as follows.

GROUP I

Five dogs received 0.9 per cent NaCl, 0.5 ml/kg body weight, iv, 21 minutes after aspiration, and every 8 hours thereafter for 72 hours.

GROUP II

Five dogs received methylprednisolone sodium succinate,¶ 0.3 mg/kg body weight, iv, 21 minutes after aspiration, and every 8 hours for 72 hours.

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TABLE 1. Arterial P_{O_2} , P_{CO_2} and pH , and Bicarbonate (Mean \pm SD) before and after Aspiration of 0.1 N HCl,* F_{I,O_2} 0.21

	Preaspiration (Min)					Postaspiration (Min)						
	-60	-20	-1	10	20	40	60	120	180	240	270	
	P_{O_2}											
Group I, no steroid	92.1 \pm 5.4	534.4 \pm 39.6	92.4 \pm 6.7	41.1 \pm 8.9	37.5 \pm 8.7	36.1 \pm 9.6	40.2 \pm 10.4	39.8 \pm 9.6	39.5 \pm 7.2	45.8 \pm 7.2	80.9 \pm 20.9	
Group II, 0.3 mg/kg methylprednisolone	91.6 \pm 7.8	533.0 \pm 36.0	92.6 \pm 10.9	38.6 \pm 11.1	38.9 \pm 9.2	41.8 \pm 5.5	44.9 \pm 6.1	50.8 \pm 12.8	46.0 \pm 14.2	49.6 \pm 25.5	168.8 \pm 182.6	
Group III and Group IV, 30 mg/kg methylprednisolone	96.8 \pm 8.6	524.0 \pm 41.8	92.3 \pm 17.4	40.9 \pm 17.3	39.1 \pm 16.3	40.6 \pm 15.9	44.1 \pm 16.4	41.3 \pm 16.4	41.7 \pm 16.6	41.0 \pm 17.9	114.0 \pm 123.0	
P_{CO_2}												
Group I, no steroid	31.5 \pm 3.4	41.9 \pm 8.7	37.5 \pm 2.4	42.5 \pm 1.9	40.4 \pm 3.3	46.2 \pm 8.2	43.7 \pm 12.5	34.4 \pm 8.8	31.3 \pm 6.6	29.9 \pm 5.5	29.8 \pm 5.8	
Group II, 0.3 mg/kg methylprednisolone	33.5 \pm 3.8	43.1 \pm 9.5	31.8 \pm 8.4	47.4 \pm 18.4	47.9 \pm 19.0	47.1 \pm 12.9	44.0 \pm 17.1	37.8 \pm 10.8	25.8 \pm 6.5	31.7 \pm 6.8	31.6 \pm 6.1	
Group III and Group IV, 30 mg/kg methylprednisolone	31.7 \pm 5.4	42.6 \pm 9.3	36.2 \pm 9.0	46.9 \pm 18.3	45.2 \pm 14.3	45.1 \pm 11.8	43.0 \pm 9.1	37.5 \pm 11.6	30.2 \pm 4.5	29.8 \pm 4.6	33.0 \pm 6.3	
pH												
Group I, no steroid	7.44 \pm 0.05	7.36 \pm 0.06	7.41 \pm 0.06	7.32 \pm 0.03	7.31 \pm 0.04	7.25 \pm 0.06	7.26 \pm 0.13	7.33 \pm 0.15	7.32 \pm 0.12	7.33 \pm 0.08	7.39 \pm 0.07	
Group II, 0.3 mg/kg methylprednisolone	7.41 \pm 0.04	7.34 \pm 0.10	7.44 \pm 0.11	7.27 \pm 0.13	7.26 \pm 0.16	7.23 \pm 0.18	7.25 \pm 0.21	7.30 \pm 0.14	7.34 \pm 0.11	7.30 \pm 0.12	7.31 \pm 0.12	
Group III and Group IV, 30 mg/kg methylprednisolone	7.43 \pm 0.03	7.34 \pm 0.06	7.40 \pm 0.05	7.29 \pm 0.15	7.27 \pm 0.12	7.25 \pm 0.14	7.24 \pm 0.14	7.25 \pm 0.20	7.35 \pm 0.07	7.35 \pm 0.10	7.29 \pm 0.12	
HCO_3^-												
Group I, no steroid	20.9 \pm 2.0	22.5 \pm 2.4	23.2 \pm 2.1	21.4 \pm 1.0	19.9 \pm 1.7	19.6 \pm 0.75	18.4 \pm 1.4	17.2 \pm 2.7	15.5 \pm 1.6	15.2 \pm 0.7	14.4 \pm 1.2	
Group II, 0.3 mg/kg methylprednisolone	20.5 \pm 1.8	22.3 \pm 0.9	20.5 \pm 0.8	20.3 \pm 3.2	19.2 \pm 2.5	18.7 \pm 2.9	17.9 \pm 2.9	17.1 \pm 4.7	13.4 \pm 3.0	15.3 \pm 4.9	15.3 \pm 2.3	
Group III and Group IV, 30 mg/kg methylprednisolone	20.6 \pm 3.0	22.0 \pm 2.8	21.3 \pm 4.0	20.9 \pm 3.9	19.6 \pm 3.0	18.8 \pm 4.4	18.1 \pm 4.1	15.8 \pm 4.2	16.0 \pm 2.9	15.7 \pm 3.9	16.0 \pm 4.0	

* Group I = 5 dogs; Group II = 5 dogs; Groups III and IV = 9 dogs.

† F_{I,O_2} = 1.0 at -20 and 270 minutes.

TABLE 2. Numbers of Dogs Surviving HCl-induced Aspiration Pneumonitis

Group	Number	Hours				Days					
		2	4	8	16	1	2	3	7	14	60
I, control	5	5	4	4	3	1	1	1	1	1	1
II, methylprednisolone 0.3 mg/kg, q8h	5	5	5	3	2	2	2	2	1	1	1
III, methylprednisolone 30 mg/kg	4	4	4	4	1	1	1	1	1	1	1
IV, methylprednisolone 30 mg/kg, q8h	5	5	4	4	2	2	1	1	1	1	1

GROUP III

Four dogs received methylprednisolone sodium succinate, 30 mg/kg body weight, iv, 21 minutes after aspiration, then 0.9 per cent NaCl, 0.5 ml/kg body weight, iv, every 8 hours for 72 hours.

GROUP IV

Five dogs received methylprednisolone sodium succinate, 30 mg/kg body weight, iv, 21 minutes and every 8 hours for 72 hours after aspiration.

Data were collected at the times shown in the tables, and chest x-rays were repeated 40 and 240 minutes after aspiration. Four and a half hours after aspiration all surviving dogs had recovered sufficiently from their anesthesia to be responsive. The endotracheal tube, thermistor probe and femoral artery catheter were removed and the dogs were placed in an oxygen tent containing 30 to 40 per cent oxygen for one week. Parameters listed in tables 1 and 2, the CBC, culture of tracheal aspirate and chest x-ray were obtained from all surviving animals at 1, 2, 3, 14 and 21 days postaspiration. Data from groups III and IV were combined for analysis during the first 8-hour period.

Necropsies of all dogs that died were done, and survivors were sacrificed after 2 months. At necropsy the trachea was exposed and cross-clamped. The thorax was opened, the lungs inspected, and the trachea and lungs were removed *en bloc*. The lungs were weighed and then inflated with 10 per cent buffered formalin to 50 cm formalin pressure

for 48 hours prior to sectioning. All lobes were inspected and any grossly abnormal areas were sampled. Eight to 14 blocks of tissue were taken from each lung and washed overnight in running water prior to processing. All sections were stained with hematoxylin and eosin. Selected sections were also stained with Masson's trichrome and with Wilder's reticulin stains.

Results

Immediately following aspiration of HCl, a brief period of apnea (10 to 20 sec) occurred, followed by marked tachypnea and coughing. With the exception of one dog in Group I, pink, frothy material developed in the tracheas of all animals 20 to 180 minutes following instillation of HCl. Heart rates decreased with aspiration, but returned to pre-aspiration levels by 3 hours. At no time did the dogs become febrile. There was no significant difference between groups with respect to heart rate, respiratory rate, or temperature at any time ($P > 0.10$).

Hematocrits decreased following induction of anesthesia, but increased to above control levels after aspiration ($P < 0.01$). Leukocyte counts were increased at 24 hours, and did not return to normal levels for 2 weeks. No significantly different hematocrits or leukocyte counts were seen in the four groups ($P > 0.10$).

PaO_2 values did not change after induction of anesthesia ($P > 0.10$). After aspiration of HCl, marked hypoxemia occurred in all dogs ($P < 0.001$) (table 1). Calculated alveolar-arterial oxygen differences at $F_{IO_2} = 0.21$

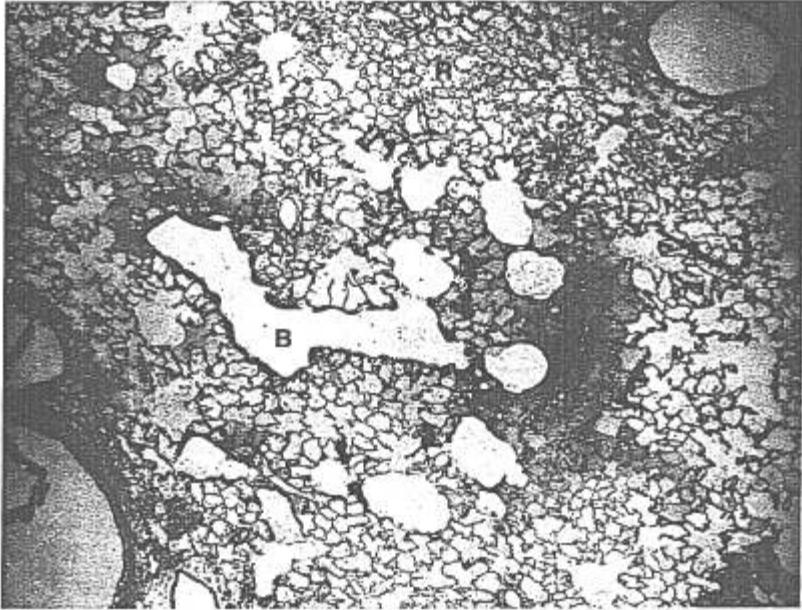


FIG. 1. Lung. Acute reaction 14 hours after instillation of acid. Note bronchiole (B) with surrounding zone of edema and necrosis (N) and a more cellular peripheral reactive border zone (R) (hematoxylin and eosin, $\times 50$).

and 1.0 remained elevated for the entire 2-week period in survivors.

P_{aCO_2} remained elevated for 3 hours after aspiration. Arterial pH declined progressively for 40 minutes, and then began to rise toward, but not to, preaspiration levels. Calculated actual bicarbonate concentration decreased for 2 to 3 hours (table 1). There was no significant difference among the four groups with respect to blood-gas tensions or acid-base status at any time before or after therapy ($P > 0.1$).

Cultures of tracheal aspirates were negative prior to aspiration. At 24 hours one control dog had a positive culture of *Staphylococcus aureus*.

Forty minutes after aspiration of 0.1 N HCl,

all chest x-rays revealed infiltration of both lung fields; generally, the right and left hilar areas were affected most, and the left apical lobe least. The infiltrate was more extensive by 4 hours in each instance. Clearing was evident by 72 hours in the five surviving animals. Two weeks later slight hyperinflation was the only radiologic abnormality in the four surviving animals. No difference in radiologic findings could be detected among the groups at any time.

Only one dog from each group was alive after a week (table 2). Upon necropsy, the lungs of all dogs that died 2.25 to 72 hours after instillation of acid looked similar. Extensive consolidation and hemorrhage involved both lungs. In some cases the con-

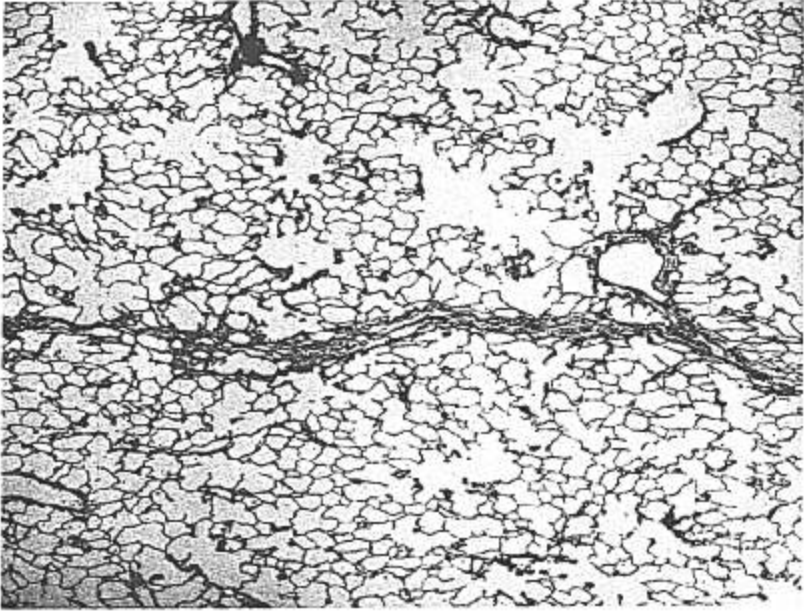


FIG. 2. Lung from dog surviving 2 months after instillation of acid. Note linear scar composed chiefly of cellular fibrous tissue which incorporates a few alveoli and replaces the pulmonary parenchyma. The remainder of the parenchyma is histologically normal (hematoxylin and eosin, $\times 50$).

solidation was patchy and in others, total. There was no apparent preferential involvement of one side over the other, or of apical over cardiac or diaphragmatic lobes. In this group of 15 animals, the lungs of four dogs were two to three times heavier than the estimated normal weights.** Seven had lung weights three to four times normal, and four, more than four times normal. In contrast, of the four dogs surviving 2 months, two had normal lung weights, while in two the lungs were slightly heavier than normal, 1.23 and 1.27 times normal respectively. All animals had evidence of acute bronchitis and

** Normal lung weight was estimated by the formula: $9.4 \times \text{body weight (kg)} = \text{lung weight (g)}$.

bronchiolitis with necrosis and sloughage of mucosa and polymorphonuclear leukocytic infiltration, and some had focal necrosis of the airway walls. Around some respiratory and terminal bronchioles there were reactive zones of variable size, with intra-alveolar edema and fibrin deposition (fig. 1). In some zones the alveolar septal capillaries were engorged and distended with erythrocytes; in others they were dilated, but appeared empty or contained eosinophilic material, while still others were collapsed. The walls of these capillaries were eosinophilic and necrotic, being devoid of nuclei or containing only pyknotic or ghost nuclei. In these areas there was also some intra-alveolar hemorrhage. In addition, around many of these

zones there was a loose peripheral infiltrate of polymorphonuclear leukocytes.

During review of all histologic sections, four dogs that appeared to have considerably less pulmonary damage than the others were selected. On identification these proved to be one dog from Group IV, one from Group III and two from Group II that had died 2.25, 14.0, 6.0, and 9.0 hours following aspiration, respectively. In the three dogs that lived 22, 30, and 72 hours, some resolution was beginning; this was characterized by a decrease in the acute inflammatory component, the appearance of macrophages, and at 72 hours, some proliferation of fibroblasts.

The lungs of the four dogs that survived 2 months were identical to each other. The pleural surfaces were pink and had a "cobblestone" appearance suggestive of emphysema. The parenchyma was crepitant and free from consolidation. On gross sectioning the depressions between the "cobblestones" appeared to result from small fibrous scars, and there was no overt emphysema. Microscopically, the acute inflammation had resolved. Scattered in the parenchyma were cellular fibrous scars which contained a few macrophages, lymphocytes, and hemosiderin granules (fig. 2). The scars were frequently linear and varied considerably in size. In addition, they were sometimes adjacent to bronchioles and associated with a minimal degree of compensatory emphysema.

Discussion

Aspiration of 0.1 N hydrochloric acid rapidly caused extensive pulmonary damage, severe hypoxia and hypercarbia. Transudation of fluid into the lung could account for the increasing hematocrit and lung weights. The metabolic acidosis may have been secondary to the acute decrease in plasma volume resulting from this fluid shift, or from tissue hypoxia secondary to the low arterial oxygen tensions. The marked tachypnea and coughing which followed aspiration probably resulted in dissemination of the acid to other than the dependent lobes. Evidence of pulmonary damage on chest x-ray correlated poorly with

PaO_2 's, an observation also made by Cameron *et al.*,⁸ who used a model similar to ours. Even though the lowest mean PaO_2 was seen 40 minutes after aspiration, the chest x-ray taken at that time did not show as marked an infiltrate as the one taken four hours later. Cultures of tracheal aspirates are in agreement with prior studies, indicating that bacterial pneumonia plays little, if any, role in HCl-induced aspiration pneumonitis.³⁻⁵⁻⁷⁻¹¹ This finding suggests that the prophylactic use of antibiotics following aspiration may be unwarranted, especially since resistant superinfection is likely after administration of antibacterial agents.¹²⁻¹³

The effects of HCl-induced aspiration pneumonitis were unaltered by low, high or multiple doses of methylprednisolone. Other investigators, using corticosteroid preparations other than methylprednisolone, have shown that aspiration of material of pH 1.1 to 1.36 resulted in 80 to 100 per cent mortality.⁷⁻¹⁴⁻¹⁵ On the other hand, Bannister *et al.*⁴ instilled material having a pH of 1.75 in the tracheas of rabbits and found that the pulmonary lesions were smaller in animals that received large doses of hydrocortisone than in those that did not. It has been shown that following aspiration of material having a pH of 1.5 or 1.75, treatment with large doses of corticosteroids combined with IPPB results in less morbidity⁶ and a more rapid resolution of the pneumonitis by x-ray⁵⁻⁷ than IPPB alone. In those experiments, however, all animals survived, even those that received IPPB alone.

Teabeaut⁹ and Taylor *et al.*¹⁶ reported that aspiration of liquid with a pH > 2.1 elicited a response similar to that which occurs following aspiration of water. They also found that as the pH of the aspirate decreased to 1.5, the pulmonary parenchymal damage increased to a maximum. It appears that once a maximal tissue response has occurred, steroid therapy is not beneficial. Thus, if steroids play a beneficial role in the treatment of acid-induced aspiration pneumonitis, it seems to be limited to animals that aspirate material in the narrow pH range of 1.5 to 2.1.

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Metabolism

ACCIDENTAL HYPOTHERMIA The authors discuss a case of accidental hypothermia (initial rectal temperature 84.0 F) in an elderly woman found in her frigid, unheated home. On admission to the hospital, blood pressure and pulse rate (atrial fibrillation) were 90/40 torr and 127/min respectively. The patient was semiconscious, with blanched, anesthetic extremities. Arterial blood pH was 7.29. Azotemia, hemoconcentration, and hyperglycemia were also present. The patient was warmed over 14 hours by immersion in hot water (104 F) and with heating blankets. With warming, administration of intravenous fluids, and basic medical support, all pathologic conditions reverted to normal; a spontaneous return to normal sinus rhythm occurred at 89 F. At discharge the patient was asymptomatic. The shifts of plasma in the peripheral vasculature (as a cause for hemodilution upon rewarming), the effects of hypothermia on renal function (poor tubular water resorption with cold), general enzyme-activity depression (van't Hoff-Arrhenius' law) and attenuation of neurologic processes are discussed. (*Meriwether, E. D., and others: Severe Accidental Hypothermia with Survival after Rapid Rewarming. JAMA* 53: 505-510, 1972.)