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Objective—To describe clinical and clinicopathologic findings from dogs with histologic pulmonary lesions consistent with human adult respiratory distress syndrome and to identify potential risk factors.

Design—Retrospective study.

Animals—19 dogs with acute respiratory distress.

Procedure—Medical records of dogs were reviewed. Signalment, physical examination and clinicopathologic findings at admission, and thoracic radiographic and necropsy findings were recorded.

Results—The most common clinical sign was dyspnea. Respiratory rate ranged from 36 to 140 breaths/min, and abnormal breathing patterns were detected. Crackles were auscultated in 7 dogs. Severe diffuse interstitial and alveolar infiltrates were observed on thoracic radiography in 9 dogs shortly after arrival and developed later in 4 dogs. Four dogs were leukopenic and neutropenic. Disseminated intravascular coagulation was diagnosed in 2 dogs, and hypocalbuminemia was found in 8 dogs. Respiratory status deteriorated rapidly in all dogs, and 10 dogs were mechanically ventilated. Death was attributed solely to respiratory failure in 8 dogs. In the other 11 dogs, severe lesions in nonpulmonary organs, sepsis, or both may have contributed to death. The most common associated conditions that may have contributed to acute respiratory failure were microbial pneumonia, sepsis, aspiration pneumonia, and shock, with more than 1 factor found in 11 of 19 dogs.

Clinical Implications—The index of suspicion for acute respiratory distress syndrome should be high in dogs with bilateral pulmonary infiltrates and acute respiratory distress that rapidly progresses to failure. (J Am Vet Med Assoc 1996;208:1419–1427)

Adult respiratory distress syndrome (ARDS) is a generic term in human medicine that refers to acute, fulminating respiratory failure resulting from various clinical states that lead to diffuse lung injury. Since Ashbaugh et al introduced the term in 1967 to describe a lethal form of respiratory distress in human trauma patients, our understanding of the syndrome has evolved such that now ARDS is recognized as part of a systemic inflammatory response that can lead to multiple organ failure. Adult respiratory distress syndrome is a common and lethal syndrome in human critical-care patients, with mortality of 50 to 70%.

Factors predisposing to development of ARDS may be pulmonary in origin, such as microbial pneumonia, smoke inhalation, and pulmonary contusions, or nonpulmonary in origin, such as pancreatitis, long-bone fracture, and massive blood transfusion. In human medicine, the syndrome is clinically recognized as acute respiratory failure, with bilateral infiltrates on chest radiography, decreased lung compliance, and severe oxygenation defect with nearly normal cardiac function, in patients with 1 or more predisposing factors.

Dogs have been used extensively in experimental models for following the development of ARDS with pancreatitis, paraquat and ethchlorvynol toxicosis, trauma, oleic acid injury, and endotoxemia. In general, however, only a single and transient inciting condition is tested, making this information less applicable to a veterinary clinical setting. Thus, although a few clinical case reports and review articles have been published, most of our information about an ARDS-like disease in dogs is based on reports of human subjects. With availability of more sophisticated and intensive care in veterinary facilities, an acute respiratory distress syndrome in dogs may be encountered more often than was previously suspected, and the ability to recognize predisposing and affected dogs is becoming a priority. The purposes of the study reported here were to identify dogs with pulmonary lesions consistent with ARDS at necropsy; to report the clinical and clinicopathologic findings from these dogs, with emphasis on the nature and progression of the respiratory failure; and to establish a list of potential risk factors for acute respiratory distress syndrome in dogs.

Criteria for Selection of Cases

Records of dogs necropsied at the veterinary hospital from December 1985 to February 1993 were reviewed for those with histologic diagnoses of interstitial pneumonia or alveolitis. From 186 records, 83 dogs with mild or local interstitial changes were excluded. After examining histologic slides from the lungs of 103 dogs, we excluded dogs with congestive heart failure, uremic pneumonia, and pneumonia attributable to canine distemper virus infection. From the remaining 34 records, only dogs that satisfied clinicopathologic and clinical criteria were included in the study.

Dogs must have had gross or histologic evidence of diffuse or extensive lung injury to be included in the study. Furthermore, each dog must have had histologic findings of alveolar inflammation, edema, hemorrhage, necrosis with formation of hyaline membranes, or vascular congestion or at least one of the histologic findings, along with type II alveolar cell proliferation or interstitial fibrosis.
The main clinical criterion for inclusion in the study was acute onset of respiratory distress. Pulmonary edema caused by left-sided heart failure was excluded by thoracic radiography or by finding pulmonary artery occlusion pressure < 18 mm Hg. Dogs with acute onset of dyspnea for which thoracic radiographs were not obtained or not available for review were included if major cardiac abnormalities that might cause left-sided heart failure were not found at necropsy.

Procedures
Clinical and laboratory evaluation—Signalement and historical and physical examination findings relevant to respiratory function were recorded for each dog at admission. The duration of illness and onset and progression of dyspnea were determined.

White blood cell and platelet counts, coagulation assays, and serum albumin concentrations when dyspnea was first detected were recorded. When measurements were repeated, the most abnormal value also was reported for comparison. For dogs in which microbiologic examination had been performed, sources of samples and bacterial isolates were recorded.

Thoracic radiographs were reviewed by one of the authors (LMW). The cardiac silhouette and vessels were evaluated to rule out underlying cardiac disease. On a ventrodorsal radiographic view, the thorax was divided into 6 sections and the lung field was evaluated in each section, using an arbitrary scale from 0 to 4+(0 = normal; 1+ = mild interstitial pattern; 2+ = severe interstitial/early alveolar pattern; 3+ = diffuse alveolar pattern; and 4+ = complete opacification with loss of cardiac silhouette).

In each case, we recorded whether death occurred naturally or whether the dog was euthanatized. Necropsy reports and lung tissue slides were reviewed by one of the authors (TJVW). Severe lesions in nonpulmonary organs and gross pulmonary findings were recorded. Histologic findings in the lungs were subjectively graded from 0 to 3+ (0 = absent; 1+ = mild; 2+ = moderate; and 3+ = severe).

Diagnosis of predisposing factors—Sepsis was diagnosed if the dog had 2 or more of the following conditions: tachycardia, tachypnea, peripheral vasodilatation or vasoconstriction, rectal temperature > 39.7 C or < 37.7 C, > 15,000 or < 5,000 WBC/mm³, > 1,000 band cells, with isolation of pathogens on microbial culture (positive culture results) of blood samples, or a verified source of infection confirmed by positive culture results before or after death.9-20 Shock was defined by systolic blood pressure < 90 mm Hg or clinical signs of poor perfusion, including altered mentation, pale mucous membranes, delayed capillary refill time, tachycardia, weak peripheral pulses, normal-to-low body temperature and, when measured, low urine output (< 1 ml/kg of body weight/hr).25-30 Oxygen toxicity was considered to be a risk factor if the dog was exposed to an inspired O₂ fraction > 0.6 for > 24 hours. Bacterial pneumonia was diagnosed in dogs with histologic lesions of bronchiolitis and 2 or more of the following conditions: fever (body temperature > 39.7 C), purulent tracheal secretions or sputum, > 15,000 or < 5,000 WBC/mm³, new pulmonary infiltrates on thoracic radiography, with positive culture results from tracheal wash samples before death or positive culture results or evidence of microorganisms on Gram's stain from lung tissue at necropsy.31 Recumbent dogs in which bacterial pneumonia was diagnosed were considered to have aspiration pneumonia when vomiting or regurgitation had been witnessed. Disseminated intravascular coagulation (DIC) was diagnosed by prolongation of the partial thromboplastin time (PTT, > 25% of control), with high fibrin split products (> 10 µg/dl), and when histocytes and thrombocytopenia (< 100,000 platelets/mm³) were evident, or when excessive bleeding or thrombosis was observed clinically and confirmed at postmortem examination.32,33

Results
Nineteen dogs (1 mixed-breed and 18 purebreds) satisfied the histopathologic and clinical criteria and were included in the study. Of the purebreds, 3 were Chinese Shar-Pei, 2 each were Dachshunds and Rottweilers, and 1 each was of the following breeds: American Pit Bull Terrier, Cocker Spaniel, Collie, Dalmatian, German Shepherd Dog, Miniature Poodle, Pointer, Pug, Newfoundland, Siberian Husky, and Yorkshire Terrier. The small number of dogs within each breed precluded comparison with the general hospital population. Ten dogs were males and 9 were females. Dogs ranged in age from 2 months to 10 years old (median, 3.5 years old). Eleven dogs were between 2 and 12 months old, and 5 dogs were between 8 to 10 years old.

On admission, most dogs had a history of dyspnea (n = 15). Onset of dyspnea ranged from 0.5 to 48 hours (median, 4.5 hours) prior to admission. The owner of 1 dog that had been dyspneic for 48 hours prior to admission reported that the dog's respiratory status had deteriorated rapidly 12 hours before the dog was admitted. Two other dogs had had chronic respiratory problems; 1 dog had been treated with antibiotics for probable aspiration pneumonia, secondary to megaesophagus, and, according to the owner, had raspy breathing that started shortly after the dog began to regurgitate. One dog with mild dyspnea for 1 week, as reported by the owner, had rapid progression to overt respiratory distress before being admitted. Other clinical signs included lethargy (5), anorexia (3), evidence of trauma (4), collapse (3), seizures and tremors (2), vomiting and diarrhea (2), and retching, with a distended abdomen (1).

On physical examination, dyspnea was observed in 17 dogs. Respiratory rate recorded on arrival in 13 dogs ranged from 36 to 140 breaths/min (mean ± SD, 58 ± 31 breaths/min). Abnormalities of breathing such as greater-than-normal effort (5), rapid and shallow breathing pattern (5), and dyspnea with paradoxical movement of the abdomen (3) were observed in 13 dogs. Of 3 dogs in which respiratory efforts, relative to the breathing phase, were monitored, 1 dog had greater-than-normal inspiratory and expiratory effort. Two other dogs, 1 of which had airway obstruction attributable to an elongated soft palate, had prolonged inspiratory phase and effort.

Crackles (7) and harsh sounds (6) often were re-
ported on auscultation of the lungs. Coughing was observed in 3 dogs, with 1 dog that had sustained blunt thoracic trauma having severe hemoptysis. During hospitalization, 2 other dogs developed hemoptysis, and 1 had concurrent epistaxis that was attributed to DIC. Mucous membranes were variable in color, ranging from pale to injected, and cyanosis was observed in only 1 dog.

Thoracentesis was performed in 6 dogs. Pneumothorax was observed in 4 dogs, with volumes of aspirated air ranging from 14 to 600 ml. In 3 dogs, 2 of which had sustained blunt thoracic trauma, pneumothorax was documented radiographically prior to performing thoracentesis. The same 3 dogs were ventilated shortly after admission, and thoracic tubes were inserted for continuous drainage of the pleural cavity. The other dog was admitted with severe subcutaneous emphysema; pneumomediastinum and tension pneumothorax were evident on thoracic radiography 30 minutes after admission. Large volumes of air were aspirated, and bronchoscopy and thoracotomy were performed to remove an intrabronchial foreign body.

Serosanguineous fluid (150 ml), secondary to lung lobe torsion, was aspirated from the right hemithorax when 1 dog's respiratory status deteriorated approximately 10 hours after admission. On auscultation, lung sounds were duller on the right side, compared with those on the left side, and thoracic radiography revealed bilateral pleural effusion that was more marked on the right. In 1 dog, thoracentesis did not reveal fluid or air, and thoracic radiography was not performed.

Predisposing factors—In 5 dogs, despite careful review of the medical records, predisposing factors could not be identified. In the other 14 dogs, the most common factors were microbial pneumonia (6), sepsis (5), and aspiration pneumonia (4).

Four of the 6 dogs with microbial pneumonia probably had ventilator-associated infections, although positive-pressure ventilation had been initiated because respiratory distress was already evident. The other 2 dogs had bacterial pneumonia secondary to smoke inhalation or parasitic pneumonitis (filarioidiasis). Sepsis was attributed to severe, necrotizing dermatitis and cellulitis in 1 dog, to a catheter-related infection in 1 dog, and to focal pulmonary infection in 2 dogs. In 1 dog in which multifocal hepatic necrosis was found at necropsy, sepsis was possibly of hepatic origin. Aspiration of gastric contents was witnessed in 3 dogs and, presumably, led to secondary bacterial pneumonia. Although aspiration was not witnessed in a fourth dog, aspiration pneumonia was diagnosed on the basis of foreign material in the dog's alveoli at necropsy.

Other predisposing factors included shock that was not responsive to IV fluid administration in 4 dogs, hyperoxia in 3 dogs supported with mechanical ventilation, and organ torsion (gastrointestinal volvulus and splenic torsion in 1 dog and lung lobe torsion in another dog that had fallen 5 feet). Acute respiratory distress also was attributed to laryngeal obstruction following strangulation with a choke chain in 2 dogs. Pulmonary contusions were suspected in 2 dogs that had had severe thoracic trauma. Disseminated intravascular coagulation was found in 2 septic dogs. Another dog that had tremors on admission developed status epilepticus, then respiratory distress attributable to aspiration of vomitus.

More than 1 risk factor was evident in 11 dogs. In 5 dogs, 2 predisposing factors were identified, whereas in the remaining 6 dogs, 3 or more risk factors were found.

Clinicopathologic findings—At admission, mean WBC count was 12,200 (SD, 7,900) cells/mm³ in 13 dogs. Four dogs were leukopenic (< 5,000 WBC/mm³) and neutropenic (1,245 ± 1,057 cells/mm³). Of 6 dogs with leukocytosis (20,200 ± 3,000 cells/mm³), 2 had > 1,000 band cells/mm³.

Coagulation profiles were normal in 3 of 8 dogs. Two dogs were mildly thrombocytopenic (106,000 and 114,000 platelets/mm³, respectively). Prothrombin time was prolonged in 1 dog (33% > control). Four dogs had prolonged PTT (range, 30 to 100% > control). Fibrin split products were between 10 and 40 μg/dl in 2 dogs and > 40 μg/dl in 1 dog. Schistoscytosis was observed in only 1 dog. Coagulation measurements were repeated in 3 dogs, 2 of which were treated with heparin and fresh-frozen plasma for presumptive DIC. These 2 dogs had a decrease in platelet count and persistently prolonged PTT.

A clinical diagnosis of DIC was made in 2 dogs, 1 of which had abnormalities in all coagulation tests. The other dog had clinical evidence of hemorrhage (hemoptysis, epistaxis, hematemesis, hemorrhage, and hematuria) and a prolonged activated clotting time (> 120 seconds). At necropsy, diffuse hemorrhage was found involving the pleural cavity, pericardium, gastrointestinal tract, lungs, and abdominal cavity.

Serum albumin concentration (mean ± SD) at admission was 2.5 ± 0.7 g/dl in 12 dogs, 8 of which were hypoalbuminemic (2.1 ± 0.4 g/dl). Serum albumin was measured again during hospitalization in 5 dogs, and 4 were hypoalbuminemic (1.9 ± 0.5 g/dl).

Microbiologic results— Aerobic and anaerobic bacterial culture of blood, skin (draining tracts), or airway samples was performed in 8 dogs. Clostridium spp was the only anaerobic organism isolated. In 4 of 6 mechanically ventilated dogs, aerobic bacteria were isolated from tracheal wash samples. In 2 of these dogs, Escherichia coli and Pseudomonas aeruginosa, respectively, were found in pure culture. In the 2 remaining dogs, multiple organisms were isolated: enterococci (2 dogs) and in 1 dog each, E. coli, Klebsiella pneumoniae, and Staphylococcus intermedius. From later tracheal wash samples in 2 dogs, 1 more organism was isolated from each dog: Clostridium spp and P. aeruginosa, respectively.

Clostridium spp and S epidermidis were isolated from blood samples in 1 dog with signs of sepsis. Two isolates of S epidermidis with different antimicrobial susceptibility were cultured from a sample from the tip of a pulmonary artery catheter in a septic dog, which also had pathogens isolated from tracheal wash samples. Clostridium spp, Enterobacter sp, and a coagulase-positive Staphylococcus sp were isolated from

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samples from the draining tracts of 1 dog with severe cellulitis and clinical signs of sepsis.

**Radiographic findings**—Thoracic radiographs from 16 of 19 dogs were available for review. Two of the remaining 3 dogs had had thoracic radiography performed by the referring veterinarian. Severe generalized pulmonary infiltrates were reported in both dogs, and the cardiac silhouette was within normal limits, but these radiographs were not available for review. One dog died before radiographs could be obtained.

Thoracic radiography was performed within 5 hours of admission in 13 dogs and later during hospitalization in 3 dogs. In 4 dogs, thoracic radiographs were normal or had a mild interstitial pattern. One dog was not dyspneic when radiographs were obtained, but developed severe respiratory distress approximately 37 hours after hospitalization. One dog with microbial pneumonia died 18 hours after radiography was performed. Dyspnea in 1 dog was attributed to severe pneumothorax and pneumomediastinum, and evaluation of the pulmonary parenchyma was difficult. The fourth dog had pharyngeal obstruction attributable to an elongated soft palate and initially did not have evidence of pulmonary changes. Review of a second set of thoracic radiographs obtained approximately 25 hours later revealed severe interstitial/early alveolar infiltrates (graded 2+) in 4 of 6 sections of the lung field. Three other dogs had radiographic changes that were graded < 2+ in 4 quadrants or more or were not bilateral.

In the remaining 9 dogs, radiographic changes were described as a combination of severe interstitial pattern and diffuse alveolar infiltrates in all lung lobes (graded > 2+; Fig 1). Repeated thoracic radiography revealed worsening of pulmonary infiltrates in 6 of 7 dogs, with development of diffuse bilateral alveolar infiltrates in 4 dogs.

**Outcome**—Respiratory status deteriorated severely and rapidly in all dogs despite oxygen supplementation. In dogs that were not mechanically ventilated, deterioration of respiratory status was associated with an increase in respiratory rate (mean ± SD, 81 ± 22 breaths/min) and severe dyspnea. Hypoxia (PaO₂ < 80 mm of Hg) was documented in dogs for which samples were obtained for arterial blood gas analysis when breathing room air.

Twelve dogs, 7 of which were mechanically ventilated, were euthanized. The other 7 dogs, 3 of which were ventilated, developed cardiopulmonary arrest and died. Duration of dyspnea prior to death in dogs not mechanically ventilated ranged from 8 to 76 hours (median, 16 hours).

Death could be attributed solely to respiratory failure in 8 dogs. The remaining 11 dogs had clinical signs of sepsis or shock or severe lesions in nonpulmonary organs that could have contributed to organ failure or systemic illness. Distribution of nonpulmonary organ involvement was as follows: renal (4), cardiac (2), hepatic (2), CNS (1), and dermatologic (1).

**Necropsy findings**—On gross examination, the lungs in 18 dogs were diffusely firm, heavy, and mottled and red, purple, or dark with some areas of normal lung tissue. When cut, the surface of the lungs oozed a clear, sometimes pinkish, fluid. In 5 dogs, 2 of which had pneumothorax, the lungs were aletectic. The tra-

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**Table 1**—Pulmonary histopathologic findings in 19 dogs with acute respiratory distress syndrome

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<tr>
<th>Finding</th>
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0 = absent; 1+ = mild; 2+ = moderate; and 3+ = severe.
All tabular values are No. of affected dogs.
Cheal lumen contained a frothy, pinkish fluid in 5 dogs. Multifocal areas of tracheal hemorrhage were reported in 1 dog. Slight serosanguineous pleural effusion was found in 12 dogs, and the dog that had had a lung lobe resection had suppurrative pleuritis. In addition, severe hemotherax was reported in a dog that had clinical evidence of DIC.

In 7 dogs, severe, diffuse suppurative alveolitis and bronchiolitis, sometimes described as necrotizing, were evident on histologic examination of lung tissue. One of these dogs, which had had smoke inhalation injury, had tracheal hemorrhage and ulceration and intrabronchial and alveolar carbon particles. In the other 12 dogs, the inflammatory process was confined to the alveoli and interstitium and was characterized as necrotizing or suppurrative in 5 dogs. Alveolar hemorrhage was described in 7 dogs, and vascular thrombi were evident in only 1 lung specimen. Congestion (16) and edema (11) of the interstitium on histologic examination corroborated gross pathologic findings (Table 1). Infiltrates of WBC (mainly neutrophils) and RBC were detected in 19 and 18 lung tissue specimens, respectively. Hyaline membranes were evident in 17 specimens (Fig 2) and proliferation of type II alveolar cells was observed in 12 specimens (Fig 3). Interstitial fibrosis had developed in 2 dogs. Colonies of bacteria were identified histologically in lung tissue specimens from 2 dogs in which microbial culture was not performed before death.

Figure 2—Photomicrograph of a section of lung tissue in a dog with lesions similar to those in the acute exudative phase of human adult respiratory distress syndrome (ARDS). Hyaline membranes (arrows) line the alveoli, and inflammatory cells are evident in the lumen. H&E stain; bar = 200 μm.

Figure 3—Photomicrograph of a section of lung tissue in a dog with lesions similar to those in the early proliferative phase of ARDS. Type II alveolar cells (arrow) line many alveoli. H&E stain; bar = 100 μm.

Important lesions in nonpulmonary organs that were attributed to a septic or systemic inflammatory process were suppurative endocarditis with intraleisonal cocci (1), intravascular and myocardial colonies of bacterial rods (1), focal acute myocardial necrosis (1), and severe, diffuse, necrotizing and ulcerative cellulitis and dermatitis, with intralesional bacilli in 1 dog. In 1 septic dog, multifocal, acute myocarditis with transmural hemorrhage (attributed to DIC) and severe multifocal hepatic necrosis were found. Acute tubular necrosis possibly related to hypotensive shock was described in 2 dogs. In 1 dog, hypoxia or anoxia, secondary to severe lung disease, was thought to have contributed to multifocal ischemic neuronal necrosis of the brain. Centrilobular hepatic necrosis, possibly related to acute pulmonary hypertension with right-sided heart failure, was found in 1 dog.

Discussion

By applying stringent histopathologic and clinical criteria, we were able to identify a group of dogs that had had acute lung injury, analogous to ARDS in human beings. Although younger dogs appeared to be overrepresented in this study, age did not seem to be associated with a predisposition for developing acute respiratory distress. In human beings, ARDS developed in adults as well as pediatric patients.7 Age should, therefore, be considered as reflective of the inciting event leading to acute lung injury. Younger dogs, by their inquisitive nature, may be more susceptible to traumatic events and strangulation with leashes, as in this study.
Pneumonia (in 10 dogs) and sepsis (in 5) most often were associated with acute lung injury in this study, similar to findings in people. Ventilator-acquired pneumonia developed in 4 dogs. In people, pneumonia is a common complication of mechanical ventilation, because airway colonization develops rapidly within 2 to 3 days after intubation. Pneumonia is reported in as many as 70% of ventilated patients with ARDS, contributing to an increase in mortality. Gastric contents were aspirated in 3 dogs, and unknown foreign material was inhaled by 1 dog. Gastric contents injure the airways chemically, causing bronchorrhea, airway constriction, and edema within hours after the injury. Because of altered lung defenses, the risk of secondary bacterial infection and lung inflammation, which may progress to ARDS, markedly increases. In smoke inhalation, as found in 1 dog in this study, hypoxia may not only be attributable to lung injury and inflammation, but also to direct effect of the inhaled gases, such as formation of carboxyhemoglobin from carbon monoxide, with impairment of oxygen delivery. Secondary bronchopneumonia is a frequent complication in patients with smoke inhalation, as was evident in our study.

Aspiration pneumonia developed after severe CNS disturbances in 1 dog. Head trauma and seizures in veterinary patients have been associated with pulmonary edema that is usually self-limiting, resolving within 24 hours with supportive care. In this dog, aspiration pneumonia may have complicated or coincided with primary neurogenic edema.

Trauma, sepsis, convulsions, and acute allergic reactions were thought to have contributed to shock in 4 dogs. Although renal lesions were suggestive of hypotension in 1 dog, shock was not documented. Shock has been reported to be associated with ARDS in human beings. Trauma was the cause of acute lung injury in 3 dogs, 2 of which sustained pulmonary contusions. Adult respiratory distress syndrome has been reported to cause respiratory failure following thoracic and nonthoracic trauma in human beings.

Hyperoxia was thought to have contributed to lung injury in 3 dogs. Exposure to high inspired concentrations of oxygen causes lung damage analogous to ARDS in animals as a result of release of oxygen free radicals. Functional and physical changes develop in canine lungs within 12 to 24 hours of breathing 100% O2. Because histopathologic changes induced by oxygen toxicity are similar to those associated with other causes of acute lung injury, we could not distinguish the effects of hyperoxia from those of the other predisposing factors. However, we believe that pulmonary oxygen toxicity may have been a contributing factor in 3 of the dogs of this study.

Disseminated intravascular coagulation developed in 2 of 19 dogs. This prevalence is much lower than that previously reported in human patients with ARDS, in whom the prevalence of DIC can be as high as 23%. Coagulation abnormalities have been reported to cause acute lung injury in animals in an experimental setting, but other studies have contradicted these data. Therefore, whether DIC directly contributed to acute lung injury in our dogs or whether it should be viewed as a complication of sepsis, the underlying risk factor, is unclear.

Laryngeal obstruction or strangulation was a predisposing factor to development of pulmonary lesions in 2 dogs. Airway obstruction is associated with pulmonary edema caused by a sudden increase in negative intrapleural pressure and, possibly, increased capillary permeability. Strangulation has been reported to be a predisposing factor for ARDS in human beings. Although conservative management in veterinary patients with pulmonary edema associated with laryngeal paralysis may result in a good outcome, the severe dyspnea in the 2 dogs in our study mandated immediate mechanical ventilation. Nosocomial pneumonia complicated the condition in 1 dog and may have contributed to the development of pulmonary lesions similar to those of ARDS.

Organ torsion was a predisposing factor in 2 dogs, although it has not been reported previously as a predisposing cause of ARDS. The mechanical effect of torsion, profound hypotension, reperfusion injury following resuscitation, bacterial translocation, and release of inflammatory mediators may all have played a role in the lung injury and systemic involvement in these dogs.

In 11 of our dogs, more than 1 potential predisposing factor was identified. In human beings, the incidence of ARDS increases at least 42% when 2 or more risk factors are present. Adult respiratory distress syndrome is often complicated by the development of nonpulmonary organ failure, which contributes to higher mortality. Irreversible respiratory failure is responsible for only about 16% of the mortality in human beings with ARDS. In contrast, death was caused by respiratory failure in 42% (8/19) of our dogs. This difference may have been attributable to our difficulty in recognizing hemodynamic disturbances and detecting foci of inflammation or infection that might have caused a systemic response. In addition, financial and technical constraints and limitations imposed by owners in the management of respiratory failure in their pets may have accounted for this difference.

The sequence of injury leading to the endothelial and epithelial damage evident in ARDS involves humoral mediators of inflammation, such as cytokines, leukotrienes, and prostaglandins, and cellular elements, such as macrophages and neutrophils. The inciting injury triggers a cascade of secondary inflammatory mediators that amplify and perpetuate the response to the initial injury. Neutrophils are thought to play an important role in ARDS by producing oxygen free radicals and releasing proteases. Peripheral leukopenia with neutropenia, observed commonly in human beings during the early stages of ARDS, was evident in 4 dogs and was attributed to neutrophil sequestration in the pulmonary vasculature. Neutrophil pooling in nonpulmonary organs following experimentally induced acute lung injury has been described in dogs. As documented in 2 dogs in our study, thrombocytopenia has been observed in the early stages of ARDS in human beings, and platelet sequestration in the lungs is thought to contribute to lung injury.

Structural and functional changes in the lungs of
patients with ARDS are caused by increased microvascular permeability, pulmonary hypertension, and airway constriction and obstruction. High concentrations of albumin in bronchoalveolar lavage fluid have been reported in patients with ARDS and aspiration pneumonia and may explain the hypoalbuminemia in many of our dogs. Because of alveolar flooding with protein-rich edema, ventilation/perfusion mismatch, and shunting of blood through nonventilated alveoli, gas exchange deteriorates substantially, leading to severe hypoxemia that cannot be corrected by oxygen supplementation alone, as was evident in the dogs of this study. Respiratory dysfunction developed in all our dogs and rapidly progressed to failure. In chronic ARDS, collagen deposition and fibrosis perpetuate the oxygenation defect by impairing oxygen diffusion and causing pulmonary hypertension attributable to vascular obstruction and occlusion.

Within hours of a precipitating event, clinical manifestations of ARDS ensue in human beings, although recognition of this phase in dogs is difficult because of the subtlety of clinical signs. Mild hypoxia and hypocapnia and slight dyspnea, tachypnea, and, sometimes, mild cough are apparent, although chest auscultation and radiographs are initially normal. As pulmonary inflammation progresses, respiratory impairment becomes more evident, with moderate-to-severe dyspnea, and overt respiratory failure that is refractory to oxygen supplementation develops, as in our dogs. Rapid progression of pulmonary disease mandated general anesthesia and positive-pressure ventilation to prevent severe discomfort or death. Oxygen therapy, ventilatory management, and assessment of lung function in these dogs has been addressed elsewhere. Respiratory crackles and harshness auscultated in our dogs have been associated with the presence of fluid, such as edema, within the alveoli. In ARDS, lung compliance decreases with the development of pulmonary edema. High respiratory rates, shallow breathing, and paradoxical respiratory patterns observed in our dogs were compatible with decreased pulmonary compliance in ARDS and likely reflected increased work of breathing. Hemoptysis, observed in 3 of our dogs, is an unusual feature of ARDS in human beings unless pulmonary contusions are present.

Early radiographic findings in these dogs were quite varied with regard to the severity of pulmonary changes. The predominant radiographic pattern was diffuse bilateral interstitial and alveolar infiltrates. When serial radiographs were available, increased severity of the alveolar infiltrates was generally observed, and air bronchograms were evident within 35 hours after the onset of lung injury. Similar findings are reported in human beings, with bilateral alveolar infiltrates developing within 48 hours of the onset of ARDS. Because radiographic abnormalities lag behind gas-exchange abnormalities and may not be detectable until 24 hours after the onset of ARDS, some radiographs obtained soon after admission in our dogs had few pulmonary changes. This delay also may explain why these radiographs may not have been representative of the pulmonary changes present at the time of death. Such delay is less likely to be a factor in patients with direct lung injury, such as severe pneumonia or lung contusions. In the study reported here, 2 dogs with thoracic trauma had marked radiographic abnormalities detectable soon after admission.

The pathologic changes in the lungs of the dogs in this study were similar to those previously reported in people and in dogs following parquat ingestion, parvovirus infection, sepsis, pancreatitis, or thoracic and nonthoracic trauma. Although the causes and initial pathophysiologic events leading to ARDS may differ, the common pathway is characterized by increased microvascular permeability. Morphologically, diffuse alveolar damage is evident and can be divided into 3 interrelated and overlapping phases: acute exudative, proliferative, and fibrotic. An initial, early phase associated with the onset of dyspnea is evident experimentally and corresponds to neutrophil sequestration in pulmonary vasculature. The exudative phase is characterized by an acute inflammatory response that causes diffuse endothelial and alveolar damage and leads to alveolar flooding with proteinaceous edema fluid, with death of type I alveolar cells. Alveolar neutrophils and RBC, along with microthrombi, vascular congestion, and hyaline membranes, can be observed. This phase begins within 12 to 24 hours after the onset of clinical signs in people and can last up to 5 days. Grossly, the lungs are heavy and hemorrhagic, with a texture similar to that of liver. As ARDS progresses, type II alveolar cells begin to proliferate in an attempt to restore the damaged epithelium. During this proliferative phase, the severity and extent of edema and vascular congestion is generally less than in the earlier phase. In addition, hyaline membranes are encountered less frequently as the phase progresses. This repair phase is followed by a fibrotic phase. With fibroblast proliferation and collagen deposition, extensive fibrosis ensue, causing alveolar, bronchiolar, and vascular obliteration, thus maintaining the oxygenation defect.

In 7 dogs, the gross pathologic and histologic findings of inflammatory cells, RBC, and hyaline membranes in lung tissue were compatible with the acute inflammatory process in the exudative phase of ARDS. In 12 dogs, the presence of type II alveolar cells, along with inflammatory exudate and hyaline membranes, indicated progression to the proliferative phase of ARDS. In all dogs, the widespread hemorrhage and congestion revealed the acute nature of the process. Although clearance of edema would be expected as the acute inflammatory phase abates, correlation could not be made between the severity of pulmonary edema, the amount of hyaline membranes, and type II alveolar cells found in all lung tissue specimens. This may be explained by the short duration of dyspnea (< 5 days) in our dogs and the overlapping of the exudative and proliferative phases of ARDS. The WBC infiltrates found in all pulmonary specimens not only may have reflected WBC sequestration developing soon after the onset of the acute respiratory distress syndrome but also, possibly, superimposed pulmonary infection. In people, fibroblast proliferation begins 7 to 10 days after the onset of ARDS. Considering that the duration of dyspnea in our dogs ranged from 8 to 102 hours until death, that fibrosis was a rare histologic finding in the study was not surprising.
In dogs that aspirated or inhaled foreign material or had nosocomial pneumonia, the pulmonary lesions had more airway involvement with diffuse alveolar and interstitial cellular infiltrates. These features differed from those typical of bronchopneumonia in which alveolar infiltrates are found in the more dependent lung lobes.

The acute respiratory distress syndrome defined in these dogs carries a grave prognosis. Similar predisposing conditions in human beings can cause a milder form of respiratory distress without progression to ARDS, or development of the severe oxygenation defect and radiographic abnormalities associated with ARDS. The progression to ARDS in people and to acute respiratory distress syndrome in dogs appears to result from amplification of the response to lung injury and subsequent ongoing disease.

References