

# Ammonia Inhalation

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**Because of the widespread use of ammonia in industry and agriculture there is a growing opportunity for ammonia burns to occur. Two fatal cases are presented. The injury is thermal as well as chemical, to skin, eyes, airway and lungs. Prompt (5–10 seconds) irrigation of the eyes is required, and immediate treatment of airway and pulmonary injuries. Fluid resuscitation and skin wound care are similar to that of other burns. Presence or absence of abnormal chest findings on admission is the best prognostic factor.**

Despite the increasing use of ammonia in agriculture and industry, the occurrence of injuries from contact with ammonia has remained relatively rare. The potential for more injuries, however, continues to increase. This is a report of two such injuries.

On 15 September 1983 the transferring of ammonia from one tank to another resulted in an explosion injuring 19 people. Two patients were transferred to the University of Miami/Jackson Memorial Hospital Burn Center.

## CASE REPORTS

**Case 1.** A 33-year-old male had second-degree burns over 12% of his total body surface area with bilateral corneal clouding, second-degree burns to the oropharynx, and severe respiratory distress. Following nasal intubation at another hospital, he was placed on ventilatory support. He required an IMV of 10 breaths/minute, tidal volume of 800 ml, PEEP of 10 cm H<sub>2</sub>O, and FIO<sub>2</sub> of 40% to achieve a PaO<sub>2</sub> of 63 torr, PaCO<sub>2</sub> of 38 torr, and a pH of 7.19. His admission laboratory data were normal except for an amylase level of 447 units (normal, 23–85 units). He was resuscitated using the Parkland formula. His vital signs remained stable; however, his respiratory function deteriorated. He was given two ampules of sodium bicarbonate before being transferred to our facility.

Upon transfer 18 hours postinjury, his laboratory data included: white blood cell count, 34,100 per ml; hematocrit, 57%; sodium, 149 mEq; potassium, 5.2 mEq; chloride, 114 mEq; BUN of 14 mg/100 ml, creatinine of 1.4 mg/100 ml, amylase 190 units (20–110 units), and CPK of 1,111 units with negative MB isoenzyme.

The corneal burns were treated with neosporin ointment and atropine. The skin burns were treated with 1% silver sulfadiazine cream (Silvadene, Marion) twice daily.

On the third postburn day (PBD), he developed small bilateral pneumothoraces. These were observed and they resolved over the next several days.

On PBD 5, thin sheets of tissue were suctioned from the trachea. Pulmonary function deteriorated on PBD 6 requiring

a stepwise increase in PEEP to 28 cm H<sub>2</sub>O. A Swan-Ganz catheter was inserted and the intrapulmonary shunt was 28%. The WBC rose to 10,500 per ml and oxacillin was begun, pending culture results.

Pulmonary function continued to worsen over the next 72 hours. The WBC rose to 33,100 per ml; amylase was 90 units. On PBD 9 the PaCO<sub>2</sub> rose to 73 torr and the peak inspiratory pressure to 80 cm H<sub>2</sub>O. Sputum cultures grew *Pseudomonas aeruginosa*; amikacin and ticarcillin were begun.

A tracheostomy was performed on PBD 14. The trachea was friable and a pseudomembranous cast was removed from the inside. The corneas were healed and the skin wounds were 90% re-epithelialized. By PBD 15 the respiratory function had improved slightly and the WBC was down to 12,100 per ml.

The following day he became oliguric. Over 2 days the BUN rose to 72 mg/100 ml, the creatinine 4.5 mg/100 ml, the potassium 5.9 mEq/L, and the WBC 27,400 per ml. He had a witnessed cardiac arrest (from a normal sinus rhythm to asystole) from which he could not be revived.

**Case 2.** In the same accident, a 51-year-old male sustained second- and third-degree burns over approximately 50% of his body, including his eyes, oropharynx, back, and legs. His past medical history was significant for 70 pack-years of smoking. On arrival at another emergency room he was in severe respiratory distress with diffuse wheezing. His room air arterial blood gas showed: PaO<sub>2</sub>, 42 torr; PaCO<sub>2</sub>, 27 torr; pH, 7.42. He was intubated and placed on ventilatory support.

Eight hours after injury, he was transferred to our facility awake and alert. He continued to have bilateral wheezing and chest X-ray showed bilateral lower lobe infiltrates. On an IMV of 8 BPM, a tidal volume of 1,000 ml, a PEEP of 15 cm H<sub>2</sub>O and FIO<sub>2</sub> of 60% his PaO<sub>2</sub> was 75 torr, PaCO<sub>2</sub> 59 torr, and pH 7.26. Admission laboratory values were: hematocrit, 45%; WBC, 2,900 per ml; sodium, 144 mEq/L; potassium, 4.1 mEq/L; chloride, 107 mEq/L; BUN, 13 mg/100 ml; creatinine, 1.1 mg/100 ml; amylase, 1,770 units.

The burns were debrided and treated with 1% silver sulfadiazine cream; his eyes were treated with neosporin ointment and atropine. Because of persistent wheezing an aminophylline drip was started; however, this had an unwanted diuretic effect and was discontinued. Terbutaline was then begun.

Over the next 2 days pulmonary function gradually improved. On PBD 2 his BUN increased to 32 mg/100 ml and creatinine to 2.1 mg/100 ml. The amylase remained elevated at 1,340 units. During the second day he had an episode of atrial fibrillation which responded to digoxin. Bilateral lower lobe infiltrates persisted.

On PBD 4 he continued to have bilateral wheezing; however,

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it was possible to decrease his respiratory support. The serum amylase was 312 units.

On the sixth day his condition began to worsen. He became less alert and no longer followed commands. Peak inspiratory pressure had risen from 30 to 46 cm H<sub>2</sub>O. Burn eschar on the legs was tangentially excised. That evening, to control frequent PVC, a lidocaine drip was begun.

On PBD 8 he underwent a tracheostomy and debridement of the burns on his chest and back. His creatinine clearance was 70 ml/min and BUN rose to 50 mg/100 ml. By the ninth day he had become unresponsive to pain, and his PaCO<sub>2</sub> remained 50–60 torr despite a minute ventilation greater than 30 liters.

On the morning of the tenth day he was oliguric. Sputum was now growing *Serratia marcescens* and oxacillin and tobramycin were instituted. He developed atrial fibrillation despite a therapeutic digoxin level; this converted to sinus tachycardia following verapamil IV. Later that day he became asystolic and could not be revived.

Both of these patients underwent postmortem examination by the Dade County Medical Examiner. They had tracheobronchial ulcerations and denuded epithelium with pseudomembrane formation. The lungs were found to be congested, with purulent exudate in the smaller bronchi. Gross examination of the heart, kidneys, and pancreas was unremarkable. Histologic examination demonstrated necrotizing bronchitis with ulceration and membrane formation. Severe intra-alveolar fibroblastic proliferation was also noted. In Case 1 micro abscesses were seen in the kidneys. In Case 2 medullary fibrosis and tubal necrosis were seen in the kidneys.

## DISCUSSION

At atmospheric pressure ammonia is a colorless gas with a characteristic pungent odor. It is approximately half as dense as air and thus rises readily. With pressurization 113 cubic feet of vapor can be condensed into one cubic foot of liquid, facilitating storage and transportation. Ammonia is extremely soluble in water; 1,300 volumes can dissolve in one volume of water. When properly mixed with air it is flammable; however, the ignition temperature is 1,200° F (12).

As an important industrial chemical, ammonia is used in the manufacture of explosives, petroleum, cyanides, plastics, and synthetic fibers (10, 24, 32). It is also widely used as a cleaning agent and as a coolant in refrigeration units. As an agricultural fertilizer, ammonia is ideal because of its high (82%) nitrogen content (12). When used for fertilizing it can be applied as liquid ammonia or as ammonia dissolved in water.

The sudden release of liquid ammonia causes damage in three ways. It has a temperature of -33° C, thus freezing any tissue it contacts (28). Ammonia vapor readily dissolves in the moisture present on the skin, eyes, oropharynx, and lungs (12, 17, 32) forming ammonium hydroxide which readily dissociates to yield hydroxyl ions (24). This exothermic reaction causes a thermal injury as well as a chemical injury. Unlike acid burns, which cause a coagulation necrosis, ammonia causes burns resembling alkali burns, resulting in liquification of the tissue and deeper penetration.

Taylor (31) first reported cases of ammonia burns in

1872. This did not become a frequent problem until the widespread use of refrigeration after World War I (3). Slot (29) reported six cases resulting from an explosion in an ice cream factory in 1938. Caplin (5) reported 47 cases in 1940 after a brewery was struck by a bomb releasing ammonia into a bomb shelter. Other cases related to the malfunctioning of refrigeration units have been reported (10, 19, 21, 28, 36).

Levy et al. (19) reported in 1964 three cases of ammonia burns from accidents involving fertilizing equipment. Helmers, Top, and Knapp (12) reported four additional cases in 1971 and predicted that the incidence would increase, as the amount of ammonia used in agriculture doubles every 10 years. Similarly, Walton (32) documented seven cases occurring in an ammonia manufacturing plant. He predicted that the incidence of injuries would increase with the industrial use of ammonia.

The severity of the injury is directly related to the concentration of the ammonia and the duration of exposure (8, 12). Those injured can be divided into three groups depending on the severity of respiratory injury (5, 8, 21, 24). Caplin (5) was the first to divide the injured into mild, moderate, and severe groups.

The mild group may present with inflammation of the conjunctiva and upper respiratory passages. They may also complain of pain and hoarseness but are not in respiratory distress. In the moderate injury group these signs are exaggerated. Dysphagia, a productive cough, and some degree of respiratory distress are usually present. This group requires hospitalization for respiratory support and may require endotracheal intubation and positive pressure therapy. Those in the severe group frequently have been overcome by the ammonia and unable to remove themselves from the area of contamination. They are in severe respiratory distress and have evidence of pulmonary edema. Despite aggressive treatment, mortality approaches 100% (2, 28, 32).

Cutaneous injuries are similar to other alkali burns. A concentration of 10,000 parts per million (ppm) will cause skin damage (2). Burns are deepest at areas where body moisture content is high. While the skin injury may be severe and disfiguring, it is not usually fatal.

Hughes (15, 16) cites experiments in which ammonia was detected in the aqueous humour 5 seconds after being instilled in the conjunctival sac of a rabbit. Because of its rapid penetration ammonia typically causes more corneal endothelial damage, corneal stromal edema, iritis, and lens damage than other alkalies (11). In severe injuries atrophy of the iris and cataract formation may result. The cornea may opacify due to scarring and neovascularization, leaving a poor bed for corneal transplant. Highman (13) reported signs mimicking acute-angle closure glaucoma within 4 hours of the injury.

The oropharynx is a commonly injured site. Upper airway obstruction may result from the edema and loss of tissue caused by this injury. This may offer some

protection to the lungs by preventing inhalation of ammonia (3, 8).

It is the pulmonary injury that is most devastating. Severe ammonia inhalation has a biphasic clinical progression (9, 28). Initial edema, congestion, hemorrhage, and atelectasis are followed by a temporary clinical improvement before the gradual onset of airway obstruction and respiratory failure (8, 17, 28, 30, 32). The severity and time course of each phase is dependent on the amount of exposure; however, most patients show some resolution of the first phase by 48–72 hours (21, 24, 32, 36).

Histologic examination frequently reveals loss of epithelium from the trachea and bronchi. The bronchial mucosa may be replaced by granulation tissue. There is bronchiectasis following destruction of mucous glands, smooth muscle, and cartilage. The alveolar walls appear thickened, the bronchioles show mucus plugging, and thrombosed capillaries are noted (3, 17, 23). Experimentally, severe damage to the bronchiolar-alveolar structures in conjunction with minimal upper airway damage suggest the lower respiratory tract is more sensitive to ammonia injury (3). In addition, the upper airway injury frequently leads to sloughing of large pieces of mucosa which may cause airway obstruction (19, 28).

The least detectable ammonia odor is at a concentration of 53 parts per million (ppm) or about 37 mg per cubic meter (12, 33). A level of about 100 ppm (70 mg per cubic meter) can be tolerated for several hours (12). Irritation to the human eye begins at about 140 ppm (98 mg per cubic meter) and immediate injury at 700 ppm (490 mg per cubic meter) (11). Throat irritation begins at about 408 ppm (285 mg per cubic meter) and laryngospasm at 1,700 ppm (1,190 mg per cubic meter). Death may result from a ½-hour exposure to 2,500 ppm (1,750 mg per cubic meter) (12).

### TREATMENT

The most important treatment is an immediate attempt to remove the ammonia from the skin and eyes by washing with water or saline. All clothing should be removed. Because ammonia penetrates rapidly, irrigation of the eyes must be begun within 5 to 10 seconds to prevent damage and should be continued for a minimum of 20 minutes or until the pH of the conjunctival sac is less than 8.5 (11).

Following this initial removal of the ammonia, patients are treated in a manner similar to a thermal injury with smoke inhalation. Because the airway and pulmonary injuries are the most life-threatening, they are addressed first. The airway is secured by nasal or oral tracheal intubation. The largest tube practical is inserted since sloughing of large pieces of mucosa may block a small tube. If upper airway obstruction interferes with intubation, a cricothyrotomy should be done.

Following intubation, the patient is placed on intermittent mandatory ventilation (IMV) at the lowest rate that will maintain a normal PaCO<sub>2</sub>. A tidal volume of 10–15 ml/kg of body weight is recommended (34). The PaO<sub>2</sub> is then controlled by adjusting the positive end expiratory pressure (PEEP), using a minimum of 5 cm H<sub>2</sub>O pressure. Increasing the FIO<sub>2</sub> above 50% risks oxygen toxicity. While some (24, 28, 32) have attempted

to treat the pulmonary edema with furosemide, others feel that it is better treated with PEEP since the edema results from lung injury rather than excess fluid (7, 26, 27). Intravenous aminophylline and inhalation bronchial dilators are used to treat bronchospasm (1, 3, 4, 9, 10). Aminophylline, however, may have a diuretic effect and complicate initial fluid resuscitation.

While steroids have been used to treat ammonia injuries (8, 10, 17, 19, 21, 24, 28, 30, 36), they are now indicated only for severe bronchospasm that does not respond to other therapy. When severe, airway obstruction may lead to hypercarbia and not respond to corticosteroids or bronchodilator therapy (2, 8, 10, 28). Steroids have not been shown to decrease mortality from ammonia injuries (7, 22, 28, 35), and may increase morbidity (10, 20).

Fluid resuscitation and skin wound care are similar to that of other thermal injuries (2, 25). Wounds should be debrided as needed and dressed with 1% silver sulfadiazine. Mafenide is a carbonic anhydrase inhibitor, and is avoided to prevent metabolic acidosis being superimposed on patients already prone to respiratory acidosis. Skin grafting is done as needed.

The initial eye irrigation may be facilitated by the use of a topical anesthetic, but this should not be continued as it may delay re-epithelialization. A mydriatic-cycloplegic drug such as atropine should be used to decrease the discomfort and prevent synechiae in the presence of iritis (11, 12, 15). Topical antibiotics prevent secondary infection. Topical steroids are not recommended because they retard re-epithelialization and cause thinning of the corneal stroma.

The use of prophylactic systemic antibiotics is not recommended (6, 18). In 29 cases discussed in detail, seven developed infection with resistant organisms after use of prophylactic systemic antibiotics (8, 10, 19, 24, 36).

### PROGNOSIS

The presence or absence of abnormal chest findings on physical examination at the time of admission is the best prognostic factor (21). Initial chest X-rays or early PaO<sub>2</sub> values correlate poorly in determining which patients go on to develop respiratory difficulties.

Walton (32), noted that all survivors showed signs of improvement by 48–72 hours; however, they developed some degree of chronic obstructive lung disease (COPD). The development of COPD along with a decreased diffusion capacity suggests residual parenchymal abnormality (10). In addition, episodes of bronchospasm may persist, necessitating continued use of bronchial dilators. Radionuclide lung imaging has been helpful in revealing the site and extent of the obstructive lung disease (30). Hatton et al. (14) found an increase in several urinary metabolites of hydroxylysine following ammonia inhalation in four patients, and attributed this to the breakdown of collagen in the lungs and suggest that this could be a useful index of the pulmonary injury.

The hyperamylasemia seen in our patients has not been reported previously. The significance of this finding is uncertain; however, it may prove to be a useful indicator of the severity of injury.

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