CHAPTER 123

Smoke Inhalation

Christopher P. Holstege Mark A. Kirk

Firefighters discovered an unresponsive 39-year-old man in a smoke-filled room at an apartment building fire. At the scene, his initial vital signs were: palpable blood pressure, 70 mm Hg; pulse, 160 beats/min; respiratory rate, 0/min. A large amount of soot was noted in the patient's upper airway during endotracheal intubation in the field. He was placed on 100% oxygen during transport. On arrival at the emergency department (ED), he was unresponsive to painful stimuli and had a palpable systolic blood pressure of 100 mm Hg. No evidence of head trauma or skin burns was noted. Pupils were equal and reactive to light; conjunctival irritation and corneal burns were noted. He had singed nasal hairs and soot in his oropharynx, and carbonaceous material was suctioned from his endotracheal tube. Diffuse wheezing was present in all lung fields. He was attached to a ventilator with 100% oxygen, and aerosolized albuterol was administered. His blood pressure improved with intravenous (IV) fluid therapy. He did no respond to IV naloxone (2 mg), thiamine (100 mg), or dextrose (25 g).

His initial electrocardiogram (ECG) revealed sinus tachycardia at 160 beats/min without evidence of ischemic changes. Initial laboratory data revealed: white blood cell count, 14,000 cells/mm^3; hemoglobin, 11.3 g/dL; sodium, 141 mEq/L; potassium, 3.5 mEq/L; chloride, 111 mEq/L; bicarbonate, 12 mEq/L; BUN, 27 mg/dL; creatinine, 0.7 mg/dL; blood glucose, 80 mg/dL. Blood lactate concentration was 14 mEq/L. Arterial blood gas analysis on 100% oxygen revealed pH, 7.17; PCO_2, 30 mm Hg; PO_2, 150 mm Hg. Cooximeter measured a carboxyhemoglobin concentration of 38% and a methemoglobin concentration of 0.8%. Blood ethanol concentration was 179 mg/dL. A chest radiograph was unremarkable.

Because of his critical condition, the presence of metabolic acidosis, and his exposure to a fire environment, the possibility of cyanide poisoning was entertained, and 12.5 g of sodium thiosulfate was given intravenously. The patient was transferred to the intensive care unit, where mechanical ventilation and fluid resuscitation continued. He had no further significant hemodynamic instability. Within 4 hours of admission, he received hyperbaric oxygen therapy. He had progressive improvement in mental status and was awake 6 hours after admission. The patient had complete recovery with no neurologic deficits. An admission whole-blood cyanide concentration of 1.80 μg/mL (<1 μg/mL normal) was reported 12 hours later.

INTRODUCTION

Smoke inhalation is the leading cause of death from fires. Smoke contains numerous toxins that are generated during combustion. Combustion, or pyrolysis, is the rapid decomposition or oxidation of a substance (fuel) by heat. Smoke is a complex mixture of heated air, suspended solid and liquid particles, gases, fumes, aerosols, and vapors. Combustion products resulting from a fire are difficult to predict; in fact, even the composition of smoke is quite variable within the same fire environment.[10,37,112] The chemical composition of the fuel, oxygen availability, and temperature determine the combustion products found in smoke (Table 123–1).[10,30,42,50,61,101,112,118,119,137] The extensive variety of materials used in our environment contributes to the broad spectrum of combustion products present in typical smoke.[30]

The association of smoke inhalation with burns produces a more serious systemic illness.[41,130,135,141,158] Burn victims with smoke inhalation injury have higher morbidity and mortality than those with burns only; the incidence of acute respiratory failure is 61% in burn victims with smoke inhalation injury versus 12% in those with burns only.[8,29,143,156,159] In addition, burn edema is accentuated and nonburned tissue has increased vascular permeability when associated with smoke inhalation injuries.[40]

HISTORY AND EPIDEMIOLOGY

Disastrous fires are frequent reminders of the role of inhalation injuries in fire deaths.[37,79] In the United States, a fire department responds to a fire every 20 seconds.[73] In 2003, the National Fire Protection Agency reported 1,584,500 fire incidents in the United States, with 3925 fire deaths and 18,125 fire injuries.[73] Compared with other countries, the United States has one of the highest fire death rates in the world.[90] An estimated 50–80% of these fire deaths result from smoke inhalation injuries, rather than dermal burns or trauma.[16,62,101,160] More than 30% of patients hospitalized in burn units develop concomitant pulmonary complications, and 75% of these patient die.[65,136] World Health Organization data show that smoke from solid fuel is one of the four most common causes of death and disease in developing countries.[15]

Fire injuries can result from an array of inhaled toxic xenobiotics and/or thermal burns. Prior to 1942, toxic inhalation from dwelling fires was considered unusual. However, in that year, a fire at the Cocoanut Grove Night Club in Boston proved that toxic gases can be generated in typical dwelling fires.[111] From 1955–1972, death from smoke inhalation injury increased 3-fold and was attributed to abundant use of newer synthetic materials for building and furnishings.[16] Despite improved firefighting resources, mass casualties from smoke inhalation continue. On November 11, 2000, 170 deaths occurred when a cable train carrying skiers caught fire in a

TABLE 123–1. Common Materials and Their Combustion Products

Products	Combustion Products
Wool	Carbon monoxide, hydrogen chloride, phosgene, chlorine, cyanide
Silk	Sulfur dioxide, hydrogen sulfide, ammonia, cyanide
Nylon	Ammonia, cyanide
Wood, cotton, paper	Carbon monoxide, acrolein, acetaldehyde, formaldehyde, acetic acid, formic acid, methane
Petroleum products	Carbon monoxide, acrolein, acetic acid, formic acid
Polystyrene	Styrene
Acrylic	Acrolein, hydrogen chloride, carbon monoxide
Plastics	Cyanide, hydrogen chloride, aldehydes, ammonia, nitrogen oxides, phosgene, chlorine
Polyvinyl chloride	Carbon monoxide, hydrogen chloride, phosgene, chlorine
Polyurethane	Cyanide, isocyanates
Melamine resins	Ammonia, cyanide
Rubber	Hydrogen sulfide, sulfur dioxide
Sulfur-containing material	Sulfur dioxide
Nitrogen-containing material	Cyanide, isocyanates, oxides of nitrogen
Fluorinated resins	Hydrogen fluoride
Fire-retardant materials	Hydrogen chloride, hydrogen bromide

tunnel in Austria. Most of the victims apparently managed to escape the burning train but were killed by "acrid smoke" as they tried to flee.[3] On February 20, 2003, a fire in a crowded Rhode Island nightclub killed 100 people and injured more than 200 people, with the majority suffering from smoke inhalation.[36] On December 31, 2004, a fire at an Argentina night club killed 175 people and injured more than 700. Most of the victims died of smoke inhalation.[4]

PATHOPHYSIOLOGY

Toxic combustion products are classified into three categories: simple asphyxiants, irritant toxins, and chemical asphyxiants (Table 123–2). Simple asphyxiants such as carbon dioxide exert a space-occupying effect; they simply displace oxygen.[37,42,133,158] In addition, combustion utilizes oxygen, potentially resulting in an oxygen-deprived environment (Chap. 119).[37]

TABLE 123–2. Toxic Combustion Products

Simple Asphyxiants	**Irritants**
Carbon dioxide	High water solubility (upper airway injury)
	Acrolein
Chemical Asphyxiants	Sulfur dioxide
Carbon monoxide	Ammonia
Hydrogen cyanide	Hydrogen chloride
Hydrogen sulfide	Intermediate water solubility (upper and lower respiratory tract injury)
Oxides of nitrogen (methemoglobinemia)	Chlorine
	Isocyanates
	Low water solubility (pulmonary parenchymal injury)
	Oxides of nitrogen
	Phosgene

Irritant xenobiotics are chemically reactive compounds that exert a local effect on the respiratory tract (Chap. 119). For example, high concentrations of acrolein are measured in air samples from fire environments and in the blood of fire victims.[2,86,150] Acrolein penetrates cell membranes easily because it is lipid soluble, injuring cells by denaturing intracellular proteins and nucleic acids.[51,160] Ammonia is generated when wool, silk, nylon, or synthetic resins are burned. It reacts with the mucosal moisture to produce the alkaline agent ammonium hydroxide.[31,81] Sulfur dioxide, an oxidation product of sulfur-containing material, is found in >50% of air samples from fires.[23] Sulfurous acid forms when sulfur dioxide reacts with the water of the respiratory mucosa. Hydrogen chloride, chlorine, and phosgene are formed from the oxidation of polyvinyl chloride (PVC), a plastic widely used in home and office furnishings, floor coverings, and electrical insulation.[17,20,37,42,88] In the presence of mucosal water, these combustion products generate damaging hydrogen chloride and reactive oxygen species.[38] Phosgene produces delayed alveolar injury.[21] Isocyanates, combustion products generated from upholstery, cause intense irritation of the upper and lower respiratory tracts.[115]

Combustion of organic material produces finely divided carbonaceous particulate matter (soot) suspended in hot air and gases. Inhalation of soot particles and aerosols enhances exposure to irritant xenobiotics in a fire environment. These particles are not just composed of carbon; organic acids, aldehydes, and reactive chemicals such as sulfur dioxide, hydrogen chloride, chlorine, and phosgene are adsorbed to their surfaces.[23,42,66,88,133,158] Soot adheres to the mucosa of the airways, allowing adsorbed irritant xenobiotics to react with the mucosal surface moisture. The deposition of these particles in the respiratory tract depends on their size, with particles of 1–3 μm reaching the alveoli.[94] Experimental animals have markedly decreased lung injury when they are exposed to smoke that was filtered to remove particulates.[76] Irritant gases can "piggyback" on aerosol droplets and alter the site of gas deposition.[63]

Water solubility is the most important chemical characteristic in determining the timing and anatomic level of respiratory tract injury. Injury from water-soluble xenobiotics occurs in the upper airway and results in damage to mucosal cells with release of mediators of inflammation and/or reactive oxygen species.[22,82,95,118] The rapidity with which this process occurs provides a warning that the environment is unsafe and prompts escape. Following more than a trivial exposure, the intense inflammatory response increases microvascular permeability and allows movement of fluid from the intravascular space into the tissues of the upper airway. The loosely attached underlying tissue of the supraglottic larynx can become markedly edematous, causing upper airway obstruction within minutes to hours.[69] The obstruction can progress such that the upper airway is completely occluded.[124] Xenobiotics with low water solubility react with the upper respiratory mucosa very slowly and do not elicit an escape response. These xenobiotics reach the distal lung parenchyma, where they react slowly to create a delayed toxic effect. In addition to water solubility, factors such as concentration of the substance inhaled, duration of exposure, particle size, respiratory rate, absence of protective reflexes, and preexisting disease influence the region of respiratory tract injury.

Tracheobronchial injuries result from inhaled particulates and toxic gases, which cause increased airway resistance from intraluminal debris, airway mucosal edema, inspissated secretions, and brochospasm.[29,87,144] Damaged cells release chemotactic factors

that stimulate production of an exudate rich in protein and inflammatory cells.[152] This reaction eventually results in sloughing of the mucosa, which combines with the exudate to create casts of the airways. In victims of smoke inhalation, casts block major airways, increasing airway resistance and mechanically preventing passage of oxygen to the alveoli.[29,33,99,144,152] Increased tracheobronchial vascular permeability leads to interstitial edema of the airways and increased airway resistance. Bronchoconstriction and subsequent wheezing are caused by a response to mediators of inflammation, a reflex response to toxic mucosal injury.[58,148]

Toxic xenobiotics that reach the alveoli injure the lung parenchyma.[105] Caustics, proteolytic enzymes, reactive free radicals, and mediators of inflammation all contribute to acute lung injury (ALI).[75,78,114,148,158] Pathophysiologic changes of ALI decrease lung compliance and bacterial defenses and lead to ventilation–perfusion mismatch with intrapulmonary shunting, increased extravascular lung water, and microvascular permeability.[29,52,148,152,155] Decreased lung compliance from atelectasis is produced when toxic chemicals deactivate pulmonary surfactant.[29,105,113,152] In animals, patchy atelectasis occurs rapidly after smoke is inspired.[29,105,152] In addition, ventilation–perfusion mismatch occurs when pulmonary blood flow is diverted by hypoxia and vasoactive mediators of inflammation.[83,84,104,148] Xenobiotics cause further injury by impairing mucociliary clearance, altering alveolar macrophage function, and impairing phagocytosis of bacteria, which all contribute to development of pulmonary infections and sepsis.[12,13,47,64,123] The combination of delayed toxic effects of some inhaled xenobiotics and slowly developing inflammatory response may explain the limited initial manifestations of parenchymal injury during the first 24 hours after smoke exposure.

Chemical asphyxiants exert their toxic effects at extrapulmonary sites. Incomplete combustion of organic materials generates carbon monoxide, which is considered the most common serious acute hazard to victims of smoke inhalation injury (Chap. 120).[1,14,37,150,160] Carbon monoxide prevents oxygen from binding to hemoglobin, creating a functional anemia. It also hinders the release of oxygen at the tissues by shifting the oxyhemoglobin dissociation curve to the left. Other mechanisms, such as lipid peroxidation, contribute to the toxicity of carbon monoxide (Chap. 120).[139] Cyanide is produced from combustion of organic nitrogen-containing products such as plastics, melamine resins, polyurethanes, wool, silk, nylon, nitrocellulose, polyacrylonitriles, synthetic rubber, and paper.[112] High concentrations of cyanide are measured in air samples from fires and elevated blood cyanide concentrations occur in both fire survivors and fire fatalities.[5,9,10,27,37,60,72,128,129,134,154] Cyanide has at least an additive, if not synergistic, effect with carbon monoxide in smoke inhalation toxicity (Chap. 121).[9,93,108,117,119] Nitrogen-containing materials generate oxides of nitrogen, which are irritants and methemoglobin inducers (Chap. 122).

Smoke inhalation associated with burns results in an elevation of systemic nitric oxide because of the increased activity of inducible nitric oxide synthase.[44-46,131] The elevation of nitric oxide may result in myocardial contractile dysfunction with subsequent hypotension.[131] Nitric oxide can combine with superoxides to form the highly reactive peroxynitrite $ONOO^-$, which may lead to further alveolar capillary membrane damage and subsequent ALI.[44]

Depending on the fuel, other combustion products are aerosolized and act by local irritation or systemic toxicity. Metal oxides, hydrocarbons, hydrogen fluoride, and hydrogen bromide may contribute to toxicity. Antimony, bromine, cadmium, chromium, cobalt, gold, iron, lead, and zinc often are recovered from air samples taken during fires and from soot removed from the surface of the trachea and bronchi of fire victims.[14,37] Unusual fires at industrial sites, clandestine drug laboratories, transportation incidents, or natural disasters such as erupting volcanoes produce additional toxic inhalants.

CLINICAL MANIFESTATIONS

The primary clinical problem in smoke inhalation victims is respiratory compromise. The patients may have voice changes, and their speech may progressively worsen as the airway becomes increasingly edematous. Stridor and acute respiratory arrest may develop. Patients may have difficulty managing airway secretions, with expectoration of copious quantities of soot containing sputum. Visualization of the vocal cords by direct laryngoscopy may be difficult because of soot accumulation, secretions, or edema.

Auscultation of the chest may demonstrate rhonchi, crackles, and wheezing suggestive of ALI.[56] ALI is defined as diffuse alveolar filling of acute onset with hypoxemia but without left atrial hypertension.[11] The most severe manifestation of ALI is the acute respiratory distress syndrome (ARDS), which is defined based on the patient's ability to oxygenate (Chaps. 22 and 119). Bronchospasm may occur, particularly in patients with underlying reactive airway disease. Breath sounds, including wheezing, may be virtually inaudible in patients with severe bronchospasm.

Tachycardia and tachypnea may be pronounced and hypotension may occur, with faint or no peripheral pulses noted.[131] Smoke inhalation victims may develop an altered mental status, including agitation, confusion, or coma. Conjunctival injection, corneal ulcerations, marked lacrimation, and blepharospasm may be noted on ophthalmologic examination.

DIAGNOSTIC TESTING

Because smoke inhalation injury causes pulmonary and airway damage, diagnostic studies should focus on assessing oxygenation and ventilation. Therefore, arterial blood gas (ABG) analysis, carboxyhemoglobin and methemoglobin concentrations, and chest radiography are the most important tests to obtain.

ABG analysis assesses both pulmonary function and blood pH. The presence of metabolic acidosis may be an early clue to tissue hypoxia. Serial measurements of arterial oxygenation and alveolar ventilation are helpful in identifying hypoxemia or ventilatory failure. The accuracy of oxygen saturation measurement depends on the method used. Oxygen saturation calculated from ABG analysis may be unreliable in the setting of carbon monoxide poisoning, but measured oxygen saturation determined by cooximeter accurately reflects the percent saturation of hemoglobin. Transcutaneous measurement of oxygen saturation by pulse oximetry is unreliable in the patient with smoke inhalation because it overestimates oxygen saturation in the presence of carboxyhemoglobin.[7,43,107,151]

A carboxyhemoglobin concentration should be obtained for all smoke inhalation victims.[28,159] Either arterial or venous samples can be used to accurately measure carboxyhemoglobin concentrations.[85,147] The carboxyhemoglobin concentration alone is a poor predictor of the severity of smoke inhalation because a low or nondetectable concentration does not exclude the possibility of developing inhalation injury.[92,132] Because elevated methemoglobin concentrations are rarely reported in fire victims, methemoglobin

concentrations should also be obtained in the initial laboratory evaluation.[67,127] Blood cyanide analysis is of little clinical use because results of analysis are not available for hours, and therapy should never await laboratory confirmation of the presence of cyanide. Accurate measurement depends on acquiring the sample soon after exposure because cyanide is rapidly eliminated from the blood following smoke inhalation.[9,74]

A chest radiograph obtained early in the course of smoke inhalation is an insensitive indicator of pulmonary injury.[28,56,116,157] The most frequent abnormal findings on initial chest radiograph are diffuse alveolar and interstitial changes found in 34% of patients, followed by focal abnormalities in 12%.[56] In one series, no significant differences in the duration of either ventilation or stay in the intensive care unit were observed between smoke inhalation victims who exhibited abnormal findings on the first chest radiographic examination and those without any abnormalities.[56] Subtle findings within 24 hours of exposure include perivascular haziness, peribronchial cuffing, bronchial wall thickening, and subglottic edema.[80,136] Serial chest radiographs following a baseline study are helpful in detecting pulmonary disease following smoke inhalation.[58] Widespread airway disease usually occurs more than 24 hours after inhalation injury and may represent ALI, aspiration, volume overload, infection, or cardiogenic pulmonary edema.[136]

Nuclear imaging and pulmonary function testing, although not readily available for initial evaluation, can detect pulmonary injury after smoke inhalation. Xenon ventilation studies can detect small airway and alveolar injuries before changes are seen radiographically.[58,96] Abnormal flow volume curves can indicate early upper airway obstruction.[57] Abnormal spirometry, especially forced expiratory volume at 1 second (FEV_1), detects early obstructive pulmonary defects of smoke inhalation, which may precede abnormalities of ABGs or radiography.[58,98]

MANAGEMENT

Critical airway compromise may be present upon the patient's arrival at the hospital, or it may develop subsequently.[34,57,124] A major pitfall in managing a patient with smoke inhalation is failing to appreciate the possibility of rapid deterioration. The history and physical findings help to determine significant smoke exposure and the potential for clinical deterioration. The clinical effects of smoke exposure and their appropriate treatment are described in Figure 123–1. Upper airway patency must be rapidly established. When obvious oropharyngeal burns are observed, upper airway injury almost certainly is present, even if overt injuries are not seen, and distal injury may be present and underestimated.[57] Direct evaluation of the upper airway, preferably with fiberoptic endoscopy, is essential for assessing patients at high risk for inhalation airway injury.[34,57,58,69] When evidence of upper airway injury exists, early endotracheal intubation should be performed under controlled circumstances. Other indications for early intubation include coma, stridor, and full-thickness circumferential neck burns.[8,57,58,124] Massive fluid resuscitation of the burned patient contributes to upper airway edema.[57,58,100,124] Therefore, early intubation may be necessary in the patient with dermal burns undergoing aggressive fluid management.[57]

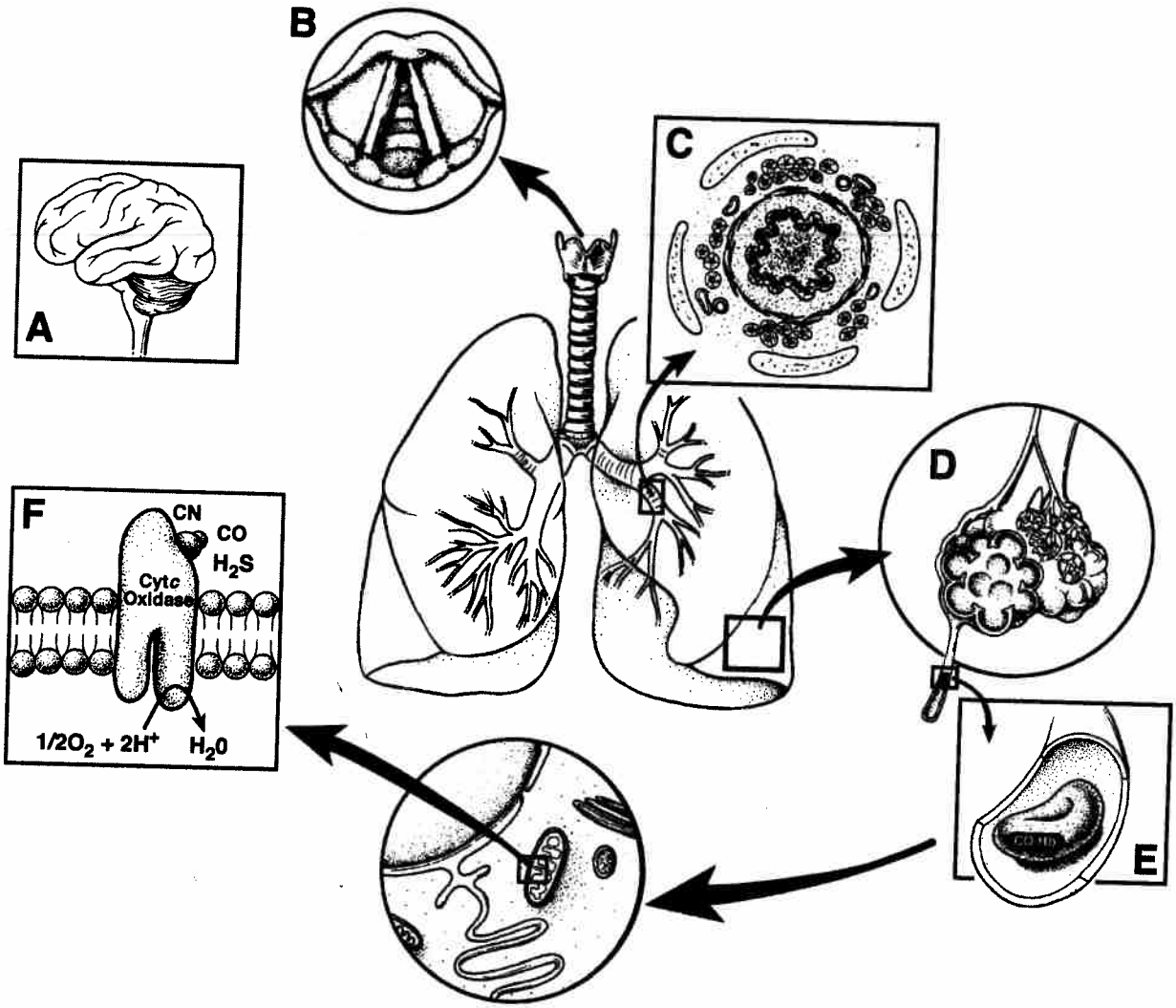
Although inhaled β_2-adrenergic agonists are effective and considered first-line therapy for acute reversible bronchoconstriction resulting from asthma or chronic obstructive pulmonary disease, their efficacy in patients with smoke inhalation is unknown.[18,89] However, pathophysiologic changes induced by irritant toxins in smoke are partially reversible, suggesting that β_2-adrenergic agonists improve airflow obstruction.[71,91] The benefits of corticosteroids given for treatment of smoke inhalation injury are not demonstrated in either clinical or animal studies.[103,125]

Pathophysiologic changes in the lung may cause progressive hypoxia over hours to days. Treatment of progressive respiratory failure includes mechanical ventilation, continuous positive airway pressure, positive end-expiratory pressure, and vigorous clearing of pulmonary secretions.[102] Frequent airway suctioning, chest physiotherapy, and therapeutic bronchoscopy can clear inspissated secretions, plugs, and casts.[33,99] Inhalation injury can progress to ALI or ARDS. Experimental treatment has examined high-frequency ventilation, percutaneous arteriovenous carbon dioxide removal, perfluorocarbons, inhaled nitric oxide, extracorporeal membrane oxygenation, instillation of natural surfactant into the lung, continuous IV infusion of heparin, and deferoxamine–hetastarch complex for improving inhalation injury.[26,32,39,59,70,77,97,106,109,110,120,121] However, none of these modalities has been definitively proven to improve outcome.

Treatment of carbon monoxide poisoning consists of supplemental oxygen therapy, administered by a high-flow, tight-fitting mask, endotracheal tube, or hyperbaric oxygen therapy, depending on the circumstances. Studies suggest that hyperbaric oxygen is superior to normobaric 100% oxygen in correcting toxicity and preventing delayed neurologic sequelae.[138,142,145,153] If readily available, hyperbaric oxygen should be considered in patients with smoke inhalation and a history of loss of consciousness, confusion, coma, headache, malaise, forgetfulness, fatigue, dizziness, visual disturbances, nausea, vomiting, cardiac ischemia, focal neurologic findings, or pregnancy.[140,153] Hyperbaric oxygen should be administered to patients only after life-threatening conditions such as associated trauma or hemodynamic instability are treated and the patient's condition has stabilized (Chap. 120 and Antidotes in Depth: Hyperbaric Oxygen).

Cyanide poisoning should be suspected in seriously ill patients with smoke inhalation and metabolic acidosis.[48,122] Plasma lactate concentrations at the time of hospital admission correlate closely with blood cyanide concentrations, with plasma lactate concentrations >10 mmol/L reported to be a sensitive indicator of cyanide toxicity.[9] Treatment of cyanide toxicity should be considered while other life support measures, including 100% oxygen therapy, are instituted.[9,93,108,117,118,129] Treatment options include supportive care alone, administration of all or part of the cyanide antidote kit, and hyperbaric oxygen therapy. Patients have survived potentially lethal cyanide concentrations with simply oxygen therapy and supportive care.[19,126] Hyperbaric oxygen has been suggested to improve the outcome of cyanide toxicity, although the data supporting its use alone are not convincing.[49,60,149] Currently, hyperbaric oxygen therapy is considered only an adjunct treatment of cyanide poisoning in the presence of concomitant carbon monoxide poisoning.[146]

The cyanide antidote kit (amyl nitrite, sodium nitrite, and sodium thiosulfate) is the only antidote for cyanide poisoning available in the United States. Amyl nitrite and sodium nitrite produce methemoglobinemia. Detoxification occurs when methemoglobin binds cyanide to form cyanomethemoglobin, but alternate mechanisms to methemoglobin formation are proposed. Sodium thiosulfate donates sulfur to the enzyme rhodanese, which converts cyanide to thiocyanate. Nitrite-induced methemoglobin and



Pathophysiology	Signs and Symptoms	Management
A) Direct CNS toxic effects	Coma Hypoventilation	Oxygen; Secure unprotected airway
B) Upper airway edema	Hypoxemia; Respiratory distress Stridor Hoarse voice	Oxygen Direct visualization of vocal cords Endotracheal intubation
C) Bronchiolar airway obstruction Mucosal edema Intraluminal debris and casts Inspissated secretions Bronchospasm	Respiratory distress Hypoxemia Wheezes Cough Increased peak airway pressures	Oxygen Removal of debris and secretions Chest physiotherapy Frequent airway suctioning Therapeutic bronchoscopy Inhaled β-adrenergic agonists
D) Atelectasis Surfactant destruction Acute Lung Injury (ALI)	Respiratory distress Hypoxemia Crackles Chest radiographic changes	Oxygen Continuous positive airway pressure Mechanical ventilation Positive end-expiratory pressure
E) Impaired oxygen-carrying capacity (carbon monoxide or methemoglobinemia)	CNS depression or seizures Myocardial ischemia Dysrhythmias Metabolic acidosis	Oxygen Consider hyperbaric oxygen Consider methylene blue
F) Impaired oxygen use at tissues (cyanide, hydrogen sulfide, or carbon monoxide)	CNS depression or seizures Myocardial ischemia Dysrhythmias Metabolic acidosis	Oxygen Assure adequate tissue perfusion Consider treating suspected cyanide toxicity with sodium thiosulfate Consider hyperbaric oxygen

Figure 123–1. The final common pathway from all pathophysiologic changes that occur in smoke inhalation is hypoxia. All treatments should be focused on improving oxygen delivery and oxygen utilization.

sodium thiosulfate work synergistically to detoxify cyanide.[24,25] Unfortunately, methemoglobin is a dysfunctional hemoglobin that is unable to carry oxygen; in addition, its presence increases the affinity of the remaining hemoglobin for oxygen, which prevents its release to the tissues.[35] Impairing oxygen-carrying capacity and oxygen delivery to tissues with nitrite-induced methemoglobinemia is a valid concern in the presence of tissue hypoxia from carboxyhemoglobinemia and other factors. In a small series of fire victims treated with sodium nitrite, methemoglobin concentrations peaked at 7.8–13.4% between 35 and 70 minutes after slow IV infusion.[74] Corresponding carboxyhemoglobin concentrations decreased before peak methemoglobin concentrations had been reached. To the contrary, a case of hypotension and prolonged impairment of oxygen-carrying capacity was reported in a smoke inhalation victim following rapid infusion of sodium nitrite.[53] Because the safety of nitrites has not been studied in a large population of concomitant cyanide and carbon monoxide poisoning and the effect of cyanomethemoglobin on oxygen-carrying capacity is not well understood, initial treatment with thiosulfate alone is reasonable, with use of nitrite reserved for refractory cases or those patients with documented low carboxyhemoglobin concentrations. Sodium thiosulfate has few adverse side effects and can be safely administered to all patients seriously ill from smoke inhalation. When hyperbaric oxygen therapy is available, sodium nitrite can be administered just before the patient enters the hyperbaric chamber, if still clinically indicated, with less concern for impairing oxygen-carrying capacity.[54] Hydroxocobalamin chelates cyanide and is a safe and effective antidote.[9,48,55,68] Because of its apparent safety and efficacy, it can be given empirically to patients seriously ill from smoke inhalation, thus eliminating the need for nitrites.[9,55] Hydroxocobalamin is designated but not yet approved for use in the United States (Chap. 121 and Antidotes in Depth: Amyl and Sodium Nitrites, Sodium Thiosulfate, and Hydroxocobalamin).

Although rarely reported in fire victims, methemoglobinemia can result from inhalation of certain toxic combustion products.[67,127] Elevated methemoglobin concentrations in the presence of elevated carboxyhemoglobin concentrations increase tissue hypoxia. Oxygen therapy alone should be effective for most cases, and the need for methylene blue therapy is rarely clinically indicated following smoke inhalation (Chap. 122 and Antidotes in Depth: Methylene Blue).

Respiratory compromise and other conditions may not result from smoke inhalation, but rather from trauma or underlying medical problems. Trauma from falls or explosions must be suspected and treatment started simultaneously with treatment of burns and inhalation injury. Comatose patients should be considered to have other etiologies for their injuries and should receive naloxone, thiamine, and hypertonic dextrose as indicated. Inhaled xenobiotics, such as carbon monoxide, can directly cause altered mental status, but drug and ethanol intoxication contribute significantly to adult fire fatalities and injuries. Blood ethanol concentrations correlate with elevated concentrations of carbon monoxide and cyanide, implying that intoxication impairs escape and prolongs toxic smoke exposure.[6,14,101] Intracranial pathology should be considered and CT scans obtained as indicated.

Xenobiotics may injure the skin or mucous membranes in addition to the respiratory mucosa.[31] The duration of contact of a xenobiotic with tissue is an important factor in determining the extent of chemical injury to the skin and eyes. Rapid removal of soot from skin or eyes may prevent continued injury. The eyes should be evaluated for corneal burns caused by thermal or irritant chemical injury. The eyes of patients with signs of ocular irritation should be irrigated. Dermal decontamination should be considered to prevent dermal burns from toxin-laden soot adherent to the skin.

SUMMARY

Smoke inhalation continues to contribute significantly to the morbidity and mortality of fire victims. Clinicians caring for these patients must have a basic knowledge of the pathophysiology of smoke inhalation injury. A spectrum of events is possible, ranging from rapid upper airway occlusion to delayed ALI and ARDS. There are controversies regarding the care of these patients and further research is warranted. However, definitive therapies are available and should be considered.

REFERENCES

1. Alarie Y: Toxicity of fire smoke. Crit Rev Toxicol 2002;32:259–289.
2. Anderson RA, Cheng KN, Harland WA: The toxicology of fire deaths. Acta Med Leg Soc 1984;34:110–121.
3. Anonymous: Cable car fire kills about 170. Richmond Times–Dispatch, November 12, 2000, p. A1.
4. Anonymous: Locked doors prevented escape from fire. Richmond Times-Dispatch, January 1, 2005, p. A4.
5. Ansell M, Lewis FA: A review of cyanide concentrations found in human organs. J Forensic Med 1970;17:148–155.
6. Barillo DJ, Goode R, Rush BF, et al: Lack of correlation between carboxyhemoglobin and cyanide in smoke inhalation. Curr Surg 1986;421–423.
7. Barker SJ, Tremper KK: The effect of carbon monoxide inhalation on pulse oximetry and transcutaneous PO_2. Anesthesiology 1987;66: 677–679.
8. Bartlett RH, Niccole M, Tavis MJ, et al: Acute management of the upper airway in facial burns and smoke inhalation. Arch Surg 1976;111:744–749.
9. Baud FJ, Barriot P, Toffis V, et al: Elevated blood cyanide concentrations in victims of smoke inhalation. N Engl J Med 1991;325:1761–1766.
10. Becker CE: The role of cyanide in fires. Vet Hum Toxicol 1985; 27:487–490.
11. Bernard GR, Artigas A, Brigham KL, et al: The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med 1994;149:818–824.
12. Bidani A, Wang C, Heming T: Cotton smoke inhalation primes alveolar macrophages for tumor necrosis factor-alpha production and suppresses macrophage antimicrobial activities. Lung 1998;176:325–336.
13. Bidani A, Wang CZ, Heming TA: Early effects of smoke inhalation on alveolar macrophage functions. Burns 1996;22:101–106.
14. Birky MM, Clarke FB: Inhalation of toxic products from fires. Bull N Y Acad Med 1981;57:997–1013.
15. Bosch X: Report highlights hazard of smoke from indoor fires. Lancet 2003;362:1902.
16. Bowes PC: Casualties attributed to toxic gas and smoke at fires: A survey of statistics. Med Sci Law 1976;16:104–110.
17. Brandt-Rauf PW, Fallon LF, Tarantini T: Health hazards of fire fighters: Exposure assessment. Br J Ind Med 1988;45:606–609.
18. Brenner BE: Bronchial asthma in adults: Presentation to the emergency department. Am J Emerg Med 1983;3:306–333.
19. Brivet F, Delfraissy JF, Duche M, et al: Acute cyanide poisoning: Recovery with non-specific supportive therapy. Intensive Care Med 1983;9:33–35.
20. Brown JE, Birky MM: Phosgene in the thermal decomposition products of poly(vinyl chloride): Generation, detection and measurement. J Anal Toxicol 1980;4:166–174.

21. Brown RF, Jugg BJ, Harban FM, et al: Pathophysiological responses following phosgene exposure in the anaesthetized pig. J Appl Toxicol 2002;22:263–269.
22. Cahalane M, Demling RH: Early respiratory abnormalities from smoke inhalation. JAMA 1984;251:771–773.
23. Charan NB, Meyers CG, Lakshminarayan S, et al: Pulmonary injuries associated with acute sulfur dioxide inhalation. Am Rev Respir Dis 1979;119:555–560.
24. Chen KK, Rose CL: Nitrite and thiosulfate in cyanide poisoning. JAMA 1952;149:113–119.
25. Chen KK, Rose CL, Clowes GH: Comparative values of several antidotes in cyanide poisoning. Am J Med Sci 1934;188:767–781.
26. Cioffi WG, deLemos RA, Coalson JJ, et al: Decreased pulmonary damage in primates with inhalation injury treated with high-frequency ventilation. Ann Surg 1993;218:328–337.
27. Clark CJ, Campbell D, Reid WH: Blood carboxyhaemoglobin and cyanide levels in fire survivors. Lancet 1981;1:1332–1335.
28. Clark WR, Bonaventura M, Meyers W: Smoke inhalation and airway management at a regional burn unit: 1974–1983. J Burn Care Rehabil 1989;10:52–62.
29. Clark WR, Nieman GF: Smoke inhalation. Burns 1988;14:473–494.
30. Clarke FB: Toxicity of combustion products: Current knowledge. Fire J 1983;77:84–101.
31. Close LG, Catlin FI, Cohn AM: Acute and chronic effects of ammonia burns of the respiratory tract. Arch Otolaryngol 1980;106:151–158.
32. Cox CS, Zwischenberger JB, Traber DL, et al: Heparin improves oxygenation and minimizes barotrauma after severe smoke inhalation in an ovine model. Surg Gynecol Obstet 1993;176:339–349.
33. Cox RA, Burke AS, Soejima K, et al: Airway obstruction in sheep with burn and smoke inhalation injuries. Am J Respir Cell Mol Biol 2003;29:295–302.
34. Crapo RO: Smoke-inhalation injuries. JAMA 1981;246:1694–1696.
35. Curry S: Methemoglobinemia. Ann Emerg Med 1982;11:214–221.
36. Dacey MJ: Tragedy and response—The Rhode Island nightclub fire. N Engl J Med 2003;349:1990–1992.
37. Davies JW: Toxic chemicals versus lung tissue—An aspect of inhalation injury revisited. J Burn Care Rehab 1986;7:213–222.
38. Decker WJ, Koch HF: Chlorine poisoning at the swimming pool: An overlooked hazard. Clin Toxicol 1978;13:377–381.
39. Demling R, LaLonde C, Ikegami K: Fluid resuscitation with deferoxamine hetastarch complex attenuates the lung and systemic response to smoke inhalation. Surgery 1996;119:340–348.
40. Demling R, Lalonde C, Youn YK, et al: Effect of graded increases in smoke inhalation injury on the early systemic response to a body burn. Crit Care Med 1995;23:171–178.
41. Demling RH, Knox J, Youn Y, et al: Oxygen consumption early postburn becomes oxygen delivery dependent with the addition of smoke inhalation injury. J Trauma 1992;32:593–599.
42. Dyer RF, Esch VH: Polyvinyl chloride toxicity in fires: Hydrogen chloride toxicity in fire fighters. JAMA 1976;235:393–397.
43. Eisenkraft JB: Pulse oximeter desaturation due to methemoglobinemia. Anesthesiology 1988;68:279–282.
44. Enkhbaatar P, Murakami K, Shimoda K, et al: Inducible nitric oxide synthase dimerization inhibitor prevents cardiovascular and renal morbidity in sheep with combined burn and smoke inhalation injury. Am J Physiol Heart Circ Physiol 2003;285:H2430–H2436.
45. Enkhbaatar P, Murakami K, Shimoda K, et al: Ketorolac attenuates cardiopulmonary derangements in sheep with combined burn and smoke inhalation injury. Clin Sci (Lond) 2003;105:621–628.
46. Enkhbaatar P, Traber DL: Pathophysiology of acute lung injury in combined burn and smoke inhalation injury. Clin Sci (Lond) 2004;107:137–143.
47. Fein A, Leff A, Hopewell PC: Pathophysiology and management of complications resulting from fire and the inhaled products of combustion: Review of the literature. Crit Care Med 1980;8:94–[illegible].
48. Fortin JL, Ruttiman M, Domanski L, et al: Hydroxocobalamin: Treatment for smoke inhalation-associated cyanide poisoning. Meeting the needs of fire victims. JEMS 2004;29(Suppl):18–21.
49. Goodhart GL: Patient treated with antidote kit and hyperbaric oxygen survives cyanide poisoning. South Med J 1994;87:814–816.
50. Guzzardi L: Toxic products of combustion. Top Emerg Med 1985;7:45–51.
51. Hales CA, Barkin PW, Jung BW, et al: Synthetic smoke with acrolein but not HCL produces pulmonary edema. J Appl Physiol 1988;64:1121–1133.
52. Hales CA, Musto SW, Janssens S, et al: Smoke aldehyde component influences pulmonary edema. J Appl Physiol 1992;72:555–561.
53. Hall AH, Kulig KW, Rumack BH: Suspected cyanide poisoning in smoke inhalation: Complications of sodium nitrite therapy. J Toxicol Clin Exp 1989;9:3–9.
54. Hall AH, Kulig KW, Rumack BH: Toxic smoke inhalation. Am J Emerg Med 1989;7:121–122.
55. Hall AH, Rumack BH: Hydroxycobalamin sodium thiosulfate as a cyanide antidote. J Emerg Med 1987;5:115–121.
56. Hantson P, Butera R, Clemessy JL, et al: Early complications and value of initial clinical and paraclinical observations in victims of smoke inhalation without burns. Chest 1997;111:671–675.
57. Haponik EF, Meyers DA, Munster AM, et al: Acute upper airway injury in burn patients. Am Rev Respir Dis 1987;135:360–366.
58. Haponik EF, Summer WR: Respiratory complications in burned patients: Diagnosis and management of inhalation injury. J Crit Care 1987;2:121–143.
59. Harrington DT, Jordan BS, Dubick MA, et al: Delayed partial liquid ventilation shows no efficacy in the treatment of smoke inhalation injury in swine. J Appl Physiol 2001;90:2351–2360.
60. Hart GB, Strauss MB, Lennon PA, et al: Treatment of smoke inhalation by hyperbaric oxygen. J Emerg Med 1985;3:211–215.
61. Hartzell GE: Overview of combustion toxicology. Toxicology 1996;115:7–23.
62. Harwood B, Hall JR: What kills in fires: Smoke inhalation or burns? Fire J 1989;84:29–34.
63. Henderson RF, Schlesinger RB: Symposium on the importance of combined exposures in inhalation toxicology. Fundam Appl Toxicol 1989;12:1–11.
64. Herlihy JP, Vermeulen MW, Joseph PM, et al: Impaired alveolar macrophage function in smoke inhalation injury. J Cell Physiol 1995;163:1–8.
65. Herndon DN, Barrow RE, Linares HA, et al: Inhalation injury in burned patients: Effects and treatment. Burns Incl Therm Inj 1988;14:349–356.
66. Hill IR: Particulate matter of smoke inhalation. Ann Acad Med Singapore 1993;22:119–123.
67. Hoffman RS, Sauter D: Methemoglobinemia resulting from smoke inhalation. Vet Hum Toxicol 1989;31:168–170.
68. Houeto P, Borron SW, Sandouk P, et al: Pharmacokinetics of hydroxocobalamin in smoke inhalation victims. J Toxicol Clin Toxicol 1996;34:397–404.
69. Hunt JL, Agee RN, Pruitt BA: Fiberoptic bronchoscopy in acute inhalation injury. J Trauma 1975;15:641–649.
70. Jackson MP, Philp B, Murdoch IJ, et al: High frequency oscillatory ventilation successfully used to treat a severe paediatric inhalation injury. Burns 2002;28:509–511.
71. Jagoda A, Shepherd SM, Spevitz A, et al: Refractory asthma, part I: Epidemiology, pathophysiology, pharmacologic interventions. Ann Emerg Med 1997;29:262–274.
72. Jones J, Mcmullen MJ, Dougherty J: Toxic smoke inhalation: Cyanide poisoning in fire victims. Am J Emerg Med 1987;5:318–321.
73. Karter M: Fire Loss in the United States During 2003. Quincy, MA, National Fire Protection Association, 2004, p. 1–35.
74. Kirk MA, Gerace R, Kulig KW: Cyanide and methemoglobin kinetics in smoke inhalation victims treated with the cyanide antidote kit. Ann Emerg Med 1993;22:1413–1418.

75. Laffon M, Pittet JF, Modelska K, et al: Interleukin-8 mediates injury from smoke inhalation to both the lung endothelial and the alveolar epithelial barriers in rabbits. Am J Respir Crit Care Med 1999;160: 1443–1449.
76. Lalonde C, Demling R, Brain J, et al: Smoke inhalation injury in sheep is caused by the particle phase, not the gas phase. J Appl Physiol 1994;77:15–22.
77. LaLonde C, Ikegami K, Demling R: Aerosolized deferoxamine prevents lung and systemic injury caused by smoke inhalation. J Appl Physiol 1994;77:2057–2064.
78. LaLonde C, Nayak U, Hennigan J, et al: Plasma catalase and glutathione levels are decreased in response to inhalation injury. J Burn Care Rehabil 1997;18:515–519.
79. Layton TR, Elhauge ER: U.S. fire catastrophes of the 20th century. J Burn Care Rehabil 1982;3:21–28.
80. Lee MJ, O'Connell DJ: The plain chest radiograph after acute smoke inhalation. Clin Radiol 1988;39:33–37.
81. Levy DM, Divertie MB, Litzow TJ, et al: Ammonia burns of the face and respiratory tract. JAMA 1964;190:873–876.
82. Lin YS, Kou YR: Acute neurogenic airway plasma exudation and edema induced by inhaled wood smoke in guinea pigs: Role of tachykinins and hydroxyl radical. Eur J Pharmacol 2000;394:139–148.
83. Loick HM, Traber LD, Stothert JC, et al: Smoke inhalation causes a delayed increase in airway blood flow to primarily uninjured lung areas. Intensive Care Med 1995;21:326–333.
84. Loick HM, Traber LD, Tokyay R, et al: The effects of dopamine on pulmonary hemodynamics and tissue damage after inhalation injury in an ovine model. J Burn Care Rehabil 1992;13:305–315.
85. Lopez DM, Weingarten-Arams JS, Singer LP, et al: Relationship between arterial, mixed venous, and internal jugular carboxyhemoglobin concentrations at low, medium, and high concentrations in a piglet model of carbon monoxide toxicity. Crit Care Med 2000;28:1998–2001.
86. Mahut B, Delacourt C, de Blic J, et al: Bronchiectasis in a child after acrolein inhalation. Chest 1993;104:1286–1287.
87. Mallory TB, Brickley WJ: Management of the Cocoanut Grove burns at Massachusetts General Hospital. Pathology: With special reference to the pulmonary lesions. Ann Surg 1943;117:865–884.
88. Markowitz JS, Gutterman EM, Schwartz S, et al: Acute health effects among firefighters exposed to a polyvinyl chloride (PVC) fire. Am J Epidemiol 1989;129:1023–1031.
89. McFadden ER: Therapy for acute asthma. J Allergy Clin Immunol 1989;84:151–158.
90. McNeil DG: Why so many more Americans die in fires? New York Times, December 22, 1991, p. 3.
91. Mellins RB, Park S: Respiratory complications of smoke inhalation in victims of fires. J Pediatr 1975;87:1–7.
92. Meyer GW, Hart GB, Strauss MB: Hyperbaric oxygen therapy for acute smoke inhalation injuries. Postgrad Med 1991;89:221–223.
93. Moore SJ, Ho IK, Hume AS: Severe hypoxia produced by concomitant intoxication with sublethal doses of carbon monoxide and cyanide. Toxicol Appl Pharmacol 1991;109:412–420.
94. Morgan WK: The respiratory effects of particles, vapours, and fumes. Am Ind Hyg Assoc J 1986;47:670–673.
95. Moritz AR, Henriques FC, McLean R: The effects of inhaled heat on the air passages and lungs: An experimental investigation. Am J Pathol 1945;21:311–331.
96. Moylan JA, Chan C: Inhalation injury: An increasing problem. Ann Surg 1977;188:34–37.
97. Murakami K, Enkhbaatar P, Shimoda K, et al: High-dose heparin fails to improve acute lung injury following smoke inhalation in sheep. Clin Sci (Lond) 2003;104:349–356.
98. Musk AW, Smith TJ, Peters JM, et al: Pulmonary function in firefighters: Acute changes in ventilatory capacity and their correlates. Br J Ind Med 1979;36:29–34.
99. Nakae H, Tanaka H, Inaba H: Failure to clear casts and secretions following inhalation injury can be dangerous: Report of a case. Burns 2001;27:189–191.
100. Navar PD, Saffle JR, Warden GD: Effect of inhalation injury on fluid requirements after thermal injury. Am J Surg 1985;150:716–720.
101. Nelson GL: Regulatory aspects of fire toxicology. Toxicology 1987;47:181–199.
102. Nieman GF, Clark WR, Goyette DA: Positive end expiratory pressure (PEEP) efficacy following wood smoke inhalation [abstract]. Am Rev Respir Dis 1986;133:A347.
103. Nieman GF, Clark WR, Hakim T: Methylprednisolone does not protect the lung from inhalation injury. Burns 1991;17:384–390.
104. Nieman GF, Clark WR, Paskanik AM, et al: Unilateral smoke inhalation increases pulmonary blood flow to the injured lung. J Trauma 1994;36:617–623.
105. Nieman GF, Clark WR, Wax SD, et al: The effects of smoke inhalation on pulmonary surfactant. Ann Surg 1980;191:171–181.
106. Nieman GF, Paskanik AM, Fluck RR, et al: Comparison of exogenous surfactants in the treatment of wood smoke inhalation. Am J Respir Crit Care Med 1995;152:597–602.
107. Nijland R, Jongsma HW, Nijhuis JG, et al: Notes on the apparent discordance of pulse oximetry and multi-wavelength haemoglobin photometry. Acta Anaesthesiol Scand Suppl 1995;107:49–52.
108. Norris JC, Moore SJ, Hume AS: Synergistic lethality induced by the combination of carbon monoxide and cyanide. Toxicology 1986;40: 121–129.
109. O'Toole G, Peek G, Jaffe W, et al: Extracorporeal membrane oxygenation in the treatment of inhalational injuries. Burns 1998;24: 562–565.
110. Ogura H, Saitoh D, Johnson AA, et al: The effects of inhaled nitric oxide on pulmonary ventilation-perfusion matching following smoke inhalation injury. J Trauma 1994;37:893–898.
111. Oliver O: Management of the Cocoanut Grove burns at the Massachusetts General Hospital. Ann Surg 1943;117:801–802.
112. Orzel RA: Toxicologic aspects of firesmoke: Polymer pyrolysis and combustion. Occup Med 1993;8:414–429.
113. Oulton MR, Janigan DT, MacDonald JM, et al: Effects of smoke inhalation on alveolar surfactant subtypes in mice. Am J Pathol 1994;145:941–950.
114. Park MS, Cancio LC, Jordan BS, et al: Assessment of oxidative stress in lungs from sheep after inhalation of wood smoke. Toxicology 2004;195:97–112.
115. Pauluhn J: Pulmonary irritant potency of polyisocyanate aerosols in rats: Comparative assessment of irritant threshold concentrations by bronchoalveolar lavage. J Appl Toxicol 2004;24:231–247.
116. Peitzman AB, Shires GT, Teixidor HS, et al: Smoke inhalation injury: Evaluation of radiographic manifestations and pulmonary dysfunction. J Trauma 1989;29:1232–1239.
117. Pitt BR, Radford EP, Gurtner GH, et al: Interaction of carbon monoxide and cyanide on cerebral circulation and metabolism. Arch Environ Health 1979;34:354–355.
118. Prien T: Toxic smoke compounds and inhalation injury—A review. Burns 1988;14:451–460.
119. Purser DA, Woolley WD: Biological studies of combustion atmospheres. J Fire Sci 1983;1:118–144.
120. Qi S, Sun W: The effects of inhaled nitric oxide on cardiac pathology and energy metabolism in a canine model of smoke inhalation injury. Burns 2004;30:65–71.
121. Reper P, Van Bos R, Van Loey K, et al: High frequency percussive ventilation in burn patients: Hemodynamics and gas exchange. Burns 2003;29:603–608.
122. Riddle K: Hydrogen cyanide: Fire smoke's silent killer. JEMS 2004;29(Suppl):5.
123. Riyami BM, Kinsella J, Pollok AJ, et al: Alveolar macrophage chemotaxis in fire victims with smoke inhalation and burns injury. Eur J Clin Invest 1991;21:485–489.
124. Robinson L, Miller RH: Smoke inhalation injuries. Am J Otolaryngol 1986;7:375–380.
125. Robinson NB, Hudson LD, Riem M, et al: Steroid therapy following isolated smoke inhalation injury. J Trauma 1982;22:876–879.

126. Saincher A, Swirsky N, Tenenbein M: Cyanide overdose: Survival with fatal blood concentration without antidotal therapy. J Emerg Med 1994;12:555–557.
127. Schwerd W, Schulz E: Carboxyhaemoglobin and methaemoglobin findings in burnt bodies. Forensic Sci Int 1978;12:233–235.
128. Shusterman D, Alexeeff G, Hargis C, et al: Predictors of carbon monoxide and hydrogen cyanide exposure in smoke inhalation patients. J Toxicol Clin Toxicol 1996;34:61–71.
129. Silverman SH, Purdue GF, Hunt JL, et al: Cyanide toxicity in burned patients. J Trauma 1988;28:171–176.
130. Soejima K, Schmalstieg FC, Sakurai H, et al: Pathophysiological analysis of combined burn and smoke inhalation injuries in sheep. Am J Physiol Lung Cell Mol Physiol 2001;280:L1233–L1241.
131. Soejima K, Schmalstieg FC, Traber LD, et al: Role of nitric oxide in myocardial dysfunction after combined burn and smoke inhalation injury. Burns 2001;27:809–815.
132. Sokal JA, Kralkowska E: The relationship between exposure duration, carboxyhemoglobin, blood glucose, pyruvate and lactate and the severity of intoxication in 39 cases of acute carbon monoxide poisoning in man. Arch Toxicol 1985;57:196–199.
133. Stone JP, Hazlett RN, Johnson JE, et al: The transport of hydrogen chloride by soot from burning polyvinyl chloride. J Fire Flammabil 1973;4:42–51.
134. Symington IS, Anderson RA, Oliver JS, et al: Cyanide exposures in fires. Lancet 1978;2:90–92.
135. Tasaki O, Goodwin C, Saitoh D, et al: Effects of burns on inhalation injury. J Trauma 1997;43:603–607.
136. Teixidor HS, Rubin E, Novick GS, et al: Smoke inhalation: Radiologic manifestations. Radiology 1983;149:383–387.
137. Terrill JB, Montgomery RR, Reinhardt CF: Toxic gases from fires. Science 1978;200:1343–1347.
138. Thom SR: Antagonism of carbon monoxide-mediated brain lipid peroxidation by hyperbaric oxygen. Toxicol Appl Pharmacol 1990;105:340–344.
139. Thom SR: Carbon monoxide mediated brain lipid peroxidation in the rat. J Appl Physiol 1990;63:997–1003.
140. Thom SR, Keim LW: Carbon monoxide poisoning: A review of epidemiology, pathophysiology, clinical findings, and treatment options including hyperbaric oxygen. J Toxicol Clin Toxicol 1989;27:141–156.
141. Thom SR, Mendiguren I, Van Winkle T, et al: Smoke inhalation with a concurrent systemic stress results in lung alveolar injury. Am J Respir Crit Care Med 1994;149:220–226.
142. Thom SR, Taber RL, Mendiguren II, et al: Delayed neuropsychologic sequelae after carbon monoxide poisoning: Prevention by treatment with hyperbaric oxygen. Ann Emerg Med 1995;25:474–480.
143. Thompson PB, Herdon DN, Traber DL, et al: Effects on mortality of inhalation injury. J Trauma 1986;26:163–165.
144. Thorning DR, Howard ML, Hudson LD, et al: Pulmonary responses to smoke inhalation: Morphologic changes in rabbits exposed to pine wood smoke. Hum Pathol 1982;13:355–364.
145. Tomaszewski CA, Rudy J, Rosenberg N, et al: Prevention of neurologic sequelae from carbon monoxide by hyperbaric oxygen in rats [abstract]. Neurology 1992;42:196.
146. Tomaszewski CA, Thom SR: Use of hyperbaric oxygen in toxicology. Emerg Med Clin North Am 1994;12:437–459.
147. Touger M, Gallagher EJ, Tyrell J: Relationship between venous and arterial carboxyhemoglobin levels in patients with suspected carbon monoxide poisoning. Ann Emerg Med 1995;25:481–483.
148. Traber DL, Linares HA, Herndon DN: The pathophysiology of inhalation injury—A review. Burns 1988;14:357–364.
149. Trapp WG: Massive cyanide poisoning with recovery: A boxing-day story. Can Med Assoc J 1970;102:517.
150. Treitman RD, Burgess WA, Gold A: Air contaminants encountered by firefighters. Am Ind Hyg Assoc J 1980;41:796–802.
151. Tremper KK, Barker SJ: Using pulse oximetry when dyshemoglobin levels are high. J Crit Illness 1988;3:103–107.
152. Wang CZ, Li A, Yang ZC: The pathophysiology of carbon monoxide poisoning and acute respiratory failure in a sheep model with smoke inhalation injury. Chest 1990;97:736–742.
153. Weaver LK, Hopkins RO, Chan KJ, et al: Hyperbaric oxygen for acute carbon monoxide poisoning. N Engl J Med 2002;347:1057–1067.
154. Wetherell HR: The occurrence of cyanide in the blood of fire victims. J Forensic Sci 1966;11:167–173.
155. Willey-Courand DB, Harris RS, Galletti GG, et al: Alterations in regional ventilation, perfusion, and shunt after smoke inhalation measured by PET. J Appl Physiol 2002;93:1115–1122.
156. Witten ML, Quan SF, Sobonya RE, et al: New developments in the pathogenesis of smoke inhalation-induced pulmonary edema. West J Med 1988;148:33–36.
157. Wittram C, Kenny JB: The admission chest radiograph after acute inhalation injury and burns. Br J Radiol 1994;67:751–754.
158. Youn Y, Lalonde C, Demling R: Oxidants and the pathophysiology of burn and smoke inhalation injury. Free Radic Biol Med 1992;12:409–415.
159. Zawacki BE, Jung RC, Joyce J, et al: Smoke, burns, and the natural history of inhalation injury in fire victims: A correlation of experimental and clinical data. Ann Surg 1977;185:100–110.
160. Zikria BA, Ferrer JM, Floch HF: The chemical factors contributing to pulmonary damage in "smoke poisoning." Surgery 1972;71:704–709.