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Acute Pulmonary Death and Forensic Pathology of the Lung

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Sudden or unexpected death after a brief illness can result from a variety of pulmonary causes, both accidental and natural, and the study of such conditions frequently falls within the realm of forensic pathology. To establish the exact cause and mechanism of death is obviously important for epidemiologic and public health considerations; in other cases it is imperative to ascertain possible criminal responsibility. In other instances, careful pathologic evaluation correlated with circumstances provides a satisfactory explanation for an otherwise unexplained death.

In this chapter, we provide an overview of the most common acute pulmonary conditions encountered by forensic pathologists (Display 19-1). Some will be only briefly mentioned because they are discussed in detail in other sections of this book. As in any other investigation, the scenario and circumstances surrounding death (*e.g.*, testimony of witnesses, police report, substances found at the scene, history of medical disease, prior therapy or resuscitative efforts) are fundamental pieces of information. Toxicologic investigation of blood and tissues and culturing for microorganisms, when indicated, are intrinsic parts of a thorough autopsy investigation.

MECHANICAL TRAUMA TO THE CHEST

Trauma is the leading cause of death in the United States in people younger than 40 years of age; overall, it ranks third after cardiovascular diseases and cancer.[1–3] In civilian life, chest injuries are directly responsible for 25% of all trauma deaths, and they contribute significantly to death in another 25% to 50% of cases, thus accounting for approximately 16,000 deaths per year.[1–4]

A significant proportion of deaths caused by chest trauma occur at the site of an accident. However, the input of skilled medical personnel and the rapid transportation of the injured person to medical facilities, including the use of helicopters, have resulted in the recovery of many patients who in the past would probably have been doomed. However, it has been estimated that of all traumatic deaths that occur after arrival at a medical facility, one sixth (17%) could have been prevented by prompt diagnosis, and an additional one sixth could have been salvaged by institution of appropriate treatment.[1–4]

Chest injuries are classified into two main categories: nonpenetrating (*i.e.*, blunt) and penetrating injuries. In blunt injuries, there is no direct communication between organs within the chest and the outside. Such injuries can be inflicted by direct or indirect forces. In the case of direct forces, the severity of the injury depends on the magnitude and duration of the applied force, its velocity, and the size of the area to which the force is applied. With indirect forces, other factors such as acceleration, deceleration, compression, torsion, and shearing determine the severity of the injury. Low-speed accidents are frequently responsible for crushing injuries; at high speeds, tissue injury results from the application of shearing forces to contiguous fixed and nonfixed intrathoracic organs and structures.[1–4]

Blunt chest trauma is responsible in the majority of patients suffering traffic accidents (55%–60%); and falls and other accidents account for a lesser proportion (10%–15%). Death is usually the result of ventilation problems and inadequate gas exchange, hemorrhage due to injury to the heart and great vessels, and to the association of intrathoracic with extrathoracic injury.[1–4]

Penetrating chest injuries are due to stabbings in 75% of these patients (Fig. 19-1). However, the ratio of stabbing to

DISPLAY 19-1. CASES OF ACUTE PULMONARY DEATH

Accidental Causes

Mechanical trauma (see Display 19-2)
Inhalation injury in fires
Aspiration injury
Immersion injury
Drug-related causes

Natural Causes

Status asthmaticus
Circulatory disorders
Infectious pneumonia
Sudden infant death syndrome

DISPLAY 19-2. TYPES OF INJURIES PRODUCED BY MECHANICAL TRAUMA TO THE CHEST

Subcutaneous emphysema
Clavicular fractures
Rib fractures
Flail chest
Sternal fractures
Open pneumothorax
Closed pneumothorax
Tension pneumothorax
Hemothorax
Pulmonary contusions, lacerations, and hematoma
Traumatic arteriovenous fistulas
Trauma due to bullets and other foreign objects
Tracheobronchial injuries
Injuries to the diaphragm, esophagus, heart and great vessels

Data from Jones KW. Thoracic trauma. Surg Clin North Am 1980;60:957, and Capan LM, Miller SM, Turndorf H. Trauma overview. In: Capan LM, Miller SM, Turndorf H, eds. Trauma anesthesia and intensive care. Philadelphia: JB Lippincott, 1991:3.

penetrating firearm wounds is apparently diminishing as the use of firearms is becoming more prevalent, particularly in large cities. The mortality of stab wounds is in the range of 2% to 4%, compared with 12% to 15% for gunshot wounds.[1–4]

Types of Thoracic Injury

Injuries to soft tissues and the thoracic cage are usually not a major cause of morbidity and mortality in themselves but provide important clues to life-threatening injuries of internal organs (Display 19-2).

SUBCUTANEOUS EMPHYSEMA

Subcutaneous emphysema occurs when air is forced into subcutaneous tissue or dissects along muscular planes that offer little resistance. Subcutaneous emphysema is usually of little clinical significance and will reverse itself once the cause is corrected. Three main mechanisms of production are recognized: disruption of pleura and intercostal muscles associated with pneumothorax, extension of mediastinal emphysema, and direct communication of tissues with open wounds.[1–4]

CLAVICULAR FRACTURES

Most clavicular fractures are not associated with major intrathoracic injury. One acute complication of significance is damage to subclavian vessels resulting in hematomas and venous thrombosis. The healing of such fractures can result in compression of neurovascular bundles at the thoracic inlet.[5,6]

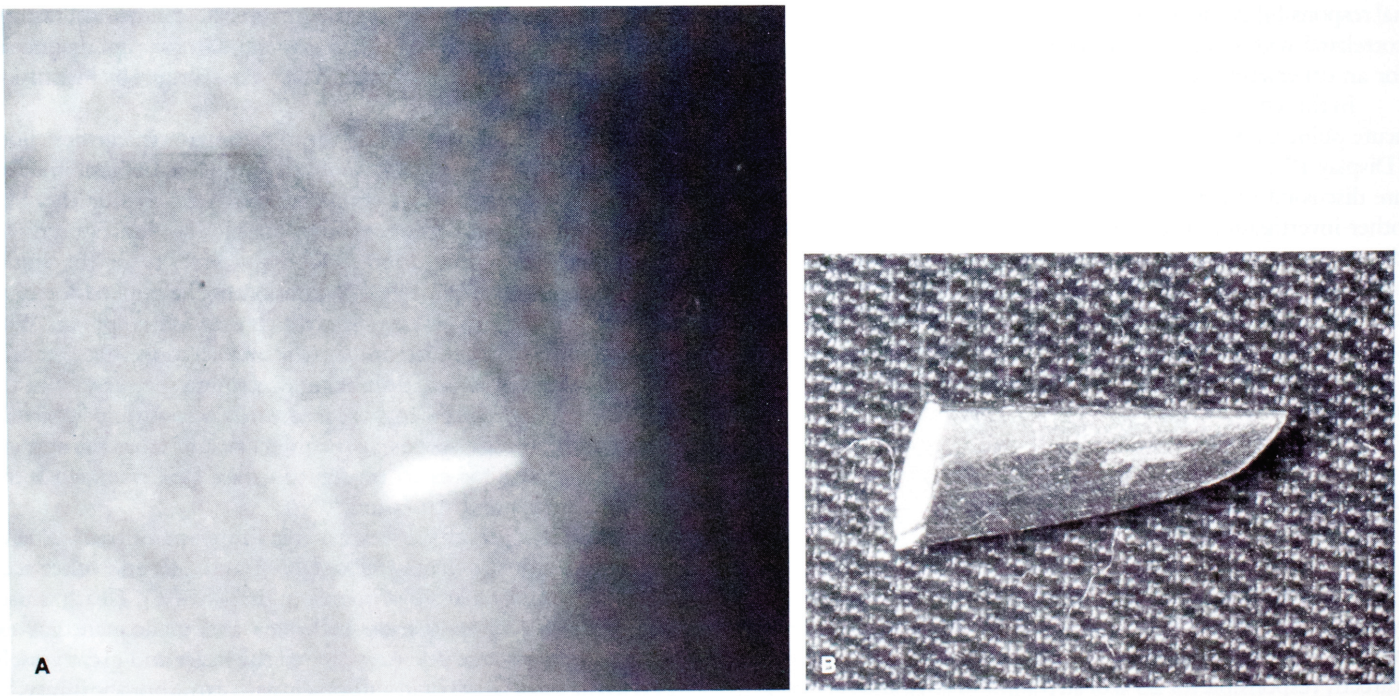

FIGURE 19-1. (**A**) Chest x-ray film from a patient with a history of a stab wound to the chest shows the presence of a foreign body. (**B**) The resected foreign body was the tip of a knife.

RIB FRACTURES

Fracture of a single rib in an otherwise normal or young person is usually trivial, but it might be significant in older people or in those with limited respiratory reserve by further limiting such reserve because of pain and muscle spasm. On the other hand, fractures of 7 or more ribs are associated with intrathoracic injury in 50% of the patients; an additional 15% have injury to an intraabdominal viscus.[1–4]

Fracture of the first rib can be a serious problem because of injury to the upper thoracic aorta, tracheobronchial tree, and neurovascular bundles to an upper extremity. The mortality associated with first-rib fractures ranges from 17% to 36%.[5,6] The pathologist should be able to recognize the common multiple rib fractures induced by forceful resuscitation measures because they occur anterolaterally along a single longitudinal line corresponding to the plane in which the manual pressure was exerted.

FLAIL CHEST

Fracture of several ribs on both sides of the point of a mechanical impact results in a loss of continuity between the fractured ribs and the remainder of the chest wall. The fractured area is unstable and shows a paradoxical movement during respiration—it caves in during inspiration and bulges out during expiration. The shift of a portion of the lungs' tidal volume back and forth between the lung on the injured side and the lung on the uninjured side (*i.e.*, pendelluft) was thought in the past to be the cause of ventilatory insufficiency in flail chest.[1] It is now recognized that the fractured segment actually interferes with the normal bellows function of the thoracic cage. Furthermore, the underlying lung damage (*i.e.*, contusion) and the hypoventilation as a result of chest pain contribute to the respiratory insufficiency.[7]

STERNAL FRACTURES

Fractures of the sternum are rare and frequently associated with severe intrathoracic injury. Injury by the steering wheel of a vehicle is a common cause of such fractures. The mortality ranges from 25% to 45% of patients, not from the fracture itself but from the internal injury to mediastinal contents.[1–4]

OPEN PNEUMOTHORAX

Open or sucking wounds of the chest wall are a serious and dramatic occurrence, usually the result of gunshot wounds at close range, both during combat and in civilian life. Respiratory insufficiency occurs instantly because of equalization of atmospheric and intrapleural pressures through the open defect. This produces marked mediastinal shifting toward the opposite side. Moreover, the decrease in venous return to the heart from the loss of negative intrapleural pressure and the massive loss of blood rapidly determine cardiorespiratory insufficiency and death.[1–4]

TENSION PNEUMOTHORAX

A tear in a bronchus or lung acting like a one-way valve may allow air to enter the pleural space. Progressive accumulation of air within the pleural space can lead to rapid cardiorespiratory collapse and death. Tension pneumothorax can also be seen in association with oblique wounds to the chest wall that allow unidirectional movement of air from the outside into the pleural space.[1–4]

HEMOTHORAX

Collection of blood within the pleural space (*i.e.*, hemothorax) is frequently associated with both blunt and penetrating injuries to the chest wall. Up to 40% of the total blood volume can accumulate within the pleural space and collapse the lung. The lung parenchyma, because of its low perfusion pressure, is seldom a cause of massive hemothorax; the latter is frequently an indication of injury to the heart, the great vessels, or another systemic artery.[1–4]

PULMONARY CONTUSIONS, LACERATIONS, AND HEMATOMAS

Pulmonary contusion occurs within minutes from a rapid, blunt deceleration injury, and it is usually limited to a segment or lobe of a lung. Pulmonary contusions can also result from high-energy shock waves produced by explosions, or from high-velocity missiles passing within a few centimeters of the chest wall. Remarkably, many of the worst contusions occur without associated rib fractures, especially in children; however, other serious injuries associated with blunt trauma may be present.

Computed tomography (CT) is the best way to demonstrate pulmonary contusions. This information plus the pathologic examination of some of these lesions indicate that a pulmonary contusion is in most cases a pulmonary laceration surrounded by intraalveolar hemorrhage. Wagner and Jameson have classified pulmonary contusions as seen in CT scans into four types.[8]

A type 1 laceration appears as an air-filled focus or an air-fluid level in an intraparenchymal cavity. The actual laceration is seen as an air-containing line or tract that does not follow the bronchial distribution. Type 1 lacerations result from sudden compression by a pliable chest wall causing the underlying air-containing lung to rupture, much like a "suddenly compressed air-filled paper bag."[8]

Type 2 lacerations appear on CT scan as air-containing cavities or as masses with an air-fluid interface. Characteristically, type 2 lacerations are seen at the paravertebral region of the lung. They result from a shearing injury of a lower lobe that is abruptly shifted across the midline by sudden compression, on one side, by a pliable lower chest wall.

Type 3 lacerations consist of linear radiolucencies in close proximity to the chest wall where a rib has been fractured. The laceration is produced by a fractured rib that has penetrated the underlying lung parenchyma. Type 3 lacerations are in fact penetrating injuries and are frequently associated with pneumothorax.

Type 4 lacerations are associated with firm pleuropulmonary fibrous adhesions that are torn apart when the chest wall is suddenly compressed or fractured.

In Wagner and Jameson's study, type 1 lacerations were the most common (75 lacerations in 50 patients), followed by type 3 (50 lacerations in 38 patients), type 2 (12 lacerations in 11 patients), and type 4, the least common (5 lacerations in 3 patients).[8] In their series of patients, at least one density could be seen in 89, and multiple lacerations were seen in 26 patients. One patient had 5 separate lacerations.

When a laceration is filled with blood or serum, the lesion is designated a pulmonary hematoma (Color Fig. 19-1; Fig. 19-2). Whereas air-filled lacerations diminish in size at rates of 2 cm per week to 1 cm in 2 weeks, hematomas decrease in size at a much slower rate; in fact, some hematomas may take as long as a year to

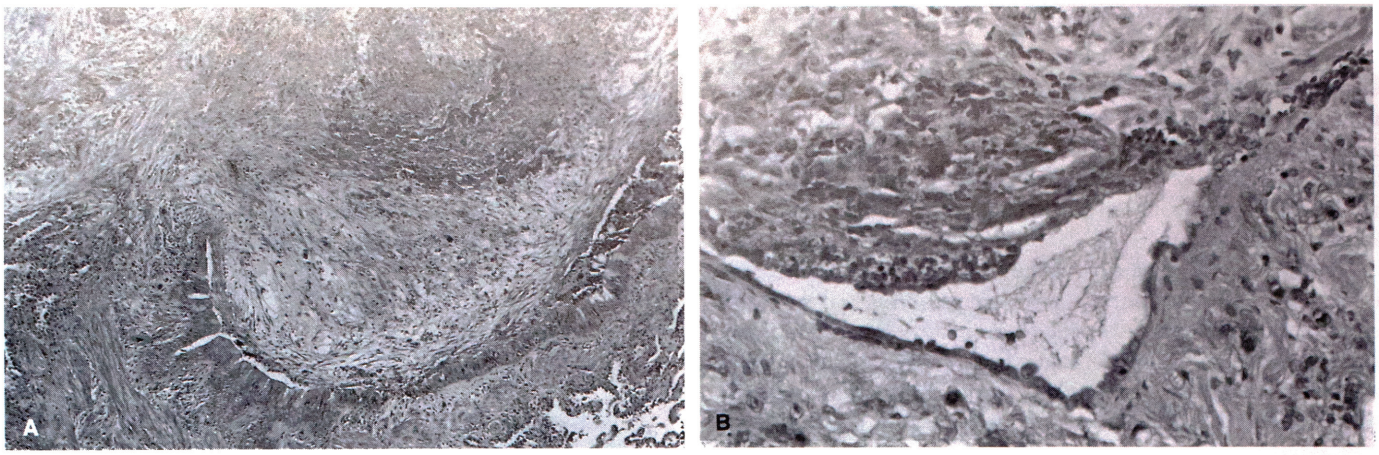

FIGURE 19-2. A 4-cm, 14-day-old pulmonary hematoma was produced by the attempted fine needle aspiration of a peripheral lesion retrospectively interpreted as a pseudotumor of the pleura (see Color Fig. 19-1). (**A**) Extensions of the fibrous capsule within airways simulate bronchiolitis obliterans. (H & E stain; low magnification.) (**B**) A collapsed and partially occluded airway in the hematoma capsule resembles a blood channel; not surprisingly, this finding led to an erroneous diagnosis of vascular malformation. (H & E stain; intermediate magnification.)

resolve. On rare occasions, a hematoma becomes infected and results in an abscess not directly connected to a bronchus.[8,9]

TRAUMATIC ARTERIOVENOUS FISTULAS

These lesions are rare, late manifestations of chest trauma, usually of the internal mammary or, less commonly, intercostal vessels. Sometimes the connection is between a systemic and a pulmonary artery.[10] If not corrected, a traumatic arteriovenous fistula may progress to a high-flow shunt with an audible murmur and congestive heart failure.[11]

INJURIES CAUSED BY BULLETS AND FOREIGN BODIES

Penetrating injuries by handguns in civilian life are virtually always low velocity and rarely result in contamination of the chest tissues by the missile itself. Many believe that the removal of a bullet may produce more injury than the projectile itself. The mere presence of a missile within the chest is, therefore, not an indication for thoracotomy. In the classic review by Harkin during World War II[12] and the long-term follow-up studies of Bland and Beebe,[13] it was shown that erosion of a bullet into vital structures is indeed a rare event.

MIGRATORY FOREIGN BODIES IN THE CHEST

Not uncommonly, a bullet winds up in a bronchus (Fig. 19-3) or in the pleural space, where it moves harmlessly under the influence of gravity until it becomes fixed by a pleural reaction and fibrosis. An anecdotal report by Spencer, however, deals with a veteran who developed scar carcinoma of the lung around a bullet embedded in lung tissue.[14]

Nonetheless, bullets entering the chest may penetrate vascular structures and travel distally. In their review of 30 such patients in civilian life, Shannon and colleagues concluded that small-caliber bullets were likely to behave in this manner (79% of patients).[15] Their proposed explanation was that small-caliber bullets, which have relatively little velocity, can penetrate one but not both sides of a vessel. According to these authors, some 70% of missiles that enter the vascular system do it through the heart or thoracic aorta.

Mattox and associates, in their series of patients with intravascular bullet emboli, found that the most common pattern of embolization was from a peripheral vein to the pulmonary artery (7 patients), peripheral vein to heart (5 patients), heart to peripheral artery (3 patients), thoracic aorta to peripheral artery (4 patients), and abdominal aorta to peripheral artery (6 patients).[16] The series also included embolism from heart to inferior vena cava (2 patients), from inferior vena cava to right atrium (2 patients), and from left atrium to abdominal aorta (1 patient). Most arterial emboli in this study (11 patients) were to the lower extremities (*i.e.*, iliac, femoral, and popliteal arteries). In one patient, the bullet traveled from the heart to a carotid artery.

TRAUMA TO THE TRACHEA AND MAJOR BRONCHI

Traumatic injury to the trachea and major bronchi is rare but is often the result of motor vehicle accidents of any type, including motorcycles. Of 1200 trauma deaths studied by Kirsh and Sloan, 33 individuals had tracheobronchial injuries.[17]

Injury to the trachea and major bronchi follows both blunt and penetrating trauma to the neck or upper chest. About 75% of tracheal injuries are to the cervical region, and penetrating wounds are more common than blunt injuries. The latter usually follow impact of the anterior neck or manubrium against a steering wheel or dashboard. Karate blows and clothesline accidents are also direct cervical injuries, the latter occurring when a motorcycle rider strikes a cable strung across the pathway.[18,19]

Complete transection of the trachea or total separation at the laryngotracheal junction can result from blunt trauma, in which case the trachea retracts into the mediastinum. Remarkably, in some of these patients the skin remains normal, but damage to the carotid artery and esophagus becomes apparent later. Fracture of the sternum at the manubrium-gladiolus junction may result in tears of the underlying trachea and avulsion of the innominate artery.

Penetrating wounds of the trachea are easy to diagnose; when

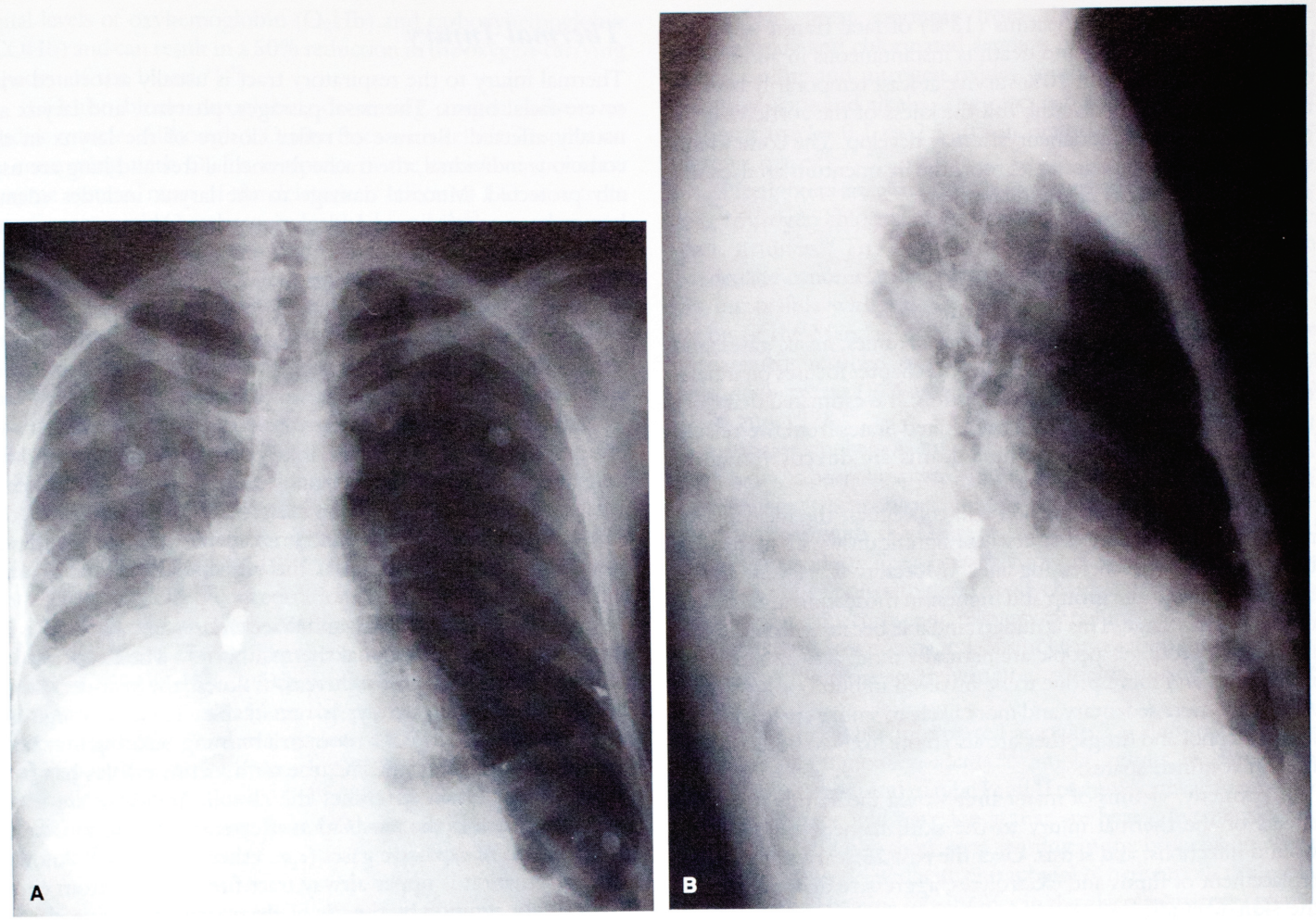

FIGURE 19-3. A bullet lodged in the right lower lobe bronchus produced obstructing pneumonia in a middle-aged man who was shot in the chest several years before. The bullet was extracted by bronchoscopy, and the pneumonic process resolved uneventfully. (**A**) Anteroposterior and (**B**) lateral chest x-ray films show the bullet and the resulting pneumonic process.

an open wound is produced, the exit of bloody air bubbles can be dramatic. There is almost always injury to other structures, such as the esophagus and the carotid artery. If the skin remains intact, subcutaneous emphysema with associated pneumothorax can occur.

Stab or gunshot wounds to the thorax may injure major bronchi, with damage to the great vessels. However, bronchial tears usually result from deceleration in car accidents and tend to occur within 2 cm of the carina. Some bronchial tears are bilateral; others involve only the upper-lobe bronchi and rarely the bronchus intermedius.[18,19]

In bronchial rupture, air escapes with each breathing cycle and dissects through the mediastinum into the cervical fascial compartment. The resulting subcutaneous emphysema can be overwhelming and can result in total obliteration of the neck and facial features. When the pleura is torn, there might be tension pneumothorax. Failure of a lobe to expand after thoracostomy for chest trauma suggests bronchial rupture, foreign-body obstruction, or both.[20]

OTHER TYPES OF INJURY

Rupture of the diaphragm is seen in about 5% of patients with chest trauma.[21] The majority of these patients have sustained blunt trauma in car accidents. Penetrating lesions from stabbings or gunshot wounds can also rupture the diaphragm. Ninety percent of these traumatic tears occur on the left side, apparently because the right hemidiaphragm is protected by the liver. Also commonly involved in these cases are the stomach, colon, small intestine, and spleen; the overall mortality is 10% to 20%.[21]

The most common cause of esophageal perforation is iatrogenic and follows injury from instrumentation.[22] It occurs most frequently at anatomic sites of esophageal narrowing (*i.e.*, the pharyngoesophageal junction, the aortic arch, and the diaphragmatic esophageal hiatus). These are also the preferred sites of perforation by ingestion of foreign bodies. Penetrating injuries of the esophagus have been noted in cases of stab wounds and gunshot injuries. Blunt trauma seldom results in perforation of the lower one third of the esophagus, and it carries an 80% mortality rate.[22]

Trauma to the heart and great vessels may result from nonpenetrating injuries and includes myocardial contusion, myocardial rupture, septal rupture, valvular tears, and thrombosis of coronary arteries.[22] Penetrating injuries to the heart, usually from stabbings and gunshots, can result in cardiac tamponade or massive exsanguination into the pleural space if a large defect of the pericardium has been produced.

One of every eight victims (13%) of fatal transit accidents sustains aortic rupture, and death is instantaneous in about 90% of these patients. About 10% survive at least temporarily because the tear does not involve the full thickness of the aortic wall; in these patients, a pseudoaneurysm may develop. The commonest sites of aortic rupture are at its root, the ligamentum arteriosum, and the aortic hiatus at the diaphragm.[22]

INHALATIONAL INJURY

The subject of inhalation injury by dusts, fumes, mists, gases, and vapors are reviewed in Chapter 17. This chapter focuses on inhalation injuries seen in victims of major fires. It is estimated that close to 10,000 persons die yearly in the United States from fire-related accidents, and a majority of these deaths are directly related to respiratory injuries.[23–27]

In the study by Thompson and colleagues, the incidence of mortality from inhalation injury rose significantly with increasing burn area and with increasing age.[28] Mortality was lowest in the 5- to 14-year-old age group and highest in those individuals older than 59 years of age. This is understandable because, according to the authors, younger people are naturally more active than older individuals and more prone to be involved in outdoor accidents. Adults are more sedentary and more likely to smoke cigarettes and ingest alcohol and drugs; they are also more likely to be victims of fires in confined spaces.

Formerly, victims of major fires would die mainly from the effects of the thermal injury to the skin, namely, burn shock, wound infections, and sepsis. Over the past 25 years, appropriate replacement of fluids and electrolytes, aggressive debridement of the skin wounds, and the use of antibiotics have resulted in a significantly lowered mortality. Specifically, burn shock, which accounted for nearly one fourth of all burn deaths until the 1940s, has been nearly eliminated as a cause of death.[24,25]

As a consequence of the above developments, respiratory complications have emerged as a main cause of death in major thermal burns. Apparently, this was not well recognized before 1942, when 491 people were killed in the Boston Cocoanut Grove nightclub fire. One hundred and fourteen of the victims were transported to the Massachusetts General Hospital, where 78 were dead on arrival or died shortly thereafter. Thirty-five of the 36 patients who survived with initial therapy died not from cutaneous burns but from pulmonary injury.[29]

The presence of inhalation injury affects mortality among burn victims more significantly than age or surface area of the skin wounds. In the series by Herndon and associates, the mortality of all burn patients was about 21%; it rose dramatically to 61% in the presence of inhalation injury.[25] Mortality due to inhalation injury was high (36%) even in the presence of relatively small burns and remained high with burns of any size.

The pathophysiology of inhalation injury in burn patients is complex and depends on the interplay of three major mechanisms: thermal injury to the airways, asphyxia as a result of carbon monoxide (CO) poisoning and other gases, and smoke inhalation. The relative importance of these three mechanisms varies from patient to patient, depending on such factors as whether the fire took place in an open or closed space, the temperature and duration of the conflagration, and the chemical composition of the generated smoke.[24–27]

Thermal Injury

Thermal injury to the respiratory tract is usually associated with severe facial burns. The nasal passages, pharynx, and larynx are usually affected. Because of reflex closure of the larynx in the conscious individual, the tracheobronchial tree and lung are usually protected. Mucosal damage to the larynx includes edema, hemorrhage, necrosis, and ulceration; these changes can occur within minutes of the accident or a few hours later. Death from asphyxiation occurs if a patent airway is not secured immediately by intubation or tracheostomy.[24,26,27]

Inhalation of hot air does occur, particularly in the unconscious individual. Experimentally, however, it has been shown that even super-heated air is rapidly cooled before it reaches the lower respiratory tract by the efficient heat exchange mechanisms of the upper airways.[27,30] Thermal injury of the distal airways and the lung proper almost never occurs, except in the case of steam inhalation, a rare occurrence in itself. Steam has 4000 times the heat-carrying capacity of air, and it is capable of producing direct mucosal injuries as far distal as the bronchioles in experimental animals.[31]

According to Heimbach and Waeckerle, essentially there is no such thing as an inhalational thermal burn.[27] The heat-carrying capacity of air is very poor, whereas, as noted, the heat-decreasing ability of the upper airways is remarkable. Thus, although the temperature at the top of a room in a burning building may be in the range of 482°C to 521°C, the air a victim inhales has been largely cooled when it reaches the alveoli. Yet there are a few exceptions, such as the production of extensive and serious burns by inhalation of explosive gases (*e.g.*, ether, propane).[27] Another unusual situation is upper airway tract fire resulting from endotracheal tube ignition by the use of electrocautery during elective tracheostomy, a hazard surgeons, anesthetists, and forensic pathologists should be aware of.[32]

Watanabe and Makino have demonstrated in dogs that inhalation of heated air at the relatively modest temperature of 130°C induces pulmonary edema if elevated levels of CO are present at the same time.[33] CO poisoning greatly deepened the breathing of their experimental animals and thus led to the inhalation of greater amounts of heated air; the authors concluded that the latter, by itself, was responsible for the pulmonary edema. This could be one possible explanation for the pulmonary edema seen in patients with CO poisoning from fires (see Asphyxia in Fires).

Asphyxia in Fires

In fire victims, a situation of hypoxemia is created by consumption of O_2 in the atmosphere by the fire itself. The O_2 concentration in air can be reduced from the normal 21% to as low as 10%. The partial concentration of O_2 in the inspired air can be further reduced by increments of other gases, such as carbon dioxide (CO_2) and nitrogen. Yet the most important cause of immediate death is CO poisoning; it is estimated that it accounts for about one half of all burn deaths.[34,35]

CO is an odorless, colorless, nonirritating gas that is produced in large amounts by incomplete combustion of organic matter. It is generated in significant amounts when a fire takes place in a close environment with production of large amounts of soot. CO has an affinity for hemoglobin (Hb) that is 210 times that of O_2; a 0.1% concentration of CO in inspired air can produce

equal levels of oxyhemoglobin (O_2Hb) and carboxyhemoglobin (COHb) and can result in a 50% reduction in the oxygen-carrying capacity of the blood.[34,35]

CO also blocks myoglobin, decreasing oxygen delivery to cardiac muscle. Although CO interferes with cellular respiration by competing with O_2 for receptors in the cytochrome oxidase enzyme system, most of the deleterious effects of CO arise from interference with O_2 transport by the blood.[34,35]

Levels of COHb in blood are used to determine the severity of CO poisoning. Normally, nonsmokers have COHb blood levels of about 1%, smokers have levels of 5%, and city dwellers have levels of about 10%. Transient levels of up to 15% to 20% can be detected in people who jog on busy thoroughfares. Levels of 15% to 20% can produce nausea and splitting headaches. At levels of about 40%, people lapse into unconsciousness; levels of 60% or more are fatal.[34,35]

Pathologic changes attributable to CO poisoning include bright cherry red discoloration of the blood, musculature, and livor mortis areas. Characteristically, the fingernails are red or pink, even in black individuals.[36] The above findings, however, are not seen with COHb concentrations below 40%.

Alcohol, barbiturates, sedatives, and many other drugs potentiate the effects of CO. It has been noted that a COHb concentration of 35% to 40%, which produces little harm to a healthy individual, may prove fatal in the presence of a blood alcohol concentration of 0.2%. Levels as low as 15% to 20% may also be fatal in people suffering from chronic anemia, emphysema, and atherosclerotic heart disease.[36] Fluidity of the blood is another peculiarity in people dying from CO poisoning, in common with very sudden death states.[36]

Cyanide Poisoning

Cyanide poisoning results from ingestion or inhalation of compounds that release cyanide ions: hydrogen cyanide and potassium cyanide. In fires, cyanide is produced by the burning of polymers containing nitrogen, such as in upholstered furniture and polyurethane foams. In the tissues, cyanide blocks the use of O_2 by cells by inhibiting the action of cytochrome oxidase, carbonic anhydrase, and other enzymatic systems.[26,27]

Spectrophotometric methods are available for the quantification of cyanide in blood and plasma.[37] Blood cyanide levels of 0.10 to 0.15 μg/mL can be found in healthy individuals from cigarette smoking, consumption of certain foods, and industrial pollution. Blood cyanide levels of 2 μg/mL or higher suggest cyanide poisoning; levels of 5 μg/mL or above are lethal.

In about one half of patients with cyanide poisoning, the body is bright cherry red because O_2 remains in red cells as O_2Hb.[38]

Smoke Inhalation

Smoke is composed of hot air, gases, and suspended carbonaceous particles in various amounts. Carbonaceous particles are not damaging in themselves but are coated with highly irritating aldehydes, ketones, and organic acids. Synthetic materials widely used in modern construction and indoor furnishings represent important sources of toxic gases. The water-lipid solubility ratio of these gases is a major determinant of their toxicity. Aldehydes are among the most toxic liquid-soluble substances. Hydrogen chloride is released in great amounts from the combustion of polyvinylchloride and chlorinated acrylics, producing severe mucosal burns. Sulfur and nitrogen oxides combine with water to yield corrosive acids and alkalis. The gases can adhere to the surface of carbon particles 0.1 to 2.5 μm in diameter and thus reach the alveolar space.[26,27,39]

Firefighters are also exposed to dangerous levels of CO, acrolein, hydrogen chloride, and nitrogen dioxide, acting in a synergistic manner.[40] The combined effects of these gases with high particulate concentrations often make effective work by firefighters impossible without respiratory protection. The implementation of the Mandatory Mask Rule by the City of Boston Fire Department resulted in a 52% reduction in smoke inhalation episodes between 1976 and 1977, and an 80% reduction between 1976 and 1978.[40]

Inhaled smoke poisons cilia throughout the tracheobronchial tree, induces bronchospasm, and in its severest form can produce hemorrhagic tracheobronchitis. The latter can progress to complete necrosis with shedding of the mucosa in membranes and casts that produce airway obstruction. If the patient escapes asphyxia and CO poisoning, the above changes may result in airway obstruction, atelectasis, and respiratory failure.[41,42] This has been designated by Stone as stage 1 of smoke inhalation injury and can be seen in the most severely injured patients during the first 36 hours.[43]

What Stone has interpreted as stage 2 is dominated by the presence of pulmonary edema.[43] Smoke results in damage to surfactant material and to type I and II pneumocytes. Patients who die at this stage will have lungs that are heavy, hyperemic, and edematous, and will show soot staining of the bronchial mucosa. The edema is associated with entrapment of neutrophils in alveolar capillaries and hyaline membranes in the alveolar spaces, a picture of diffuse alveolar damage (DAD; see Chap. 14). This permeability type of pulmonary edema is seen in 5% to 30% of patients 6 to 72 hours after the initial injury, and the condition is associated with a 60% to 70% mortality rate.[43]

Stone's stage 3 is dominated by the presence of infection and appears in 15% to 60% of patients; the mortality is 50% to 86%.[43] Infection is usually coincidental with expectoration of large mucus casts formed within the tracheobronchial tree, 3 to 10 days after the injury. Initially, the infective bacteria are frequently penicillin-resistant staphylococci superseded by gram-negative species, especially *Pseudomonas* species.[25] In a study by Shirani and colleagues, inhalation injury alone increased mortality by 20%, and pneumonia increased mortality by 40%, with a maximum increase of approximately 60% when both factors were present.[44] In children suffering from smoke inhalation, *Branhamella catarrhalis*, a common inhabitant of the upper respiratory tract, has been identified as a cause of lower airway infection and sepsis.[45]

Another analysis of the respiratory tract pathology in smoke inhalation has been conducted by Toor and colleagues on 6 child and 27 adult burn victims.[46] DAD was observed in 16 patients, acute bronchopneumonia in 7 patients, and necrotizing pneumonia in 7 patients. DAD and pneumonia coexisted in 11 patients; children most consistently developed pneumonia. In addition to the inhalation injury *per se*, their explanation for the pathogenesis of DAD included septicemia (12 patients), hypotension (9 patients), necrotizing pneumonia (6 patients), and oxygen toxicity (4 patients). The onset of DAD in 8 patients was late in the disease, suggesting causative factors other than the inhalation injury. Survival rates

did not differ in patients with or without DAD, and there was no correlation between DAD and the extent of burns.

Homma and associates have described the pulmonary pathology in two soldiers fatally injured by accidental inhalation of zinc chloride (hexite) from a smoke bomb.[47] Acute injury was minor, but 10 days later the patients developed severe manifestations of DAD with pulmonary hypertension. Autopsy examination revealed extensive interstitial and intraalveolar fibrosis. Thrombosis and fibrous obliteration of small vessels were other major findings, particularly on the venous side of the pulmonary circulation.

Sequelae of smoke inhalation are few and include bronchiectasis and subglottic stenosis, the latter in patients who have had nasotracheal intubation.[24,26] Bronchiolitis obliterans has been described in patients who were exposed to oxides of nitrogen,[48] or following inhalation burns.[49] In 11 of 14 survivors of a major fire, there was evidence of small airway disease, by physiologic tests, at 6 months after the accident, and in all 7 patients evaluated at 2 years.[50] There is also substantial evidence that prolonged airway hyperresponsiveness and asthma may follow smoke inhalation.[51] In particular, polyvinylchloride pyrolysis products pose a high risk, but other toxic inhalants are probably implicated.[51]

ASPIRATION INJURY

As noted by LoCicero, aspiration may be classified into two main categories: silent and active.[52] Silent aspiration occurs during anesthesia or while a patient is intubated in an intensive care unit. Approximately 16% to 27% of anesthetized patients will have silent aspiration to some extent. The latter is favored by such mechanisms as insufflation of the stomach with air during anesthesia induction, lower esophageal sphincter relaxation secondary to reflux or medications, or a combination of both mechanisms. Even manipulation of bowel loops during abdominal surgery may produce reflux of intestinal contents into the oropharynx, whence silent aspiration occurs.

Active pulmonary aspiration, on the other hand, produces three main clinicopathologic syndromes: pneumonia due to aspiration of oropharyngeal bacterial pathogens, aspiration of inert fluids or particulate material, and aspiration of acidic gastric contents. Each of these three syndromes displays, to a considerable degree, a characteristic pattern of pulmonary injury depending on the circumstances of the aspiration and the nature and the amount of the aspirate.[53]

Pneumonia Resulting From Aspiration of Oropharyngeal Bacterial Pathogens

Aspiration of contaminated oropharyngeal secretions in people with poor dental hygiene or periodontal disease is the major source of infection; not surprisingly, edentulous patients do not develop this type of pneumonia. The latter is typically an indolent pleuropulmonary infection.[54] The early stage is that of a localized infectious process, but many of these patients postpone evaluation for 1 or 2 weeks, at which time the picture has progressed to necrotizing pneumonia, the hallmark of the syndrome. In addition to putrid sputum, there is lung cavitation, abscess formation, and empyema.

The lesions characteristically affect the right lung more frequently than the left, and the apical-posterior segments of the upper lobes and apical segments of the lower lobes. This is clearly a gravitational effect, but the affected region can vary depending on the patient's position at the time of the aspiration. The majority of the pathogens are community-acquired (*i.e.*, anaerobic bacteria). In hospitalized patients, anaerobic bacteria are usually accompanied by enteric gram-negative bacteria and *Staphylococcus aureus* (see Chap. 39).

Aspiration of Inert Fluids or Particulate Material

Aspiration of inert and nontoxic solid particles, or fluids such as water, saline, and barium solution, can result in reflex bronchoconstriction and mechanical obstruction. Cyanosis, atelectasis, and respiratory failure can result from abundant particulate material in the airways. Although aspiration of an inert fluid (*e.g.*, water) produces no distinctive radiologic findings, it is frequently followed by infectious pneumonia that progresses to consolidation, cavitation, and empyema, particularly if particulate material remains lodged in the peripheral airways (Fig. 19-4).

In a case reported by Elliott and colleagues, a 16-year-old woman developed respiratory insufficiency following aspiration of activated charcoal.[55] The latter substance was administered for a drug overdose that led to her demise 14 days later. Although no charcoal was noted in bronchi during bronchoscopy, there was extensive evidence of this material in bronchioles in association with obliterative bronchiolitis and a prominent giant cell reaction.

Aspiration of activated charcoal was also the cause of death in a 56-year-old man reported by Menzies and colleagues.[56] Microscopic examination of the lungs 15 days after the suicidal episode showed inflammatory changes with charcoal and crystalline material lying free within alveoli, in the cytoplasm of alveolar macrophages, and in the sinusoidal space of regional lymph nodes. The authors observed that activated charcoal (Medicoal, England) contains povidone as a nonabsorbable suspending agent, a substance implicated in the production of pneumonitis after inhalation of hair spray.[57]

Aspiration of Acidic Gastric Contents

Also known as Mendelson syndrome,[58,59] this is the most serious aspiration syndrome, with a mortality ranging from 30% to 70%. Aspiration of gastric acid induces a chemical injury of the alveolocapillary membrane and the lining of the bronchi. As a result, there is a rapid exudation of fluid and protein into the alveolar space. In fatal cases, the lungs are very heavy, edematous, and hemorrhagic, and the picture is that of DAD (see Chap. 14).

Hypoxia develops rapidly in patients with Mendelson syndrome. There is markedly reduced pulmonary compliance and a rapid rise in pulmonary artery pressure. Typically, the full syndrome is expressed within 2 hours of aspiration, a fact that distinguishes it from other forms of pneumonia.

In his 1952 study, Teabeaut showed that in rabbits a *p*H of aspirated gastric contents greater than 2.5 was not important in the production of aspiration pneumonia, and that the severity of the pulmonary damage increased proportionally as the *p*H of the aspirate decreased.[60] Roberts and Shirley, in 1974, proposed that a threshold volume of at least 0.4 mL/kg (*e.g.*, 20–25 mL) of gastric

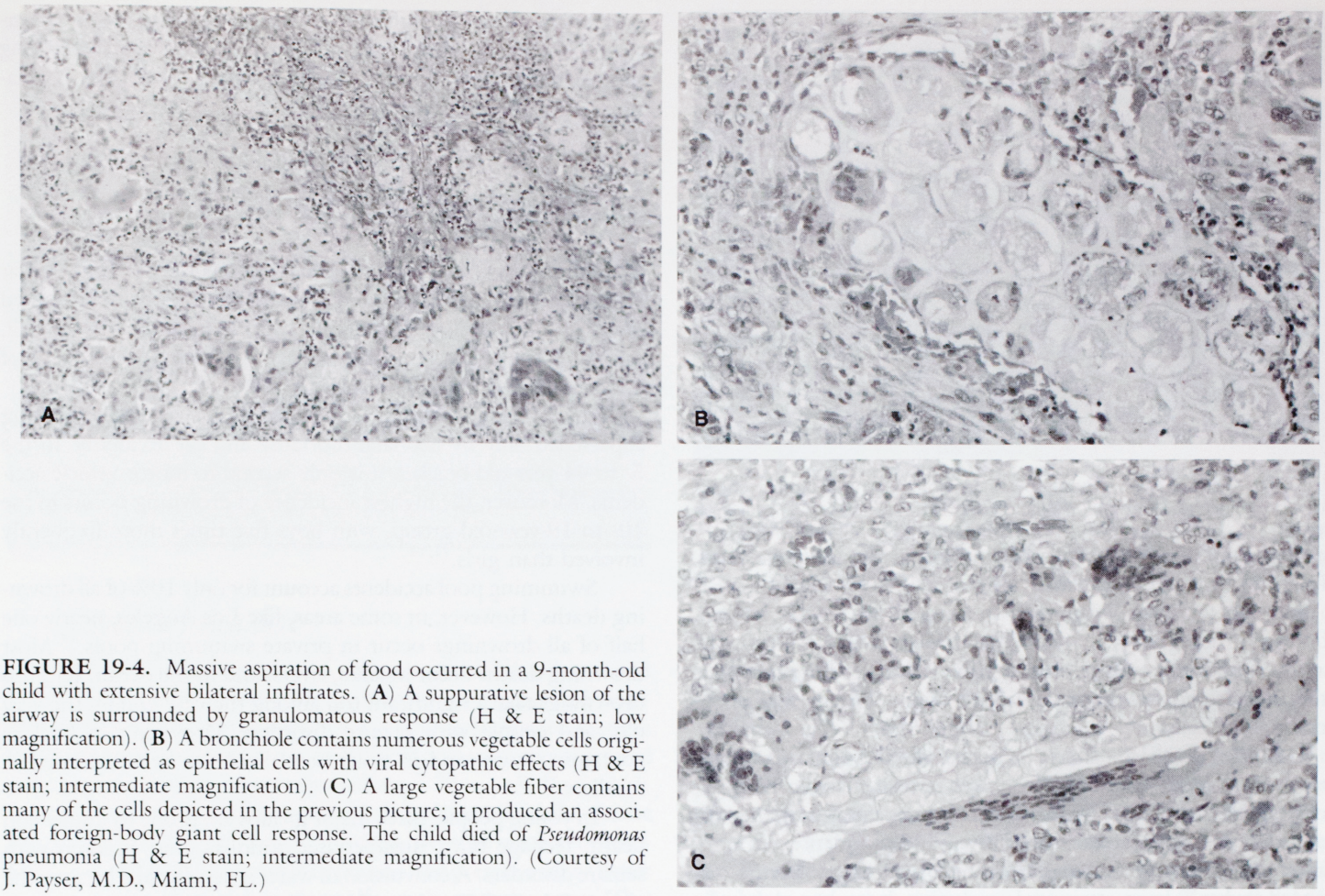

FIGURE 19-4. Massive aspiration of food occurred in a 9-month-old child with extensive bilateral infiltrates. (**A**) A suppurative lesion of the airway is surrounded by granulomatous response (H & E stain; low magnification). (**B**) A bronchiole contains numerous vegetable cells originally interpreted as epithelial cells with viral cytopathic effects (H & E stain; intermediate magnification). (**C**) A large vegetable fiber contains many of the cells depicted in the previous picture; it produced an associated foreign-body giant cell response. The child died of *Pseudomonas* pneumonia (H & E stain; intermediate magnification). (Courtesy of J. Payser, M.D., Miami, FL.)

juice is required to produce aspiration pneumonia in adults.[61] Although this suggestion was based on unpublished data from experiments performed on rhesus monkeys, the critical values for aspirate *p*H (<2.5) and volume (>25 mL) are widely recognized factors that place the patient at increased risk for Mendelson syndrome.[61]

Aspiration of Foreign Bodies

Most foreign-body aspiration accidents occur in children younger than 3 years of age, and the event usually passes unnoticed. If the aspirated foreign body lodges in the glottis, death may be rapid. More often, the aspirated foreign body enters the esophagus, but if it does enter the trachea it usually passes into a bronchus, causing unilateral obstruction.[62]

In Brooks' study, foreign bodies occurred in 51 patients in a 10-year interval.[63] Obstruction of the air passages was most frequently found in the pediatric age group, and the left main bronchus was most often involved. The greatest single offender was the peanut (19 patients), followed by plastic bullets (6 patients), screws (2 patients), a safety pin (1 patient), a sewing needle (1 patient), and various other objects. There were only two adults in the study; one had aspirated a peanut and the other a safety pin.

Adults with foreign-body aspiration and resulting pneumonic changes may be unaware of the original episode of aspiration. Two such cases were reported by Ben-Dov and Aelony, one following aspiration of a coffee bean and the other following aspiration of a pumpkin seed.[64] These authors discuss the complications of foreign-body aspiration, which include lung abscesses, cysts and cavities, asthmalike symptoms, bronchiectasis, bronchial stenosis, granulomatous process, bronchiolitis obliterans, empyema, pneumothorax, and bronchocutaneous fistula.

In Kollef and Winn's experience, most aspirated materials are foods and other organic materials (*e.g.*, fruits, seeds, nuts, meat particles, hot dog fragments, vegetable peels, chicken bones, candy, gum).[65] Figure 19-5 shows a lobectomy specimen from a young patient with large bronchiectasis and pneumonic consolidation due to aspiration of a vegetal spike. The first recorded case of this condition seems to be that in a book entitled *Some Account of Lord Boringdon's Accident on July 21st, 1817, and its Consequences*:

> In 1662, Armand de Boutree, son of the Compte de Nogent, was seized with a violent fever, accompanied by a great difficulty in breathing, a dry cough, afterwards spotting of blood, sleeplessness, and great pain in the right side. A tumor at length appeared on that side, and surgeon extracted from it an ear of barley almost entire which was quite green and had undergone no change.[65a]

Nonorganic aspirated materials include pins, needles, dental fillings, dental drill fragments, stones, small toys, marbles, broken thermometers, rubber earplugs, suture material, and nails. In

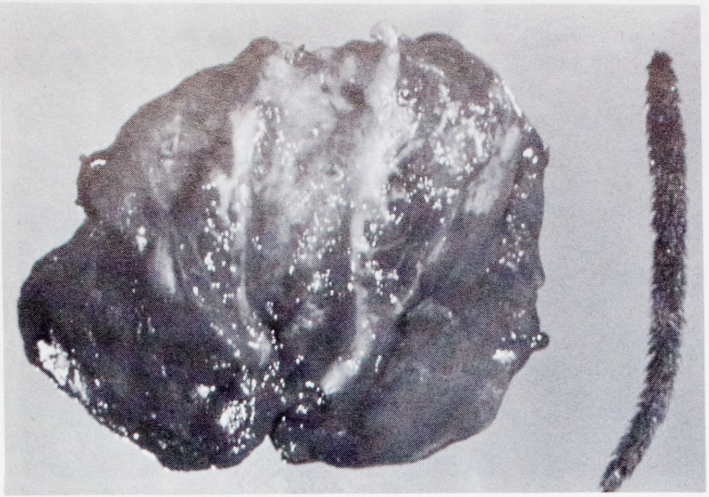

FIGURE 19-5. A lobectomy specimen from a young patient shows large bronchiectasis and pneumonic consolidation as a result of aspiration of a vegetal spike (*i.e.*, timothy grass influorescence). (Courtesy of Teaching Pathology Collection, University of Miami School of Medicine, Miami, FL.)

another patient, a coiled drinking straw obstructed the bronchus intermedius and was associated with a picture of recurrent pneumonia.[65]

Sudden death of a child due to accidental aspiration of black pepper is a bizarre event. In the report by Sheahan and colleagues, a 4-year-old boy with a history of pica (*i.e.*, the eating of such items as rocks, dirt, feline fecal material) suffered sudden respiratory arrest, collapse, and death after eating black pepper from a discarded shaker.[66] In an attempted intubation, it was noted that the airway was heavily coated with pepper, and the child died 4 days after the aspiration incident. Microscopic examination of the lungs at postmortem revealed vegetal material consistent with pepper in the airways; there was also alveolar edema with hyaline membranes and moderate acute inflammation. The authors noted that the active ingredient of black pepper is piperine, the amide of piperidine, which belongs to the alkaloid group of organic substances. Death of this patient probably resulted from a combination of the mechanical obstruction of the airways by pepper and the highly irritant effects of piperine.[66]

Another bizarre incident is a report of the aspiration of large amounts of polyurethane foam by a 33-year-old mentally retarded female who developed acute respiratory failure.[67] The foam was identified by flexible bronchoscopy and successfully removed.

BRONCHOLITHS

Broncholiths are masses of calcareous material that have been coughed up or that can be observed eroding into a bronchus. Conceivably, broncholiths can be mistaken for an aspirated foreign body by both patient and doctor. Broncholiths represent, in fact, necrotic and calcified lymph nodes eroding through the bronchial wall and penetrating the bronchial lumen. The most common etiologic factor is granulomatous lymphadenitis (tuberculosis and histoplasmosis). The lesion is rare, but Arrigoni and colleagues, in their classic paper of 1971 at the Mayo Clinic, were able to collect 253 cases in a 30-year period.[68]

Broncholiths are important because they can be associated with severe clinical manifestations, some requiring extensive surgery. Complications of broncholithiasis include suppurative lung disease, hemoptysis, bronchoesophageal fistula, and their association with bronchogenic carcinoma.[68]

IMMERSION INJURY

Drowning accounts for an estimated 140,000 deaths per year around the world; of these deaths, nearly 5500 occur in the United States, and an additional 1000 to 1300 in Canada.[69,70] Overall, drowning is exceeded only by car accidents and falls as a cause of accidental death in the United States.[71]

In children, drowning ranks third as a cause of death, being superseded only by neonatal mortality and car accidents. In the 5- to 44-year-old bracket, it is only second to motor vehicle accidents. Moreover, the highest incidence of drowning occurs in the 10- to 19-year-old group, with boys five times more frequently involved than girls.[71,72]

Swimming pool accidents account for only 10% of all drowning deaths. However, in some areas, like Los Angeles, nearly one half of all drownings occur in private swimming pools.[73] Most drowning deaths occur in lakes, rivers, and in the ocean. Bathtub drownings take a significant toll among the very young, the very old, and people with seizure disorders. Drowning in buckets containing water and in toilet bowls has also been recorded in toddlers.[74,75]

In young people, three major groups are prone to immersion death: teenage boys, unsupervised toddlers, and children with seizure disorders. A convulsion in water is usually fatal because the victim sinks and disappears from view, and also because the convulsion itself blocks airway reflexes and impedes the struggle needed to survive.[76]

Drowning and Near-Drowning

SEQUENCE OF EVENTS

Initially, the victim panics and struggles violently while holding his or her breath; then some automatic swimming movements are made. The movements stop, and a small amount of air is exhaled while large amounts of water are swallowed; spasmodic movements resembling convulsions occur, with gasping respirations and further aspiration of water and regurgitated gastric contents. Finally, the airway reflexes disappear, water passively fills the trachea and lungs, and the victim succumbs. According to Brooks, on a time scale, laryngospasm occurs at 1 minute, swallowing-vomiting-aspiration at 3 minutes, circulatory collapse at 4 minutes, microscopic central nervous system damage at 6 minutes, and the beginning of brain cell death at 9 minutes.[77]

Patients are classified into groups depending on whether or not they survive the first 24 hours (*i.e.*, drowned *versus* near-drowned) and whether or not they aspirate (*i.e.*, wet *versus* dry). The nature of the medium (*i.e.*, salt water *versus* fresh water) is also taken into account. Delayed death subsequent to near-drowning applies to those who survive for more than 24 hours and develop respiratory complications after successful resuscitation. The most commonly used terminology for immersion injury is that proposed by Modell (Display 19-3).[78,79]

DISPLAY 19-3. TYPES OF IMMERSION INJURY

Drowning With Aspiration

Death within 24 hours with aspirated fluid material in the lungs

Near-Drowning With Aspiration

Immersion episode in which patient aspirates fluid material but survives for at least 24 hours

Near-Drowning Without Aspiration

Immersion episode without associated aspiration in which patient survives the first 24 hours

Delayed Death Subsequent to Near-Drowning

Death due to respiratory and other complications more than 24 hours after immersion episode

Data from Modell JH. Pathophysiology and treatment of drowning and near drowning. Springfield, IL: Charles C Thomas, 1971;1, and Modell JH. Drown versus near-drown: a discussion of definition. Can Care Med 1981;9:351.

PATHOPHYSIOLOGY

Earlier studies emphasized changes in blood volume and serum electrolytes in the pathogenesis of drowning and near-drowning. More recent studies, however, have established that the most important mechanism in both fresh and sea water is arterial hypoxemia, which is almost immediate.[77–80]

Both the type and the amount of aspirated fluid determine the pathophysiology of these conditions. Because sea water osmolality is three to four times that of plasma, the presence of sea water in the alveolar space draws plasma from the vascular space. This results in hypovolemia and hemoconcentration with increased serum electrolyte concentrations. On the other hand, aspirated fresh water is absorbed and produces hemodilution with decreased concentrations of Hb and electrolytes, as well as hypervolemia.[78–80]

The influx of large quantities of fresh water, a hypotonic fluid, into the intravascular space also produces lysis of red cells. These changes have been documented in experimental animals and probably occur in some drowning victims. They are, however, rare in patients who survive long enough to reach the hospital, probably because the volume of aspirated water is relatively small. Indeed, it is well known that about 10% of near-drowning victims aspirate no water at all, and in those who do, the amount of aspirate is less than 22 mL/kg.[80,81]

It is clear that the major pathophysiologic event in drowning and near-drowning is hypoxemia. Indeed, hypoxic damage to the central nervous system accounts for almost all late morbidity and mortality in near-drowning victims. Hypervolemia in the case of hypotonic fresh water immersion injury is capable of producing cerebral edema. Resuscitation often involves infusion of large quantities of salt-containing fluids, which further increases blood volume. Cerebral edema may also be exacerbated by postasphyxial increased capillary permeability, allowing fluid to leak into the tissues, including the brain.[82]

In certain circumstances, two factors may ameliorate the degree of cerebral damage: the diving reflex and immersion hypothermia. The former is a neurogenic response that diverts blood from nonessential organs to the heart and brain. This reflex is independent of chemoreceptors and baroreceptors, and it is stimulated by facial immersion and reflex or involuntary breath-holding. The diving reflex is more potent in children, and it is activated by fear and by cold water.[83]

The second protective mechanism is immersion hypothermia resulting in a core temperature of less than 35°C.[84] In the majority of immersion accidents, water temperature is significantly lower than body temperature, and the loss of body heat is very fast because the thermal conductivity of water is 32 times greater than that of air. Alcohol, a common cause of hypothermia, further accelerates heat loss through cutaneous vasodilation. It is thus possible that both the diving reflex and immersion hypothermia explain remarkable, documented examples of survival for up to 40 minutes after immersion in cold waters.[83,84]

PATHOLOGY

As noted by Copeland, the pathologic diagnosis of drowning is one of exclusion.[85] Enlarged, edematous lungs, hemorrhage in the middle ears, and the presence of diatoms in the tissues are useful criteria, but none are exclusively seen in drowning (Fig. 19-6). Furthermore, because the presence of dry lungs is a well-known occurrence in some drowning victims, the question of whether such a case indeed represents a drowning victim or a body immersed in water after death needs to be established.

Copeland compared the lung weights of 220 patients who drowned with a sample of the average (*i.e.*, "natural") population as well as average (*i.e.*, "normal") controls.[85] He found that 80% to 90% of fresh- or salt-water drowning cases had heavier (*i.e.*, wet) lungs than did the natural and normal population. No differences were noted in weights between fresh-water and salt-water cases.

According to Auer and Möttönen, the presence of diatoms in the lungs and other organs is highly indicative of actual drowning.[86] Furthermore, qualitative analysis of the diatoms in the body as well as in the surroundings may help in ascertaining the location of the drowning accident.

The mechanisms of pulmonary injury in fresh and salt water are different. Surfactant is washed out or inactivated by fresh water, resulting in atelectasis;[87,88] production of new surfactant material requires at least 24 to 48 hours. On the other hand, salt water does not affect surfactant but alters the permeability of the alveolocapillary membrane and results in alveolar edema.[89] In either case, hypoxemia is the result of ventilation-perfusion mismatch with continued perfusion of nonventilated alveoli.

In experimental animals, mitochondrial swelling has been noted in the pulmonary vascular endothelium. It has been interpreted as resulting from excessive catecholamine secretion rather from the effects of aspirated water.[90] In fact, pathologic findings consistent with catecholamine release have been demonstrated in the hearts of human and animal drowning victims and include smooth muscle contraction banding in the media of coronary arteries, focal myocardial necrosis, and ventricular myocyte contraction banding.[91] The smooth muscle contraction banding of the coronary arteries suggests spasm; thus, many drowning victims may die from complications of decreased or abolished myocardial perfusion rather than aspiration of water.

Delayed pulmonary manifestations in near-drowning victims include superimposed bacterial pneumonia, pulmonary barotrauma, mechanical lung damage from resuscitation, foreign-body or chemical pneumonitis, O_2 toxicity, and neurogenic pulmonary edema.[70,71,90]

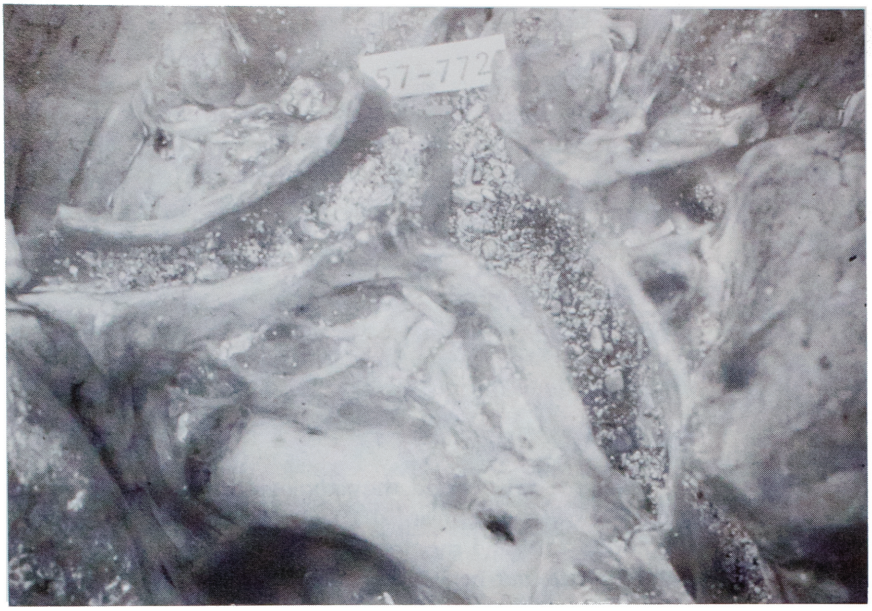

FIGURE 19-6. The lungs of a drowned victim show extensive deposits of sand in the tracheobronchial mucosa.

Decompression Sickness Among Scuba Divers

Diving underwater with a breathing apparatus (*i.e.*, scuba diving) is an increasingly popular sport practiced by millions of people throughout the world.[92–94] Decompression sickness and arterial gas embolism are two serious clinical risks attending this activity. Whereas decompression sickness is a disease that involves gas bubbles forming in tissues and venous blood, arterial gas embolism results from the introduction of gas bubbles into the arterial circulation. Although both pathogenesis and pathology are different in these conditions, the basic treatment is the same—recompression in a hyperbaric chamber, as soon as possible.[95]

After a dive, the affected individual experiences pain in the extremities (*i.e.*, the bends), neurologic deficits, or both. The most serious symptoms are paresthesia of the legs and ataxic gait, which may precede paraplegia. The bends may occur in different locations, but the shoulder and elbows are preferentially involved. Caisson disease of bone (*i.e.*, dysbaric osteonecrosis) is characterized by regions of bone and marrow necrosis that can lead to secondary deforming osteoarthrosis of the hip, shoulder, or other joints.[96,97] Caisson disease can be seen in divers as well as in workers in a compressed air environment, such as during the construction of tunnels under rivers.[96] In Caisson disease, there is evidence of an increase in marrow fat cell size resulting from hyperoxia. This phenomenon may play a role in the production and localization of gas bubble emboli, which are thought to be the cause of the bone and marrow necrosis.[96,97]

In divers, neurologic injury to the spinal cord is usually confined to the white matter of the thoracic and upper lumbar segments. The lesions consist of petechiae, perivascular hemorrhages, edema, and microscopic cystic changes. The gray matter is involved secondary to the white matter lesions.[98]

The brains in 12 amateur and 13 professional divers, all of whom died accidentally, were studied by Palmer and colleagues, who noted grossly distended empty vessels, presumably caused by gas bubbles, and extensive lesions of white and gray matter of the brain and cerebellum, with hyalinization of blood vessels.[99]

Decompression sickness among aviators is a condition that occurs almost exclusively at altitudes above 6098 m (20,000 ft).[100–102] The primary cause of decompression is loss of cabin or cockpit pressurization. There have been reports of decompression sickness at altitude exposures of 3049 to 4878 m (10,000–16,000 ft), but these accidents involved individuals with a prior history of trauma, surgery, or obesity.[100]

Although air embolism is distinct from decompression sickness, it is an important pressure-related hazard of scuba diving.[92–95] As the diver ascends toward the surface, gas within the lung expands, particularly if the glottis is kept closed. As a result, there is overdistention and rupture of lung tissue, causing interstitial emphysema (Fig. 19-7), air embolism, mediastinal and subcutaneous emphysema, and pneumothorax. The most serious complication is arterial air embolism, because bubbles of gas are disseminated systemically. In the brain, this can result in a strokelike clinical picture with hemiplegia, blindness, unconsciousness, and death.[92–95]

Prevention of air embolism requires, foremost, that the diver never hold his or her breath during ascent. In addition, the medical examination that precedes scuba-diving training should include respiratory function tests and roentgenograms to rule out pulmonary disease. In two accidents during submarine escape training described by Liebow and colleagues,[103] the victims suffered interstitial emphysema and air embolism because of involuntary air trapping. In one victim, a broncholith of tuberculous origin acted as a ball-valve within a segmental bronchus. In the other patient, who survived, a large bulla was demonstrated roentgenologically and subsequently reabsorbed; no apparent anatomic cause of airway obstruction was noted.

DRUG-RELATED DEATHS

Fatal acute pulmonary edema caused by heroin overdose is a well-known occurrence to forensic pathologists. As discussed in Chapter 13, this form of pulmonary edema is centrally mediated and

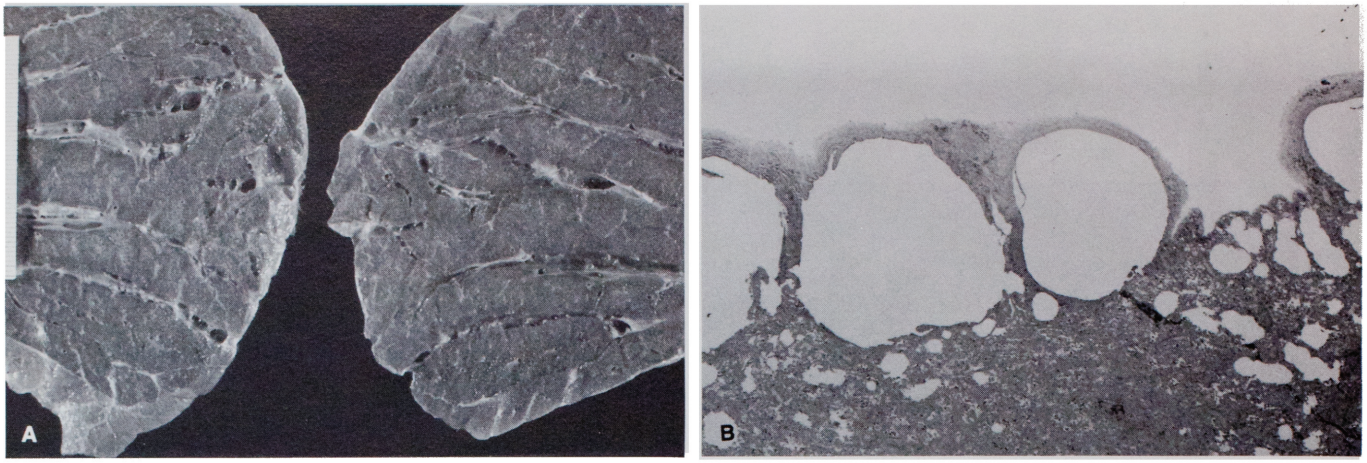

FIGURE 19-7. Interstitial emphysema caused by barotrauma. (**A**) Although the lesions in this patient were induced by high ventilatory pressures, the picture is identical to that seen in immersion accidents (*i.e.*, drowning and near-drowning). (**B**) Microscopic view of a drowned patient shows subpleural blebs of interstitial emphysema. (H & E stain; low magnification.)

probably results from an intense venular constriction in the pulmonary circulation. The resulting protein-rich pulmonary edema (*i.e.*, large pore edema) is reflected in the large amount of foam noted in the mouth and nose of these victims (Fig. 19-8). Characteristic and impressive as it is, the change is not pathognomonic of heroin overdose and can be seen in other forms of pulmonary edema, for instance, that seen at high altitude (see Chap. 24). In heroin overdose victims, the pathologist should always look for the telltale sign of injection needle tracks or marks, usually in the arms but sometimes in less obvious locations. Serious pulmonary parenchymal and vascular disorders are associated with intravenous injections in drug addicts; they are discussed in Chapter 22 and are also illustrated in Color Figure 19-2 and Figure 19-9.

Mention should be made of the observation that inhalation of crack cocaine can produce diffuse pulmonary hemorrhage (see Chap. 16). Accidental burns of the face and upper airway passages and mouth are common in patients with this habit. Paraquat poisoning as an occupational hazard has already been mentioned in Chapters 17 and 19. Ingestion of this substance for suicidal purposes leads to a picture of acute respiratory insufficiency, and the pathology is that of DAD and acute pulmonary fibrosis (Color Fig. 19-3; Fig. 19-10).

Intravenous drug administration is a common cause of serious pulmonary disease. Cardiopulmonary disease in this patient population is inherently important because of three major associations: transmission of AIDS by the use of contaminated needles and syringes (see Chap. 45); development of tricuspid valve bacterial endocarditis with secondary septic embolization to the lungs, pneumonia, and abscesses (see Chaps. 18 and 38); and hypertensive pulmonary arteriopathy (see Chaps. 22 and 45).

ACUTE PULMONARY DEATH DUE TO NATURAL CAUSES

Bronchial Asthma

Acute death caused by bronchial asthma frequently follows status asthmaticus, which is discussed in Chapters 17 and 29.

Acute Pulmonary Thromboembolism

Among circulatory disorders of the lung, acute pulmonary thromboembolism is doubtless the most common cause of sudden death, and the subject is discussed in Chapter 18. The syndrome is frequently seen with saddle emboli obstructing 75% or more of the total pulmonary arterial cross-sectional area at or near the main pulmonary artery bifurcation. Death can be the result of unilateral pulmonary artery occlusion. In such patients, careful dissection of the unobstructed pulmonary artery will frequently disclose fragments of a major embolus. When this is not the case, it is probable that reflex vasoconstriction played a major role in the production of acute cor pulmonale. Another possibility is the presence of chronic thromboembolic pulmonary hypertension (see Chap. 22). In any event, an effort should be made to disclose the source of the emboli, usually in the legs, thighs, or pelvis (Color Fig. 19-4; Fig. 19-11).

Venous Air Embolism

As noted in the section on decompression sickness, two types of air embolism are recognized—venous and arterial. The latter has much more serious consequences. Venous embolism with the presence of air in the right chambers of the heart and pulmonary artery was documented by Adams and Hirsch in 16 autopsies from patients with shotgun and gunshot wounds of the head, traffic fatalities with head trauma, and one patient with a neck incision.[104]

Venous air embolism is also a well-recognized complication of central venous catheterization in a number of ways, including during initial catheterization, when catheters crack or are disconnected, after catheter removal, or when a guide wire is left in place.[105] Even the residual venous catheter tract can be an occult source of lethal air embolism.[106]

Another relatively frequent source of venous air embolism occurs during cesarean delivery. In the report by Handler and Bromage, subclinical venous air embolism was demonstrated in 50% to 65% of patients during cesarean delivery.[107] Venous air embolism has been documented after operative hysteroscopy with

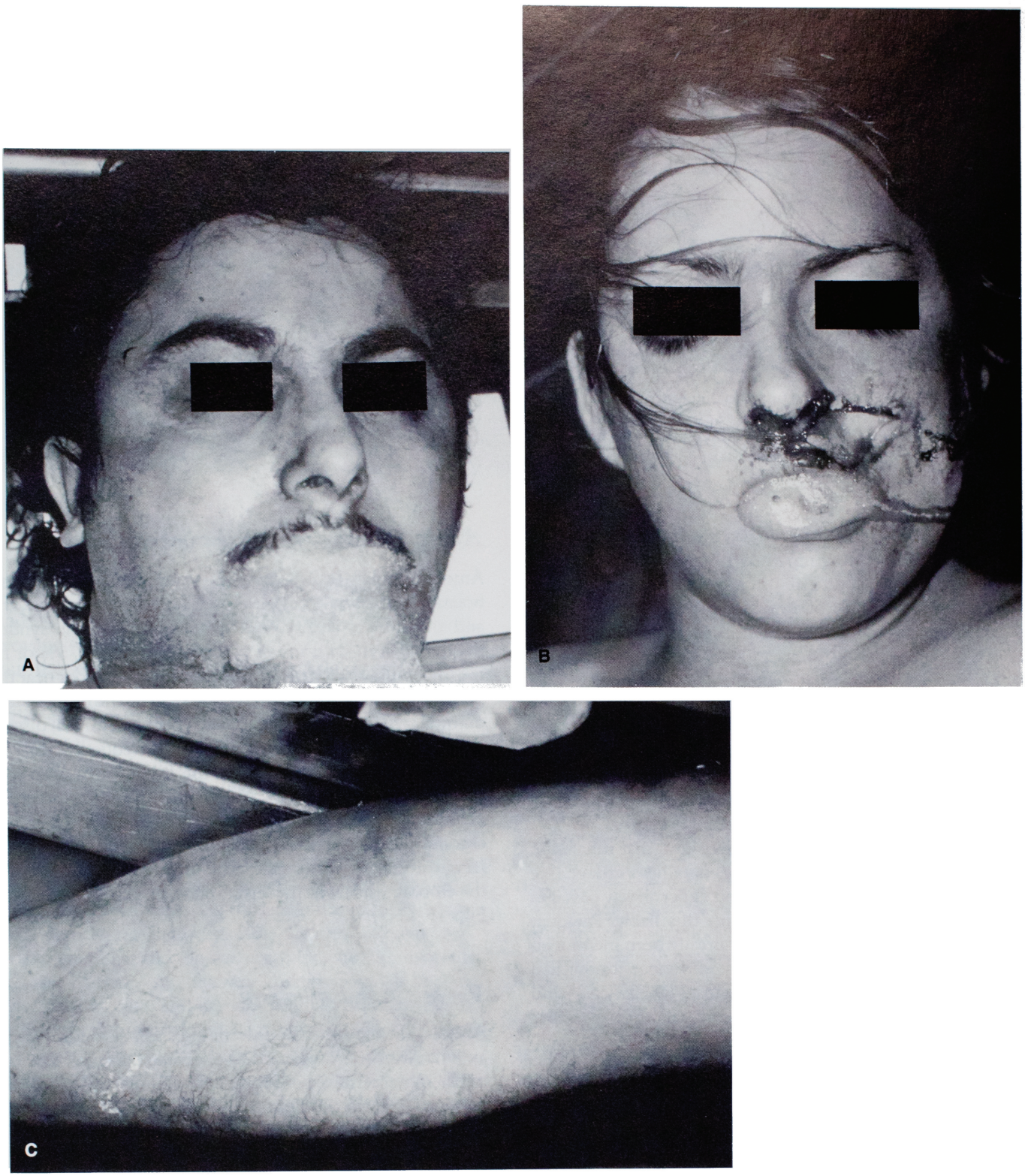

FIGURE 19-8. (**A**) A man and (**B**) a woman died as a result of heroin overdose. The protein-rich large pore pulmonary edema is evidenced by the tenacious foam sticking to the mouth and nose. (**C**) The arm of the man in **A** shows the telltale needle tracks and marks of an intravenous drug abuser.

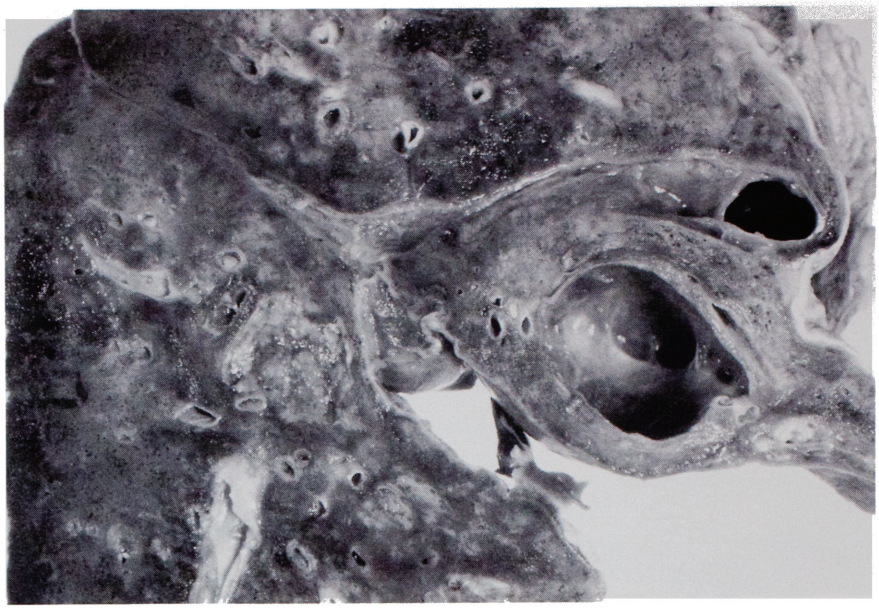

FIGURE 19-9. The lung of a middle-aged man with a long history of crack cocaine inhalation shows extensive fibrotic and cystic changes (see Color Fig. 19-2).

use of a 32% dextran-70 pump,[108] and during radical retropubic prostatectomy.[109]

Arterial Air Embolism

Left-sided or systemic air embolism is a life-threatening event that is usually fatal. It may arise from a peripheral, tearing lung injury due to barotrauma in excess of 60 mm Hg, or from right-sided air embolism that either traverses the lung circulation or reaches the left atrium through a patent foramen ovale. The presence of systemic air embolism is an indication for thoracotomy to repair the source of the embolism and to aspirate air from the left ventricle and the ascending aorta prior to cardiac resuscitation.[110]

Embolization of Gastric Contents

A bizarre case of embolization of gastric contents to the lungs has been described in a 54-year-old man who had most of his stomach located posteriorly in the right chest cavity because of prior esophageal surgery.[111] He died from acute upper gastrointestinal blood loss and perforation of a gastric ulcer into the inferior vena cava and from there to the lungs.

Primary Pulmonary Hypertension

This syndrome is associated with high mortality and occasionally presents as sudden, unexpected death (see Chap. 23). In patients known to suffer from this disease, a frequent cause of death is a

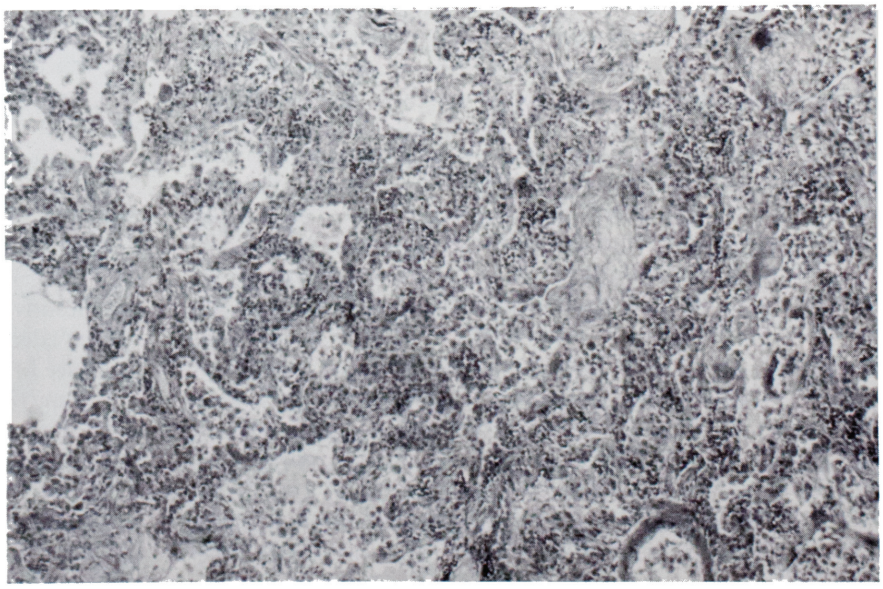

FIGURE 19-10. In a victim of paraquat poisoning, a clinical picture of fatal respiratory insufficiency is associated with diffuse alveolar damage in an organizational stage (*i.e.*, acute pulmonary fibrosis; see Color Fig. 19-3). (Masson trichrome stain; low magnification.)

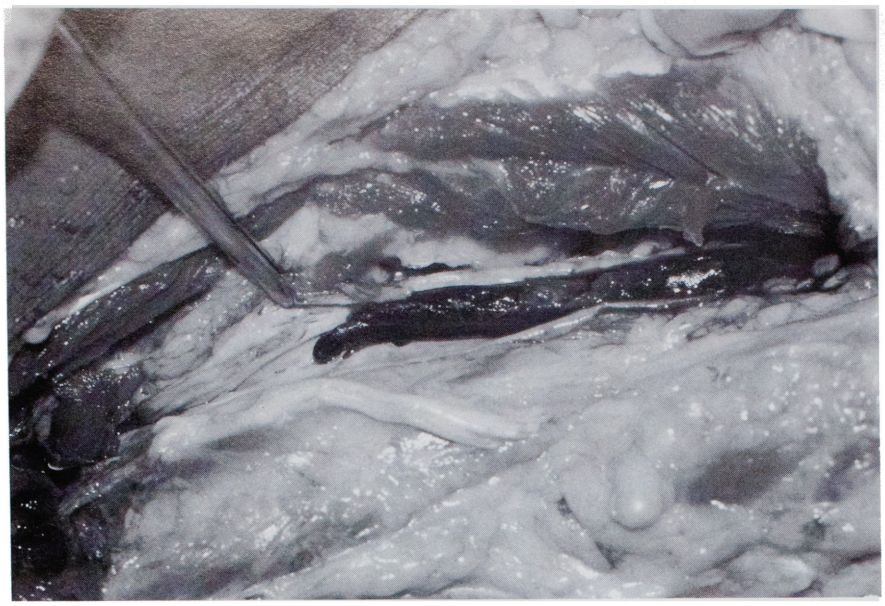

FIGURE 19-11. Acute pulmonary thromboembolism. *In situ* thromboemboli are seen in the thigh of a man who had embolic lesions to his lungs (see Color Fig. 19-4).

fatal arrhythmia; this is also the likely explanation in patients with unsuspected primary pulmonary hypertension who die suddenly. The gross findings at autopsy may be minimal, and the cause of death may be easily overlooked. However, right ventricular hypertrophy or dilatation in the absence of a pulmonary embolus, heart anomalies, or valvular defects, and the presence of grossly normal lungs should suggest the diagnosis of primary pulmonary hypertension. Careful dissection and histologic examination of the conduction system of the heart are warranted in these patients.

Histologic findings in the lungs include the presence of plexiform lesions (Fig. 19-12*A*); however, some patients will show only medial hypertrophy or a combination of medial hypertrophy and concentric intimal fibroelastosis (Fig. 19-12*B*). Thrombotic forms of the disease have been recognized, as well as medial defects or focal dysplasia of pulmonary arteries. Rarely, sudden death has been associated with pulmonary venoocclusive disease (see Chap. 23).

Infectious Pneumonia

Some pulmonary infections may pursue a highly fulminant clinical course and result in death of an apparently undetermined cause. This is particularly true if the patient lived alone or if death occurred at home or when the patient was medically unattended.

The most commonly involved agents are viral, mycoplasmic, or rickettsial infections, and they are discussed in Chapter 42. Overwhelming respiratory insufficiency in adults is usually associated with DAD, as in influenza. In children, the presence of bronchiolitis must be entertained, although both gross and microscopic findings may be deceptively mild. As noted in Chapters 11 and 38, β-streptococcal infections in the newborn may simulate hyaline membrane disease. Appropriate cultures for viral and bacterial organisms and proper fixation of tissue for electron microscopy are indicated in any patient suspected of being infectious.

Sudden Infant Death Syndrome

The term "sudden infant death syndrome" (SIDS) is applied by pediatric and forensic pathologists to a fatal condition in which the autopsy fails to identify a probable cause of death. Indeed, the autopsy in many such patients may be entirely negative, yet the concept of SIDS is valid, provided it takes into account the infant's medical history, knowledge of the circumstances surrounding death, and the complete postmortem examination to rule out recognized causes of sudden death.

The following definition of SIDS was agreed on at the 1969 International Conference on Causes of Sudden Death in Infants: "The sudden death of any infant or young child which is unexpected by history and in which a thorough postmortem examination fails to demonstrate an adequate cause of death."[112] A panel of experts convened by the National Institute of Child Health and Development in 1987 recommended the following rewording of the definition: "The sudden death of an infant under one year of age which remains unexplained after a thorough case investigation, including performance of a complete autopsy, examination of the death scene, and review of the clinical history."[113]

From a number of surveys, it appears that the incidence of SIDS varies between 0.6% and 3.0% of 1000 live births.[114] Remarkably, SIDS is the most common cause of postnatal infant mortality, accounting for one third to one fourth of all deaths under 1 year of age.[115,116] Low birth weight and prematurity are significantly associated with SIDS but by themselves do not provide an adequate basis for identifying patients at risk.[117,118] The incidence of SIDS peaks between 2 and 3 months of age.

Many of the gross and microscopic findings attributed to, or to be distinguished from, SIDS have been comprehensively reviewed and compiled in a publication by Valdés-Dapena and colleagues.[119] The typical gross and microscopic findings of SIDS are presented in Displays 19-4 and 19-5, respectively. Causes of explained sudden death that must be carefully separated from SIDS are presented in Display 19-6.

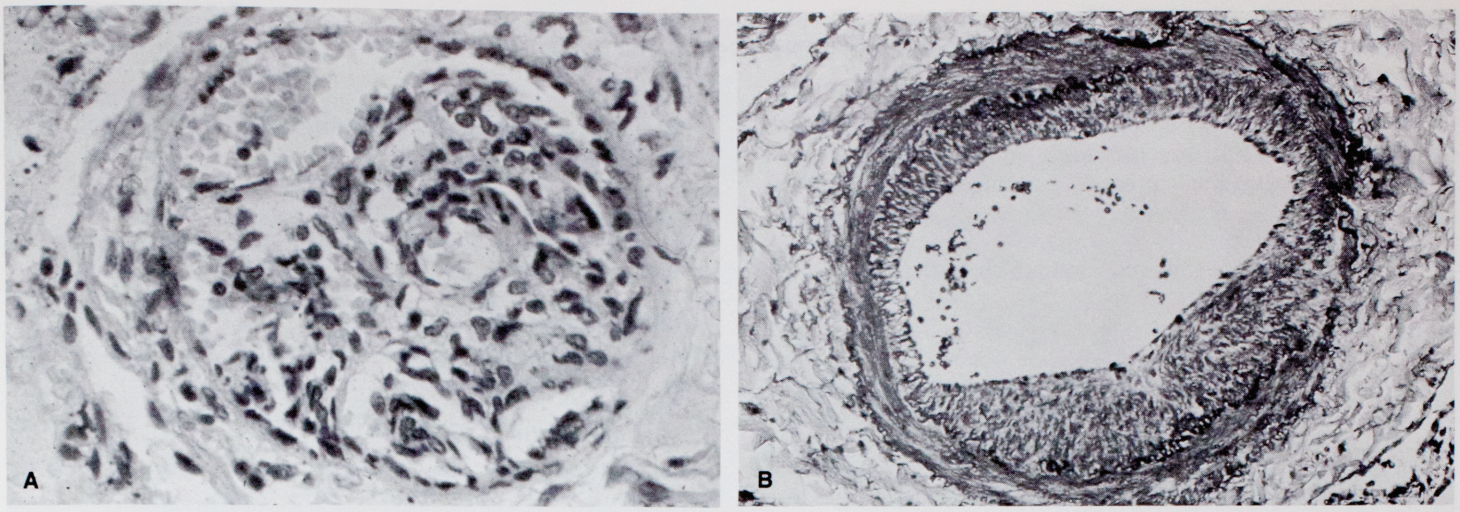

FIGURE 19-12. (**A**) An angiomatoid lesion is present in a man with a history of primary pulmonary hypertension (PPH) who died suddenly, probably of an arrhythmia. (H & E stain; low magnification.) (**B**) The pulmonary artery in a middle-aged woman with unsuspected PPH who died suddenly showed no angiomatoid or plexiform lesions. The main pathology consisted of medial hypertrophy and concentric fibroelastosis of medium-sized and small pulmonary arteries. (Elastic tissue stain; low magnification.)

PULMONARY PATHOLOGY

As noted in Displays 19-4 and 19-5, petechiae of the visceral and parietal pleura are a common finding in SIDS. They probably represent an agonal event found grossly and microscopically in 63% of SIDS patients *versus* 38% of explained deaths. They are often associated with petechiae of the heart and thymus.

Congestion of lung parenchyma can also be an impressive finding in SIDS, frequently giving rise to a mistaken gross impression of pneumonia. Alveolar hemorrhage is frequently associated with congestion, particularly in the dependent portions of the lung, and probably represents an agonal event. Interlobular septal hemorrhages and interstitial emphysema are usually seen in patients subjected to artificial ventilation and may progress to pneumothorax.

Pulmonary edema is another finding in classic cases of SIDS; it can vary from mild to severe. Although the possibility of a hypoxic agonal injury to pulmonary capillaries is favored, the possibility of a postmortem artifact cannot be excluded. An increased number of desquamated alveolar macrophages within alveoli is another poorly understood finding.

Patchy atelectasis alternating with areas of overdistention of alveoli can be seen following attempted resuscitation. This finding probably represents uneven aeration of alveolar tissue, because air is forcibly blown into the lungs of these babies and forced out by manual compression of their chest wall. Because alveolar septae in infants are normally thicker than those in the adult, collapse of lung tissue may give rise to a mistaken impression of pneumonia or fibrosis by the unaware pathologist.

ETIOLOGY AND PATHOGENESIS

Although the exact cause and pathogenesis of SIDS remain elusive, there is significant evidence supporting the role of chronic hypoxemia as an underlying state.In 1974, Naeye identified seven markers of chronic hypoxia in SIDS victims: increased muscularity of pulmonary arterioles, brain stem gliosis, retention of brown fat, liver extramedullary hematopoiesis, adrenal medullary hyperplasia, carotid body abnormalities, and hypertrophy of the right ventricle.[120] These findings have been confirmed by other investigators, including increased brown fat retention,[121] brain stem gliosis,[122] increased muscularization of pulmonary arterioles,[123] and increased extramedullary hematopoiesis.[124] Naeye and colleagues also described normoblastic hyperplasia in the bone marrow, thus providing evidence that the primary as well as the secondary sites of erythropoiesis in SIDS victims are under hypoxic stress.[125] The authors proposed that the increased erythropoiesis was secondary to erythropoietin production by the kidney under hypoxic stimulation.[125]

Also supporting the hypoxic pathogenesis of SIDS is the evidence uncovered by Gillan and associates of an abnormal pattern of neuroendocrine cells in the lungs of victims with SIDS.[126] This is probably the result of brain stem dysfunction or chronic hypoxia affecting the lungs secondarily. Another important finding is the presence of increased fetal hemoglobin (HbF) levels in SIDS victims. In their study, Gilbert-Barness and colleagues, using high-performance liquid chromatography, showed that HbF is clearly elevated in SIDS patients in comparison with normal controls.[127] This gives further support for an underlying hypoxic state and provides a useful marker to identify SIDS at necropsy.

Haque and Mancuso have recently demonstrated by immunohistochemical methods that there are greater numbers of peribronchiolar dendritic cells (Langerhans histiocytes) in SIDS victims than in control infants.[128] The authors hypothesize that the proliferation of dendritic cells is the result of exposure to environmental antigens, resulting in thickening of the bronchiolar walls, narrowing of the lumen, and reduction in airflow, thus causing chronic persistent hypoxemia.

DISPLAY 19-4. CLASSIC OR TYPICAL GROSS FINDINGS IN SUDDEN INFANT DEATH SYNDROME

Skin

Purple blotches in face, extremities, and dependent portions of body, frequently mistaken as evidence of abuse; cyanosis of mucous membranes, vermilion border, and fingernails and toenails

Mouth and Nose

Scant amount of blood, mucus, and froth about the nares and mouth

Petechiae

Showers of petechiae on the external surface of the thymus, the visceral and parietal pleura, and the epicardium and myocardium

Thymus

Prominent and heavy; weight, however, within normal range; involution of thymus indicates SIDS not cause

Heart Blood

Intraventricular blood in liquid state

Lungs

Gross impression of congestion, edema, and pneumonia is frequently mistaken

Lymphoid Tissues

Prominent tonsils, mesenteric lymph nodes, and Peyer patches of intestine

Gastric Contents

Partly digested food (*i.e.*, pasty curd), clear or hemorrhagic mucus caused by agonal capillary oozing of gastric mucosa

Acute Iatrogenic Lesions

Mucosal erosion of airways caused by intubation, acute interstitial emphysema, needle punctures in the heart

Chronic Iatrogenic Lesions

Occur after days or weeks in artificial life-supporting systems; bacterial bronchopneumonia, pressure-induced ulcers of airways by endotracheal tube, hyaline membranes due to O_2 toxicity

Data from Valdés-Dapena M, McFeeley PA, Hoffman HJ, et al. Histopathology atlas for the sudden infant death syndrome. Washington, DC: Armed Forces Institute of Pathology, 1993:1.

DISPLAY 19-5. CLASSIC OR TYPICAL HISTOLOGIC FINDINGS IN SUDDEN INFANT DEATH SYNDROME

Epicardium

Multiple petechiae

Larynx

Foci of fibrinoid necrosis with acute and chronic inflammation. Nonspecific acute and chronic laryngitis of a mild to moderate degree

Trachea

Nonspecific acute and chronic tracheitis

Lung

Pleural petechiae, congestion, hemorrhage, septal hemorrhages and interstitial emphysema, edema, desquamated alveolar macrophages, atelectasis, overdistention

Liver

Microvesicular fatty degeneration of liver

Thymus

Multiple petechiae

Brain

Perivascular hemorrhages

Data from Valdés-Dapena M, McFeeley PA, Hoffman HJ, et al. Histopathology atlas for the sudden infant death syndrome. Washington, DC: Armed Forces Institute of Pathology, 1993:1.

DISPLAY 19-6. MOST COMMON CAUSES OF EXPLAINED SUDDEN INFANT DEATH

Respiratory

Upper airway obstruction, cystic remnant of thyroglossal duct cyst causing obstruction of airway, cervical cellulitis (*i.e.*, Ludwig angina), bronchopneumonia, bronchiolitis, accidental or deliberate suffocation by soft plastic sheet, CO poisoning (toxicologic analysis required), drowning

Cardiovascular

Viral myocarditis, congenital heart disease such as aortic stenosis, endocardial fibroelastosis, anomalous origin of left coronary artery, cardiomyopathy, rhabdomyoma in tuberous sclerosis, coronary arteritis (*i.e.*, Kawasaki disease), polysplenia, asplenia (*i.e.*, Ivemark syndrome)

Gastrointestinal, Liver and Pancreas

Enterocolitis with diarrhea and dehydration, viral hepatitis (*i.e.*, coxsackievirus), boric acid poisoning, cystic fibrosis hyperthermia, viral pancreatitis (*i.e.*, coxsackievirus)

Other

Trauma such as skull fracture in a battered child, meningitis, sickle cell disease, viral encephalitis, arteriovenous malformation, subdural hematoma, dehydration, hyperthermia caused by cystic fibrosis, congenital adrenal hypoplasia, or hyperplasia

Data from Valdés-Dapena M, McFeeley PA, Hoffman HJ, et al. Histopathology atlas for the sudden infant death syndrome. Washington, DC: Armed Forces Institute of Pathology, 1993:1.

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