# Toxin-induced Respiratory Distress

Charles A. McKay Jr, MD[a,b,*]

**KEYWORDS**

• Acute lung injury • Inhalation injury • Simple asphyxiant • Respiratory irritant
• Reactive airways dysfunction syndrome • Impaired oxygen transport
• Water solubility

**KEY POINTS**

- When an exposure history is unclear or unknown, the presenting symptoms and signs referable to a particular airway component should guide assessment and treatment.
- Useful categories include lack of oxygen delivery from exposure to a simple asphyxiant, airway irritation from a water-soluble irritant, airways irritation from a water-insoluble irritant, direct pulmonary toxicity from a recent or remote event, altered oxygen transport from acquired dyshemoglobinemia, and altered oxygen use by cells because of a mitochondrial toxin.
- Treatment should focus on supportive care and addressing the specific dysfunction identified.

## INTRODUCTION

Most poisoning and overdose events involve unintentional or intentional ingestions by the oral route. However, the possibility of inhalation exposure to volatile compounds or suspended particulates is a daily concern for everyone. Most people go through each day without respiratory or systemic complaints, which is as much a tribute to people's pulmonary defensive capabilities as it is to the low ambient concentration of most commonly occurring xenobiotics, allergens, and infectious agents. High-dose exposure, inadequate defenses, and genetic or acquired susceptibility can affect multiple components of the airway from the point of air entry to the level of gas exchange. Examples of these varied maladies include allergic rhinitis, viral pharyngitis, fungal

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[a] Occupational Health Services, Division of Medical Toxicology, Department of Emergency Medicine, Hartford Hospital, 80 Seymour Street, Hartford, CT 06102-5037, USA; [b] Connecticut Poison Control Center, Division of Medical Toxicology, University of Connecticut Health Center, University of Connecticut School of Medicine, 263 Farmington Avenue, Farmington, CT 06030, USA
* Division of Medical Toxicology, Department of Emergency Medicine, Hartford Hospital, 80 Seymour Street, Hartford, CT 06102-5037.
*E-mail address:* charles.mckay@hhchealth.org

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sinusitis, irritant-induced bronchospasm, chemical or bacterial pneumonitis, alpha-1 antitrypsin deficiency–mediated emphysema, granulomatous diseases such as sarcoidosis or berylliosis, as well as many other occupational pneumoconioses such as silica-mediated pulmonary fibrosis. This article focuses on the variety of chemical compounds that can result in injuries to the airways, resulting in a patient presenting to the emergency department.

## PULMONARY ANATOMY AND PHYSIOLOGY AND RESPONSE TO INJURY

### *Ventilatory Capacity*

A basic understanding of respiratory anatomy and physiology is essential in characterizing its response to external insults. Of all biologic systems in the human body, the pulmonary system has the greatest potential surface area of exposure. Under a heavy workload, adult minute ventilation can increase more than 10-fold from an average baseline of 6 L. Roughly equal contributions from increased respiratory rate and recruitment of additional alveolar units contribute to this capacity. The alveoli, estimated at 300 million in the adult, are the sites of gas exchange. One aspect of increased susceptibility to inhalation injury in children is the smaller number of alveolar units (at birth, ~15% of adult capacity), and the requisite higher respiratory rate, resulting in a greater concentration-time exposure at any given pulmonary site.[1] In addition, at all ages, changes in ventilation/perfusion matching with exertion increase the potential for pulmonary and systemic exposure to inhaled compounds.

### *Gas Exchange*

Oxygen delivery and carbon dioxide excretion follow the principles of the gas laws, whereby the total pressure of gas within a system is composed of the partial pressure contributed by each constituent (Dalton's law of partial pressures), and the exchange of those gases at an interface (ie, the alveolar air and the blood of the alveolar capillaries) is proportional to their concentrations (Henry's law). The critical role of a properly functioning gas carrier (hemoglobin) is shown by the Bohr and Haldane effects, which result in increased tissue release of oxygen from, and increased binding of carbon dioxide to, hemoglobin at the tissue level; whereas increasing binding of oxygen and release of carbon dioxide take place at the alveoli, respectively. This efficiently engineered system of gas exchange can be disrupted in several ways, including changes to hemoglobin affinity based on inhaled toxins such as carbon monoxide (CO) and methemoglobin (MetHb) inducers. Other agents can injure the thin gas exchange membrane composed of alveolar epithelial cells and capillary endothelium, increasing diffusion distance by acute lung injury with edema and inflammatory injury, or decreasing the number of functioning alveolar units.

### *Ventilatory Mechanics*

The mechanics of ventilation are not extensively addressed in this article. However, because they can be affected by the toxicity of various compounds, it is important to define a few terms.[2] Air is conducted through the fixed-volume ventilatory dead space of the upper airways and the more dynamic intrathoracic airways. The ventilatory process is depicted in **Fig. 1** as the volumes and capacities present within the lungs. For example, a tidal volume ($V_T$) of approximately 500 mL for an adult with an average respiratory rate of 12 breaths per minute results in a minute ventilation volume of 6 L. Additional air can be inhaled (inspiratory reserve volume [IRV]) and actively exhaled beyond the passive recoil of the chest wall (expiratory reserve volume [ERV]) to make up the total lung capacity (TLC; total lung volume of a single maximal