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Exhibit D45

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INTRODUCTION

This topic will discuss the clinical toxicity, evaluation, and diagnosis of acute hydrocarbon exposure. The management of acute hydrocarbon exposure and inhalant abuse in children and adolescents are discussed separately. (See "Inhalant abuse in children and adolescents".)

EPIDEMIOLOGY

Hydrocarbon exposures account for over 28,000 cases reported annually to United States regional poison control centers and are an important cause of poisoning worldwide [1]. About 85 percent of hydrocarbon exposures are unintentional. Children five years of age and younger account for the majority of the nearly 14,000 annual pediatric exposures [1]. Although fatalities are rare, moderate effects requiring supportive care are common, especially after hydrocarbon ingestion. Hydrocarbon ingestion is the most common form of exposure in this age group, occurring in about 75 percent of cases [2]. In young children (≤5 years of age), the ingestion typically occurs as a result of exploratory behavior. Frequently, the hydrocarbon is unsecured or improperly stored in a drinking container (eg, soda or water bottle). Among adolescents and adults, hydrocarbon exposure often arises from recreational inhalant abuse (see "Inhalant abuse in children and adolescents"). Fuel siphoning is an important source of unintentional ingestion in adults [3].

PATHOPHYSIOLOGY

The specific toxicity of a hydrocarbon exposure is determined by the route, type of chemical compound, and amount of exposure (see 'Clinical toxicity' below). Although hydrocarbons are toxic to essentially all body systems, the most important toxicities occur in the lungs, brain, and heart [4-6]:

- **Lungs** – Pulmonary aspiration and chemical pneumonitis are major features of hydrocarbon ingestion. Based on animal studies, the primary pathologic finding is severe necrotizing pneumonia [7]. Other findings include direct destruction of the airway epithelium, alveolar

septae, and pulmonary capillaries, as well as solubilization of the lipid surfactant layer. Secondary changes include atelectasis, interstitial inflammation, and hyaline membrane formation. The inflammatory response from chemical irritation generally causes temperature elevation, usually within hours of exposure. The aspiration hazard of hydrocarbon compounds is determined by three properties [4,5]:

- **Viscosity** – Viscosity refers to the resistance to flow through an orifice or the tendency of a compound to resist stirring. Lower viscosity facilitates deeper penetration into the tracheobronchial tree. Viscosity is the most important chemical characteristic that determines the aspiration potential for hydrocarbons.

Literature review current through: Nov 2021. | **This topic last updated:** Jun 26, 2020.

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