108: Hydrocarbons

David D. Gummin

HISTORY AND EPIDEMIOLOGY

The modern world could not exist without hydrocarbons. Virtually everything we touch is either coated with or made up primarily of hydrocarbon products. Organic chemistry originated during the Industrial Revolution, evolving largely due to advances in coal tar technology. In the coking process, bituminous (soft) coal is heated to liberate coal gas. This gas contains volatile hydrocarbons that can be captured and separated into a variety of natural gases. The viscous residue left over from the coking process forms coal tar, which can, in turn, be distilled into kerosene and other hydrocarbon mixtures.

Over the years, petroleum has replaced coal tar as the principal source of commercial organic compounds. Crude oil processing involves heating to a set temperature within processors that separate (distill) hydrocarbon fractions by vapor (or boiling) point. Because of the relationship between boiling point and molecular weight, distillation roughly divides hydrocarbons into like sized molecules. The most volatile fractions come off early as gases, and these are used primarily as heating fuels. The least volatile fractions (larger than about 10 or 12 carbons) are used chiefly for lubricants or as paraffins, petroleum jelly, or asphalt. The remaining mid sized distillation fractions (5 to 10 carbons) are those most commonly used in combustion fuels and as solvents. Petroleum distillates are used as chemical feedstocks and as precursors or intermediates in feedstock production.

For decades in the United States, kerosene ingestion in children was a major public health concern. Only through public education, consumer product safety initiatives, and modernization of the use and distribution of cooking and heating fuels has this problem been largely eliminated. However, in the developing world, these same challenges have yet to be resolved, with large numbers of children ingesting kerosene from poorly labeled and poorly secured containers.

Recent public attention and debate surrounds the potential for hydrocarbon exposures following environmental spills. Even more controversial is the practice of “induced hydraulic fracturing” of rock or shale, commonly called “fracking.” Fracking is performed on up to 60% of oil and gas wells drilled today, to liberate pockets of trapped gas or oil from within the fractured rock. The intent is to capture and collect trapped hydrocarbons, but some escape into nearby aquifers, thereby entering water supplies or otherwise contaminating human environments. Critics are concerned about the composition of the hydraulic fluids used, as these may be comprised mainly of methanol, ethylene glycol, benzene, or other hydrocarbons. Components of these fluids are found in area groundwater, with resultant risk of human exposure and untoward health effects.
The true epidemiology of hydrocarbon exposure and illness is difficult to ascertain from available data sources. But three populations appear to be at particular risk for hydrocarbon-related illness. These are children who suffer unintentional exposures, often ingestion with pulmonary aspiration; workers with occupational exposures, often inhalational and dermal; and adolescents or young adults who intentionally abuse solvents by inhalation. People in specific occupations who are at risk for exposure include petrochemical workers, plastics and rubber workers, printers, laboratory workers, painters, and hazardous waste workers. Most hydrocarbon exposures do not involve ingestion, and most do not result in illness. Exposures may range from self-pumping gasoline, to painting a spare bedroom, or to applying or removing fingernail polish. Because hydrocarbon solvents are often volatile, inhalation is extremely common. Lipid solubility results in dermal absorption when skin is exposed. Data from US poison centers suggest that about 30% of reported exposures to hydrocarbons were in children younger than 6 years of age (Chap. 136). Largely not captured in these data is an alarming rate of intentional misuse of volatile solvents by young people, which is discussed in more depth in Chap. 84.

Most commonly encountered hydrocarbons are mixtures of compounds, often obtained from a common petroleum distillation fraction. The many applications for these in consumer and household products include paints and thinners, furniture polish, lamp oils, and lubricants. Table 108–1 lists frequently encountered hydrocarbon compounds and their properties. This chapter focuses principally on toxicity of hydrocarbons present in these commercially available mixtures. Individual hydrocarbons are discussed only when they are commonly available in purified form, or when specific xenobiotics result in unique toxicologic concerns.

### TABLE 108–1. Classification and Viscosity of Common Hydrocarbons

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**CHEMISTRY**

A hydrocarbon is an organic compound made up primarily of carbon and hydrogen atoms, typically ranging from 1 to 60 carbon atoms in length. This definition includes products derived from plants (pine oil, vegetable oil), animal fats (cod liver oil), natural gas, petroleum, or coal tar. There are two basic types of hydrocarbon molecules, *aliphatic* (straight or branched chains) and *cyclic* (closed ring), each with its own subclasses. The aliphatic compounds include the *paraffins* (*alkanes*, with a generic formula \( \text{C}_n\text{H}_{2n+2} \)); the *olefins* (*alkenes* have one double bond and *alkadienes* have two double bonds); the *acetylenes* (*alkynes*) with at least one triple bond; and the *acyclic terpenes* (polymers of isoprene, \( \text{C}_5\text{H}_{10} \)). Some aliphatic compounds have branches in which the subchain also contains carbon atoms; both the chain and branches are essentially straight.

The cyclic hydrocarbons include *alicyclic* (three or more carbon atoms in a ring structure, with properties similar to the aliphatics), and *aromatic* compounds, as well as the *cyclic terpenes*. The
Alicyclics are further divided into cycloparaffins (napthenes) such as cyclohexane, and the cycloolefins (two or more double bonds) such as cyclopentadiene.

**Saturated** hydrocarbons contain carbon atoms that exist only in their most reduced state. This means that each carbon is bound to either hydrogen or to another carbon, with no double or triple bonds present. Conversely, **unsaturated** compounds are those with hydrogens removed, in which double or triple bonds exist.

**Solvents** are a heterogenous class of xenobiotics used to dissolve and provide a vehicle for delivery of other xenobiotics. The most common industrial solvent is water. The common solvents most familiar to toxicologists are **organic solvents** (containing one or more carbon atoms), and most of these are comprised of hydrocarbons. Most are liquids in the conditions under which they are used. Specifically named solvents (Stoddard solvent, white naphtha, ligroin) represent mixtures of hydrocarbons emanating from a common petroleum distillation fraction.

Aromatic hydrocarbons are divided into the **benzene** group (one ring), **naphthalene** group (two rings), and the **anthracene** group (three rings). Polycyclic aromatic hydrocarbons (polynuclear aromatic hydrocarbons) have multiple, fused benzenelike rings. Aromatic organic compounds may also be **heterocyclic** (where oxygen or nitrogen substitutes for carbon in the ring). Structurally, all of these molecules are flat, with reactive electron clouds above and below the ring.

The cyclic terpenes are the principal components of the variety of plant-derived essential oils (Chap. 43), often providing color, odor, and flavor. Limonene in lemon oil, menthol in mint oil, pinene in turpentine, and camphor are all terpenes.

Physical properties of hydrocarbons vary by the number of carbon atoms and by molecular structure. Unsubstituted, aliphatic hydrocarbons that contain up to 4 carbons are gaseous at room temperature, 5 to 19 carbon molecules are liquids, and longer-chain molecules tend to be tars or solids. Branching of chains tends to destabilize intermolecular forces, so that less energy is required to separate the molecules. The result is that, for a given molecular size, highly branched molecules have lower melting and boiling points and tend to be more volatile.

The various definitions of paraffin warrant discussion. In chemistry, **paraffin** is a general term for any alkane. In North American common use, paraffin describes either medicinal paraffin or paraffin wax. **Medicinal paraffin** is the same as mineral oil, a viscous mixture of longer-chained alkanes (typically 15–50 carbon atoms per molecule) derived from a petroleum source. The molecules in mineral oil exhibit considerable branching, making it a viscous liquid at room temperature and pressure. Molecules in **paraffin wax** are nearly identical to these in size, but less branching increases the number of intermolecular interactions, forming a waxy/solid at room temperature. Outside North America, the term **paraffin** often refers to kerosene—a mixture of medium-chain alkanes typically used for lighting and heating.

Gasoline is a mixture of alkanes, alkenes, napthenes, and aromatic hydrocarbons, predominantly 5 to 10 carbon atoms in size. Gasoline is separated from crude oil in particular distillation fractions and
then usually blended with several other fractions in refinery processors. More than 1500 individual molecular species may be present in commercial grades, but most analytical methods isolate only 150 to 180 constituent compounds in gasoline. Notably, \( n \)-hexane is present at up to 6\%, and benzene is present between 1\% and 6\%, depending on the origin and processing technique. A number of additives may go into the final formulation: alkyl leads, ethylene dichloride, and ethylene dibromide in leaded gasoline, and oxygenates such as methyl \( t \)-butyl ether (MTBE), as well as methanol and ethanol.

Organic halides contain one or more halogen atoms (fluorine, chlorine, bromine, iodine) usually substituted for a hydrogen atom in the parent structure. Examples include chloroform, trichloroethylene, and the freons.

Oxygenated hydrocarbons demonstrate toxicity specific to the oxidation state of the carbon, as well as to the atoms adjacent to it (the “R” groups). The alcohols are widely used as solvents in industry and in household products. Their toxicity is discussed in Chaps. 80 and 109. Ethers contain an oxygen atom bound on either side by a carbon atom. Acute toxicity from ethers tends to mirror that of the corresponding alcohols. Aldehydes and ketones contain one carbon–oxygen double bond (C = O), the former at a terminal carbon, the latter somewhere in the middle. Organic acids, esters, amides, and acyl halides represent more oxidized states of carbon; human toxicity is agent specific.

 Phenols consist of benzene rings with an attached hydroxyl (alcohol) group. The parent compound, phenol, has only one hydroxyl group attached to benzene. The toxicity of phenol can be dramatically altered by addition of other functional groups to the benzene ring (Chap. 104). Cresols, catechols, and salicylate are examples of substituted phenols.

A variety of amines, amides, nitroso and nitro compounds, as well as phosphates, sulfites, and sulfates are used commercially and industrially. The addition of these functional groups to hydrocarbons dramatically alters the characteristics, including the toxicity of the compound.

**PHARMACOLOGY**

The effects of hydrocarbons on humans are chiefly related to interactions with lipid bilayers in cellular membranes. Inhaled hydrocarbon vapor depresses consciousness. As such, acute central nervous system (CNS) toxicity from occupational overexposure or recreational abuse parallels the effect of administering an inhaled general anesthetic. The concentration of volatile anesthetic that produces loss of nociception in 50\% of patients defines the minimum alveolar concentration (MAC) required to induce anesthesia. Similarly, inhaled solvent vapor produces unconsciousness in 50\% of subjects, when the partial pressure in the lung reaches its median effective dose (ED\(_{50}\)). The ED\(_{50}\) in occupational terms is effectively the same as the MAC in anesthesiology terms (Chap. 68). Virtually all patients will be anesthetized when the partial pressure is raised 30\% above the MAC (MAC × 1.3). If ventilation is not supported, death typically occurs when the concentration reaches two to four times the MAC. Dose–response curves suggest that essentially no individual will be rendered
unconscious by an inhaled dose 30% below the MAC. Nonetheless, impaired cognitive and motor function may occur at much lower doses.23

The physical property of an inhaled anesthetic that correlates most closely with its ability to extinguish nociception is its lipid solubility. Inhalational exposure to lipid-soluble solvents, such as aromatic, aliphatic, or chlorinated hydrocarbons, is more likely to cause acute and chronic CNS effects than exposure to water-soluble hydrocarbons such as alcohols, ketones, and esters. The Meyer-Overton hypothesis, proposed more than 100 years ago, implies that an anesthetic dissolves into some critical lipid compartment of the CNS, causing inhibition of neuronal transmission. According to this hypothesis, the target structure for general anesthetics is the neuronal lipid membrane itself.66

Unfortunately, this hypothesis is likely too simplistic. Numerous protein receptor interactions also occur. Halothane, isoflurane, sevoflurane, enflurane, and desflurane inhibit fast sodium channels.117 Toluene, trichloroethylene, perchloroethylene, and others inhibit neuronal calcium currents.114,135 The halogenated hydrocarbons increase the outward potassium rectifying current.136 Specific ligand-receptor interactions occur, as such as the inhibition of receptor function at nicotinic,145 and at glutamate receptors,146 as well as enhancement of type-A γ-aminobutyric acid (GABA_A) and glycine receptor currents.12 Independent of other mechanisms, halogenated hydrocarbons appear to decrease exocytosis of neuronal synaptic vesicles.16

Pharmacodynamic properties of inhaled hydrocarbons and other volatile xenobiotics (Chap. 68) suggest some receptor–ligand interaction, and a growing body of evidence suggests that the Meyer-Overton hypothesis cannot explain the many neurochemical activities demonstrated by this broad class of xenobiotics.24 Perhaps a more elegant approach to the lipid bilayer interaction has been termed the “modern lipid hypothesis.” The hypothesis is thermodynamically derived, purporting an increase in lateral pressure on protein receptors within the neuronal bilayer. Lateral pressure leads to conformational changes in membrane ion channels, modulating the capacity for activation.22 While this hypothesis is mechanistically plausible and thermodynamically defensible, no in vitro or in vivo work has yet substantiated it. Thus, to date, no single mechanism fully explains the pharmacologic and toxicologic activity of volatile hydrocarbons on neuronal tissues.

TOXICOKINETICS

Hydrocarbons are variably absorbed into human systems by ingestion, inhalation, or dermal routes. Human toxicokinetic data are lacking for most of these xenobiotics, so much of our understanding derives from in vitro studies and animal research. Partition coefficients, in particular, are useful predictors of the rate and extent of the absorption and distribution of hydrocarbons into tissues. A partition coefficient for a given chemical species is the ratio of concentrations achieved between two different media at equilibrium. The blood-to-air, tissue-to-air, and tissue-to-blood coefficients directly relate to the pulmonary uptake and distribution of hydrocarbons. The tissue-to-blood partition coefficient is commonly derived by dividing the tissue-to-air coefficient by the blood-to-air
The higher the value, the greater the potential for distribution into tissue. Table 108–2 lists partition coefficients for commonly encountered hydrocarbons. Where human data are limited, rat data is presented in the table, because human and rat data often correlate.

**TABLE 108–2. Kinetic Parameters of Selected Hydrocarbons**

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Inhalation is a major route of exposure for most volatile hydrocarbons. Most cross the alveolar membrane by passive diffusion. The driving force is the difference in vapor concentration between the alveolus and the blood. The absorbed dose is determined by the air concentration, duration of exposure, minute ventilation, and the blood-to-air partition coefficient. Hydrocarbons that are highly soluble in blood and tissues are readily absorbed, and blood concentrations rise rapidly following inhalation exposure. While aromatic species are generally well absorbed, absorption of aliphatic hydrocarbons varies by molecular weight: aliphatic hydrocarbons with between 5 and 16 carbons are readily absorbed through inhalation, whereas those with more than 16 carbons are less extensively absorbed.

Absorption of aliphatic hydrocarbons through the digestive tract is inversely related to molecular weight, ranging from complete absorption at lower molecular weights, to approximately 60% for C-14 hydrocarbons, 5% for C-28 hydrocarbons, and essentially no absorption for aliphatic hydrocarbons with more than 32 carbons. Oral absorption of aromatic hydrocarbons with between 5 and 9 carbons ranges from 80% to 97%. Oral absorption of aromatics with more than 9 carbons is poorly characterized, as data are lacking.

While the skin is a common area of contact with solvents, the dose of dermally absorbed hydrocarbons is quite small relative to that through other routes such as inhalation. The skin is comprised of both hydrophilic (proteinaceous portion of cells) and lipophilic (cell membranes) regions (Chap. 18). While many hydrocarbons can remove lipids from the stratum corneum, permeability is not simply the result of lipid removal; permeability also increases with hydration of the skin. The rate of skin absorption is highest when xenobiotics have a water-to-lipid partition coefficient near one. Solvents that contain both hydrophobic and hydrophilic moieties (eg, glycol ethers, dimethylformamide, dimethylsulfoxide) are particularly well absorbed through skin. Other factors that determine penetration across the skin include the thickness of the skin layer, the difference in concentration of the solvent on either side of the epithelium, the diffusion constant, and skin integrity (ie, normal vs. cut or abraded).

The dose absorbed through skin is proportional to the exposed surface area and the duration of contact. Although highly volatile compounds may have a short duration of skin contact because of evaporation, skin absorption can also occur from contact with hydrocarbon vapor. In studies with human volunteers exposed to varying concentrations of hydrocarbon vapors, the dermal dose accounted for only 0.1% to 2% of the inhalation dose. With massive exposure (eg, whole-body
immersion), dermal absorption may contribute significantly to toxicity. Significant dermal absorption with resultant toxicity is described with carbon tetrachloride, tetrachloroethylene, and phenol.

Once absorbed into the central compartment, hydrocarbons are distributed to target and storage organs based on their tissue-to-blood partition coefficients and on the rate of perfusion of the tissue with blood. During the onset of systemic exposure, hydrocarbons accumulate in tissues that have tissue/blood coefficients greater than 1 (eg, for toluene, the fat-to-blood partition coefficient is 60). Table 108–2 lists the distribution half-lives of selected hydrocarbons.

Hydrocarbons can be eliminated from the body unchanged, for example, through expired air, or can be metabolized to more polar compounds, which are then excreted in urine or bile. Table 108–2 lists the blood elimination half-lives (for first-order elimination processes) and metabolites of selected hydrocarbons. Some hydrocarbons are metabolized to toxic compounds (eg, methylene chloride, carbon tetrachloride, n-hexane, methyl-n-butyl ketone). The specific toxicities of these metabolites are discussed later in this chapter.

PATHOPHYSIOLOGY AND CLINICAL FINDINGS

Respiratory
Several factors are classically associated with pulmonary toxicity after hydrocarbon ingestion. These include specific physical properties of the xenobiotics ingested, the volume ingested, and the occurrence of vomiting. Physical properties of viscosity, surface tension, and volatility are primary determinants of aspiration potential.

Dynamic (or absolute) viscosity is the measurement of the ability of a fluid to resist flow. This property is measured with a rheometer and is typically given in units of pascal-seconds. More frequently, engineers work with kinematic viscosity, measured in square millimeters per second, or centistokes. Dynamic viscosity is converted to kinematic viscosity by dividing the dynamic viscosity by the density of the fluid. An older system for measuring viscosity was initially popularized by the petroleum industry and expresses kinematic viscosity in units of Saybolt Universal seconds (SUS). Unfortunately, many policy statements were developed in an era when SUS units were popular, and many still describe viscosity in SUS units. Various look-up tables and calculators are available to convert kinematic viscosity to SUS units. Table 108–1 shows kinematic viscosity of common hydrocarbons, measured in SUS. A unit conversion approximation is given in the table’s footnote.

Hydrocarbons with low viscosities (<60 SUS; eg, turpentine, gasoline, naphtha) have a higher tendency for aspiration in animal models. The US Consumer Products Safety Commission issued a rule in 2001, requiring child-resistant packaging for products that contain 10% or more hydrocarbon by weight and have a viscosity less than 100 SUS.

Surface tension is a cohesive force generated by attraction due to the Van der Waals forces between molecules. This influences adherence of a liquid along a surface (“its ability to creep”). The
lower the surface tension, the more effectively the liquid will creep, producing a higher aspiration risk.

*Volutility* is the tendency for a liquid to become a gas. Hydrocarbons with high volatility tend to vaporize, displace oxygen, and potentially lead to transient hypoxia.

Early reports conflicted in their attempts to relate risk of pulmonary toxicity (1) to the amount of hydrocarbon ingested or (2) to the presence or absence of vomiting. One prospective study addressed both these variables. The cooperative kerosene poisoning (COKP) study was a multicenter study that enrolled 760 patients with hydrocarbon ingestion. Of these, 409 individuals could provide an estimate of the amount ingested. Patients who reportedly ingested more than 30 mL had a 52% chance of developing pulmonary complications, compared with 39% of those who ingested less than 10 mL. Risk of central nervous complications was 41%, compared with 24% using the same criterion. There was a 53% incidence of pulmonary toxicity when vomiting occurred, compared with 37% when there was no history of vomiting. While this knowledge may help modify the index of suspicion regarding possible pulmonary toxicity, none of these parameters is completely predictive. Severe hydrocarbon pneumonitis may occur after ingestion of "low-risk" hydrocarbons. Patients may develop severe lung injury after low-volume (<5 mL) ingestions, as well as after ingestions with no history of coughing, gagging, or vomiting.

It is widely held that aspiration is the main route of injury from ingested simple hydrocarbons. The mechanism of pulmonary injury, however, is not fully understood. Intratracheal instillation of 0.2 mL/kg of kerosene causes physiologic abnormalities in lung mechanics (decreased compliance and total lung capacity) and pathologic changes such as interstitial inflammation, polymorphonuclear exudates, intraalveolar edema and hemorrhage, hyperemia, bronchial and bronchiolar necrosis, and vascular thrombosis. These changes most likely reflect both direct toxicity to pulmonary tissue and disruption of the lipid surfactant layer.

Most patients who develop pulmonary toxicity following hydrocarbon ingestion will have an initial episode of coughing, gagging, or choking. This usually occurs within 30 minutes after ingestion and is presumptive evidence of aspiration. The majority of patients who have respiratory signs and symptoms in addition to the initial history of gagging, choking, and coughing develop radiographic pneumonitis. Pulmonary toxicity may manifest as crackles, rhonchi, bronchospasm, tachypnea, hypoxemia, hemoptysis, acute respiratory distress syndrome (hemorrhagic or nonhemorrhagic), or respiratory distress. Cyanosis develops in approximately 2% to 3% of patients. This may result from simple asphyxiant effects from volatilized hydrocarbons, from ventilation–perfusion mismatch, or, rarely, from methemoglobinemia (aniline, nitrobenzene, or nitrite-containing hydrocarbons). Clinical findings often worsen over the first several days but typically resolve within a week. Death is distinctly uncommon and typically occurs after a severe, progressive respiratory insult marked by hypoxia, ventilation–perfusion mismatch, and barotrauma.

Intravenous (IV), subcutaneous, and even intrapleural injection of hydrocarbons are reported. Severe hydrocarbon pneumonitis may occur following IV exposure. Animal
experiments show that intravascular hydrocarbons injure the first capillary bed encountered. The clinical course after IV hydrocarbon injection is comparable to that of aspiration injury.

Radiographic evidence of pneumonitis develops in 40% to 88% of patients admitted following aspiration. Findings can develop as early as 15 minutes or as late as 24 hours after exposure. Chest radiographs performed immediately on initial presentation are not useful in predicting infiltrates in either symptomatic or asymptomatic patients. Ninety percent of patients who develop radiographic abnormalities do so by 4 hours postingestion. Clinical signs of pneumonia (eg, crackles, rhonchi) are evident in 40% to 50% of patients. A small percentage (<5%) are completely asymptomatic after a period of observation, yet to have radiographic findings.

(A)
Initial: Patchy densities appear in the basilar areas of both lung fields with increased interstitial markings and peribronchial thickening.

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(B)
Day 2: More extensive diffuse alveolar infiltrates are apparent.

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(C)
Day 6: Dense consolidation and atelectasia are evident in the right lower lobe. (Used with permission of Nancy Genieser, MD, Professor of Radiology, New York University.)

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Specific radiologic findings include perihilar densities, bronchovascular markings, bibasilar infiltrates, and pneumonic consolidation. Right-sided involvement occurs in 75% of cases and bilateral involvement in approximately 50%. Upper-lobe involvement is uncommon. Pleural effusions develop in 3% of cases, with one-third appearing within 24 hours. Pneumothorax, pneumomediastinum, and pneumatoceles occur uncommonly. Initial radiographs after ingestion may reveal two liquid densities in the stomach, known as the “double-bubble” sign. This represents an air–fluid (hydrocarbon or water) and a hydrocarbon–water interface, as the hydrocarbon is not miscible with gastric (aqueous) fluid and may have a specific gravity less than that of water.

Radiographic resolution does not correlate with clinical improvement but rather lags behind by several days to weeks. There are few reports of long-term follow-up on patients with hydrocarbon
pneumonitis. Frequent respiratory tract infections are described after hydrocarbon pneumonitis, but these studies are not well controlled. Delayed formation of pneumatoceles may occur. Bronchiectasis and pulmonary fibrosis are reported but appear to be uncommon. In one study, 82% of patients examined 8 to 14 years after hydrocarbon-induced pneumonitis had asymptomatic minor pulmonary function abnormalities. The abnormalities were consistent with small-airway obstruction and loss of elastic recoil. The authors hypothesized that this group may be predisposed to chronic obstructive pulmonary disease.

Cardiac
The most concerning cardiac effect from hydrocarbon exposure is precipitation of dysrhythmias through myocardial sensitization. Malignant dysrhythmias may occur after exposure to high concentrations of volatile inhalants or inhaled anesthetics. Such events are described with all classes of hydrocarbons, but halogenated compounds are most frequently implicated, followed by aromatic compounds. Atrial fibrillation, ventricular tachycardias, junctional rhythms, ventricular fibrillation, and cardiac arrest are reported. This is termed the “sudden sniffing death syndrome.” Prolongation of the QT interval in some cases raises additional concern for the development of torsade de pointes.

Cardiac sensitization is incompletely understood. Halothane and isoflurane inactivate sodium channels, whereas chloroform and others attenuate potassium efflux through voltage-gated channels. Sensitization may be mediated by slowed conduction velocity through membrane gap junctions. Dephosphorylation of connxin-43 results in a conformational change that increases gap junctional resistance. Halocarbons, in the presence of epinephrine, cause dephosphorylation of this gap junction protein, thereby increasing resistance and slowing conduction velocity in myocardial tissue.

Any route of exposure to hydrocarbons may result in cardiotoxicity. Classically, sudden death follows an episode of sudden exertion, presumably associated with an endogenous catecholamine surge. Tachydysrhythmias, cardiomegaly, and myocardial infarction are rarely reported after ingestion of hydrocarbons. A retrospective follow-up cohort of exposed methylene chloride workers did not find evidence of excess long-term cardiac disease.

Central Nervous System
Transient CNS excitation may occur after acute hydrocarbon inhalation or ingestion, but more commonly, CNS depression or general anesthesia occurs. In cases of aspiration, hypoxemia from pulmonary damage may contribute to CNS depression. Coma and seizures are reported in 1% to 3% of cases. Chronic occupational exposure or volatile substance use may lead to a chronic neurobehavioral syndrome, the painter’s syndrome, most notably described after toluene overexposure. Clinical features include ataxia, spasticity, dysarthria, and dementia, consistent with leukoencephalopathy. Autopsy studies of the brains of chronic toluene abusers show atrophy and mottling of the white matter, as though the lipid-based myelin were dissolved away. Microscopic examination shows a consistent pattern of myelin and oligodendrocyte loss with relative preservation of axons. Animal models of toluene poisoning reveal norepinephrine and dopamine
depletion. The severity and reversibility of this syndrome depends on the intensity and duration of toluene exposure. Infrequent exposure may produce no clinical neurologic signs, whereas severe (daily) use can lead to significant neurologic impairment after as little as 1 year, but more commonly after 2 to 4 years of continuous exposure. The specific cognitive and neuropsychological findings in toluene-induced dementia have been termed a white matter dementia. Initial findings of white matter dementia include behavioral changes, impaired sense of smell, impaired capacity to concentrate, and mild unsteadiness of hand movements and gait. Further exposure leads to slurred speech, head tremor, poor vision, deafness, stiff-legged and staggering gait, and subsequent dementia. Physical findings may include nystagmus, ataxia, tremor, spasticity with hyperreflexia, plantar extension, deafness, impaired vision, and a broad-based, staggering gait. An abnormal brainstem auditory-evoked response appears to be a sensitive indicator of toluene-induced CNS damage. The electroencephalogram can show mild, diffuse slowing. Computed tomography in severe cases shows mild-to-moderate cerebellar and cortical atrophy. Magnetic resonance imaging (MRI) findings are consistent with white matter disease. Most cases show clinical improvement after 6 months of abstinence, although with moderate to severe abuse, improvement may be incomplete. While toluene abuse is addicting, withdrawal or abstinence syndrome is surprisingly uncommon and, when present, appears relatively benign.

Exposures in the occupational setting are rarely as extreme as those that occur with intentional volatile substance misuse. Given the significantly lesser exposures, the findings among workers overexposed to solvent concentrations above permissible exposure limits are often subclinical and detected primarily through neurobehavioral testing. In rare cases, however, a worker may be acutely overexposed to solvent concentrations that can produce acute CNS depression. Repeated, symptomatic overexposures over a protracted period of time have the potential to lead to a chronic encephalopathy, as evident from the experience with solvent abusers.

Peripheral Nervous System
Peripheral neuropathy is well described following occupational exposure to \(n\)-hexane or methyl-\(n\)-butyl ketone (MnBK). This axonopathy results from a common metabolic intermediate, 2,5-hexanedione. The mechanism by which this intermediate causes peripheral neuropathy probably relates to decreased phosphorylation of neurofilament proteins, with disruption of the axonal cytoskeleton. Methyl ethyl ketone may exacerbate this neurotoxicity, probably by interfering with metabolic pathways of \(n\)-hexane and MnBK. Other organic solvents, such as carbon disulfide, acrylamide, and ethylene oxide, may cause a similar peripheral axonopathy. Cranial and peripheral neuropathies are reported after acute and chronic exposure to trichloroethylene (TCE). Pathologically, TCE appears to induce a myelinopathy.

TCE exposure is associated with trigeminal neuralgia. Symptoms can develop within 12 hours of a single intense exposure and persist for many years. Trigeminal nerve damage was documented by evoked potentials following 15 minutes of TCE inhalation. Some evidence suggests that decomposition products or impurities in TCE may be responsible for cranial neuropathy.
Axonopathy from MnBK or n-hexane exposure typically begins in the distal extremities and progresses proximally (a classic, “dying-back” neuropathy) (Chap. 24). Exposure to one of these hydrocarbons should be considered in the differential diagnosis of the patient with Guillain-Barré syndrome (GBS), although sensory findings are present with MnBK and absent in GBS. The longest axons appear to be affected initially, so that the patient manifests a “length-dependent polyneuropathy.” With discontinuation of exposure many of the effects reverse over weeks to months. Alternatively, the phenomenon of “coasting” may occur, in which neuropathy progresses for a time (weeks to months) after discontinuation of the toxic insult. A reversible peripheral neuropathy occurred in 40% of chronic toluene abusers and was characterized by severe motor weakness without sensory deficits or areflexia. It is unclear whether the toluene in this series might have been contaminated by n-hexane or MnBK.

**Gastrointestinal**

Hydrocarbons irritate gastrointestinal mucous membranes. Nausea and vomiting are common after ingestion. As discussed earlier, vomiting may increase the risk of pulmonary toxicity. Hematemesis was reported in 5% of cases in one study, and gastrointestinal ulcerations are reported in animal studies.

**Hepatic**

The chlorinated hydrocarbons (Table 108–1) and their metabolites are hepatotoxic. In most cases, activation occurs via a phase I reaction to form a reactive intermediate (Chap. 13). In the case of carbon tetrachloride, this intermediate is the trichloromethyl radical. This radical forms covalent bonds with hepatic macromolecules and may initiate lipid peroxidation. Carbon tetrachloride causes centrilobular necrosis after inhalational, oral, or dermal exposure. Hepatotoxicity in animals has been ranked for common hydrocarbons as follows: carbon tetrachloride is greater than benzene, and trichloroethylene is greater than pentane. Vinyl chloride is a liver carcinogen, and trichloroethylene, tetrachloroethylene, and 1,1,1-trichloroethane are considered less acutely hepatotoxic than vinyl chloride. Hepatotoxicity rarely follows ingestion of petroleum distillates. Hepatic injury, manifested as aminotransferase elevation and hepatomegaly, is usually reversible except in massive exposures.

**Renal**

Halogenated hydrocarbons such as chloroform, carbon tetrachloride, ethylene dichloride, tetrachloroethane, 1,1,1-trichloroethane, and TCE are nephrotoxic. Acute kidney injury (AKI) and distal renal tubular acidosis occur in some painters and volatile-substance abusers. Toluene causes a renal tubular acidosislike syndrome (see Toluene later in the chapter). 

**Hematologic**

Hemolysis has been sporadically reported to occur following hydrocarbon ingestion. One retrospective study of 12 patients showed hemolysis in three individuals and disseminated intravascular coagulation in another. Although one patient required transfusion, hemolysis is usually mild and typically does not require red blood cell transfusion (also see discussion of the effects of benzene on bone marrow, under Benzene later in the chapter).

**Immunologic**
Hydrocarbons disturb the integrity of membrane lipid bilayers, causing swelling and increased permeability to protons and other ions. This alters the structural and functional integrity of the membrane. Changes in the lipid composition of the membrane occur, and membrane lipopolysaccharides and proteins are disturbed. Resultant toxicity may directly destroy capillary endothelium. Additionally, there appears to be significant basement membrane dysfunction, and this is postulated to underlie both alveolar and glomerular toxicity of hydrocarbons. Immune mechanisms may account for basement membrane dysfunction in chronic exposures. Hydrocarbon exposure is suggested as one possible cause of the Goodpasture syndrome (immune dysfunction causing both pulmonary damage and glomerulonephritis), although the association is not widely accepted. Measurable changes in immune function occur after hydrocarbon exposure, but our knowledge of any clinical relevance is incomplete.

**Dermatologic**

Most hydrocarbon solvents cause nonspecific irritation of skin and mucous membranes. Repeated, prolonged contact can dry and crack the skin. The mechanism of dermal injury appears to be defatting of the lipid layer of the stratum corneum. Up to 9% of workers may develop eczematous lesions from dermal contact. Limonene and turpentine contain sensitizers that can rarely result in contact allergy (Chap. 18).

Contact dermatitis and blistering may progress to partial- and even full-thickness burns. Severity is proportional to duration of exposure. Hydrocarbons are irritating to skin. Acute, prolonged exposure can cause dermatitis and even full-thickness dermal damage. Chronic dermal exposure to kerosene or diesel fuel can cause oil folliculitis. A specific cutaneous lesion called chloracne is associated with exposure to chlorinated aromatic hydrocarbons with highly specific stereochemistry such as dioxins and polychlorobiphenyls.

Soft tissue injection of hydrocarbon is locally toxic, leading to necrosis. Secondary cellulitis, abscess formation, and fasciitis can occur. Infectious complications are treated by meticulous wound care, with surgical débridement as necessary. A particularly destructive injury involves high-pressure injection gun injury. These injuries typically involve the extremities, with high-pressure injection of grease or paint into the fascial planes and tendon sheaths. Emergent surgical débridement is necessary in most of these cases.

**HYDROCARBONS WITH SPECIFIC AND UNIQUE TOXICITY**

*n*-Hexane

Hexane is a six-carbon simple aliphatic hydrocarbon. It is a constituent of some brake-cleaning fluids, rubber cement, glues, spray paints, coatings, and silicones. Outbreaks of *n*-hexane–related neurotoxicity have occurred in printing plants, sandal shops, furniture factories, and automotive repair shops. Human exposure occurs primarily by inhalation. Both *n*-hexane and MnBK are well-known peripheral neurotoxins that cause a classic “dying-back” peripheral polyneuropathy.
Neurotoxicity does not appear to be directly caused by the parent compounds but results from a common metabolic intermediate—2,5-hexanedione. Toxicity appears related to the ability of this intermediate to form a ringed pyrrole structure, which causes decreased phosphorylation of neurofilament proteins, disrupting the axonal cytoskeleton. Similar five- and seven-carbon species do not induce similar neurotoxicity, except those that are direct precursor intermediates in the metabolic pathway producing 2,5-hexanedione (Fig. 108–2).

FIGURE 108–2.
The metabolism of both organic solvents n-hexane and methyl n-butyl ketone produces the same common metabolite, 2,5-hexanedione.

Methylene Chloride
Methylene chloride is commonly found in paint removers, cleansers, degreasers, and aerosol propellants. Like other halogenated hydrocarbons, it can rapidly induce general anesthesia by inhalation or ingestion. Unlike other hydrocarbon agents, methylene chloride and similar one carbon halomethanes such as methylene dibromide are metabolized by liver P450 2E1 mixed-function oxidase to carbon monoxide. Significant, delayed, and prolonged carboxyhemoglobinemia can occur (Table 108–2 and Chap. 125).

Carbon Tetrachloride
Carbon tetrachloride (CCl₄), although not actually a hydrocarbon, has been used as an industrial solvent and reagent. Its use in the United States has declined dramatically since recognition of its toxicity caused the Environmental Protection Agency to restrict its commercial use. Absorption occurs by all routes, including dermal. CCl₄ is an irritant to skin and mucous membranes and gastric mucosa when ingested. As in the case of other halogenated hydrocarbons, aspiration can result in pneumonitis, and systemic absorption may result in ventricular dysrhythmias.

CCl₄ exposures are hepatotoxic and nephrotoxic. Both occur more commonly with repetitive occupational exposure. Toxicity follows phase-I dehalogenation of the parent compound, which produces free radicals and causes lipid peroxidation and the production of protein adducts. Localization of specific phase I hepatic enzymes in the centrilobular area of the liver results in regionalized (zone 3) centrilobular injury after CCl₄ exposure (Chap. 23). Hepatotoxicity is typically manifested as reversible aminotransferase concentration elevations with or without hepatomegaly. Cirrhosis is reported in both animal models and in humans with prolonged excessive exposures. Nephrotoxicity is less studied but may result from a similar mechanism. CCl₄ is a suspected human carcinogen.

Trichloroethylene
TCE is a commonly used industrial solvent, cleanser, and degreaser. Systemically absorbed TCE, as might occur in the occupational setting, may competitively inhibit aldehyde dehydrogenase. Concomitant ethanol consumption may result in a disulfiramlike reaction that has been termed “degreaser’s flush” (Chap. 79).

TCE was used for years as a general anesthetic, and hundreds of disposal sites in the United States remain sources of ongoing human exposure. The use of TCE as a general anesthetic was abandoned because of associated acute cardiotoxicity. TCE is also hepatotoxic, neurotoxic, and nephrotoxic in humans and animals. TCE exposure is linked to the development of neurodegenerative diseases, such as parkinsonism. Evidence suggests that TCE is a human carcinogen.

**Benzene**

Benzene is hematotoxic and associated with acute hemolysis or with the delayed development of aplastic anemia and acute myelogenous leukemia. Other aromatic hydrocarbons that are reported to cause similar hematologic effects most likely are contaminated with benzene. An excess risk of hematologic toxicity has not been demonstrated in groups with long-term exposure to toluene, xylene, or other aromatic hydrocarbons. Other hematologic malignancies also may be linked to benzene, including chronic myelocytic leukemia, myelodysplastic syndromes, and lymphoma. Chromosomal changes are believed to provide a marker for carcinogenicity. Because of the carcinogenic risk, most benzene-based solvents have been removed from the US market, and the Occupational Safety and Health Administration has limited the permissible worker exposure concentration to 1 ppm.

**Toluene**

Toluene has essentially replaced benzene as the primary organic solvent in many commercial products. Many oil paints and stains primarily contain toluene as solvent. As such, it is readily available and readily abused as an inhalant. The CNS sequelae of chronic solvent inhalation are most frequently related to chronic toluene exposure.

Chronic toluene abuse can also cause a syndrome that resembles transient distal renal tubular acidosis (RTA). Although the mechanism is incompletely understood, the acidosis results in great part from the urinary excretion of hippuric acid (Table 108–2). Renal potassium loss may be severe and can result in symptomatic hypokalemia. Clinical findings are a hyperchloremic metabolic acidosis, hypokalemia, and aciduria. Typically an associated transient azotemia occurs, as well as proteinuria and an active urine sediment. Some also report a proximal RTA, or the Fanconi syndrome. A metabolic acidosis resulting from the metabolism of toluene to benzyl alcohol through alcohol dehydrogenase to benzoic acid may be an adequate explanation for the serum and urine acid–base disturbances.

**Pine Oil and Terpenes**

Pine oil is an active ingredient in many household cleaning products. It is a mixture of unsaturated hydrocarbons composed of terpenes, camphenes, and pinenes. The major components are
terpenes, which are found in plants and flowers. Wood distillates including pine oil and turpentine are derived from pine trees. Patients who ingest pine oil often emit a strong pine odor. Wood distillates are readily absorbed from the gastrointestinal tract, and ingestion may cause CNS and pulmonary toxicity without aspiration.

The clinical features of pine oil ingestion can include CNS depression, respiratory failure, and gastrointestinal dysfunction, which are rarely fatal. Aspiration pneumonitis remains the primary clinical concern. Acute toxicity and management are similar to that of petroleum distillate ingestion. Rare reported complications of wood distillate ingestion include turpentine-associated thrombocytopenic purpura, AKI, and hemorrhagic cystitis.

**Lipoid Pneumonia**

Ingestion of low-viscosity hydrocarbons poses risk of pulmonary aspiration with subsequent acute pneumonitis. Conversely, viscous hydrocarbons rarely lead to pulmonary aspiration. Alternatively, inhalation of aerosolized oil droplets can occur in various occupational settings, and exogenous lipoid pneumonia may result. The most common xenobiotics involved are mineral or vegetable oils.

Initially, inhaled oil droplets are emulsified in the alveoli by surfactant, and then they are engulfed by alveolar macrophages. Unfortunately, the macrophages are unable to readily process the internalized, exogenous oil. Microscopically, persistent cytoplasmic droplets give a “foamy” appearance to these “lipophages” that may persist for weeks to years. Not uncommonly, the initial manifestations are limited or even subclinical, but once symptoms arise, illness may be prolonged from months to years. Ultimately, irreversible proliferative fibrosis may develop.

Silicone-based polymers share structural similarities and some physical properties with long-chain hydrocarbons. Silicone polymers such as dimethicone exist as oily, viscous liquids at room temperature are widely used as lubricants, antifoaming agents, and even as medicine and food additives. Pulmonary aspiration or inhalation of aerosolized silicone droplets causes clinical pneumonitis that is indistinguishable from that caused by their viscous hydrocarbon counterparts. The time course of lung injury is similarly protracted, and complications may be expected.

**Tar and Asphalt Injury**

Tar and asphalt injuries are common occupational hazards among construction workers. Asphalt workers are at risk for toxic gas exposure of hydrogen sulfide, carbon monoxide, propane, methane, and volatilized hydrocarbons. In addition, cutaneous exposure to these hot hydrocarbon mixtures can cause severe burns. The material quickly hardens and is very difficult to remove. However, immediate cooling with cold water is important to limit further thermal injury. Complete removal is essential to ensure proper burn management and to limit infectious complications. Attempts to remove hardened tar or asphalt mechanically often cause further damage. Dissolving the material with mineral oil, petroleum jelly, or antibacterial ointments are met with variable success. Surface-active agents combined with an ointment (De-Solv-it, Tween-80, Polysorbate 80) are more effective.
DIAGNOSTIC TESTING

Laboratory and ancillary testing for hydrocarbon toxicity should be guided by available information regarding the specific xenobiotic, the route of exposure, and the best attempt at quantifying the exposure. Inhalation or ingestion of hydrocarbons associated with pulmonary aspiration is most likely to result in pulmonary toxicity. The use of pulse oximetry, end-tidal CO₂, and arterial blood gas testing in this group of patients is warranted when clinically indicated. Early radiography is indicated in patients who are severely symptomatic; however, radiographs performed immediately after hydrocarbon ingestion have a poor predictive value for the occurrence of aspiration pneumonitis. In the asymptomatic patient, early radiography is not cost effective. Patients observed for 6 hours after an ingestion, who adequate oxygenation, are not tachypneic, demonstrate no abnormal pulmonary findings, and have a normal chest radiograph obtained after the 6-hour observation period have a good medical prognosis with very low risk of subsequent deterioration.

The choice of specific diagnostic laboratory tests to assess organ system toxicity or function following exposure to a hydrocarbon depends on the type, dose, and route of exposure, and on the assessment of the patient’s clinical condition. Useful clinical tests may include pulse oximetry, end-tidal CO₂, and an ECG. Laboratory tests may include serum or urine electrolytes, venous or arterial blood gas, complete blood counts, and creatine phosphokinase as clinically indicated. If a hydrocarbon has specific target organ toxicities (eg, benzene/bone marrow, CCl₄/liver, or n-hexane/peripheral nervous system), evaluating and monitoring target organ system function is indicated.

Specific diagnostic testing for hydrocarbon poisoning can include (a) bioassays for the specific hydrocarbon or its metabolites in blood, breath, or urine, or (b) assessment of toxicity. Bioassays for a hydrocarbon are seldom necessary for diagnosis or management of hydrocarbon poisoning in the emergency setting and rarely clinically available. Exceptions might include testing to assist in differential diagnosis (eg, testing for CCl₄ in a comatose patient with unexplained hepatic and renal toxicity or a carboxyhemoglobin determination in a paint stripper with chest pain), testing for worker compensation purposes (eg, testing for urinary trichloroethanol and trichloroacetic acid in a worker exposed to TCE with unexplained bouts of dizziness), or for forensic purposes (eg, sudden death in a huffer).

Chronic overexposures to hydrocarbons, as occur with volatile substance use, can result in persistent damage to the CNS. Damage can be detected and quantified using neuroimaging methods such as MRI or positron emission tomography. Major MRI findings in patients with chronic toluene abuse include atrophy, white matter T2 hyperintensity, and T2 hypointensity involving the basal ganglia and thalamus. Neurobehavioral testing can be used to detect subtle central nervous system effects following chronic occupational overexposures.

MANAGEMENT
Identification of the specific type, route, and amount of hydrocarbon exposure is rarely essential to achieve effective management.

Decontamination is one of the cardinal principles of toxicology, with priority that is second only to stabilization of the cardiopulmonary status. Safe decontamination can avoid further absorption and also avoids secondary casualties in those attempting to provide care. Protection of rescuers with appropriate personal protective equipment and rescue protocols is paramount, especially in situations where the victim has lost consciousness. The principle of removing the patient from the exposure (eg, vapor or gaseous hydrocarbon) or the exposure from the patient (eg, hydrocarbon liquid on skin or clothing), while protecting the rescuer, implies that personal protective equipment be considered at each level of the health care delivery system.

Exposed clothing should be removed and safely discarded as further absorption or inhalation of hydrocarbons from grossly contaminated clothing can worsen systemic toxicity. Decontamination of the skin should have a high priority in massive hydrocarbon exposures, particularly those exposures involving highly toxic hydrocarbons. Water alone may be ineffective in decontaminating most hydrocarbons, but early decontamination with soap and water may be adequate. The caregiver should remain aware that certain hydrocarbons are highly flammable and pose a fire risk to hospital staff (Chap. 131).

Several studies have attempted to evaluate the role of gastric decontamination after hydrocarbon ingestion. Results were largely inconclusive and the level of evidence, poor. In the subset of patients who were randomized to receive gastric lavage, 44% had pulmonary complications, compared with 47% of those who were not lavaged. Although available studies do not offer a conclusive answer to the question of gastric emptying after hydrocarbon ingestion, the high incidence of spontaneous emesis and the risk of aspiration essentially eliminate any consideration of gastric emptying in all but the rarest of cases.

Activated charcoal (AC) has limited ability to decrease gastrointestinal absorption of hydrocarbons and may distend the stomach and predispose patients to vomiting and aspiration. The use of AC may be justified in patients with mixed overdoses, but its role in isolated hydrocarbon ingestions appears very limited.

Antibiotics were once frequently administered in the setting of hydrocarbon pneumonitis to treat possible bacterial superinfection, and they are still occasionally used today as fever and infiltrates are common. Although animal models rapidly demonstrate superinfection, prophylactic antibiotics only appear to alter pulmonary flora. Prophylactic antibiotics did not affect length of stay or otherwise impact the outcome of 48 pediatric patients admitted for respiratory distress from hydrocarbon poisoning. Similarly, in a randomized controlled study of pediatric patients suffering from kerosene-induced pneumonitis, prophylactic amoxicillin did not affect signs or symptoms, the rate of clinical deterioration (treatment failure), or duration of hospitalization. However, antibiotic administration may be justified in severely poisoned patients. Ideally, sputum Gram stain or culture results should direct antibiotic use.
Corticosteroids, like antibiotics, have been prophylactically administered in the setting of hydrocarbon pulmonary toxicity. The rationale for their use is prevention and limitation of the pulmonary inflammatory response after hydrocarbon injury. Animal models do not show any benefit of corticosteroid administration and may increase the risk of bacterial superinfection. Furthermore, a controlled human trial failed to show a benefit from corticosteroid administration. It is clear that corticosteroid use does not improve the acute course of hydrocarbon pulmonary toxicity, although some authors suggest improved outcome with delayed corticosteroid therapy there is little supporting evidence. Coupled with the possible increased risk of bacterial superinfection, corticosteroid administration in this setting is not recommended.

Patients with severe hydrocarbon toxicity pose unique problems for management. Respiratory distress requiring mechanical ventilation in this setting may be associated with a large ventilation-perfusion mismatch. The use of positive end-expiratory pressure (PEEP) in this setting is often beneficial. However, very high levels of PEEP may be required, with subsequent increased risk of barotrauma. High-frequency jet ventilation (HFJV), using very high respiratory rates (220–260) with small tidal volumes, has helped to decrease the need for PEEP. Patients who continue to have severe ventilation-perfusion mismatch despite PEEP and HFJV have benefited from extracorporeal membrane oxygenation (ECMO). ECMO appears to be a useful option in severe pulmonary toxicity after other treatments have failed. Early administration of surfactant may reduce pulmonary toxicity, but experience under these circumstances is limited.

Cyanosis is uncommon after hydrocarbon toxicity. Although this is most often caused by severe hypoxia, methemoglobinemia associated with hydrocarbon exposure is reported. The potential for methemoglobinemia should be investigated in patients who remain cyanotic following normalization of arterial oxygen tension (Chap. 127).

Hypotension in severe hydrocarbon toxicity raises additional concerns. The etiology of hypotension in this setting is often compromise of cardiac output because of high levels of PEEP. Hydrocarbons do not have significant direct cardiovascular effects, and decreasing the PEEP may improve hemodynamics. The use of β-adrenergic agonists such as dopamine, epinephrine, isoproterenol, and norepinephrine should be avoided if possible, as certain hydrocarbons predispose to dysrhythmias.

Management of dysrhythmias associated with hydrocarbon toxicity should include consideration of electrolyte and acid–base abnormalities such as hypokalemia and acidosis result from toluene, hypoxemia, hypotension, and hypothermia. Ventricular fibrillation poses a specific concern, as common resuscitation algorithms recommend epinephrine administration to treat this rhythm. If it is ascertained that the dysrhythmia emanates from myocardial sensitization by a hydrocarbon solvent, catecholamines should be avoided. In this setting, lidocaine has been used successfully, as have β-adrenergic antagonists.

Hyperbaric oxygen (HBO) was studied in a rat model of severe kerosene-induced pneumonitis. HBO at 4 ATA showed some benefit in 24-hour survival rates. No follow-up studies
have been performed. Patients with CCl₄ poisoning, however, may benefit from hyperbaric oxygen⁴ (Antidotes in Depth: A37).

In the past, hospital admission was routinely recommended for patients who ingested hydrocarbons, because of concern over possible delayed symptom onset and progression of toxicity. Several reports documented patients with relatively asymptomatic presentations who rapidly decompensated with respiratory compromise. However, progressive symptoms after hydrocarbon ingestion are rare,⁸ and these recommendations predate noninvasive assessments of gas exchange. In a retrospective study of 950 patients, only 14 (1.5%) had progression of pulmonary toxicity.⁸ Of these 14, seven had persistence of symptoms for less than 24 hours. Eight hundred patients were asymptomatic on initial evaluation with normal chest radiographs, remained asymptomatic after 6 to 8 hours of observation, and had a normal repeat radiograph. No patient in this group of 800 had progressive symptoms, and all were discharged without clinical deterioration. Seventy-one of the 950 patients had initial respiratory symptoms but were asymptomatic at initial medical evaluation. Of the 71 patients, 36 had radiographic evidence of pneumonitis. Of these 36 patients, two (6%) developed progression of pulmonary symptoms during the 6-hour observation period. Of the 35 who had a normal radiograph, two (6%) developed pulmonary symptoms and radiographic pneumonitis during the 6-hour observation period. The four patients who were hospitalized for progression of symptoms became asymptomatic over the next 24 hours and had no complications.

A separate poison center–based study evaluated 120 asymptomatic patients over an 18-hour telephone follow-up period.⁴ Sixty-two patients had initial pulmonary symptoms that quickly resolved. One of the 62 patients (1.6%) developed progressive pulmonary toxicity. This patient was hospitalized and had resolution of symptoms within 24 hours without complications.

A number of investigators have suggested protocols for determining which patients can be safely discharged.⁸¹⁄₂⁴ None of these protocols has been prospectively validated. However, rational guidelines for hospitalization can be recommended. Those patients who have clinical evidence of toxicity, and most individuals with intentional ingestions, should be hospitalized. Patients who do not have any initial symptoms, have normal chest radiographs obtained at least 6 hours after ingestion, and who do not develop symptoms during the 6-hour observation period can be safely discharged. Care should be individualized for patients who are asymptomatic but who have radiographic evidence of hydrocarbon pneumonitis and for patients who have initial respiratory symptoms but quickly become asymptomatic during medical evaluation. Reliable patients may be considered for possible discharge with next-day follow-up.

**SUMMARY**

- Hydrocarbons are a diverse group of xenobiotics that can cause toxicity by inhalation, ingestion, or dermal absorption.
- Populations at particular risk for toxicity include children who ingest hydrocarbon compounds, workers who are occupationally exposed by inhalation or dermal absorption, and youths who intentionally inhale volatile hydrocarbons.

- Aspiration pneumonitis is the primary concern after hydrocarbon ingestion, with the risk of aspiration dependent on many factors including viscosity, volatility, surface tension, amount ingested, and the presence of emesis.

- Many hydrocarbons are poorly absorbed from the gastrointestinal tract and unlikely to produce systemic poisoning. Acute systemic toxicity is unlikely to occur in the absence of CNS effects such as excitation or sedation.

- An exposed child who is asymptomatic after 6 hours of observation and who has a normal chest radiograph taken after 6 hours of observation is most likely safe for discharge.

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