06 - 20.6 Inhalant Related Disorders

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fifth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-5) excludes anesthetic gases (e.g., nitrous oxide and ether) and short-acting vasodilators (e.g., amyl nitrite) from the inhalant-related disorders, which are classified as other (or unknown) substance-related disorders and are discussed in Section 20.12. EPIDEMIOLOGY Inhalant substances are easily available, legal, and inexpensive. These three factors contribute to the high use of inhalants among poor persons and young persons.

Approximately 6 percent of persons in the United States had used inhalants at least once, and about 1 percent of persons are current users. Among young adults 18 to 25 years of age, 11 percent had used inhalants at least once, and 2 percent were current users. Among adolescents 12 to 17 years of age, 7 percent had used inhalants at least once, and 1.1 percent were current users. In one study of high school seniors, 18 percent reported having used inhalants at least once, and 2.7 percent reported having used inhalants within the preceding month. White users of inhalants are more common than either black or Hispanic users. Most users (up to 80 percent) are male. Some data suggest that inhalant use may be more common in suburban communities in the United States than in urban communities. Inhalant use accounts for 1 percent of all substance-related deaths and less than 0.5 percent of all substance-related emergency room visits. About 20 percent of the emergency room visits for inhalant use involve persons younger than 18 years of age. Inhalant use among adolescents may be most common in those whose parents or older siblings use illegal substances. Inhalant use among adolescents is also associated with an increased likelihood of conduct disorder or antisocial personality disorder. NEUROPHARMACOLOGY Inhalants most used by American adolescents are (in descending order) gasoline, glue (which usually contains toluene), spray paint, solvents, cleaning fluids, and assorted other aerosols. Sniffing vapor through the nose or huffing (taking deep breaths) through the mouth leads to transpulmonary absorption with very rapid drug access to the brain. Breathing through a solvent-soaked cloth, inhaling fumes from a glue-containing bag, huffing vapor sprayed into a plastic bag, or breathing vapor from a gasoline can are common. Approximately 15 to 20 breaths of 1 percent gasoline vapor produce several hours of intoxication. Inhaled toluene concentrations from a glue-containing bag may reach 10,000 ppm, and vapors from several tubes of glue may be inhaled each day. By comparison, one study of just 100 ppm of toluene showed that a 6-hour exposure produced a temporary neuropsychological performance decrement of approximately 10 percent. Inhalants generally act as a central nervous system (CNS) depressant. Tolerance for inhalants can develop, although withdrawal symptoms are usually fairly mild. Inhalants are rapidly absorbed through the lungs and rapidly delivered to the brain. The effects appear within 5 minutes and can last for 30 minutes to several hours, depending on the inhalant substance and the dose. The concentrations of many inhalant substances in blood are increased when used in combination with alcohol, perhaps because of competition for hepatic enzymes. Although about one fifth of an inhalant substance is excreted unchanged by the lungs, the remainder is metabolized by the liver. Inhalants are detectable in the blood for 4 to 10 hours after use, and blood samples should be taken in the emergency room when inhalant use is suspected. Much like alcohol, inhalants have specific pharmacodynamic effects that are not well understood. Because their effects are generally similar and additive to the effects of

other CNS depressants (e.g., ethanol, barbiturates, and benzodiazepines), some investigators have suggested that inhalants operate by enhancing the γ-aminobutyric acid (GABA) system. Other investigators have suggested that inhalants work through membrane fluidization, which has also been hypothesized to be a pharmacodynamic effect of ethanol. DIAGNOSIS Inhalant Use Disorder

Most persons probably use inhalants for a short time without developing a pattern of long-term use resulting in dependence and abuse. Nonetheless, dependence and abuse of inhalants occur and are diagnosed according to the DSM-5 (see page 621). Inhalant Intoxication The diagnostic criteria for inhalant intoxication specify the presence of maladaptive behavioral changes and at least two physical symptoms. The intoxicated state is often characterized by apathy, diminished social and occupational functioning, impaired judgment, and impulsive or aggressive behavior, and it can be accompanied by nausea, anorexia, nystagmus, depressed reflexes, and diplopia. With high doses and long exposures, a user's neurological status can progress to stupor and unconsciousness, and a person may later be amnestic for the period of intoxication. Clinicians can sometimes identify a recent user of inhalants by rashes around the patient's nose and mouth; unusual breath odors; the residue of the inhalant substances on the patient's face, hands, or clothing; and irritation of the patient's eyes, throat, lungs, and nose. The disorder can be chronic, as in the following case. A 16-year-old single Hispanic female was referred to a university substancetreatment program for evaluation. The patient had been convicted for auto theft, menacing with a weapon, and being out of control by her family. By age 15, she had regularly been using inhalants and drinking alcohol heavily. She had tried typewritererasing fluid, bleach, tile cleaner, hairspray, nail polish, glue, and gasoline, but preferred spray paint. She had sniffed paint many times each day for about 6 months at age 15, using a maximum of eight paint cans per day. The patient said, "It blacks out everything." Sometimes she had lost consciousness, and she believed that the paint had impaired her memory and made her "dumb." (Courtesy of Thomas J. Crowley, M.D.) Inhalant Intoxication Delirium Delirium can be induced by the effects of the inhalants themselves, by pharmacodynamic interactions with other substances, and by the hypoxia that may be

associated with either the inhalant or its method of inhalation. If the delirium results in severe behavioral disturbances, short-term treatment with a dopamine receptor antagonist, such as haloperidol (Haldol), may be necessary. Benzodiazepines should be avoided because of the possibility of increasing the patient's respiratory depression. Inhalant-Induced Persisting Dementia Inhalant-induced persisting dementia, as with delirium, may result from the neurotoxic effects of the inhalants themselves; the neurotoxic effects of the metals (e.g., lead) commonly used in inhalants; or the effects of frequent and prolonged periods of hypoxia. The dementia caused by inhalants is likely to be irreversible in all but the mildest cases. Inhalant-Induced Psychotic Disorder Clinicians can specify hallucinations or delusions as the predominant symptoms. Paranoid states are probably the most common psychotic syndromes during inhalant intoxication. Inhalant-Induced Mood Disorder and Inhalant-Induced Anxiety Disorder Inhalant-induced mood disorder and inhalant-induced anxiety disorder allow the classification of inhalant-related disorders characterized by prominent mood and anxiety symptoms. Depressive disorders are the most common mood disorders associated with inhalant use, and panic disorders and generalized anxiety disorder are the most common anxiety disorders. Other Inhalant-Induced Disorders Other Inhalant-Induced Disorder is the recommended DSM-5 diagnosis for inhalantrelated disorders that do not fit into one of the diagnostic categories discussed earlier. CLINICAL FEATURES In small initial doses, inhalants can be disinhibiting and produce feelings of euphoria and excitement as well as pleasant floating sensations, the effects for which persons presumably use the drugs. High doses of inhalants can cause psychological symptoms of fearfulness, sensory illusions, auditory and visual hallucinations, and distortions of body size. The neurological symptoms can include slurred speech, decreased speed of talking, and ataxia. Long-term use can be associated with irritability, emotional lability, and impaired memory. Tolerance for the inhalants does develop for some users; a

withdrawal syndrome can accompany the cessation of inhalant use. The withdrawal syndrome does not occur frequently; when it does, it can be characterized by sleep disturbances, irritability, jitteriness, sweating, nausea, vomiting, tachycardia, and (sometimes) delusions and

hallucinations. Organ Pathology and Neurological Effects Inhalants are associated with many potentially serious adverse effects. The most serious of these is death, which can result from respiratory depression, cardiac arrhythmias, asphyxiation, aspiration of vomitus, or accident or injury (e.g., driving while intoxicated with inhalants). Placing an inhalant-soaked rag and one's head into a plastic bag, a common procedure for inhalant users, can cause coma and suffocation. Chronic inhalant users may have numerous neurological problems. Computed tomography (CT) and magnetic resonance imaging (MRI) reveal diffuse cerebral, cerebellar, and brainstem atrophy with white matter disease, a leukoencephalopathy. Single photon emission CT (SPECT) of former solvent-abusing adolescents showed both increases and decreases of blood flow in different cerebral areas. Several studies of house painters and factory workers who have been exposed to solvents for long periods also have found evidence of brain atrophy on CT scans, with decreased cerebral blood flow. Neurological and behavioral signs and symptoms can include hearing loss, peripheral neuropathy, headache, paresthesias, cerebellar signs, persisting motor impairment, parkinsonism, apathy, poor concentration, memory loss, visual-spatial dysfunction, impaired processing of linguistic material, and lead encephalopathy. White matter changes, or pontine atrophy on MRI, have been associated with worse intelligence quotient (IQ) test results. The combination of organic solvents with high concentrations of copper, zinc, and heavy metals has been associated with the development of brain atrophy, temporal lobe epilepsy, decreased IQ, and a variety of electroencephalography (EEG) changes. Other serious adverse effects associated with long-term inhalant use include irreversible hepatic disease or renal damage (tubular acidosis) and permanent muscle damage associated with rhabdomyolysis. Additional adverse effects include cardiovascular and pulmonary symptoms (e.g., chest pain and bronchospasm) as well as gastrointestinal (GI) symptoms (e.g., pain, nausea, vomiting, and hematemesis). There are several clinical reports of toluene embryopathy, with signs such as those of fetal alcohol syndrome. These include low birth weight, microcephaly, shortened palpebral fissures, small face, low-set ears, and other dysmorphic signs. These babies reportedly develop slowly, show hyperactivity, and have cerebellar dysfunction. No convincing evidence indicates, however, that toluene, the best-studied inhalant, produces genetic damage in somatic cells. TREATMENT Inhalant intoxication, as with alcohol intoxication, usually requires no medical attention and resolves spontaneously. However, effects of the intoxication, such as coma, bronchospasm, laryngospasm, cardiac arrhythmias, trauma, or burns, need treatment. Otherwise, care primarily involves reassurance, quiet support, and attention to vital

signs and level of consciousness. Sedative drugs, including benzodiazepines, are contraindicated because they worsen inhalant intoxication. No established treatment exists for the cognitive and memory problems of inhalantinduced persisting dementia. Street outreach and extensive social service support have been offered to severely deteriorated, inhalant-dependent, homeless adults. Patients may require extensive support within their families or in foster or domiciliary care. The course and treatment of inhalant-induced psychotic disorder are like those of inhalant intoxication. The disorder is brief, lasting a few hours to (at most) a very few weeks beyond the intoxication. Appropriate is vigorous treatment of such lifethreatening complications as respiratory or cardiac arrest, together with conservative management of the intoxication itself. Confusion, panic, and psychosis mandate special attention to patient safety. Severe agitation may require cautious

control with haloperidol (5 mg intramuscularly per 70 kg body weight). Sedative drugs should be avoided because they may aggravate the psychosis. Inhalant-induced anxiety and mood disorders may precipitate suicidal ideation, and patients should be carefully evaluated for that possibility. Antianxiety medications and antidepressants are not useful in the acute phase of the disorder; they may be of use in cases of a coexisting anxiety or depressive illness. Day Treatment and Residential Programs Day treatment and residential programs have been used successfully, especially for adolescent abusers with combined substance dependence and other psychiatric disorders. Treatment addresses the comorbid state which, in most cases, is conduct disorder or, in other instances, may be attention-deficit/hyperactivity disorder (ADHD), major depressive disorder, dysthymic disorder, and posttraumatic stress disorder (PTSD). Attention is also directed to experiences of abuse or neglect, which is very common in these patients. Both group and individual therapy are used that are behaviorally oriented, with immediate rewards for progress toward objectively defined goals in treatment and punishments for lapses to previous behaviors. Patients attend on-site schools with special education teachers, together with planned recreational activities, and the programs provide birth control consultations. The patients' families, often very chaotic, are engaged in modifications of structural family therapy or multisystemic therapy, both of which have good empirical support. Participation in 12-step programs is required. Treatment interventions are coordinated closely with interventions by community social workers and probation officers. Progress is monitored with urine and breath samples analyzed for alcohol and other drugs at intake and frequently during treatment. Treatment usually lasts 3 to 12 months. Termination is considered successful if the youth has practiced a plan to stay abstinent; is showing fewer antisocial behaviors; has a plan to continue any needed psychiatric treatment (e.g., treatment for comorbid depression); has a plan to live in a supportive, drug-free environment; is interacting with the family in a more productive way; is working or attending school; and is

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