Inhalant Use Disorders

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Introduction

Though a less common substance use disorder, the unique features of inhalant use disorder create significant potential for severe morbidity and mortality. As defined by the DSM 5, inhalant use disorder is a problematic pattern of use of a hydrocarbon-based inhalant substance leading to clinically significant impairment or distress, as manifested by at least two of the ten criteria listed in Table 6.1 and occurring in a 12-month period [1].

Unique among its class and adding to its inconspicuous nature, inhalant use disorder has no corresponding withdrawal disorder. The differential diagnosis for inhalant use disorder includes unintentional inhalant exposure from industrial or other accidents; intentional inhalant use or intoxication that does not meet criteria for inhalant use disorder; inhalant-induced disorders (such as psychotic or depressive disorders); other substance use disorders, especially those involving sedating substances; other toxic, metabolic, traumatic, neoplastic, or infectious disorders impairing central or peripheral nervous system function; and disorders of other organ systems. Included among this class of substances are volatile solvents, aerosols, gases, and nitrites [1].

This chapter includes background information and epidemiology, two clinical cases on the topic at hand, physiologic consequences, and ends with treatment and prevention measures. Distinct features of this disorder include the multitude of substances which it encompasses and the variation of usage by population. The volume of specific substances in the category of inhalants results in difficulty classifying specific traits of this disorder and contributes to limited understanding of pharmacologic effects.

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Table 6.1 Criteria of inhalant use disorder from DSM-5

Inhalant Use Disorder: a problematic pattern of use of a hydrocarbon-based inhalant substance leading to clinically significant impairment or distress
Occurs within a 12-month period
Includes at least two of the following criteria: 1. The inhalant substance is often taken in larger amounts or over a longer period than was intended. 2. There is a persistent desire or unsuccessful efforts to cut down or control use of the inhalant substance. 3. A great deal of time is spent in activities necessary to obtain the inhalant substance, use it, or recover from its effects. 4. Craving, or a strong desire or urge to use the inhalant substance. 5. Recurrent use of the inhalant substance resulting in a failure to fulfill major role obligations at work, school, or home. 6. Continued use of the inhalant substance despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of its use. 7. Important social, occupational, or recreational activities are given up or reduced because of use of the inhalant substance. 8. Recurrent use of the inhalant substance in situations in which it is physically hazardous. 9. Use of the inhalant substance is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance. 10. Tolerance, as defined by either of the following: (a) A need for markedly increased amounts of the inhalant substance to achieve intoxication or desired effect (b) A markedly diminished effect with continued use of the same amount of the inhalant substance

Epidemiology

There is some difficulty in establishing who meets criteria for inhalant use disorder, which is among the least prevalent substance use disorders. Broadly, inhalant use is most common among adolescents, with younger girls initially more likely to use than younger boys. This pattern eventually reverses with age, and young men are more likely to use inhalants than young women. Inhalant use occurs with higher prevalence in rural areas [2, 3].

According to the 2019 National Survey on Drug Use and Health, 807,000 people age 12 or older used inhalants in the prior month. That number increased to 2.1 million people (0.8% of the population) when the time frame was extended to a year, more than methamphetamine (2.0 million) and heroin (745,000). Estimates of the past year use increased since 2016 for people age 12 or above, with the primary shift seen in those aged 12–17 (from 2.2 percent in 2016 to 3.0 percent in 2019). Rates of use in young adults (ages 18–25) and adults above age 26 remained stable from 2015 to 2019. Of the 730,000 individuals who initiated inhalant use in 2019, slightly more than half were adolescents aged 12–17 (381,000) with an average of 1,000 adolescents initiating use each day. Across age groups, the number diagnosed with

inhalant use disorder has remained stable at 0.4% since 2017 with adolescents constituting the highest proportion (0.3%) [4].

According to the national Youth Risk Behavior Survey (YRBS) published by the Centers for Disease Control and Prevention, the percentage of teens in grades 9–12 who have ever used inhalants– which is defined as having sniffed glue, breathed the contents of aerosol spray cans, or inhaled any paints or sprays to get high one or more times during their life– has decreased since 1995 (earliest data available). The percentage of lifetime use was 6.4% in 2019 [5].

Case 1

Helen is a 14-year-old female with no significant medical history. She is preparing to begin 9th grade and lives in a rural part of her home state with her grandmother, who works as a cashier at the local grocery store, and two younger siblings. Both of Helen's parents have unknown substance use disorders. Her grandfather had bipolar I disorder and died 20 years prior from suicide.

Helen presents to her pediatrician, Dr. Chen, for her pre-high school physical exam. Before walking into the exam room where Helen and her grandmother are waiting, Dr. Chen looks over Helen's intake assessment. He immediately notices Helen's weight has dropped from the 40th percentile last year to below the 5th percentile. Her height has remained in the 50th percentile. Dr. Chen makes a note to evaluate for an eating disorder, as well as two things he sees more often than he would like in his rural pediatric practice: inadequate access to nutritious food and substance misuse.

Dr. Chen, Helen, and her grandmother discuss how things have been going since they met last winter when Helen was sick with a cold. He is relieved to know the grandmother is still working at the grocery store, where he knows she receives a discount on food. Helen describes that she spent the summer, "hanging out with my friends," and shrugs when pressed for details about how they were spending their time. Dr. Chen examines Helen, noticing as he checks her oropharynx that there are small erythematous papules on the skin surrounding her mouth. The remainder of Helen's exam is normal.

Dr. Chen tells Helen and her grandmother that he would like to speak with Helen individually. Helen opens up a little more and tells him that it has been difficult to have both of her parents away. Helen is open about having tried smoking a cigarette but did not like that it made her cough. She denies alcohol or cannabis use. When asked about other substances, she looks down and states that she started "bagging." Helen reports some friends were sniffing glue six months ago, since then she has been inhaling fumes, mostly from spray paint, out of a paper bag at least once a day. Dr. Chen asks Helen if she would be okay discussing this with her grandmother present. Helen is hesitant but agrees.

With Helen and her grandmother, Dr. Chen discusses the dangerous nature of using inhalants, answers their questions about it, and provides information about peer support groups for teenagers. Additionally, Dr. Chen makes a referral for Helen

to see the child and adolescent psychiatrist in the closest nearby city, about half an hour from their rural town. He explains the importance of seeing the psychiatrist for additional help with inhalant use management and for psychiatric screening, especially with Helen's family history. When ordering lab tests, Dr. Chen includes urine hippuric acid and benzylmercapturic acid tests as well as a broad urine toxicology screen [2, 6, 7].

Case 2

Benny is a 33-year-old gay male who works as a high school chemistry teacher. His medical history includes asthma and alcohol use disorder, which has been in remission since age 27. Following graduate school, Benny's alcohol use increased to the point that he was drinking every day and found he was unable to go without alcohol ingestion for more than a few days. But it was only after narrowly avoiding a car accident while driving intoxicated that he realized he needed to get professional help to stop using alcohol. Benny met with an addiction specialist who offered him a 30-day detoxification and rehabilitation program, as well as monthly injections of intramuscular naltrexone (Vivitrol). With an active Alcoholics Anonymous program and this medication, Benny has been able to refrain from using alcohol for over 5 years.

Benny lives in a large city with his dog. His family history includes alcohol use disorder in his father and grandfather. When his long-term relationship abruptly ended last year, Benny started attending parties with some younger friends to "blow off steam." At these parties he was introduced to "poppers." In addition to making him feel euphoric, the poppers were an enhancement to his sexual encounters.

Since the effects of poppers lasted only several minutes, Benny found that he was not impaired by them like he had been with alcohol. After attending a few parties where he used them, he learned the ease of buying them himself. His usage increased from occasional social use, to then using at home alone, and then bringing them to work. Inconspicuous and with a lingering odor indistinguishable from others in his chemistry laboratory classroom, Benny regularly used poppers at work between classes or on his lunch break.

This occurred for several weeks, until one Tuesday afternoon when Benny woke up confused in an ambulance. Another teacher found him unconscious and immediately called 911. In the emergency department, the EMS worker informed Dr. Willis that Benny was found holding a small canister of "liquid gold." He complained of a headache and gave inappropriate answers to orientation questions. On exam, he was tachycardic with a heart rate in the 140's and hypoxic with an oxygen saturation of 88% on room air. When nurse Chris drew his blood, he noticed how dark it appeared and informed Dr. Willis of this anomaly. Dr. Willis requested a nitrate test and a hemolysis panel in addition to basic lab tests. Due to a high index of suspicion for methemoglobinemia, she treated Benny with supplemental oxygen and IV methylene blue.

After recovery, Dr. Willis helped Benny call his addiction specialist and schedule an appointment for the following day [6, 8].

Inhalant Classification, Psychosocial Impacts, Physiologic Effects, and Proposed Mechanisms

As a result of the wide range of products which vaporize, there were more than 200 different categories of inhalants reported between 1993 and 2008. To organize and classify the variety of inhalants, Storck et al. grouped them by chemical properties. In Group I are aliphatic, aromatic, or halogenated hydrocarbons, including propellants. Examples are fuels, such as toluene and gasoline, and computer sprays, which have seen a substantial increase in use since the early 2000s. Group II includes gases and other aerosols such as nitrous oxide, found in whipped cream dispensers and referred to colloquially as "whippets." Least used are inhalants in Group III which are the alkyl nitrates such as chlorohexyl nitrite [6].

The psychosocial impacts of inhalant use disorder are numerous though little is known about the natural history of inhalant use disorders and comorbidities in the general population. A common thread through the cases above is the association of inhalant use disorder with psychiatric conditions and, as in the second case, with other substance use disorders. Psychiatric conditions and symptoms notably more common among inhalant users include depressive disorders, anxiety disorders, suicidal ideation, and suicide attempts. Rates of depression and anxiety were higher in groups studied with occupational exposure to inhaled hydrocarbons. Though evident, differentiating whether this association is due to a similar spectrum of risk factors or if one is premorbid to the other is unclear. One hypothesis remarks on inhalant use as a global vulnerability marker, rather than a direct precipitant of psychiatric illness [6].

As there are many types of inhalants, the mechanism of use as well as signs and symptoms of intoxication or recent use can vary. The most common methods by which a vapor is inhaled are through direct inhalation from a container, inhalation from a product vaporized into a bag, or inhalation of fumes from a soaked cloth that covers the nose and/or mouth [8]. Signs of use can directly correlate to the method of ingestion. In the case of Helen, a perioral rash was evidence of recent use by inhaling fumes out of a paper bag, also known as "bagging."

Physiologic effects of inhalants correlate specifically to the substance ingested and broadly affect every organ system. Systems impacted are neurocognitive, metabolic, hepatic, renal, cardiovascular, hematopoietic, neuromuscular (including peripheral nerves), and reproductive. It is difficult to distinguish acute effects from those that result from sustained use as there have been reports of long-term impacts, such as in memory and processing speed, from a single occupational exposure. Occupational exposure studies allowed for the discovery of the effects of these substances on the body; however, these data serve only as a model due to higher exposure level in intentional inhalant use (whether by quantity, duration, or repetitious use) [6].

Acute physiologic effects mimic those of alcohol intoxication, such as dizziness, dysarthria, tremor, vision changes and involuntary eye movement, stupor, and coma, as well as impairments in cognition, coordination, and reflexes. With repetitive use, these temporary consequences progress to the development of encephalopathy, parkinsonism, cerebral atrophy, ataxia, and decreased cerebral perfusion. On brain imaging, hypointensities are visible in the thalamus and basal ganglia. Pulmonary dysfunction and disease are also highly common, with associations noted between duration of inhalant use and development of bronchitis, asthma, sinusitis, and tuberculosis. One study demonstrated an accelerated rate of radioisotope pulmonary clearance in those who were using inhaled solvents, indicating dysfunction at the level of the alveolar capillary membrane [6]. A particular example of physiologic impact relates to Benny from Case 2, which is that of amyl nitrate and its potential to cause methemoglobinemia; this can be fatal without recognition and timely treatment [8].

Additional adverse consequences of inhalant use are chemical and thermal burns, persistent mental illness, and medical emergencies. Severe and imminent life-threatening consequences of inhalant use are sudden sniffing death, asphyxiation, and unintentional injuries. Sudden sniffing death refers to heart failure precipitated by fatal arrhythmia [2, 6].

Cognitive and neurological effects can be temporary though with repeated exposure compounded deficits can be long-lasting. Global brain atrophy, as seen in Image B in Fig. 6.1, can occur in those with chronic toluene use [9]. Other effects of prolonged toluene exposure include impaired growth such that a person with

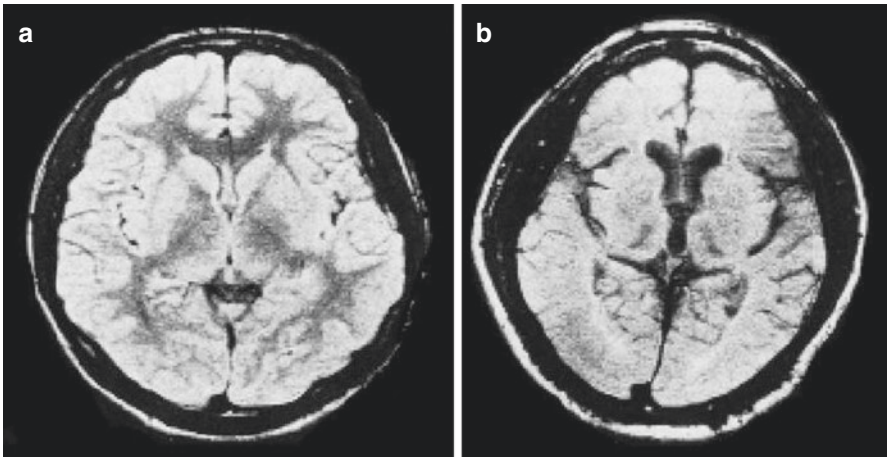

Fig. 6.1 Normal brain (**a**) and brain with chronic exposure to inhalant (**b**). (Image **a** features the brain of a patient with no history of inhalant use. Image **b** features the brain of an individual who chronically uses toluene. The brain in image **b** has atrophied, evidenced by the smaller appearance and increased space inside the skull (the white outer circle in each image). *This image is used with permission from NIDA, Courtesy of Neil Rosenberg, M.D., NIDA Research Report (NIH 05-3818)* [9])

repeated use can develop failure to thrive, such as Helen in Case 1 [10]. Systemically, toluene inhalation can cause imminently harmful problems such as lactic acidosis, rhabdomyolysis, and acute hepatorenal injury [11].

Teratogenic effects occur with intrauterine exposure to inhaled substances. The presentation is similar to fetal alcohol syndrome with prominent features of facial and cranial deformities, poor brain development, low birth weight, developmental delays, as well as a variety of additional complications [4, 6].

The proposed mechanism for the neurobiology of inhalant use again varies by substance. Toluene and trichloroethylene promote motor excitation at low concentrations, whereas at high concentrations they potentiate anesthesia, sedation, coma, and even death. A proposed mechanism for toluene is that it blocks NMDA receptors in a similar way to PCP [4]. In studies with rats, toluene exposure increased dopamine levels in the prefrontal cortex and striatum, leading to increased neuron firing in the ventral tegmental area. This mechanism is similar to other substances which are misused. Benzene and diethyl ether work as depressants to the central nervous system as positive modulators to GABA-a receptors [4].

Treatment

Treatment options for inhalant use disorder are limited; psychosocial treatments have shown some efficacy and pharmacologic options are minimal. Inadequate initiatives to develop treatment options can be attributed to lack of research, inadequate screening, and underreporting of use [4]. As with the case of Dr. Chen and Helen, directly approaching the patient is the foundation of treatment of inhalant use disorder. This method begins with the implementation of screening at every opportunity as well as looking out for signs of use, such as Helen's perioral dermatitis and failure to thrive. The SBIRT model offers a standardized approach to screening and intervention that includes questions on topics of frequency and amount of use, as well as impacts of use on personal and interpersonal functioning [12]. As with other substance use disorders, the motivational interview is crucial in determining the state of readiness of change for a particular patient, as well as guiding them along in the process [13]. Outpatient and inpatient substance use treatment programs, which utilize structured environments, peer support, individual and group counseling, education, and accountability, can be useful in the treatment of inhalant use disorder [4].

Primary prevention methods aim to deter the use of commonly used volatile compounds and are a key area of focus in reducing harm from inhalant abuse [4]. Examples of primary prevention include clearer labeling for misused products and chemicals, changing the composition of products so the volatile chemicals causing intoxication are replaced or masked, monitoring quantity of particular products purchased, and the addition of age restrictions. Other harm reduction strategies are to make usage safer, such as advising persons to avoid the use of compounds containing propane and butane, refrain from placing a plastic bag over one's head, and take precautions to avoid burns, overdose, and aspiration of vomitus.

Treatment at the community level is multipart. Nearly every rural community needs increased access to mental health care and substance use treatment. Educational initiatives and outreach programs directly addressing substance use are imperative in prevention of all substance use disorders, including inhalants. Opportunities for youth engagement such as recreational programs offer a means of alternative time spent for youth most vulnerable to early substance use. Culturally sensitive outreach and education may be critical in certain vulnerable communities. In Canada and Australia, for example, holistic approaches that utilize components drawn from indigenous cultures have been shown to be efficacious treatment options for inhalant use disorder in indigenous populations [4].

Pharmacological treatments for inhalant use disorder have not been well researched, though some antipsychotics and antiepileptic agents demonstrate benefit for symptom relief. In one case report of a patient who developed psychotic symptoms after repeated gasoline inhalation, the administration of risperidone led to both decreased psychotic symptoms and decreased cravings. Haloperidol and carbamazepine similarly have some limited evidence for decreasing symptoms in those with inhalant-induced psychotic disorders. A case report showed reduction in cravings and increased abstinence with lamotrigine [4].

Conclusion

Although inhalant use disorder is relatively rare compared to other substance use disorders, it can nevertheless cause significant injury to those affected by it, including several potentially fatal complications. Inhalant use should be part of any comprehensive substance use screening, particularly when working with populations with higher prevalence of the disorder. Although treatment options are limited, some of the psychosocial treatments with efficacy in other substance use disorders have also been shown to work in this patient population.

Key Points

- Inhalant use disorder describes problematic use of a heterogeneous group of substances including volatile solvents, aerosols, gases, and nitrites.
- Inhalants can exert their effects across body systems both acutely (including life-threatening hematologic, respiratory, and cardiac risks) and more chronically.
- Careful screening, harm reduction, and community-level interventions are critical to reducing the burden of disease.
- Treatment options for inhalant use are primarily psychosocial and overlap with those for other substance use disorders.

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