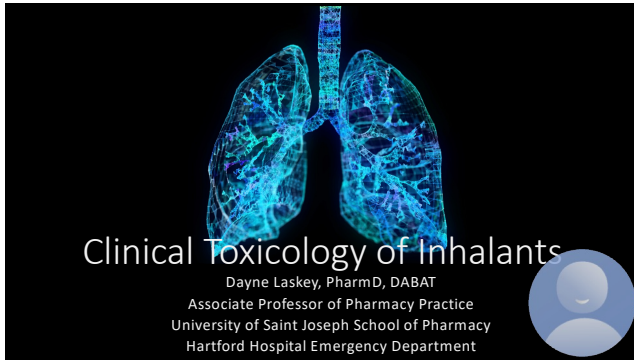
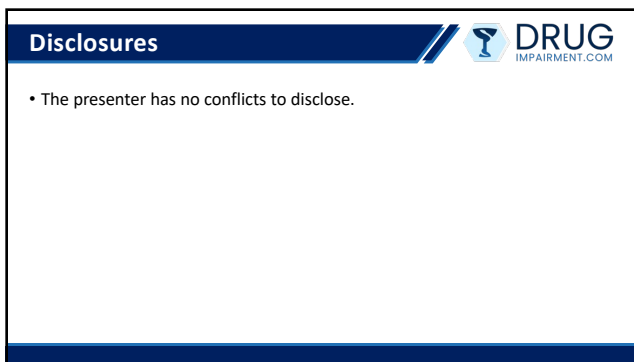
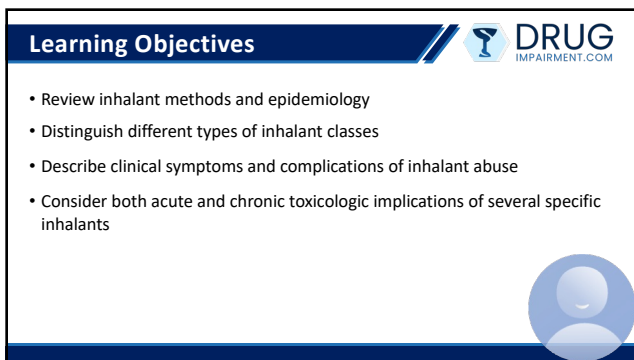




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3

Inhalants

- Inhalant: deliberate inhalation of vapors for the purpose of getting high
- Often appeals to adolescents
 - Easy to obtain
 - Mistakenly viewed as harmless

4

Inhalants – Epidemiology

Key Substance Use and Mental Health Indicators in the United States: Results from the 2021 National Survey on Drug Use and Health

Table 1.108 Inhalant Use in Past Year: Among People Aged 12 or Older, by Age Group and Demographic Characteristics, Percentages, 2021

Demographic Characteristics	Age 12-17 (2021)	Age 18-24 (2021)	Age 25-34 (2021)	Age 35-44 (2021)	Age 45-54 (2021)
TOTAL	8.1	1.8	2.3	8.3	9.1
GENDER					
Male	11.1	8.2	11.4	8.6	11.7
Female	7.2	9.2	7.1	7.6	7.6
HISPANIC ORIGIN AND RACE					
Non-Hispanic or Latino	8.8	9.0	8.8	8.1	10.0
White	11.1	9.8	11.1	8.6	11.7
Black or African American	1.0	7.8	1.2	1.4	9.2
Asian	2.8	7.8	2.2	7.4	8.2
NIHPI	7	7	7	7	7
Asian	4.4	10	4.1	6.6	10.7
Two or More Races	12.5	7.5	14.8	11.8	12.5
Hispanic or Latino	6.5	6.5	6.9	7.2	7.7
EDUCATION LEVEL					
< High School	da	da	5.9	8.2	1.6
High School Graduate	da	da	7.3	7.6	7.2
Some College Associate's Degree	da	da	10.8	8.4	11.4
College Graduate	da	da	15.4	8.2	10.2
EMPLOYMENT STATUS					
Full-Time	da	da	10.2	8.2	10.8
Part-Time	da	da	10.7	8.4	11.1
Unemployed	da	da	11.6	9.2	12.4
Other	da	da	4.7	7.2	9.4

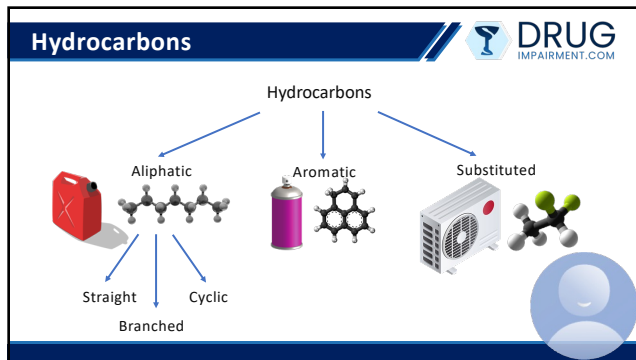
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NSDUH – Last Month Use

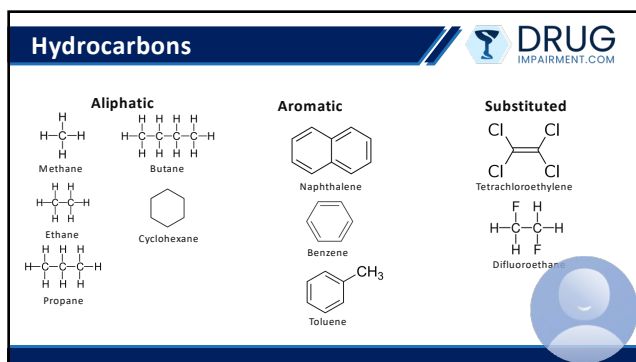
Table 1.109 Inhalant Use in Past Year: Among People Aged 12 or Older, by Age Group and Demographic Characteristics, Percentages, 2021

Demographic Characteristics	Age 12-17 (2021)	Age 18-24 (2021)	Age 25-34 (2021)	Age 35-44 (2021)	Age 45-54 (2021)
TOTAL	9.1	2.4	0.9	1.2	0.5
GENDER					
Male	11.1	2.2	0.9	1.8	0.8
Female	0.5	2.2	0.3	1.1	0.2
HISPANIC ORIGIN AND RACE					
Non-Hispanic or Latino	0.8	2.2	0.8	1.8	0.5
White	0.8	2.8	0.7	1.8	0.5
Black or African American	0.1	1.2	0.3	0.3	0.5
Asian	0.1	0.5	0.4	0.4	0.5
NIHPI	0.1	0.2	0.1	0.1	0.1
Asian	0.9	2.8	0.8	2.7	0.5
Two or More Races	1.1	2.8	1.0	2.2	0.7
Hispanic or Latino	0.7	2.2	0.3	1.1	0.4
EDUCATION LEVEL					
< High School	da	da	0.2	0.8	0.2
High School Graduate	da	da	0.8	1.2	0.4
Some College Associate's Degree	da	da	0.8	1.2	0.4
College Graduate	da	da	0.8	1.0	0.7
EMPLOYMENT STATUS					
Full-Time	da	da	0.7	1.4	0.8
Part-Time	da	da	0.7	1.4	0.5
Unemployed	da	da	1.1	2.4	0.7
Other	da	da	0.3	1.4	0.4

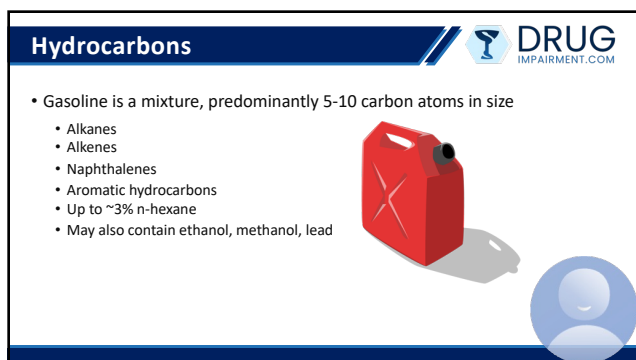
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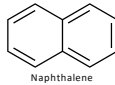


12

Hydrocarbons - Mechanism



- Organic compounds made of carbon and hydrogen atoms
 - Aliphatics ≤ 4 carbons are gaseous at room temp
 - 5-18 are liquid
 - >19 are tars or solids
- Highly lipophilic, passive absorption
 - Aromatics absorb very quickly following inhalation
 - Aliphatics with <16 carbons absorb readily
 - >16 carbons absorbed poorly
- Rapidly enter CNS
 - More lipophilic = more CNS depression
 - Aromatic, aliphatic, halogenated

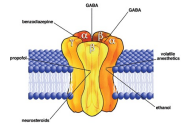


13

Hydrocarbons - Mechanism



- Organic compounds made of carbon and hydrogen atoms
- Highly lipophilic, passive diffusion across membranes
 - Aromatics absorb very fast
 - Aliphatics with <16 carbons good, >16 carbons poor
 - Rapidly enter CNS
 - More lipophilic = more CNS depression
- Stimulate CNS inhibitory neurotransmission, antagonize excitatory neurotransmission **similarly to ethanol**
 - Increase GABA-mediated activity, hyperpolarize cells, slow rate of neuronal firing
 - Toluene, Trichloroethane (TCE), trichloroethylene
- Complex – no single mechanism explains clinical effects



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Blood:Gas Partition Coefficient



Veridical	Blood:Gas Partition Coefficient (B/G)	Routes of Elimination	Important Metabolites
Acetone	145–200	largely unchanged via exhalation	None
Diethyl ether	0.009	largely unchanged via exhalation	Metabolized to 2-butoxy and 2-butoxy
Carbon tetrachloride	0.6	10% unchanged via exhalation, 90% hepatic metabolism and urinary excretion	CYP2C1 to trichloroethyl radical, trichloroethyl peroxyl radical, phosgene
n-Hexane	2	10%–20% exhaled unchanged; hepatic metabolism and urinary excretion	CYP2C1 to 2-hexanol, 2,5-hexanedione, γ -hexolactone
Methylene chloride	1–10	90% exhaled unchanged; hepatic metabolism and urinary excretion	1. CYP2C1 to CO and CO ₂ 2. Glutathione transferase to CO ₂ , formaldehyde, and formic acid
Nitrous oxide	0.47	99% exhaled unchanged	None
Toluene	0.14	<10% exhaled unchanged; 90% hepatic metabolism and urinary excretion	CYP2C1 to benzoic acid, then: 1. Glutathione conjugation to form hippuric acid (90%) 2. Glutathione conjugation to form glucuronide (significant pathway except after large exposure)
1,1,1-Trichloroethane	1–2	90% exhaled unchanged; hepatic metabolism and urinary excretion	CYP2C1 to trichloroethanol, then: 1. Conjugated with glucuronic acid to form trichloroethanol glucuronide 2. Further oxidized to trichloroacetic acid
Trichloroethylene	0	90% exhaled unchanged; 10% hepatic metabolism and urinary excretion	CYP2C1 to epoxide intermediate (transient), chloral hydrate (transient), trichloroethanol (stable), trichloroacetic acid (stable). Urinary trichloroacetic acid peaks 2–3 days postexposure
1,2-Dichloro-1,1-difluoroethane	NA	NA	CYP2C1 to 2-chloro-1,2-difluoroethyl glucuronide, 2-chloro-2,2-difluoroethyl glucuronide, chlorodifluoroacetic acid, chlorodifluoroacetylaldehyde, hydroxychlorodifluoroacetylaldehyde, and organic fluorides, no bound metabolites to liver proteins

Drug Metabolism: Molecular Basis of Pharmacokinetics, 4th ed. Lewis J. Nelson, et al. Wolters Kluwer 2019



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Hydrocarbons – Signs

- Solvent odor
- Discoloration around nose/mouth
- Mucous membrane irritation
 - Sneezing
 - Coughing
- Dyspnea
- GI complaints

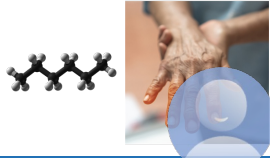


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Hydrocarbons – Clinical Effects

- Acute CNS effects
 - Initial: Euphoria and hallucinations
 - Progressive: Dizziness, headache, slurred speech, tremor, weakness, ataxia
 - Finally: Seizures, coma, respiratory depression
- Irreversible CNS damage with chronic use
 - White matter degeneration
 - "Painter's syndrome"
- Peripheral nervous system effects
 - Peripheral neuropathy
 - N-hexane, methyl-n-butyl ketone, carbon disulfide, acrylamide, ethylene oxide, trichloroethylene

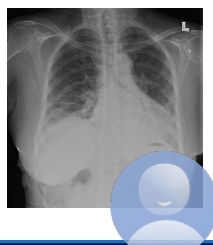


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Hydrocarbons – Lung Injury

- Aspiration injury
 - Chemical pneumonitis
 - Interstitial edema
 - Bronchospasm
 - ARDS
- Choking/gagging/coughing within 30 minutes → x-ray
 - Re-check within 6 hours
 - 90% develop radiographic findings within 4 hours



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Hydrocarbons – Aspiration Risk

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Three hydrocarbon properties influence risk of aspiration injury:

1. Viscosity

2. Volatility

3. Surface Tension

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Hydrocarbons – Viscosity

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Viscosity comparison of common hydrocarbons

Compound	Common Uses	Viscosity (cSt) ^a
Aliphatics		
Gasoline	Motor vehicle fuel	30
Naphtha	Charcoal lighter fluid	29
Kerosene	Heating fuel	35
Turpentine	Paint thinner	33
Mineral spirits	Paint and varnish thinner	30-35
Mineral seal oil	Furniture polish	30-35
Heavy fuel oil	Heating oil	>450
Aromatics		
Benzene	Solvent, reagent, gasoline additive	31
Toluene	Solvent, spray paint solvent	28
Xylene	Solvent, paint thinner, reagent	28
Halogenated		
Methylene chloride	Solvent, paint stripper, propellant	27
Carbon tetrachloride	Solvent, propellant refrigerant	30
Trichloroethylene	Degreaser, spot remover	27
Tetrachloroethylene	Dry cleaning solvent, chemical intermediate	28

^a Hogen, Morgan A., and David B. Guerin. "Hydrocarbons." Goldstein's Toxicologic Emergencies, 11e Ed. Lewis J. Nelson, et al. McGraw Hill, 2018.

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Hydrocarbons: Cardiac toxicity

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- “Sudden Sniffers Death Syndrome”
 - Acute cardiotoxicity following a stressful situation
- Hydrocarbons can sensitize myocardium to catecholamines
 - **Most common with halogenated, followed by aromatic**
 - Block potassium current (I_{K}), prolonging repolarization
- Cardiac dysrhythmia and arrest can be triggered by a startle response, stressful situation, or strenuous physical activity
 - Described with difluoroethane, butane, air freshener, many more.

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Physical risks



Figure 1. Bullae filled with clear fluid on the right cheek, lateral aspect of the upper lip, and lower lip.



Figure 2. Bullae filled with clear fluid on the index, middle, and ring fingers on the left hand.

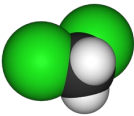
Koehler MM, Henninger CA. Orofacial and digital frostbite caused by inhalant abuse. *Cutis*. 2014;93(5):256-260.



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Methylene Chloride

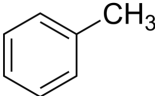
- Paint stripper, degreaser, aerosol propellant, carburetor cleaner
- Metabolized in liver by CYP2E1 to carbon dioxide (CO₂) and carbon monoxide (CO)
- Significant, delayed carbon monoxide toxicity may occur, typically peaking ~8 hours after exposure
- CNS effects may be related to solvent OR to CO toxicity




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Toluene

- Found in gold/silver metallic paint, paint thinners, glue
 - Has replaced benzene as a solvent in many products
- Acute abuse causes:
 - Intoxication
 - Metabolic acidosis
 - Hypokalemia (low potassium)
- Chronic abuse can have irreversible effects
 - Dementia, ataxia, eye movement disorders, psychological changes, memory impairment

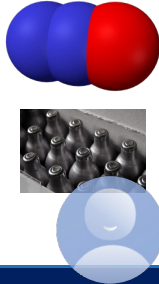



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Nitrous Oxide (N₂O)



- “Laughing gas” used in medical and dental procedures
 - Used in racing as “nitrous”, propellant in whipped cream canisters “whippets”
- Causes short-lived euphoric effect, hallucinations, and relaxation
 - Inhibits NMDA (stimulation), but does not enhance GABA (inhibition), and stimulates dopamine neurons
- Abuse danger: hypoxia, loss of motor control



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Nitrous Oxide (N₂O)



- Chronic abuse leads to neurotoxicity
 - Oxidation of vitamin B12
 - Myeloneuropathy
 - Bone marrow suppression
 - Leukopenia, anemia, thrombocytopenia
- Inhibits methionine synthase prevents conversion of homocysteine to methionine
 - Results in impaired DNA and myelin synthesis
 - Myeloneuropathy – numbness, paresthesias, ataxia, incontinence

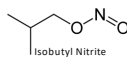
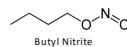
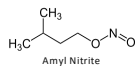


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Alkyl Nitrites



- Amyl, butyl, and isobutyl nitrites, sometimes called “poppers”
- Used recreationally for sexual enhancement
 - Sold covertly in sex paraphernalia shops as “air freshener”, “liquid incense”, “VHS tape cleaner”, and others

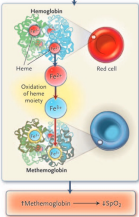


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Alkyl Nitrites



- No direct effect on CNS, rather, effects are due to smooth muscle relaxation
- Use can result in methemoglobinemia
 - Mild cases may be asymptomatic
 - Slate grey cutaneous coloration
 - Blue nail beds/lips
 - Dyspnea, dizziness, syncope
 - Severe cases can lead to coma, seizures, death



Pallua JC, Maxwell RT, Pimentel MR. Case 7-2011: a 52-year-old man with upper respiratory symptoms and low oxygen saturation levels. Cobelli RC, Harris NL, Sheppard JAD, et al., eds. N Engl J Med. 2011;364(3):357-366.

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Summary



- Thank you

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