Hydrocarbons

Hydrocarbon Classification

- From - Plants - Petroleum Coal Tar
  - Animal fats - Natural gas
- Aliphatics: Straight or branched chain
  - Paraffins…alkanes \((C_nH_{2n+2})\)
  - Olefins
    - Alkenes… Double bond
    - Alkadienes… Two double-bonds
    - Acetylenes …Triple bond
  - Acyclic terpenes

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Hydrocarbon Classification

- **Cyclic**: Closed ring
  - Allycyclics (≥ 3 carbons in a ring; act like aliphatics)
  - Cycloparaffins (Naphthenes) i.e. cyclohexane
  - Cycloolefins... ≥ 2 double-bonds
- **Aromatics**
  - Benzenes... one ring
  - Naphthalenes... two rings
  - Anthracenes... three rings
  - Polycyclic aromatic hydrocarbons...
    Multifused benzene rings
  - Heterocyclic... Include an oxygen or nitrogen substitution for a carbon
  - Cyclic terpenes... Key in plant derived essential oils

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The Naphths

- Cycloparaffins (Naphthene) (Cyclohexane)
  - Acts like an aliphatic
  - Charcoal Lighter Fluid

- Naphthalene
  - Old Moth Ball item...mostly replaced
  - Pure white with noxious odor
  - #1 component of coal tar
  - Metabolized to active alpha-naphthol...
    - thus delayed clinical
  - Clinical
    - Hemolysis #1 (esp G6PD deficient)
    - Methemoglobinemia

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Hydrocarbons

- Inhalation: #1 route of exposure
- Cross alveolus by passive diffusion
- Aromatics pass particularly well
- Aliphatic diffusion: 5-16 carbons good, > 16 poor
- GI absorption: Inverse to the weight
- Small HC: Almost complete
  - > 32 carbons: Very little
- Skin absorption
  - Often minor.
  - Solvents with both hydrophilic and hydrophobic groups absorbed best i.e. glycol ethers
Hydrocarbons: Pulmonary

• Aspiration is #1 injury route
• Direct toxicity & lipid surfactant layer disruption
• Physical Properties...? Which is most important
  • Viscosity…………Low (< 60 SSU)
  • Surface Tension…Low
  • Volatility ………… High
• Radiographic…CXR
  • 90% w/ Pneumonitis w/ 4 hrs
  • < 5% have but w/o symptoms
  • Changes usually peak at 5-7 days
  • Chronic (Bronchiectasis or pulm fibrosis) are uncommon

Hydrocarbon: Neuropathy

• Peripheral
  • Classic axonopathy: N-Hexane
    Methyl-n-butyl ketone
  • Also:
    • CS₂
    • Acrylamide
    • Ethylene Oxide
    • Styrene

• Cranial
  • Classic: Trichloroethylene (TCE) ➔
    • Trigeminal neuralgia & other facial neuropathies
    • Likely due to the decomposition product...
  • Dichloroacetylene
    • Reported:
      • Trichloroethanol ➔ Periph & Cranial neuropathies
      • Perchloroethylene (PERC) … likely due to TCE being a contaminant in a PERC preparation
Hydrocarbon: Liver

- Chlorinated HCs are #1 bad boys
- # of halogens ↑ & atomic weight of halogens ↑ → Toxicity ↑
  - CCl₄ >> Benzene, Trichloroethylene
  - Less toxic: trichloroethylene, tetrachloroethylene, and 1,1,1-trichloroethane
  - AST/ALT ↑ & Hepatomegaly; Reversible
  - Phase I activation → Reactive intermediate → Lipid Peroxidation, Free Radicals → Direct Membrane Injury
- Also
  - Vinyl chloride → Liver carcinogen
  - Aromatic HCs

Hydrocarbons: Cardiac

- Halogenated #1 group among HCs; Aromatics #2
- Chronic Occupational Solvent Exposure
  - No change in CV mortality except with…
    - Carbon Disulfide
  - Acute solvent abuse (Sudden Sniffing Deaths)
    - Toluene, 1,1,1-Trichloroethane
    - Chlorofluorocarbons, Trichloroethylene
    - Less Likely
      - Trichloromethane (chloroform)
      - PERC
  - Dysrhythmia Mechanisms:
    - Heart Sensitization to catecholamines
    - CNS Depression → Hypoxia & CV Depression

Hydrocarbons

- Renal
  - Halogenated HCs (degree correlates with hepatotoxicity)
    - Toluene → Distal RTA
- Dermal
  - Nonspecific irritation
  - Drying to the skin
  - Agents with lower boiling points are more irritating…
    - gasoline
  - Contact dermatitis… to…full burns
    - Erythema…Dryness…Fissures…Eczema
    - Folliculitis, Hyperpigmentation, Hyperkeratotic
Hydrocarbons

- Dermal (Con’t)
  - Involved in up to 20% of occupational dermatitis
  - Irritant Order: Aromatic > Aliphatic > Chlorinated > Turpentine > Alcohols > Esters > Ketones
  - Burns most associated with the aromatics
  - Degreaser’s Flush...Disulfiram-like reaction associated with Trichloroethylene

Hands, wrists & forearms are the # 1 sites for industrial contact dermatitis. This case – chronic kerosene for cleaning. Note - thickened, hyperpigmented, dry and fissured. Itching is usually a major symptom.

Hydrocarbons

- Dermal (Con’t)
  - Chloracne
    - Chlorinated aromatic HCs...ones with stereochemistry
    - Chronic inflammation, eruption of comedones and epidermal cysts ➔ may get scarring
    - # 1 Areas - eyes, malar areas of the face, behind the ears, and on the scrotum in males.
    - Pathognomonic (almost) - presence of numerous straw-colored cysts early in the course of the disease.
    - Progression - inflammatory lesions and abscesses develop, and intense itching.

Aliphatic Hydrocarbons

n-Hexane

- Colorless; Gasoline-like odor; Highly flammable
- Uses: Extract vegetable oils from crops such as soybeans; Solvent in rubber cement industry
- Key: Metabolism ➔ Methyl-n-Butyl Ketone
Methyl-n-Butyl Ketone

- Clear, colorless solvent
- Smells of acetone
- Peripheral neuropathy
  - Chronic exposure
    - Agents with ≥ 6 carbons → γ-diketone (functional group spacing is key to toxicity) → Form a ringed pyrrole structure
    - Phosphorylation of neurofilament proteins
    - Axonal cytoskeleton disruption
- Methyl ethyl ketone (MEK) & Methyl isopropyl ketone (MIBK) → Not Toxic
- 2,5-hexanadione → Peripheral neurotoxicity
- 2-Hexanol likely → Narcotic effects

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\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 & \quad \text{N-Hexane} \\
\text{CH}_3\text{CCH}_2\text{CH}_2\text{CH}_3 & \quad \text{Methyl-n-Butyl Ketone} \\
\text{CH}_3\text{CCH}_2\text{CH}_2\text{CH}_3 & \quad \text{2-Hexanol} \\
\text{CH}_3\text{CH}_2\text{CCH}_2\text{CH}_3 & \quad \text{5-Hydroxy-2-hexanone} \\
\text{CH}_3\text{CCH}_2\text{CH}_2\text{CH}_3 & \quad \text{2,3-Hexanediol} \\
\text{CH}_3\text{CCH}_2\text{CH}_2\text{CH}_3 & \quad \text{2,5-Hexanedione}
\end{align*}
\]

Hexane Neuropathy

- Gradual sensorimotor neuropathy with demyelinating features.
- #1 initial complaint is numbness and tingling of the toes and fingers → progressive motor function
- Only Rx - Removal from n-hexane
- Prognosis for n-hexane neuropathy generally is favorable, but recovery may take months to years, depending on disease severity.
Halogenated Hydrocarbons

- Each individual one with low % impurities… Usually other chlorinated HCs. These confound the issues of adverse effects of a product.
- Clinical Effects
  - CNS depression initially
  - Secondary: Possible Hepatic and renal injury
- Radio-opaque

Aromatic Hydrocarbons

Toluene

- Colorless; Benzene-like odor; Flammable
- Natural from crude oil and in the tolu tree.
- Uses: Big solvent! Has replaced benzene as the top solvent. Paints, Thinners, Glues, etc. Some printing and leather tanning processes.
- Inhalation: Rapid intoxication
- Chronic Use
  - Distal RTA
  - Metabolic acidosis (Hippuric acid)
  - Hypokalemia and associated symptoms
  - Leukoencephalopathy

Toluene Metabolism

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\begin{align*}
\text{Toluene} & \rightarrow \text{Benzy alcohol} \\
\text{Benzy alcohol} & \rightarrow \text{Benzaldehyde} \\
\text{Benzaldehyde} & \rightarrow \text{Benzoic Acid} \\
\text{Benzoic Acid} & \rightarrow \text{Glycine} \\
\text{Glycine} & \rightarrow \text{Hippuric Acid}
\end{align*}
\]
Halogenated HCs that have 1 or 2 Carbons

- \( \text{CCl}_4 \) - Carbon Tetrachloride
- \( \text{CHCl}_3 \) - Chloroform
- \( \text{CH}_2\text{Cl}_2 \) - Methylene Chloride
- \( \text{Cl}_2\text{H-C-C-HCl}_2 \) - Tetrachloroethane
- \( \text{CH}_2\text{Cl}-	ext{C-CH}_2\text{Cl}_2 \) - Trichloroethane
- \( \text{Cl}_2 \cdot \text{C}==\text{C-Cl}_2 \) - Tetrachloroethylene (PERC)
- \( \text{CH}_2\text{C}==\text{C-Cl}_2 \) - Trichloroethylene (TCE)
- \( \text{Cl}_2 \cdot \text{C}==\text{C-H}_2 \) - Monochloroethylene (Vinyl Chloride)
- \( \text{Cl}_2\text{H-C(OH)}_2\text{H} \) - Choral Hydrate

Halogenated Hydrocarbons: Hepatotoxins

- **Worst**
  - Tetrachloromethane (\( \text{CCl}_4 \))
  - Trichloromethane (Chloroform)

- **Middle**
  - Tetrachloroethane
  - Trichloroethylene (TCE)

- Most metabolism

- **Weakest**
  - Tetrachloroethylene (PERC)

10% metabolism
  - Trichloroethane (TCA)
  - Dichloromethane

Epoxide
- Binds Liver Cells
- Cell injury / Death

Halogenated Hydrocarbons
Carbon Tetrachloride

- Usually a gas
- Uses:
  - Former: Refrigerant (Freon 10); Propellants; Cleaning agent
  - Now: Only used in some industrial applications.
- Chronic exposures
  - The most hepatotoxic of known HCs (Zone 3)
  - Simple metabolism with free radical formation as cause of toxicity (like trichloroethane)
  - Nephrotoxicity may also occur
Halogenated Hydrocarbons

**Methylene chloride**

- Dichloromethane; Freon 30; Methane dichloride; Methylene dichloride; Methylene chloride;
- Uses: Solvent and paint stripper. Also: some aerosol and pesticide products; Film production
- Absorbed by inhalation or dermally
- Highly lipophilic
- Released from adipose; Liver metabolism
- Metabolized → CO$_2$ (70%) and CO (30%).
- CO levels up to 50%...Peak up to 8 hours after exposure
- AMS after exposure likely solvent related, but changes later may be due to CO

**Vinyl chloride**

- Chloroethene; chloroethylene; ethylene monochloride; Monochloroethene
- Gas; Flammable
- Uses: Make Polyvinyl chloride (PVC)
- Hepatic angiosarcoma ...clear association
- Acrosclerosis...Classic Rheum Problem
- Acroosteolysis...osteolysis in terminal phalanges of some fingers
- Raynaudts
- Scleroderma...thickening of the skin or raised nodules on the arms

**Acrosclerosis / AcroOsteolysis Vinyl Chloride**

- First described in 1950
- Blacksmith
- Reversible
- Bony destructive lesions of the distal phalanges of one or more fingers (most frequently involving the thumbs)
- Seen in < 2% workers involved with the polymerization of vinyl chloride
Halogenated Hydrocarbons
Perchloroethylene

- Tetrachloroethylene; PERC
- Heavier than water (unlike Stoddard agent)
- First: an antihelminthic in 1920s… preferable to CCl₄
- Uses:
  - Dry cleaning – At its Peak…
  - Used as “the” agent in 95% of dry cleaning
  - > 50% of all PERC used is used in dry cleaning
- Degreasing, Glues; Intermediate; Paint removers; Inks; Water repellents; Semiconductor manufacture; Heat transfer medium
- Being phased out and replaced with other agents including glycol ethers; now used in ~ 70% dry cleaning

Halogenated Hydrocarbons
Perchloroethylene

- Metabolism
  - 90% eliminated unchanged by exhalation
  - 10% \( \rightarrow \) (P450 2E1) \( \rightarrow \) Epoxide \( \rightarrow \) Trichloroacetic & Oxalic acid
- Trichloroethanol is a PERC “metabolite.” However, this substance likely results from a typical PERC contaminant… trichloroethylene!
- The extensive pulmonary elimination distinguishes PERC from other halogenated HCs
- Longer T ½ than other halogenated HCs \( \rightarrow \) accumulation and / or slower symptom clearance
- Decomposes \( \rightarrow \) Phosgene & Dichloroacetylene …the latter is the likely culprit behind the cranial neuropathies
Halogenated Hydrocarbons
Trichloroethylene (TCE)

- Uses: Solvent for metal parts, paint removers, typewriter correction fluids, and spot removers.
- Was replaced by tetrachloroethene (PERC) b/c TCE is more hepatotoxic than PERC.
- Metabolism: Epoxide (like PERC) … but … this is its 1st route Trichloroacetic acid and Trichloroethanol.
- Hepatic injury (DUE TO Epoxide intermediate).

Halogenated Hydrocarbons
Trichloroethylene (TCE)

- Degreaser’s Flush
- TCE #1, but other solvents associated i.e. xylene
- Only need to be exposed to the vapor
- Disulfiram-like reaction; Altered EtOH metabolism
- Mechanism is unclear
- Starts w/ 30 min of alcohol exposure; Peaks within 30-60 min; Clears w/ 1-hour.
- Starts: Nose and cheeks: May → upper torso
- Trigeminal Neuropathy is classic…also…other cranial nerve neuropathies

Essential Oils

- photo of Essential Oils
- Anybody Seen My Cat?
Essential Oils

- Organic compounds distilled from plants
- Aromatic and volatile
- Fragrance...flavor...Medicinal...Massage...Religious ceremony...bathing
- Camphor, pine oil, menthol, peppermint oil, eugenol, cinnamon oil, oil of wintergreen, pennyroyal oil
- Very irritating to mucous membranes
- Large ingestions ➔ CNS

Essential Oils

- 1st Part - Hydrocarbon base
  - Most compounds found in essential oils are terpenoid molecules - carbon backbone and consist of 10-30 carbon atoms - made up from the 5 carbon isoprene units.
  - Isoprene is not a terpene, yet all terpenes have isoprenes
  - Monoterpene – has two isoprenes. React with air and heat and thus do not last well (citrus oil – have many monoterpenes). Have proposed anti-inflammatory, antiseptic activity. Also with stimulating effect on the mucus membranes & thus used as decongestants.
- 2nd Part - Compounds with oxygen atoms including alcohols, esters, aldehydes, ketones, lactones, coumarins, ethers

Camphor

- Vicks Vapo Rub (4.7%) & Campho-Phenique (10.8%)
- US products < 11%, but ↑ outside US and in Industry
- May ➔ local analgesia / antipruritic effects
- Absorbed all routes; Very lipid soluble
- Symptoms:
  - GI: N/V and upset
  - CNS excitation...the key
    - Fasciculation; Restless and agitated
    - Seizures (early as 1-2 hours)
  - But also...CNS depression
  - Treatment – Supportive; Benzodiazepines

Old place – Mothballs