Exposure Assessment

What Is the Dose and What Can the Dose Do?

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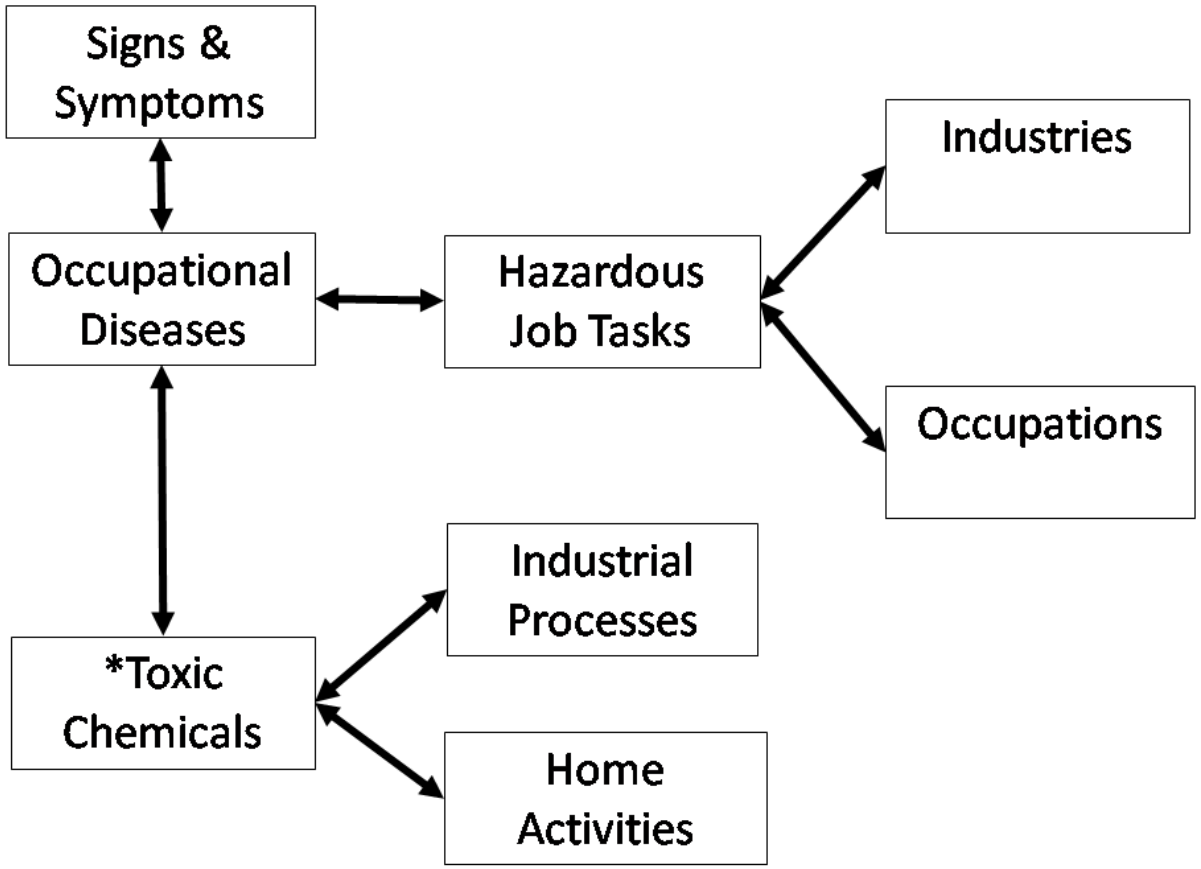
Outline of Talk

- What is Haz-Map?
- Lessons Learned:
  - Toxicology
  - Industrial Hygiene
  - Epidemiology
  - More Research Needed

What Is Haz-Map?

- A relational database of occupational toxicology accessible on the NLM website since 2002;
- Collects into one database the best information available regarding occupational exposures and diseases and supports the early recognition and prevention of work-related diseases;
- Links chemicals to occupational diseases, in which causality has been established by current scientific evidence;

Eight Major Tables in Haz-Map



** Toxic chemicals include biological agents, e.g., latex rubber.*

Haz-Map Sources of Information

- Best and most up-to-date journals, monographs, textbooks, online databases, and websites;
- Sources of information in Haz-Map are referenced. For example, the reference tag [Sullivan, p. 79] refers to the Sullivan & Krieger textbook.
- See www.haz-map.com/referenc.htm for a complete bibliography and a list of all reference tags.

Toxicology

- In which the adverse effects of chemicals are established.

What Is Exposure Assessment?

- "Exposure assessment is the quantification and evaluation of the dose of chemical incurred from the exposure situation under consideration." [Sullivan, p. 79]
- "Exposure assessment is the step that quantifies the intake of an agent resulting from contact with various environmental media (e.g., air, water, soil, food). . . . It determines the degree of contact a person has with a chemical and estimates the magnitude of the absorbed dose." [Hayes, p. 477]

What Is a Toxic Chemical?

- “What is there that is not poison? All things are poison and nothing without poison. Solely, the dose determines that a thing is not a poison.” [Paracelsus, 1492-1541]
- “Hazard evaluation involves both the toxicity of the chemical or material and the opportunity for exposure to cause disease." [Sullivan, p. 32]

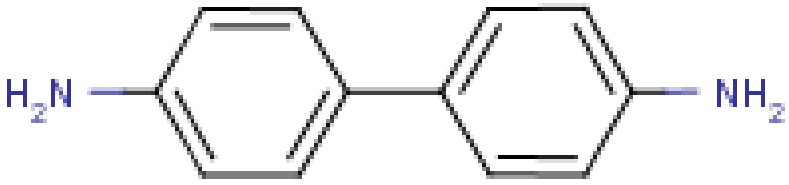
What Makes a Chemical Hazardous?

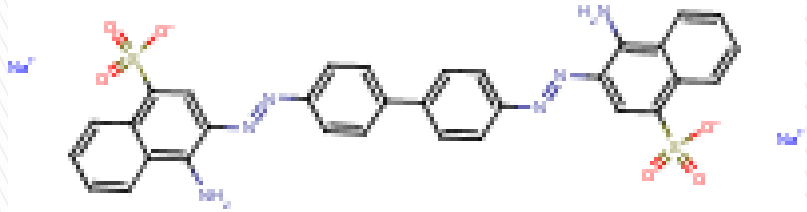
- "A distinction is made between toxicity and hazard. An extremely toxic chemical that is in a sealed container on a shelf has inherent toxicity but presents little or no hazard. When the chemical is removed from the shelf and used by a worker in a closed space and without appropriate protection, the hazard becomes great. Thus the manner of use affects how hazardous the substance will be in the workplace." [LaDou, p. 175]
- Hazard = Toxicity X Exposure

Internet Resources

- ChemIDplus
- ExPub
- Use these two portals to enter the name or CAS number of a chemical and to find information from many different websites.
- Both portals show the matching Haz-Map records.

Chemical Toxicity Is Related to Chemical Structure



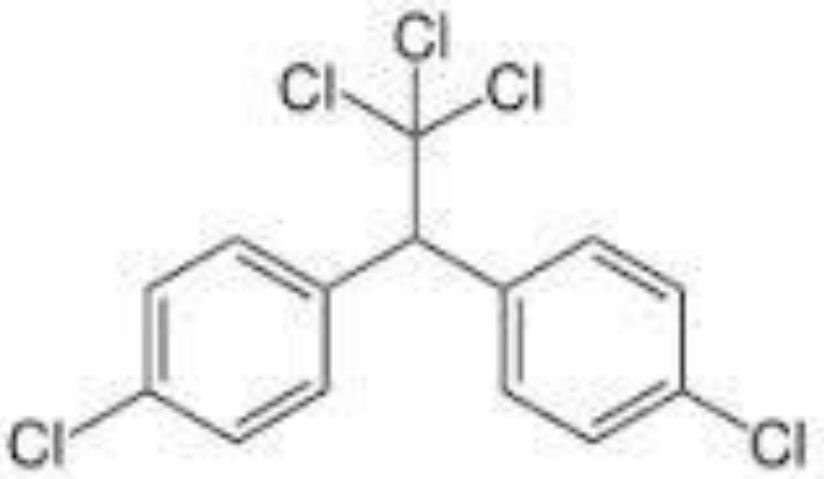


Benzidine

Congo Red

Structure-Activity Relationships

- For an unknown chemical, find a known chemical with a similar structure;
- Chemicals in the same class inherit the properties of that class;



Structure of DDT

Major and Minor Categories of Hazardous Chemicals

- See http://hazmap.nlm.nih.gov and click "By Types of Agents."
- Click a Major Category to see Minor Categories (250 total).
- Click a Minor Category to see Agents (8000 total).
- The 12 major categories are Metals, Solvents, Pesticides, Mineral Dusts, Toxic Gases & Vapors, Plastics & Rubber, Biological Agents, Nitrogen Compounds, Other Classes, Other Uses, Dyes, and Radiation/Physical Agents.

Saturated Vapor Concentration

- The vapor pressure (VP) is a measure of a chemical's volatility at room temperature (20–25° C or 68–77° F).
- Multiply VP times 1300 to estimate in ppm the saturated VP of the chemical after a spill in a confined space. [Sullivan, p. 34]
- For example, if the VP is 76 mm Hg (1/10 of atmospheric pressure), then the saturated VP is 76 X 1300 = 98,800 ppm, i.e., about 1/10 of a million parts per million.

Saturated Vapor Concentration

- This means that a chemical with vapor pressure of 760 mm Hg (atmospheric pressure) has the potential to reach a concentration of one million parts per million (760 X 1300 = 1,000,000).
- If you know that the VP of toluene is 28.4 mm Hg at room temperature, then you can estimate the maximum concentration after a spill in a confined space (28.4 X 1300 = 36,920 ppm).

Odor Threshold, LC50, and IDLH

- How does the saturated vapor concentration of the chemical compare to these values?
- If the victim smelled the chemical, then you know the concentration was higher than the odor threshold.
- The LC50 is the lethal concentration in 50% of the animals tested in an inhalation experiment.
- IDLH is an estimated concentration that is “Immediately Dangerous to Life or Health.”

Conversion of ppm to mg/m^3

- See links to the Molecular Weight Calculator and Conversion Calculator at the bottom of this page: http://www.haz-map.com/glossary.htm

Dose-Response Relationship

- Relationship between the dose of a toxic chemical and the incidence of an adverse effect;
- This is a fundamental law of toxicology expressed as, "The dose makes the poison."
- For any poison, there exists a threshold dose below which adverse effects do not occur.

The Placebo Effect Does Not Depend on Dose

- The placebo effect is real and measurable, but it is a subjective phenomenon.
- The placebo effect can occur below the threshold dose.
- In toxicology, the placebo effect is called the nocebo effect, i.e., an adverse effect rather than a pharmaceutical effect.
- The placebo effect may occur without detection in studies that are not double-blinded.

Public Health Implications of Nocebo Effect

- Public announcements in news media that reinforce fear of chemicals or radiation can cause adverse health effects.
- There are no public health agencies that monitor the dissemination of chemical information.
- Results of isolated studies are often disseminated without providing any context of the current state of knowledge.

Hormesis

"Based on the nearly 6000 hormetic dose-response examples entered into the database, the stimulatory component of the dose-response begins immediately below the quasi-threshold, the toxicological NOAEL."

Hayes AW (ed). *Principles and Methods of Toxicology*, 5th Ed. Boca Raton: CRC Press, 2008, p. 84-85.

Hormesis: What Does It Mean?

- The human body is not a passive sponge.
- Rather we are active, adapting organisms.
- Every healing professional knows about the body's amazing power to heal itself.
- A toxic dose causes the body to make an adjustment.
- This adjustment may stimulate the body.
- For example, exercise can damage muscles and also make the muscles stronger.

Half-Life

- Time required to reduce by one half the amount of a chemical absorbed by the body;
- Half-life can be calculated accurately only for those substances eliminated linearly, independent of concentration.
- For linearly eliminated substances, it takes approximately 3.5 half-lives to eliminate 90% of the substance. [LaDou, p.183]
- Bioaccumulation is the progressive increase of a poison in the body where the rate of intake exceeds the rate of elimination.

Half-Life: What Does It Mean?

- Most chemicals are rapidly eliminated from the body.
- After drinking alcohol the “inebriation” lasts for only a few hours.
- After eating asparagus, the urine odor lasts less than 24 hours.
- Metals like lead can accumulate in the body of workers exposed daily to lead dust.
- Many of the halogenated polyaromatic hydrocarbons, e.g., PCBs, PBBs, DDT, and TCDD, bioaccumulate and have been banned.

Controlled Vocabulary of Adverse Effects in Haz-Map

Category	Adverse Effects
Lung Toxin	Asthma, Pneumonitis, Chronic Bronchitis, and Fibrosis
Neurotoxin	Neuropathy, Parkinson's Syndrome, and CNS Solvent Syndrome
Hematotoxin	Methemoglobinemia, Aplastic Anemia, and Hemolytic Anemia
Dermatotoxin	Contact Dermatitis, Chloracne, and Skin Burns
Carcinogen	Known, Probable, or Possible
Other Tissue Toxin	Hepatotoxin, Nephrotoxin, and Reproductive Toxin
Other Poison	Organophosphate, Carbamate, Organochlorine, Uncoupler, Chemical Asphyxiant, and Simple Asphyxiant

Adverse Effects in Haz-Map

- The most important adverse effects in occupational toxicology, based on my research;
- Each chemical is tagged with all adverse effects that apply;
- Adverse effects include those seen in high-dose animal experiments and in human cases of poisoning by ingestion;
- Not the same as occupational diseases—relatively small daily doses, usually by skin or inhalation routes;

Industrial Hygiene

- In which the health hazards of industrial processes are recognized.

What is a TLV?

- "The concentration in air to which it is believed that most workers can be exposed daily without an adverse effect (i.e., effectively, the threshold between safe and dangerous concentrations). The values were established (and are revised annually) by the ACGIH and are time-weighted concentrations (TWA) for a 7- or 8-h workday and 40-h workweek, and thus are related to chronic effects. A short-term exposure limit (STEL) is defined as a 15-min TWA exposure, which should not be exceeded at any time during a workday even if the 8-h TWA is within the TLV-TWA." IUPAC Gold Book

Guide to Occupational Exposure Values

- Published annually by ACGIH;
- Can find chemical by name or CAS number;
- Includes TLVs, PELs, MAKs, and IARC classifications;
- All of these values are included and updated in Haz-Map.

Biological Monitoring

- Has some advantages over measuring air contaminant levels;
- Measures uptake through all exposure routes;
- Determines dose whether or not personal protective equipment is used;
- Individual differences are reflected in results;
- Updates of Biological Exposure Indices are published each year by ACGIH in *TLVs and BEIs*.

Key Industrial Processes

- Agents in Haz-Map are linked to one or more of the 54 processes.
- Most of these are industrial processes as described in *Recognition of Health Hazards in Industry* by William A. Burgess.
- Covered industrial processes include abrasive blasting, forging, welding, machining, heat treating, electroplating, painting, soldering, mining, smelting, and production of steel, aluminum, pulp & paper, and textiles.

Epidemiology

- In which the causal agents of occupational diseases are established.

Acute or Chronic?

- Usually acute exposures (phosgene) cause acute diseases and chronic exposures (coal dust) cause chronic diseases.
- Animal studies are often helpful in understanding acute diseases (pneumonitis) but less helpful in understanding chronic diseases (pneumoconiosis).
- Epidemiological studies are often necessary to establish the causal agents of chronic occupational diseases.

Reversible and Irreversible Health Effects

- Epidemiological studies of occupational risk factors for COPD may be misleading when pulmonary function results are used as markers of disease because the impairment may be reversible.
- Workers exposed to high levels of cadmium in the past suffered chronic renal disease, but recent studies have shown reversibility of microproteinuria in some cadmium workers. [PMID 9099369 and 12397419]

Time, Place, and Causality

". . . the profile of agents used in the industry has changed significantly over time, necessitating caution in applying the results of studies of health effects in prior decades, especially those evaluating carcinogenic risks of the industry, for currently exposed workers."

Steven Markowitz, p. 1025 "Synthetic Rubber Industry" in *Textbook of Clinical Occupational and Environmental Medicine*

Health Effects of Ionizing Radiation

- A known human carcinogen that may be toxic to the lung, bone marrow, skin, CNS, liver, kidney, eye (cataracts) and reproductive system.
- After acute exposure, high doses can cause acute radiation sickness.
- There is no conclusive evidence that background radiation, averaging about 350 mrem/yr, causes disease, but national (NCRP) and international (ICRP) regulatory agencies still promote the linear-no-threshold (LNT) dose model.

Metals and Occupational Diseases

Disease Name	Caused by Compounds Containing
Toxic Neuropathy	As (inorganic); Tl; Pb; Hg
Pneumoconiosis, Other	Sb; Rare Earth Metals
Pneumoconiosis, Benign	Fe; Ba; Sn; Sb; Rare Earth Metals
Parkinsonism	Mn
Bone Cancer	Pu; Ra
Nasal Sinus Cancer	Ni; Ra
Skin Cancer	As (inorganic)
Occupational Asthma	Cr(VI); Ni
Contact Dermatitis, Allergic	Cr(VI); Ni
Acute Tubular Necrosis	Cr(VI); U; Pb
Chronic Renal Failure	Cd; Pb

Occupational Exposures and Reproductive Health

- See the chapter on “Disorders of Reproduction and Development” by Luderer and Cullen in *Textbook of Clinical Occupational and Environmental Medicine,* edited by Rosenstock, Cullen, Brodkin, and Redlich.

Mineral Dusts and Pneumoconioses

- "It is suspected that this lung airway defense system can be overcome by several different mechanisms: by the physical characteristics of the particle that prevent phagocytosis or cell movement, as seen in asbestosis; by direct cytotoxicity, as in the case of silica dust or cytotoxic metals and compounds; or by simply overloading the clearance capacity of the system, which is most likely the mechanism of injury from normally non-fibrogenic 'nuisance' dusts." [Hendrick, p. 167]

Chemicals Linked to Occupational Cancer

- See the chapter on "Occupation" by Siemiatycki, Richardson, and Boffetta in *Cancer Epidemiology and Prevention*, edited by Schottenfeld & Fraumeni.
- See "Haz-Map Changes Resulting from 2012 IARC Changes to Group 1 Carcinogens" at the bottom of this page: www.haz-map.com/cancer.htm
- Also in 2012-13, IARC linked asbestos to ovarian cancer and trichloroethylene to kidney cancer.

More Research Needed

- In which links between diseases and occupational exposures have not been clearly established.

More Research Needed

- Atherosclerosis: An Occupational Disease?
- Hypertension: An Occupational Disease?
- Do solvents cause hearing loss?
- Porphyria: An Occupational Disease?
- Occupational RA & Scleroderma?
- Environmental Tobacco Smoke (ETS) and Occupational Diseases?
- See http://www.haz-map.com/research.htm.

Carbon Nanotubes & Lung Cancer

- "The fibrous shape of carbon nanotubes (CNTs) raises concern that they may pose an asbestos-like inhalation hazard, leading to the development of diseases, especially mesothelioma."
- "Our data confirm the hypothesis that, although a proportion of all deposited particles passes through the pleura, the pathogenicity of long CNTs and other fibers arises as a result of length-dependent retention at the stomata on the parietal pleura." [PMID 21641383]

More Information Needed

If you need help with this:	Call this number or see website:
Local emergency response	911
Poison Center	800-222-1222
CDC	800-CDC-INFO
CDC Emergency Response Hotline	770-488-7100
State or Local Health Department	www.cdc.gov/mmwr/international/relres.html
HAZMAT Communications Center	800-262-8200
Radiation Emergency Assistance	865-576-1005
Occupational Medicine Clinics	www.aoec.org/directory.htm
Workplace Health Hazard Evaluation	www.cdc.gov/niosh/hhe/Request.html