

Toxicology 101

Indra Frank, MD, MPH

Region 5 Pediatric Environmental Health Specialty Unit



(866) 967-7337

www.uic.edu/sph/glakes/childrenshealth/



This material was supported by the American Academy of Pediatrics (AAP) and funded (in part) by the cooperative agreement FAIN: 1U61TS000237-02 from the Agency for Toxic Substances and Disease Registry (ATSDR).

*Acknowledgement: The U.S. Environmental Protection Agency (EPA) supports the PEHSU by providing partial funding to ATSDR under Inter-Agency Agreement number **DW-75-95877701**. Neither EPA nor ATSDR endorse the purchase of any commercial products or services mentioned in PEHSU publications*

Outline

- How do chemicals get into the body?
- What do they do once they are there?
- How do they leave?

Toxicology in the News

Animas River fouled by 1 million gallons of contaminated mine water

EPA accidentally releases water; Durango residents warned to cut back on water use as health officials evaluate river

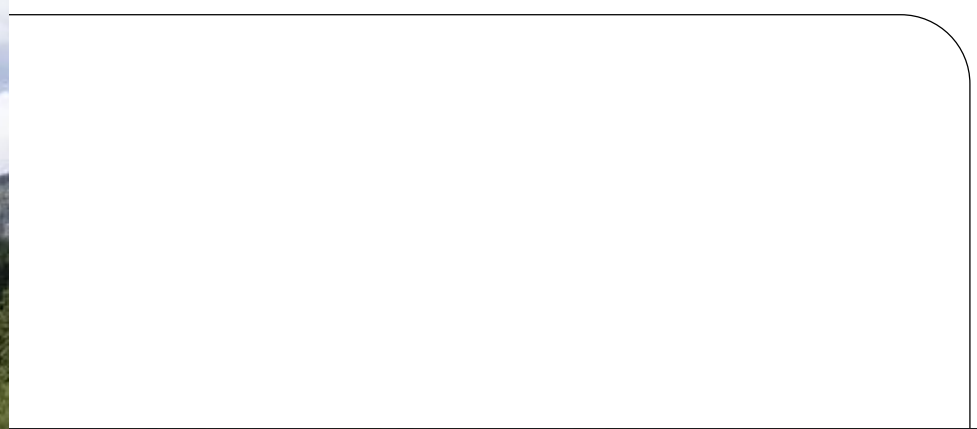
By Jesse Paul and Bruce Finley

The Denver Post

POSTED: 08/06/2015 11:27:26 AM MDT | UPDATED: 5 DAYS AGO

279 COMMENTS

www.denverpost.com/news/ci_28595759/animas-river-contaminated-by-1-million-gallons-contaminated



Pre-spill photo Angela Adams

August 6, 2015

Brent Lewis/The Denver Post/Getty Images

EPA proposes cleaning up toxic drinking water problem on Indy's west side

POSTED 4:22 PM, SEPTEMBER 29, 2015, BY [JESSE WELLS](#)

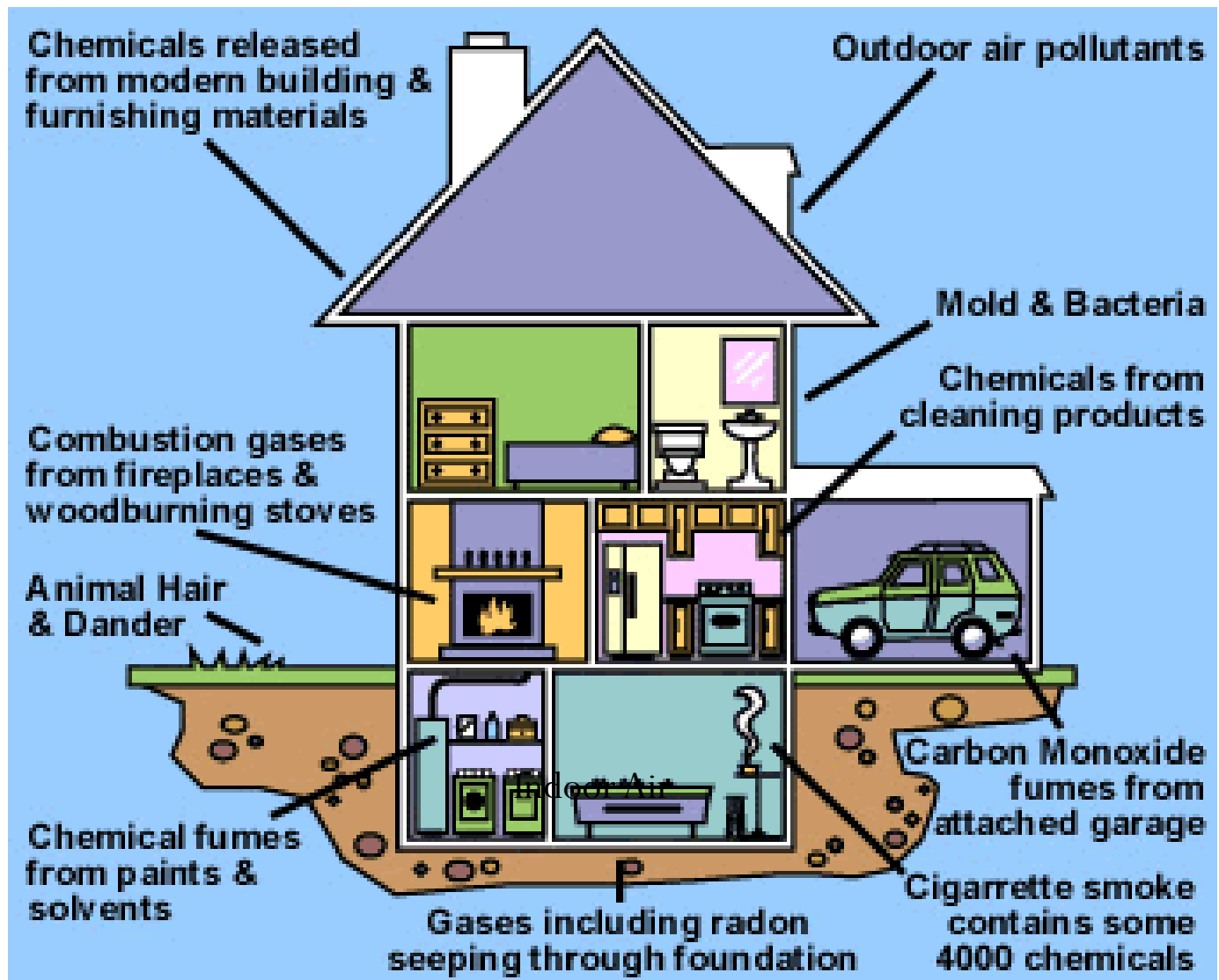
Crop duster spray hits teens working in field

[Dylan Peers McCoy](mailto:dmccoy@jconline.com), dmccoy@jconline.com 1:37 p.m. EDT July 16, 2015



(Photo: [John Terhune/Journal & Courier](#), [John Terhune/Journal & Courier](#))

Indoor Air



How do chemicals get into the body?

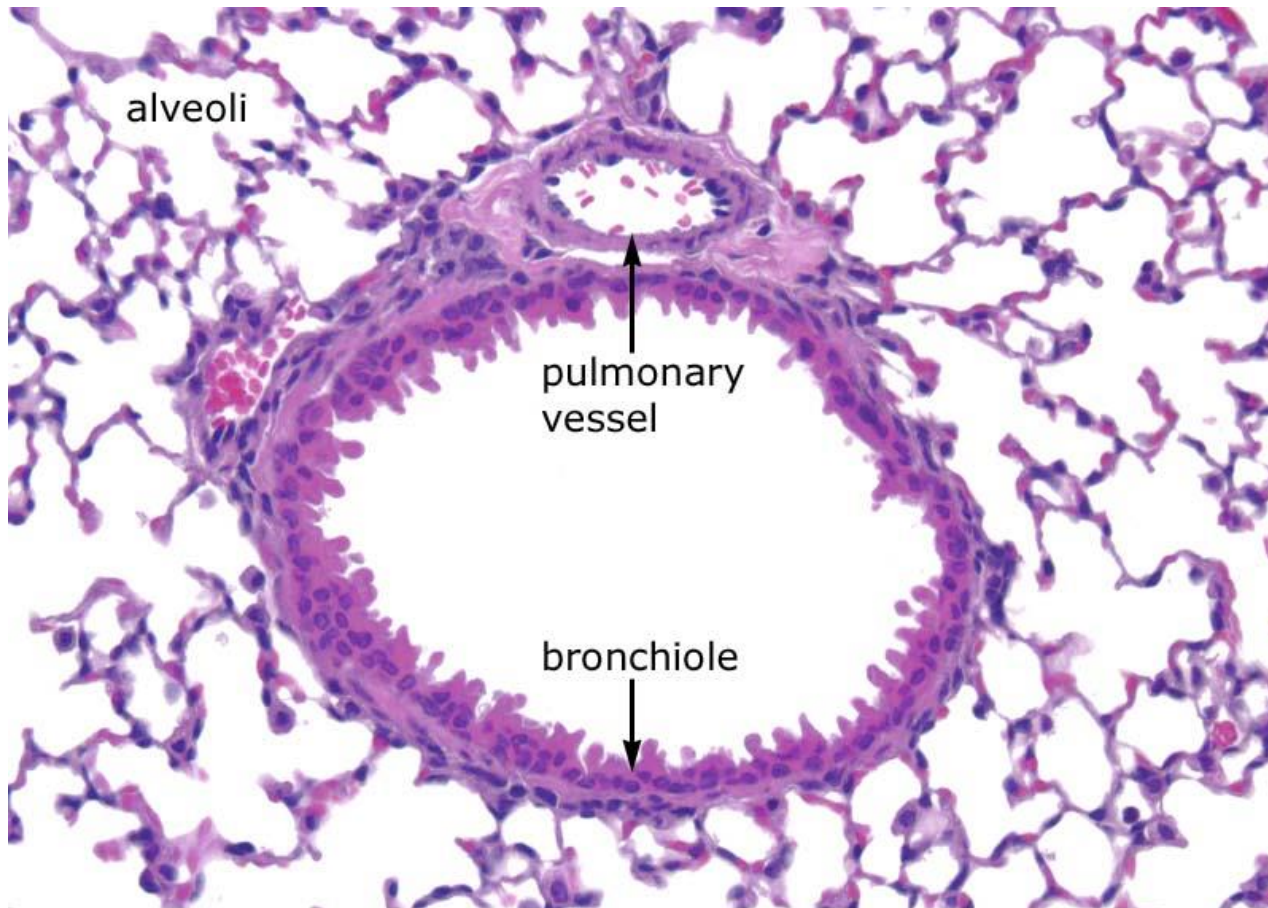
Inhalation



©Ron Leishman * illustrationsOf.com/1047868



Lung Histology



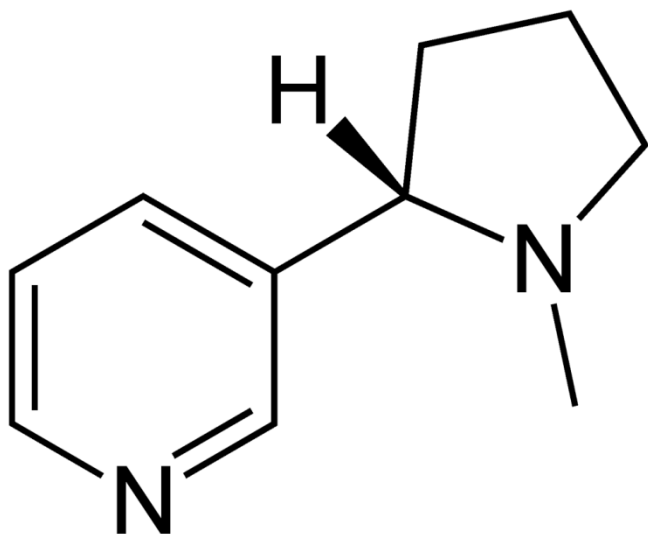
© Deltagen Inc.

How do chemicals get into the body?

Skin absorption



Nicotine



How do chemicals get into the body?

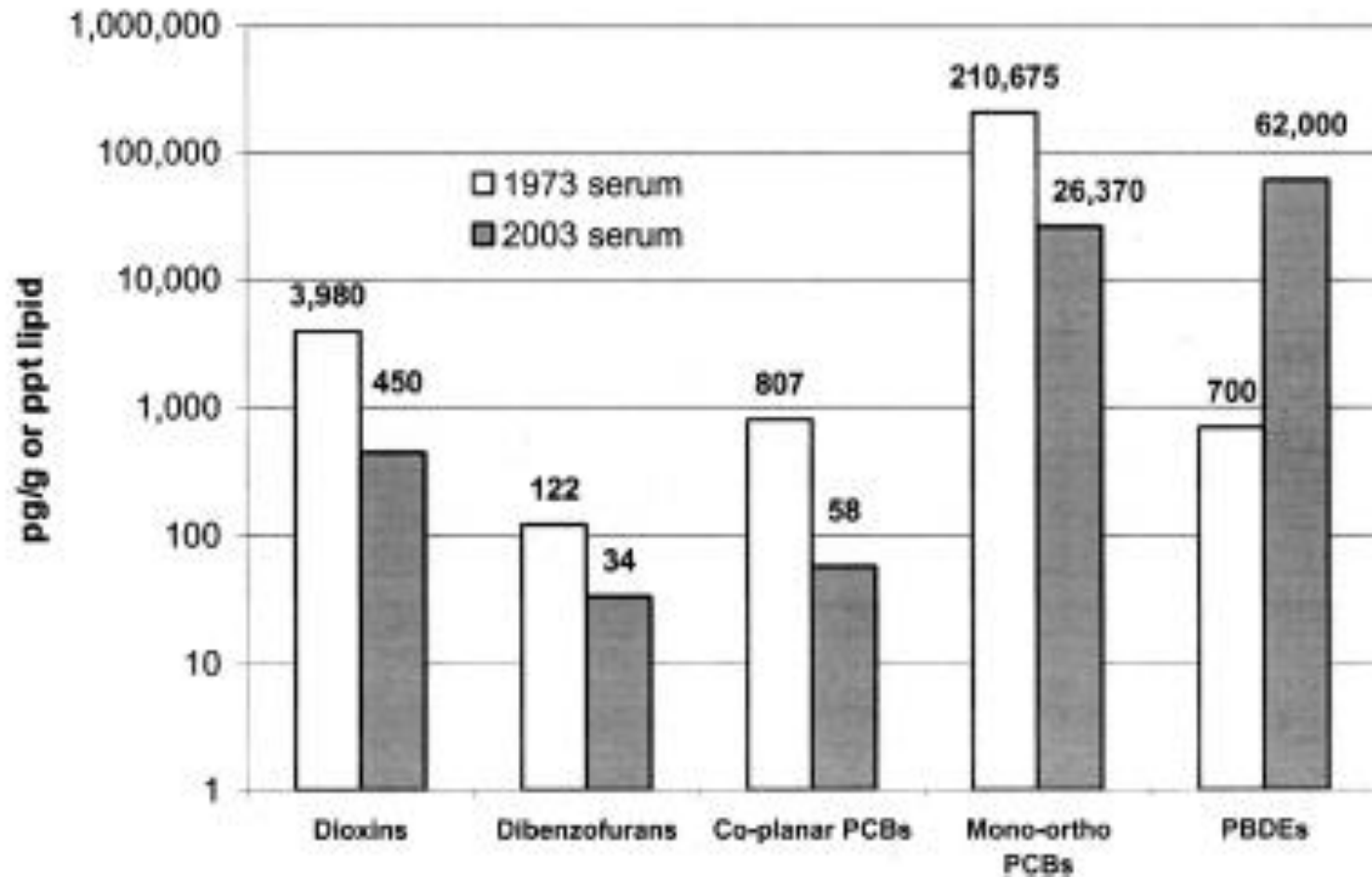
Ingestion



EPA Standard Default Exposure Factors

Exposure path	Daily intake
Ingestion of water	2 Liters
Ingestion of dust (child)	200 mg
Ingestion of dust (adult)	100 mg
Inhalation (total)	20 m ³

Chemicals get into the body even if they were never intended to do so.



Outline

- How do chemicals get into the body?
- What do they do once they are there?
- How do they leave?

What do they do once they are there?

- Distribution
- Storage
- Metabolism
- Toxicity

What do they do once they are there?

- Distribution
 - The blood carries the chemical throughout the body
- Storage
- Metabolism
- Toxicity

What do they do once they are there?

- Distribution
 - The blood carries the chemical throughout the body
- Storage
 - Some chemicals have an affinity for an organ and stay there. Ex. Lead is stored in bone.
- Metabolism
- Toxicity

What do they do once they are there?

- Distribution

- The blood carries the chemical throughout the body.

- Storage

- Some chemicals have an affinity for an organ and stay there. Ex. Lead is stored in bone.

- Metabolism

- The body's chemical processes alter the chemical.

- Toxicity

What do they do once they are there?

- Distribution

- The blood carries the chemical throughout the body.

- Storage

- Some chemicals have an affinity for an organ and stay there. Ex. Lead is stored in bone.

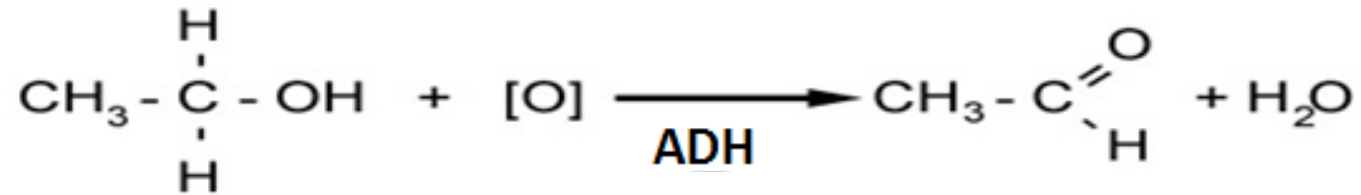
- Metabolism

- The body's chemical processes alter the chemical.

- Toxicity

- The chemical acts on the body.

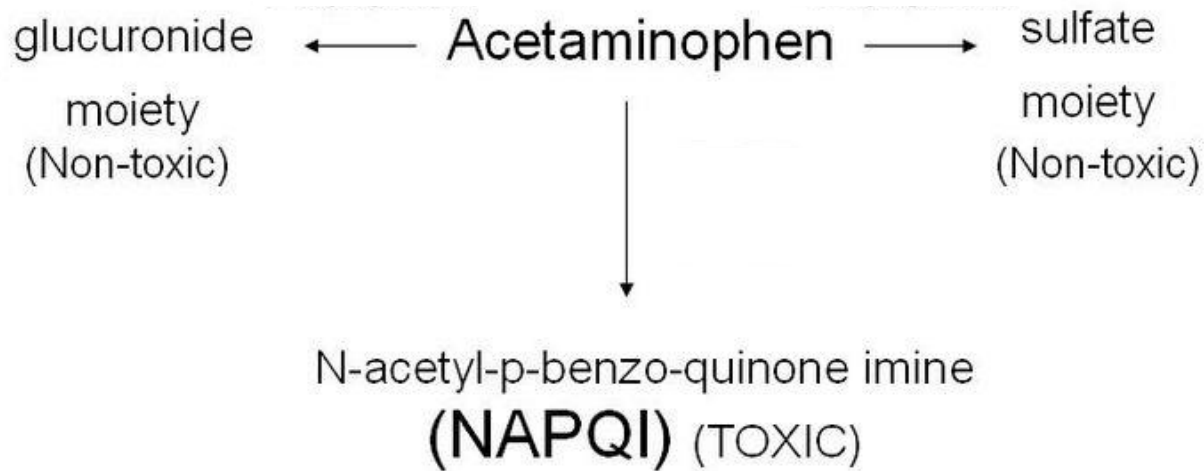
Purpose of Toxicant Metabolism



ADH = alcohol dehydrogenase

1. Detoxify
2. Make the toxicant easier to eliminate

Some metabolites are more toxic, not less



Toxicity: How chemicals cause health problems

- Toxicity begins at the molecular level
 - Examples:
 - Binding to protein
 - Binding to DNA
 - Disrupting cell membranes

Toxicity: How chemicals cause health problems

- Molecular interaction



- Cellular dysfunction

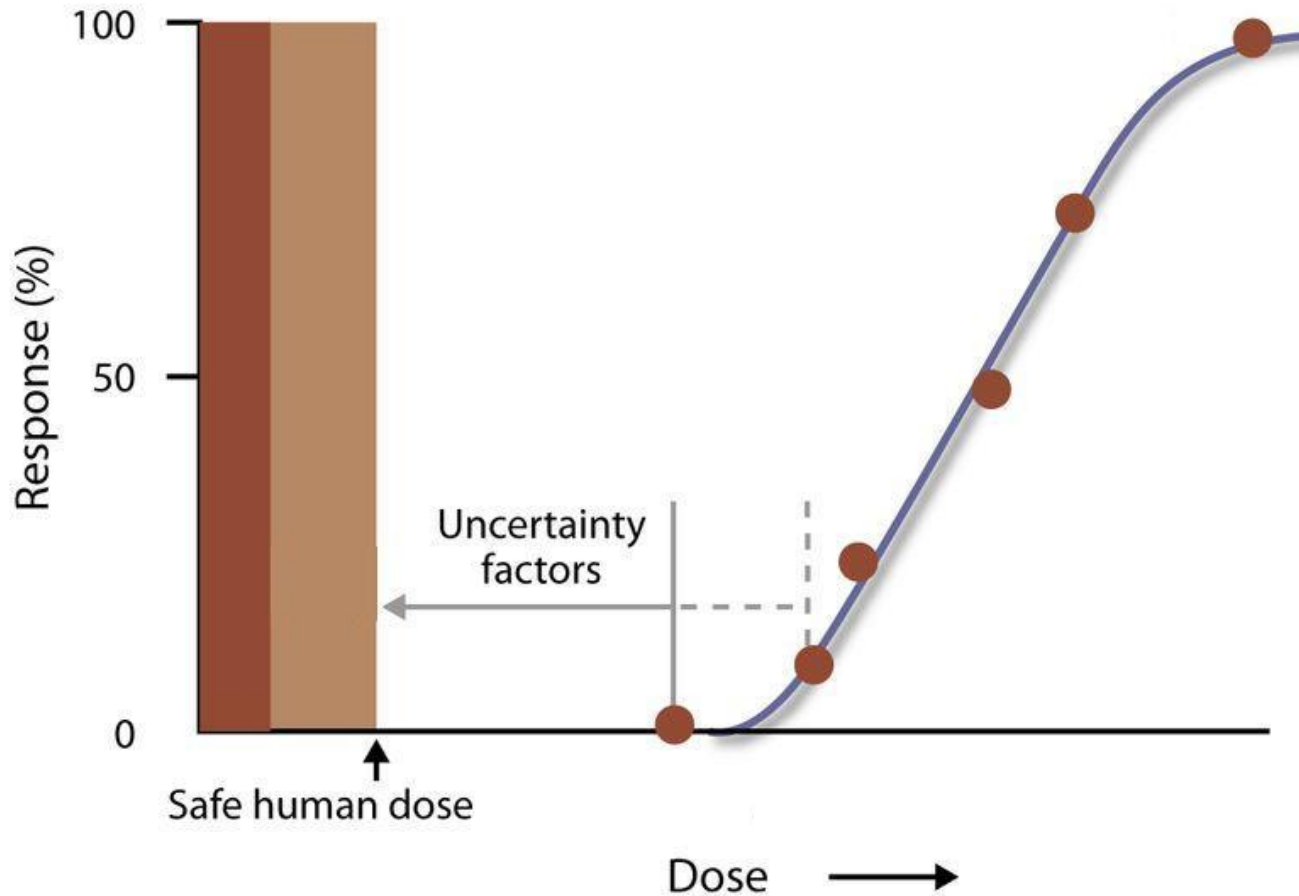


- Organ dysfunction



- Symptoms

The dose determines how much toxicity



Adapted by CTLT from Principles of Toxicology: Environmental & Industrial Application, 2nd ed. Williams, James & Roberts, eds, John Wiley & Sons, Inc., NY, 2000.

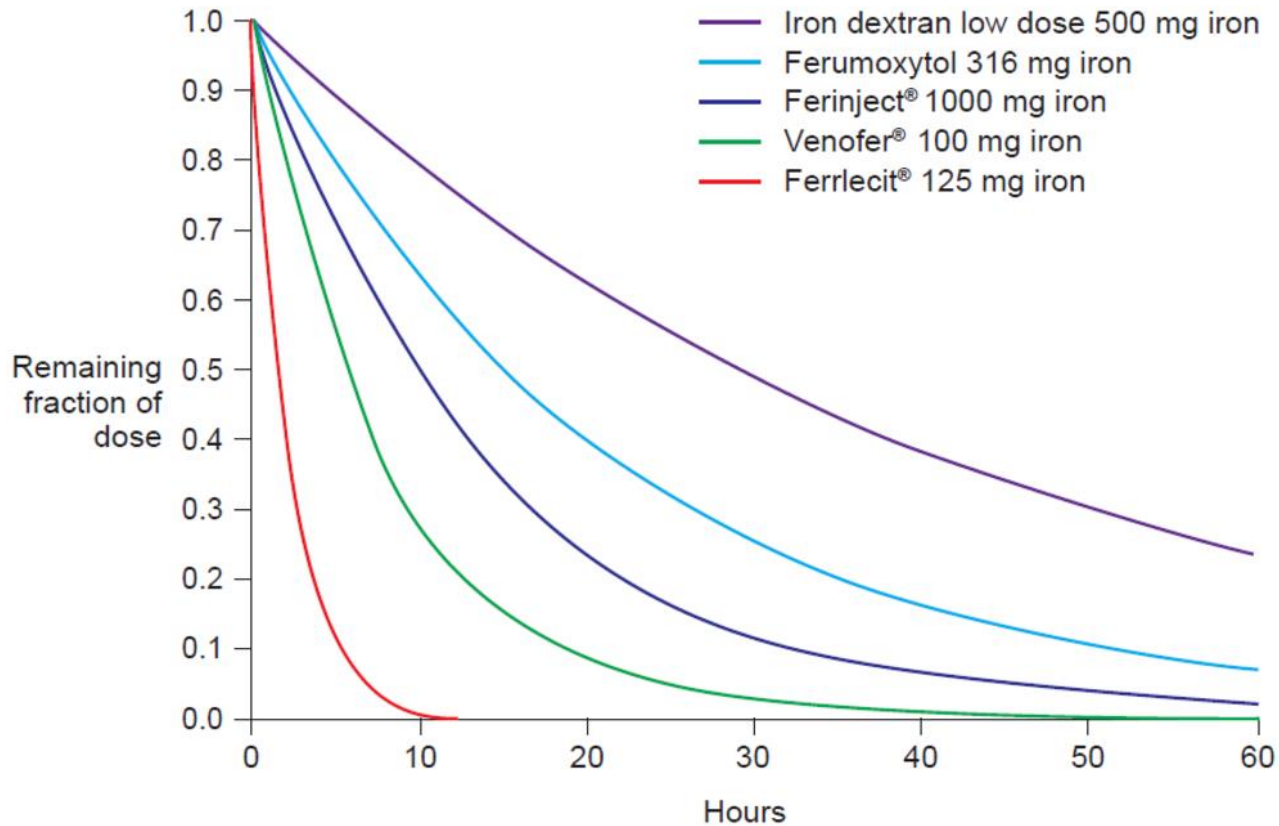
Outline

- How do chemicals get into the body?
- What do they do once they are there?
- How do they leave?

Toxicant Elimination

- Urine > Feces > Lungs
- Minor routes (e.g., sweat, milk, hair, and nails)

Timing of Elimination



After a single dose

Half life

- How long it takes for the body to get rid of half the chemical

Example half lives

- Epinephrine – 2 minutes
- Morphine - 2 hours
- Mercury - 2 months
- PCBs - 5 to 10 years

Repeated Exposures

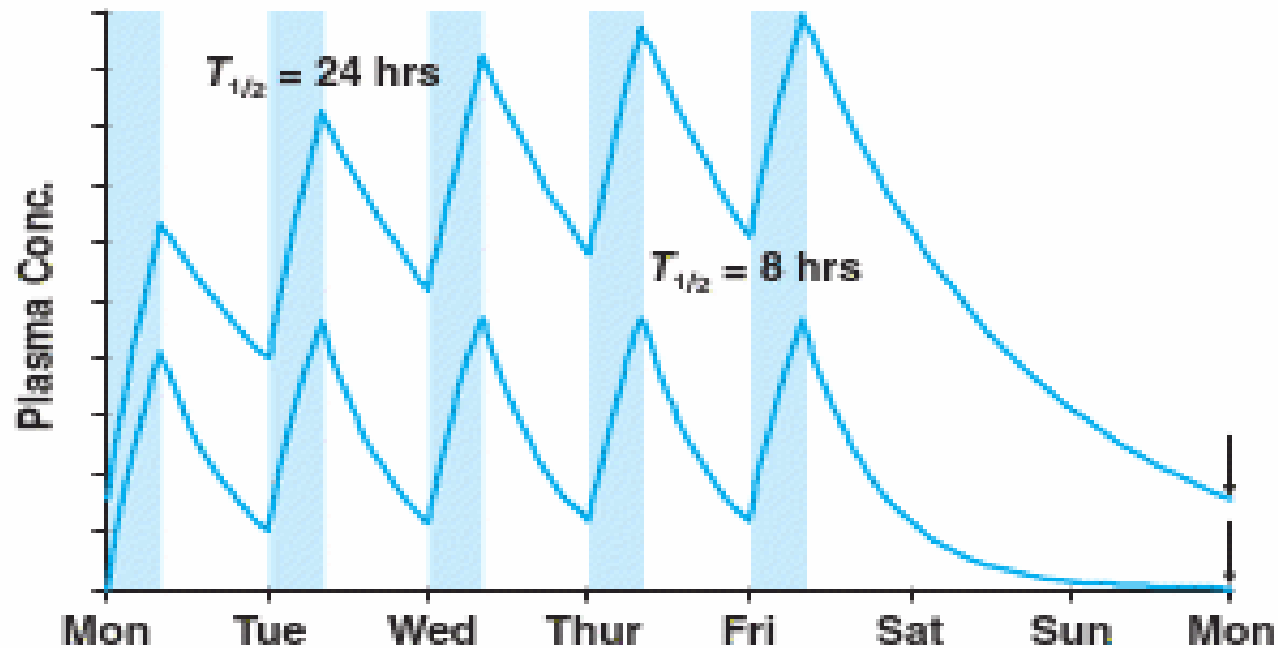


Figure 7-10. Simulated accumulation of plasma concentration from occupational exposure over the cycle of a work week compared between two industrial chemicals with short and long elimination half-lives.

Example: Carbon Monoxide

- How does the chemical get into the body?
- What does it do once it is there?
- How does it leave?

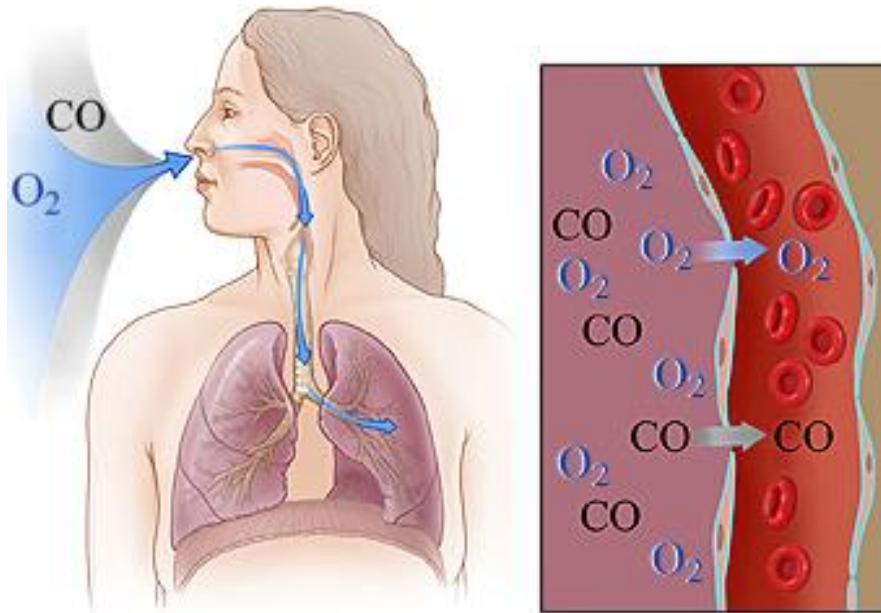
Example: Carbon Monoxide

- Sources



Example: Carbon Monoxide

- How does the chemical get into the body?



1) Oxygen (O₂) and carbon monoxide (CO) are inhaled

2) O₂ and CO enter blood

Example: Carbon Monoxide

- What does it do once it is there?
 - Distribution
 - Storage
 - CO binds to proteins
 - Metabolism
 - the body converts some CO to CO₂
 - Toxicity
 - CO binds to hemoglobin which blocks O₂

Example: Carbon monoxide

- The dose determines toxicity

Concentration of CO	Symptoms
35 ppm	Headache after 6 – 8 hours
400 ppm	Headache after 1 - 2 hours
800 ppm	Dizziness, nausea, convulsions in 45 minutes
3,200 ppm	Death within 30 minutes

Example: Carbon monoxide

- How does it leave?
 - If the person is removed from the CO source,
 - CO is displaced by oxygen
 - Then CO is exhaled

Example: Carbon monoxide

- How does it leave?

	Half-life of CarboxyHb
Breathing ambient air	3 hours
Breathing 100% oxygen	20 minutes

Children are especially vulnerable

- Exposure – may be higher
- Absorption – may be higher
- Metabolism – may be immature
- Elimination – may be immature

Children are especially vulnerable

- A child's organs are still growing
- Cells are multiplying and organizing
- Growth and development are carefully orchestrated through biochemical signals and are therefore easily disrupted

There are more than 80,000 chemicals in commercial use in the U.S.

In the U.S., toxicity testing prior to commercial production is required for

- Food additives
- Pharmaceuticals
(Drugs)
- Pesticides

There are more than 80,000 chemicals in commercial use in the U.S.

Approximately 7% of them have been fully assessed for their toxicity.

Synopsis

- How do chemicals get into the body?
- What do they do once they are there?
- How do they leave?
- Children are especially vulnerable
- The toxicology of most chemicals is poorly understood.