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The Environmental Science Education for Sustainable Human Health

in commemoration of Prof. Armen Saghatelyan

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Environmental Toxicology

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CENS



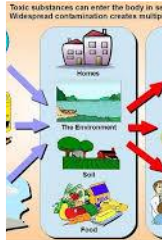
IACRA



ISEC

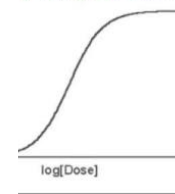


Environmental Toxicology Course



Essentials of Toxicology. Terminology.

Dose-Response Relationship



Dose-Response Relationship.



Toxins and Toxicants.

Toxicokinetics

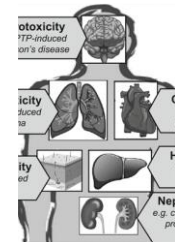
internal concentration over time

toxicodynamics

Toxicodynamics. Toxicokinetics.



Toxicity.



Target Organ Toxicity.

How Toxic Is It?



Exposure Pathway. Route of Exposure.



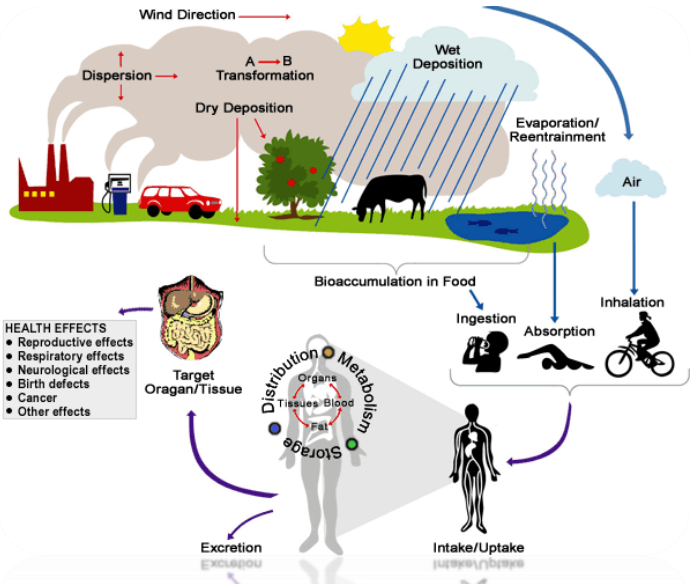
Why should we care?



Environmental Toxicology



the study of poisons around us



atoms, molecules, substances, chemical, reaction, energy, substance

Chemistry

BIOCHEMISTRY

lab, toxic, patients, development, placebo, glass, abuse, solution, effects, helping, business, biotechnology, biology, untreated, side, medical, health, experiment, equipment, analysis, research, pharmacy, medication, pharmaceutical, laboratory, reagents, industry, medicine, discovery, pill, technology, instrument, substance, clinical, diagnosis, diagnosis, health, test, active, ingredient, pharma, healthcare, patient, prevention, science, control, drug, stimulate, treatment, liquid

Pharmacology

Multidisciplinary science

BIOLOGY

Physiology
Anatomy

REGULATION

"upon" "study"
epidemiology
"people"



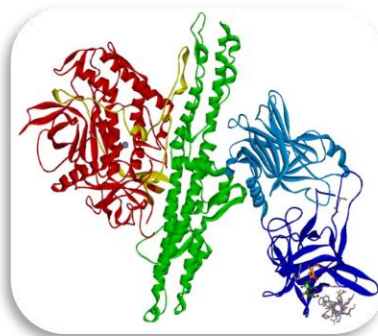
Toxins

Poisonous substances produced by...

animals
(*zootoxins*)



bacteria
(*bacteriotoxins*)



plants

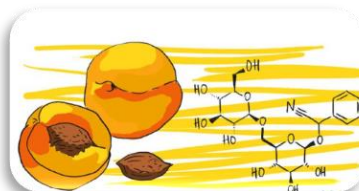
Alkaloids ← (*phytotoxins*) → *Glycosides*



Solanine



Toxic mushrooms



Amigdaline



Toxicants

Xenobiotics (*xenos* – a stranger)

substances, that are not naturally produced in organism



from a variety of industrial, automotive, agricultural, household, or natural sources



Xenobiotics

Classification

Categories

Physical state

Gas, liquid, solid

Chemical structure

Aromatic amines, aliphatics, glycols

General action

Air pollutants, chronic poisons, industrial toxins

Poisoning potential

Slightly toxic, moderately toxic, supertoxic

Effect

Carcinogens, mutagens, teratogens

Target organ

Neurotoxins, hepatotoxins, nephrotoxins

Mechanism of action

Stimulants, inhibitors

General or use class

Plastics, organic chemicals, heavy metals, food additive

Labeling requirements

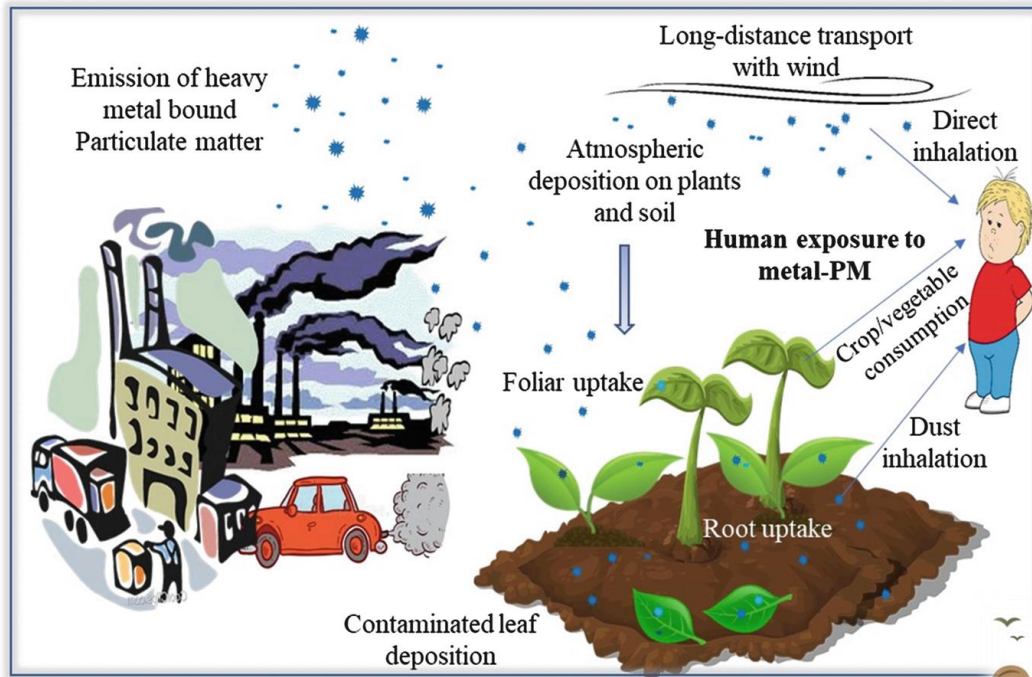
Oxidizer, acid, explosive



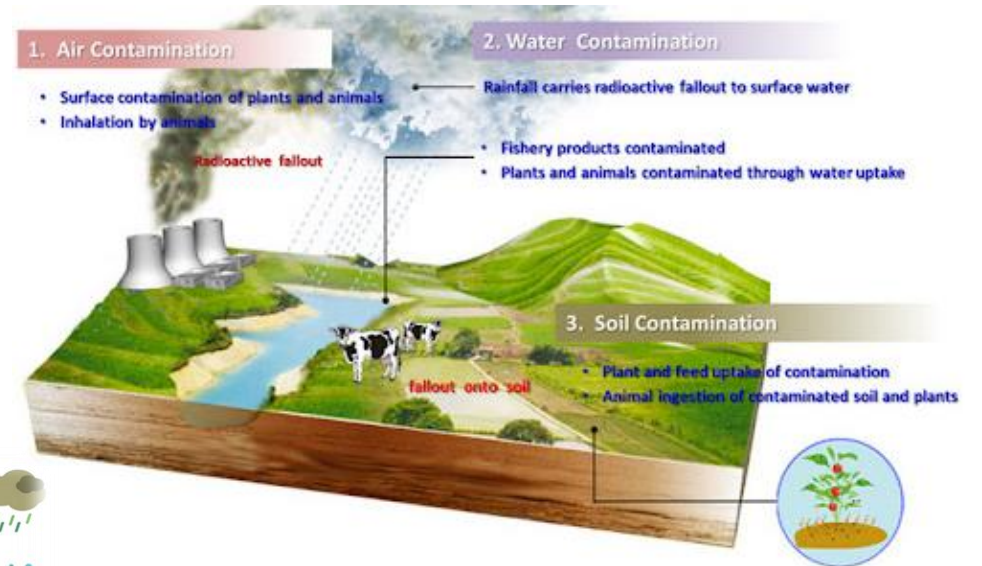
Environmental Toxicants

Hazardous substances that can have adverse effects...

Metals



Radioactive contaminants

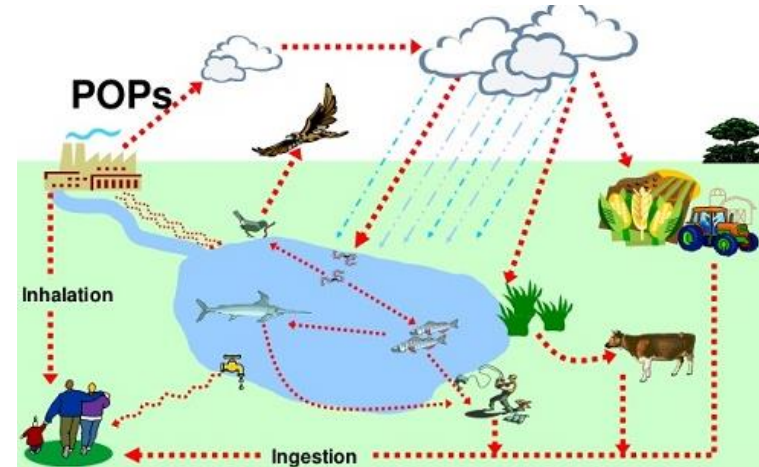


Environmental Toxicants (2)

Pesticides



Persistent Organic Pollutants



- Aldrin
- Dieldrin
- Endrin
- Toxaphene
- Heptachlor
- Mirex
- Chlordane
- PCBs
- HCB
- Dioxins & Furans
- DDT

Dirty dozen

PESTICIDES AND INDUSTRIAL CHEMICALS - ELIMINATION - (ANNEX A)

UNINTENTIONAL PRODUCTION - (ANNEX C)

PESTICIDE - RESTRICTION - (ANNEX B)



Environmental Toxicants (3)

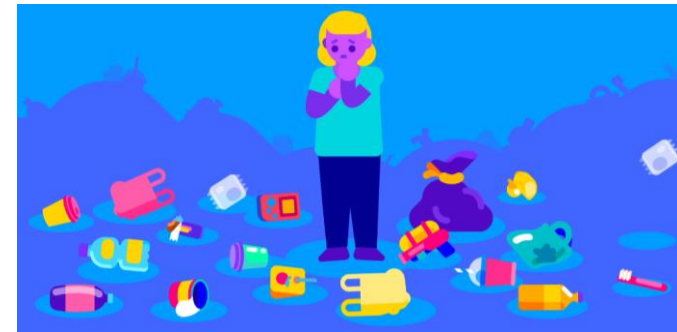
Organic Solvents



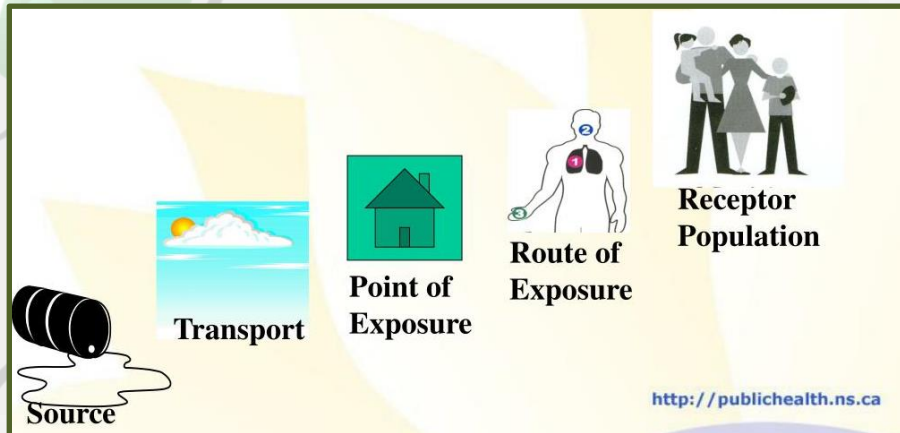
Solvents create quickly high concentrations of vapors



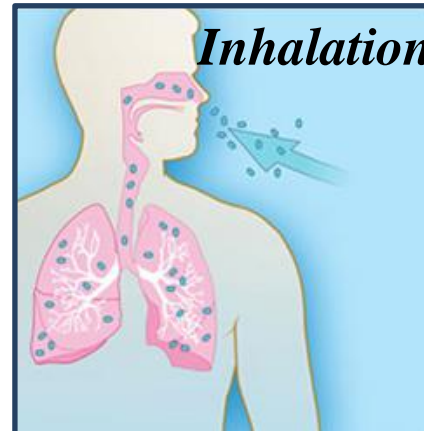
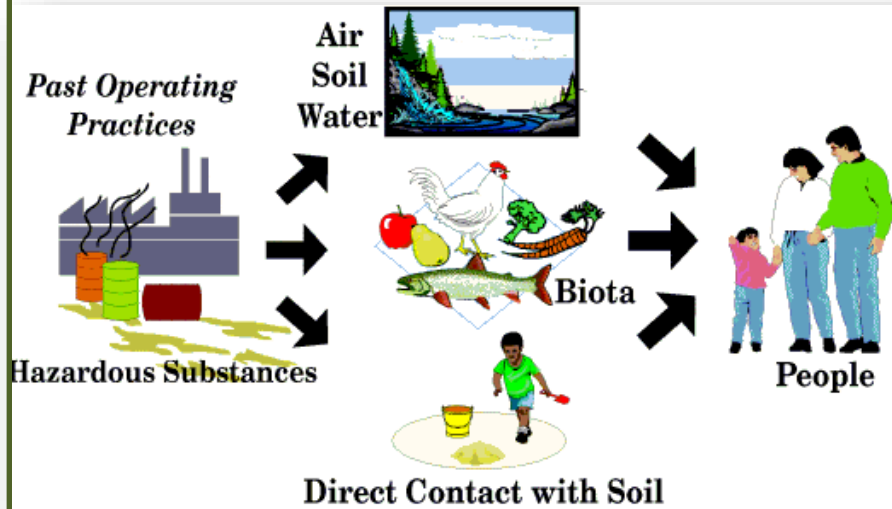
Plastic



Exposure Pathway and Route of Exposure

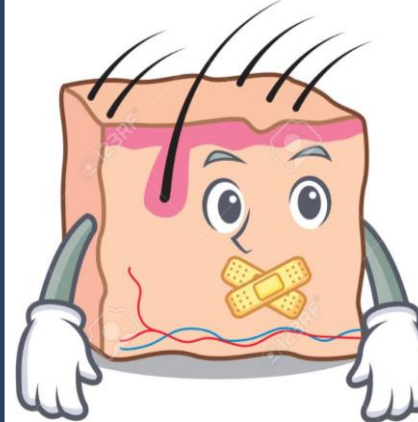


Exposure Pathway

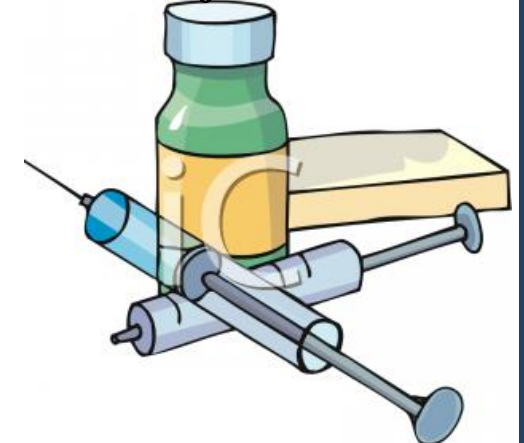


Routes of Exposure

Dermal contact



Injection



Exposure Duration

Acute
less than 24 h

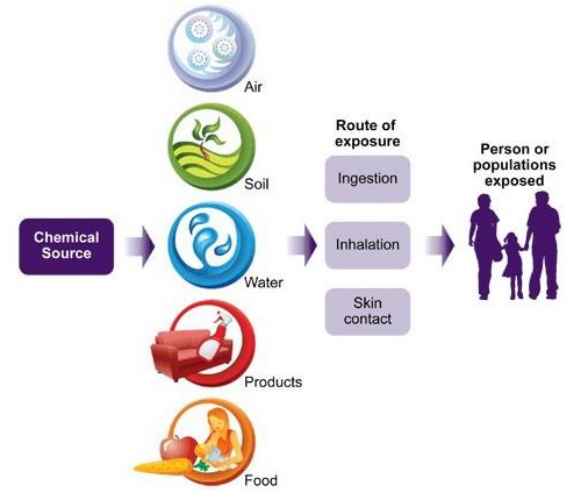


Subacute
from several days to 1 month

Subchronic
generally 1-3 months



Chronic
greater than 3 months



Toxicity

*The state of being poisonous and general term used to indicate **adverse effects***

Duration

Acute toxicity - sudden symptoms last for a short period of time (~24h).

Chronic toxicity - symptoms that are of a long, continuous duration.



Location

Local toxicity - the symptoms are restricted to the site of initial exposure.

Systemic toxicity - adverse effects occur at sites far from the initial site of exposure



How is toxicity determined since chemicals vary in toxicity?



“upon”
epidemiology
“study”
“people”



Target Organ Toxicity

Each organ will respond to a toxicant in a different way.

• **Hematotoxicity** (e.g. by benzene, chlordane, naphthalene)



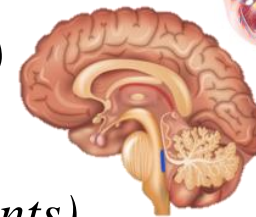
• **Hepatotoxicity** (e.g. chronic ethanol toxicity, organic chemicals)



• **Nephrotoxicity** (e.g. some xenobiotics, such as lead, cadmium, heroin)



• **Neurotoxicity** (e.g. botulin toxin, tetrodotoxin, hexachlorophene)



• **Dermatotoxicity** (e.g. organic solvents, numerous industrial agents)



• **Pulmonotoxicity** (e.g. asbestos fibers, coal dust, beryllium)





Dose

How harmful a chemical is depends on:

- Size of dose over a certain period of time
- How often exposure occurs, who is exposed
- How well the body's **detoxification system** work
- Substance's **properties** (e.g. solubility, persistence)



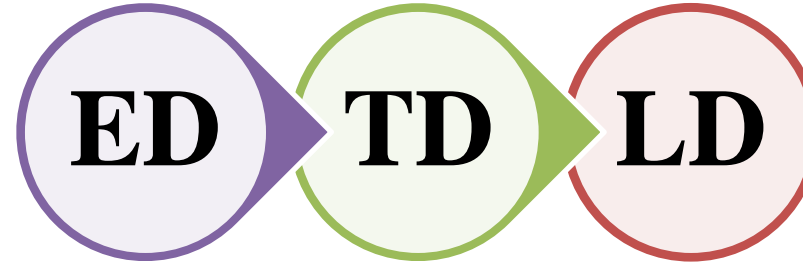
“**All substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy.**”



Dose

Effective Dose

at which the desirable response is observed



Toxic Dose

at which toxicity is present in test organisms

Lethal Dose

resulting in the death of the test organism

Don't compare the dose at which an **LD₀₁** occurs for toxicant **A** with the dose at which an **LD₅₀** occurs for toxicant **B**.

LD₀₁ ~~VS~~ LD₅₀

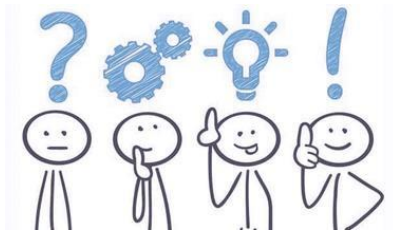
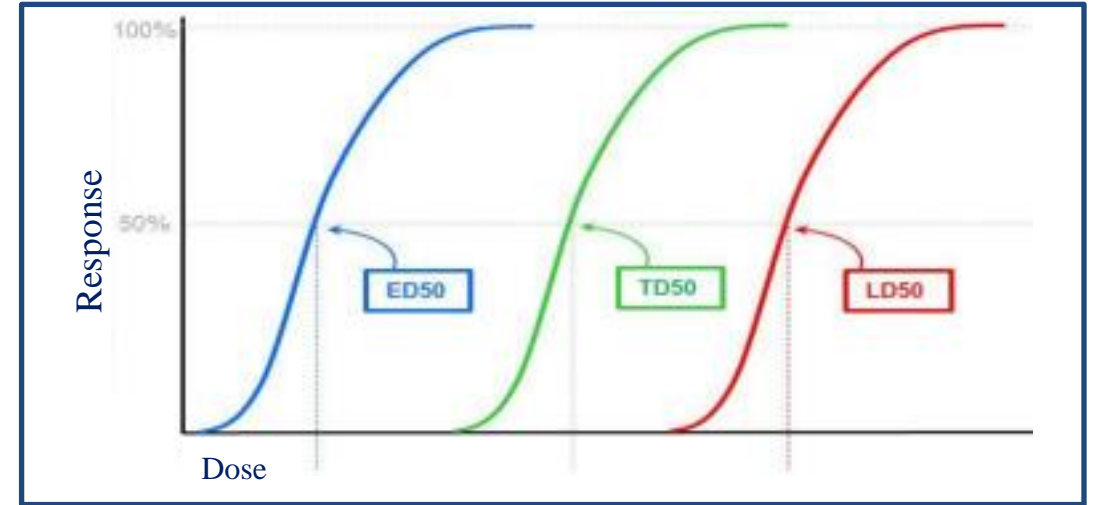
EXAMPLE

Agent	LD ₅₀ (mg/kg)	Toxicity
Ethyl alcohol	9,000	
Sodium chloride	4,000	
BHA/BHT (antioxidants)	2,000	Slight
Morphine sulfate	900	
Caffeine	200	Moderate
Nicotine	1	High
Curare	0.5	
Shellfish toxin	0.01	
Dioxin	0.001	
Botulinum toxin	0.00001	Extreme



Dose-Response Relationship

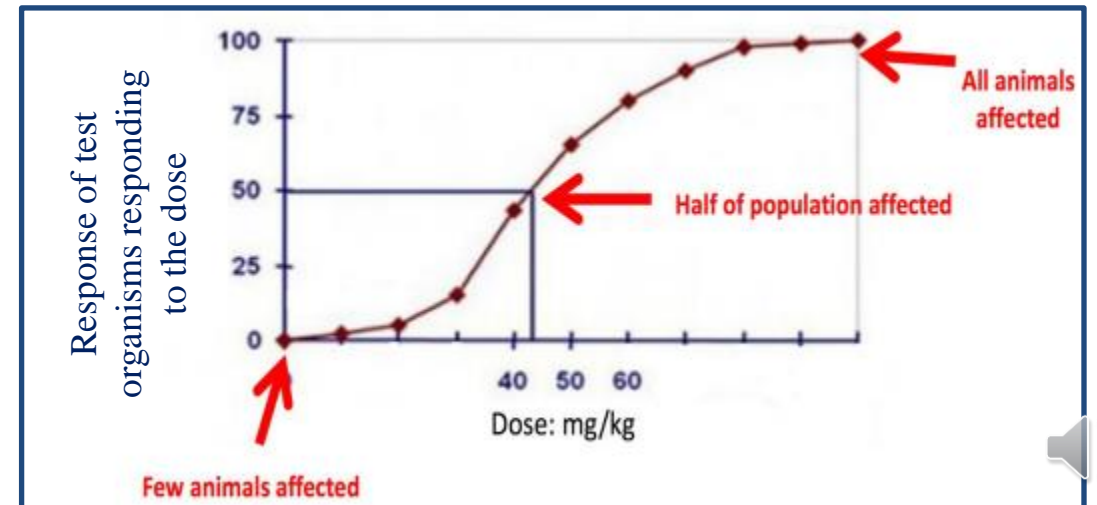
Dose-response relationship – when a consistent mathematical relationship describes the **proportion of test organisms responding to a specific dose** for a given exposure period.



What is LD_{50} ?



The individual dose required to kill **50%** of a population of test animals.



Factors Influencing Dose-Response

- Route of exposure, exposure conditions
- Age and gender characteristics
- Genetic and health status



Effects of chemical interaction

chemical interactions can decrease or multiply the harmful effects of a toxin



Effect	Relative Toxicity (hypothetical)	Example
Additive	$2 + 3 = 5$	Organophosphate pesticides
Synergistic	$2 + 3 = 20$	Cigarette smoking + asbestos
Potentialiation	$2 + 0 = 10$	Alcohol + carbon tetrachloride
Antagonism	$6 + 6 = 8$ or	Toluene + benzene or
	$5 + (-5) = 0$ or	caffeine + alcohol or
	$10 + 0 = 2$	BAL + mercury

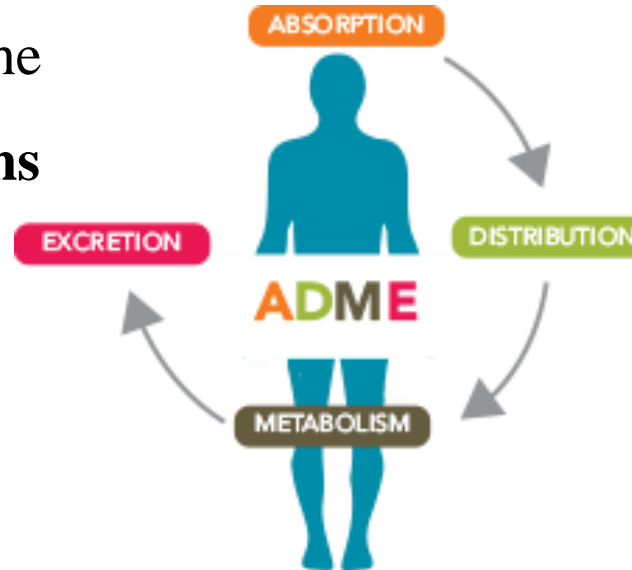
Mathematical Representation of Chemical Interaction



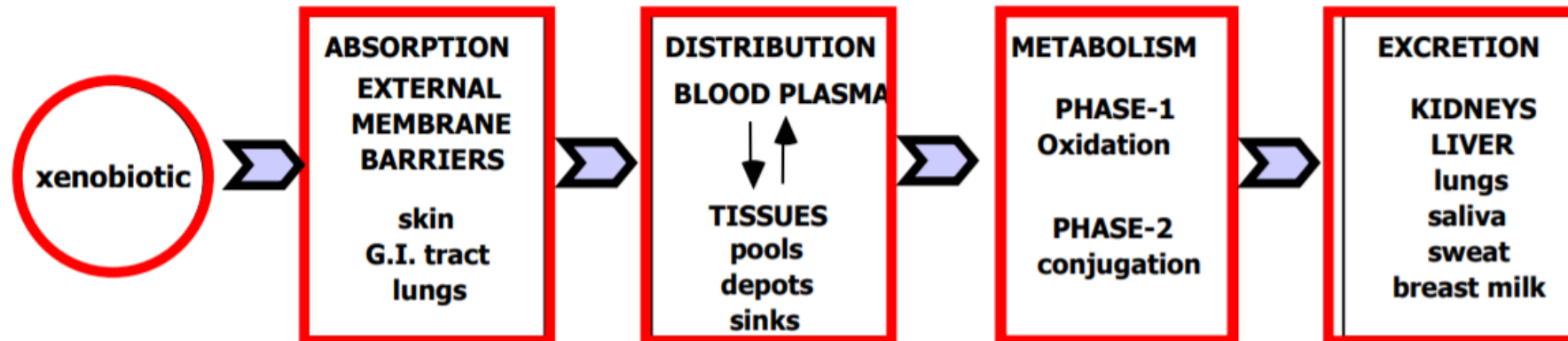
Toxicokinetics

Toxicodynamics

A substance gets into the body and **what happens to it** in the body.



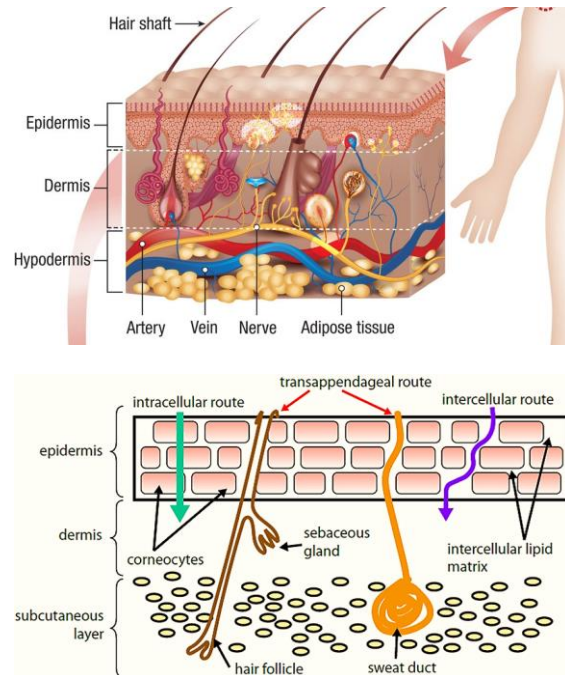
It is concerned with **what the toxicant do** to the body.



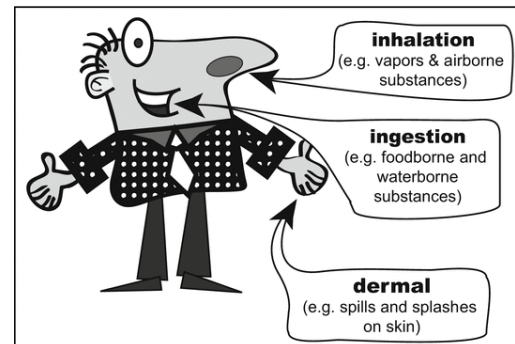
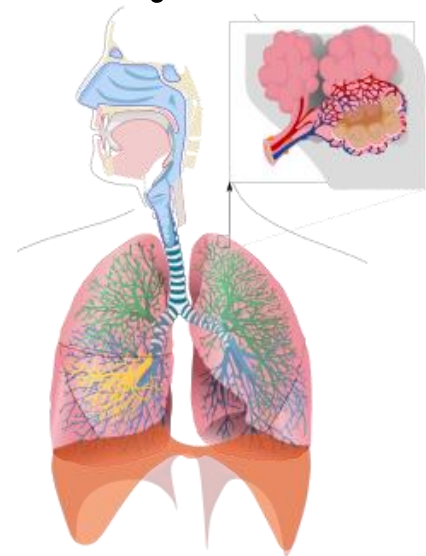
Absorption

3 primary routes of absorption

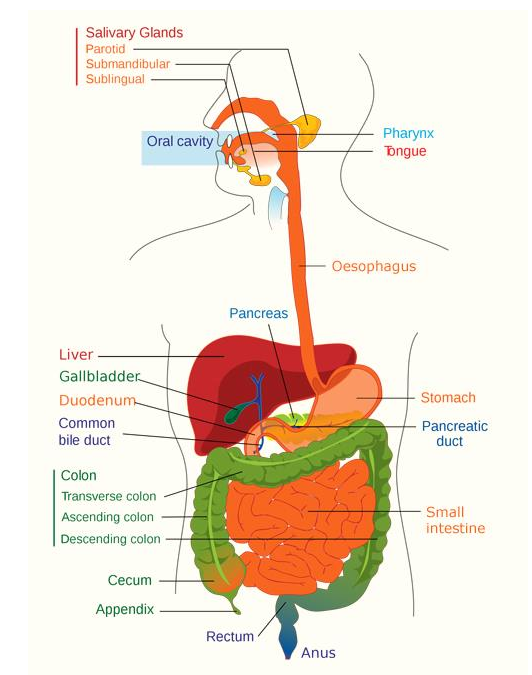
1. Integumentary system



2. Respiratory system

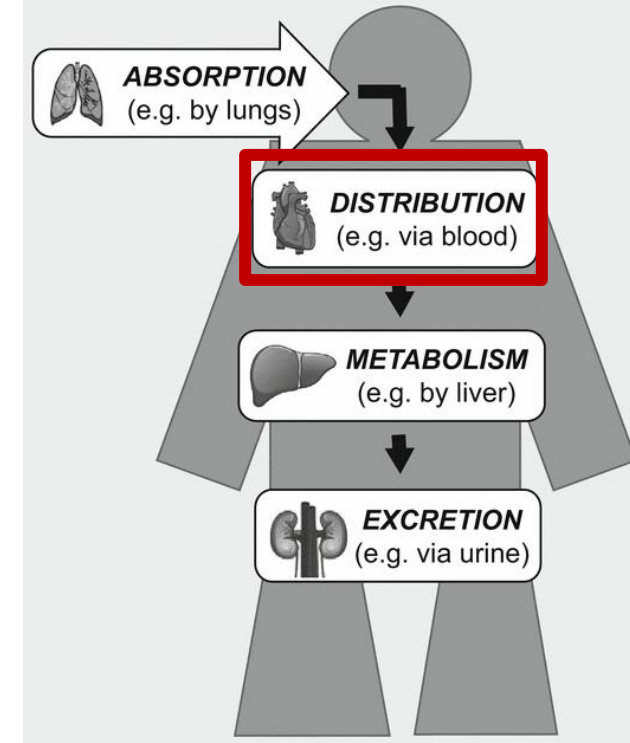


3. Digestive system

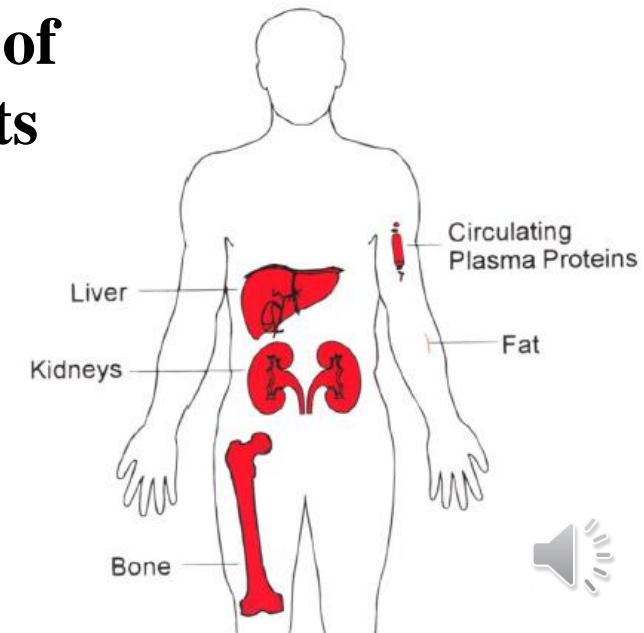


Distribution

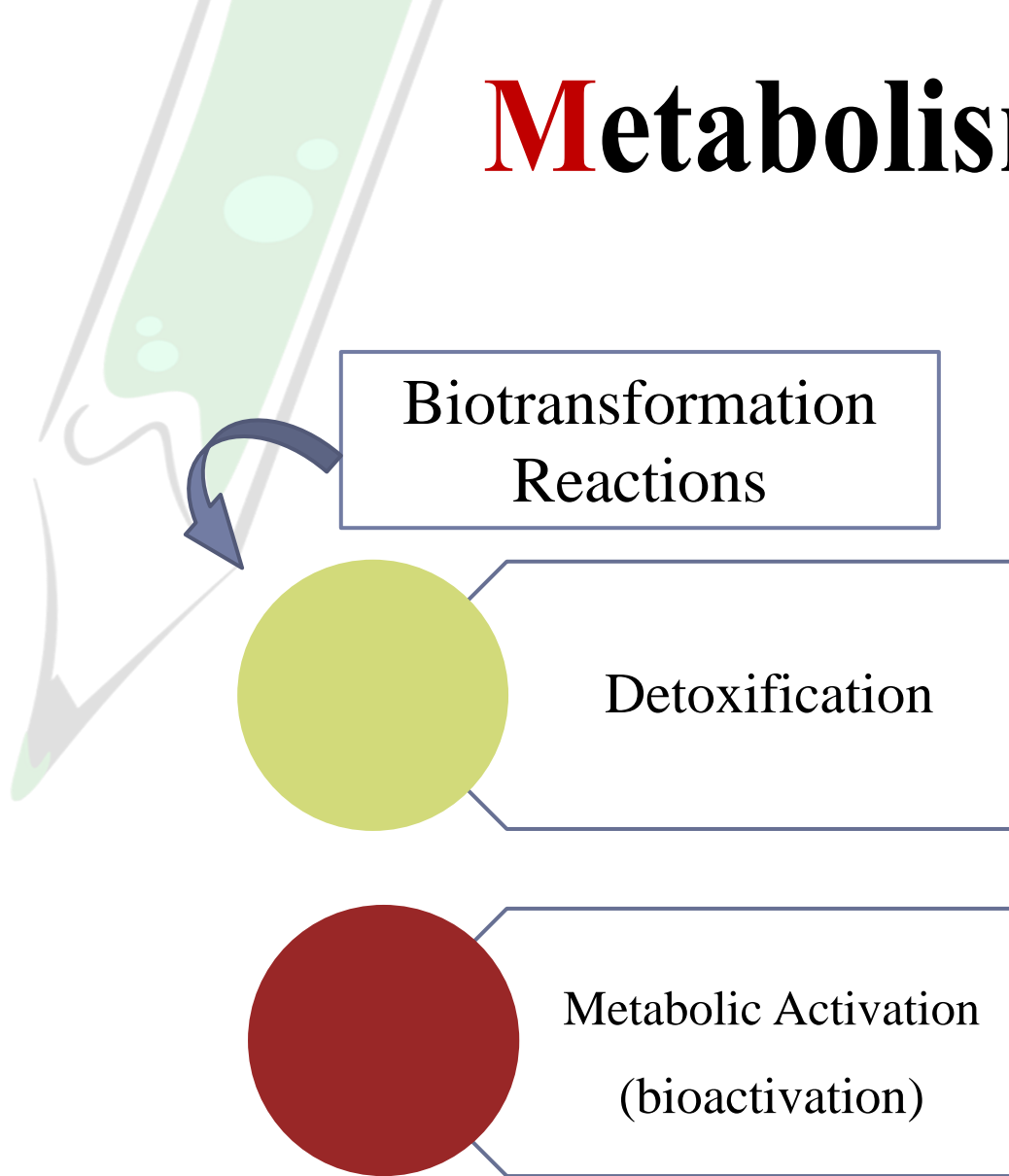
- physical and chemical properties of the toxicant
- concentration of the toxicant in the blood and in the tissues
- volume of blood flowing through a specific tissue
- tissue specificity or preference of the toxicant
- presence of special “barriers” to slow down toxicant entrance



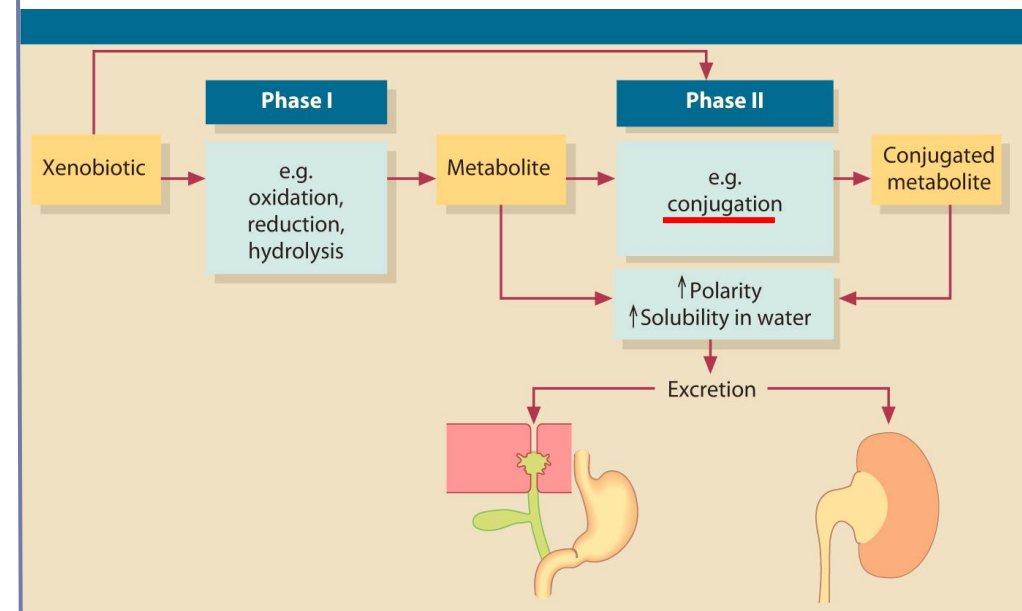
Storage of Toxicants



Metabolism (biotransformation)



The goal is to facilitate detoxication, thus producing water-soluble metabolites - more readily eliminated by the urinary and biliary systems.

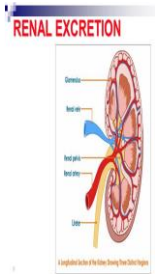
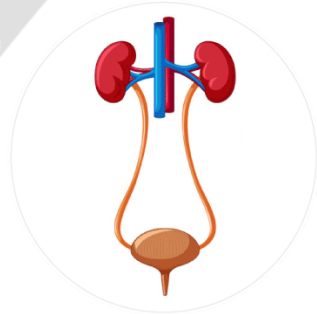


The highest capacity for biotransformation is in the liver.

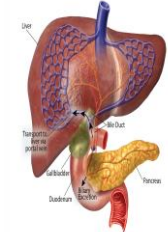


Excretion

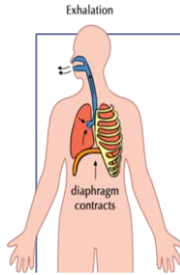
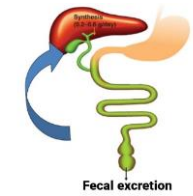
Toxicants or their metabolites are eliminated from the body by many different routes.



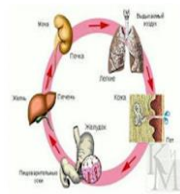
Urinary, renal



Fecal, biliary



**Respiratory
(exhalation)**



Additional Routes

(saliva, sweat, hair, skin, nails, milk)



Information Sources



<https://www.efsa.europa.eu/en>

A screenshot of the EFSA website's "Topics" page. The page has a white background with a blue header. The EFSA logo is in the top left, and a search bar is in the top right. Below the header is a navigation menu with links for "ABOUT", "NEWSROOM", "TOPICS", "RESOURCES", "PUBLICATIONS", "APPLICATIONS", "ENGAGE", and "CALENDAR". The "TOPICS" link is highlighted. Below the navigation is a breadcrumb trail "Home / Topics" and the heading "Topics". A grid of 12 topic cards is displayed, each with a representative image and a title with a right-pointing arrow. The "Chemical contaminants" card is highlighted with a blue border. The topics are: Animal health, Animal welfare, Biological hazards, Chemical contaminants, Contaminants in feed, Cross-cutting science, Data, Emerging risks, Feed additives, Food ingredients and packaging, GMO, Methodology, Nutrition, Pesticides, and Plant health.



A screenshot of the EFSA website's "Scientific Opinion on Lead in Food" page. The page has a white background with a blue header. The EFSA logo is in the top left, and a search bar is in the top right. Below the header is a navigation menu with links for "ABOUT", "NEWSROOM", "TOPICS", "RESOURCES", "PUBLICATIONS", "APPLICATIONS", "ENGAGE", and "CALENDAR". The "PUBLICATIONS" link is highlighted. Below the navigation is a breadcrumb trail "Home / Publications / Scientific Opinion on Lead in Food" and the heading "Scientific Opinion on Lead in Food". Below the heading, the publication date "Published: 20 April 2010" and the adoption date "Adopted: 18 March 2010" are shown. There are two buttons: "Read the article" and "Access the PDF". Below the buttons, the text "EFSA Journal on the Wiley Online Library" is displayed, along with the DOI: "https://doi.org/10.2903/j.efsa.2010.1570".



International Agency Research on Cancer



IARC

https://www.iarc.who.int/cards_page/iarc-publications/

IARC MONOGRAPHS ON THE IDENTIFICATION OF CARCINOGENIC HAZARDS TO HUMANS

The screenshot shows the IARC website with a navigation menu including MEDIA CENTRE, RESEARCH, PUBLICATIONS, TRAINING, EVENTS, JOBS & CAREERS, and ABOUT IARC. The main content area features several publication cards:

- The publications programme of the International Agency for Research on Cancer (IARC)**: Describes the agency's mission to promote international collaboration in cancer research for cancer prevention.
- IARC STAFF JOURNAL ARTICLES**: A card with a 'SHOW ALL' button.
- WORLD CANCER REPORT**: A card with a 'MORE INFORMATION' button and the text 'Cancer research for cancer prevention'.
- IARC MONOGRAPHS ON THE IDENTIFICATION OF CARCINOGENIC HAZARDS TO HUMANS**: A card with a 'VISIT WEBSITE' button.
- IARC PUBLICATIONS PROGRAMME**: A card showing various IARC reports.
- IARC EVIDENCE SUMMARY BRIEFS SERIES**: A card with the text 'IARC Evidence Summary Briefs'.
- WHO CLASSIFICATION OF TUMOURS**: A card with a microscopic image of cells.
- IARC HANDBOOKS OF CANCER PREVENTION**: A card with a photo of people in a meeting.

IARC Monographs on the Identification of Carcinogenic Hazards to Humans

IARC Classifications

GROUP	WHAT IT MEANS	EXAMPLES
<p>Group 1</p> <p>Carcinogenic to Humans</p>	There is sufficient evidence the agent causes cancer in humans.	Solar radiation, processed meats, alcoholic beverages, smoking, asbestos, talc-based baby powder contaminated with asbestos
<p>Group 2A</p> <p>Probably Carcinogenic to Humans</p>	There is sufficient evidence the agent causes cancer in humans.	Anabolic steroids, high temperature frying, HPV, red meat, Roundup (glyphosate), Actos (pioglitazone), N-nitrosodiethylamine (NDMA)
<p>Group 2B</p> <p>Possibly Carcinogenic to Humans</p>	Limited evidence in humans and less than sufficient evidence in animals.	Aloe vera leaf extract, marine diesel fuel, gasoline, engine exhaust, Asian pickled vegetables, progestin, perineal use of talc-based body powder
<p>Group 3</p> <p>Not Classifiable as to its Carcinogenicity in Humans</p>	Evidence is inadequate in humans and inadequate or limited in animals.	Coffee, low-frequency electric fields, dental materials, ceramic implants, chlorinated drinking water, tea, printing inks



US EPA



An official website of the United States government. [Here's how you know](#)

EPA United States Environmental Protection Agency

Search EPA.gov

Environmental Topics ▾ Laws & Regulations ▾ Report a Violation ▾ About EPA ▾

CONTACT US

U.S. Environmental Protection Agency



Paving the Way for a Zero-Emission Future

EPA's proposed clean cars plan would reduce greenhouse gas emissions, expand the use of clean technologies, and save consumers billions in fuel costs.

[Read the news release.](#)
[Read the proposed rule.](#)

1 2 3 4

Resources related to COVID-19

- [Read the Biden-Harris Plan to Beat COVID-19.](#)
- [Coronavirus \(COVID-19\) information from EPA.](#)

Find COVID-19 Vaccines Near You



An official website of the United States government. [Here's how you know](#)

EPA United States Environmental Protection Agency

Search EPA.gov

Environmental Topics ▾ Laws & Regulations ▾ Report a Violation ▾ About EPA ▾

CONTACT US

Integrated Risk Information System



Assessments in Development

- IRIS Assessment for Perfluorobutanoic Acid (PFBA) (Public Comment and External Review Draft)
- IRIS Assessment Plan for Vanadium and Compounds (Inhalation Exposure)
- Systematic Review Protocol for Vanadium and Compounds (Oral) IRIS Assessment

[See the Full List of Assessments in Development](#)

1 2 3 4

Basic Information

- [Learn About IRIS](#)
- [Guidance & Tools](#)
- [IRIS Process](#)
- [History of IRIS](#)

IRIS Assessments

- [Browse A to Z List of Chemicals](#)
- [Browse by Organ/System](#)
- [Assessments in Development](#)

Staying Connected

- [How IRIS connects with you](#)
- [How you can connect with IRIS](#)

<https://www.epa.gov/>

<https://www.epa.gov/iris>

Lead and compounds (inorganic)

CASRN 7439-92-1 | DTXSID2024161

- [IRIS Summary \(PDF\)](#) (15 pp, 128 K)

[Key IRIS Values](#) | [Other EPA Information](#)

Noncancer Assessment

[Reference Dose for Oral Exposure \(RfD\) \(PDF\)](#) (15 pp, 128 K)
Information reviewed but value not estimated. Last Updated: 07/08/2004

[Reference Concentration for Inhalation Exposure \(RfC\) \(PDF\)](#) (15 pp, 128 K)
Not assessed under the IRIS Program.

Cancer Assessment

[Weight of Evidence for Cancer \(PDF\)](#) (15 pp, 128 K) Last Updated: 09/26/1988

WOE Characterization	Framework for WOE Characterization
B2 (Probable human carcinogen - based on sufficient evidence of carcinogenicity in animals)	Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1986)

Related Links

- [CDC Guidelines on Lead](#)
- [EPA Chemicals Dashboard - Lead and compounds \(inorganic\)](#)

Chemical Structure for Lead and compounds (inorganic)

Pb




ATSDR




CSPECE Disaster Recovery Supplement


Learn how ATSDR is protecting children's environmental health after disasters.

The **Agency for Toxic Substances and Disease Registry (ATSDR)**, based in Atlanta, Georgia, is a federal public health agency of the **U.S. Department of Health and Human Services**. ATSDR protects communities from harmful health effects related to exposure to natural and man-made hazardous substances. We do this by responding to environmental health emergencies; investigating emerging environmental health threats; conducting research on the health impacts of hazardous waste sites; and building capabilities of and providing actionable guidance to state and local health partners.

 **Toxic Substances Portal**
One-stop-shop on the health effects of toxic substances

 **Toxicological Profiles**
Comprehensive evaluation of toxicological information on a substance

 **Public Health Assessments and Health Consultations**
Evaluations to find out if people are being exposed to hazardous

 **State Cooperative Program**
The Program funds 28 partner organizations to build their ability to

Most Viewed

- [Lead](#)
- [Arsenic](#)
- [Aluminum](#)
- [Benzene](#)

[TSP Home](#)

Substances List

Lead

[Toxicological Resources Listing](#)

[Health Effects of Exposures to Substances](#)

[Chemical Classifications](#)

[Community Members](#)

[Emergency Responders](#)

[Medical Education and Training](#)

[Toxicological and Health Professionals](#)

Lead

CAS ID#: 7439-92-1

Affected Organ Systems: Neurological (Nervous System), Renal (Urinary System or Kidneys)

Cancer Classification: Please contact [NTP](#), [IARC](#), or [EPA](#) with questions on cancer and cancer classification.

Chemical Classification: Inorganic substances

Summary: Lead is a naturally occurring bluish-gray metal found in small amounts in the earth's crust. Lead can be found in all parts of our environment. Much of it comes from human activities including burning fossil fuels, mining, and manufacturing. Lead has many different uses. It is used in the production of batteries, ammunition, metal products (solder and pipes), and devices to shield X-rays. Because of health concerns, lead from gasoline, paints and ceramic products, caulking, and pipe solder has been dramatically reduced in recent years.

*CDC has updated its recommendations on children's blood lead levels. Experts now use an upper reference level value of 97.5% of the population distribution for children's blood lead. In 2012-2015 that value is 5 micrograms per deciliter ($\mu\text{g}/\text{dL}$) to identify children with blood lead levels that are much higher than most children's levels. The information on this page refers to CDC's previous "blood lead level of concern" of 10 $\mu\text{g}/\text{dL}$. This information will be updated in future ToxProfile and ToxFAQ editions. To learn more about CDC's updated recommendations on children's blood lead levels, please visit: http://www.cdc.gov/nceh/lead/ACCLPP/blood_lead_levels.htm.





*Thank you for your kind
attention!*

**KEEP CALM
AND STUDY
TOXICOLOGY**



UNIVERSITÀ
DEGLI STUDI DELLA
TUSCIA

Meline Beglaryan meline.beglaryan@cens.am

