Concepts in Toxicology

Instructor: Min Wu
Kunming University of Science and Technology

Learning Objectives

Part 1. Some Definitions

Part 2. Different Types of Toxic Responses

Part 3. Intensity of Toxic Response

Part 4. General Factors Affecting Toxicity

Part 5. Risk to Next Generation

Part 1

Silent Spring

"Over increasingly large areas of the United States spring now comes unheralded（悄无声息的）by the return of birds, and the early mornings are strangely silent where once they were filled with the beauty of bird song."

Rachael Carson, 1962,
Silent Spring

Publication of “Silent Spring”

- Silent Spring” published in 1962.
- Written by Rachel Carson, a respected marine biologist.
- An expose of the damage to the environment from indiscriminate（ use of chlorinated pesticides.

1962年美国海洋生物学家卡尔逊女士出版的《寂静的春天》，向人们描述了人们使用化学农药给环境带来的严重后果，加深了人们对化学农药的全面认识，人们开始全面审视化学农药的功与过、利与弊。

1.1 Definitions: Environment

- The circumstances, objects, or conditions by which one is surrounded.

or

- The complex of climatic, edaphic (soil-based), and biotic factors that act upon an organism or an ecologic community.

所处的情况、对象、条件。

对生物有机体和生态群落发生作用的气候、土壤（以土壤为基础）以及生物因素的复合体。

1.2 Definitions: Safe

- *Free* from harm or risk.
- *Secure* from the threat of danger, harm, or loss.
- *Zero* risk.

没有伤害和危险

不受到危险、伤害、损失的威胁

零风险

1.3 Definitions: Toxicity

- Toxicity: The degree to which a substance can harm humans or animals.

  毒性：(一种)化学物质能够造成机体损害的程度。

1.4 What is Toxicology?

Toxicology: The study of the adverse effects of chemicals and physical agents on **living organisms**.

Environmental Toxicology: The study of the nature, properties, effects and detection of toxic substances in the environment and in any environmentally **exposed species, including humans**.

Ecosystem Toxicology: the study of the fate and effect of a toxic compound on an **ecosystem**.

1.5 What is a Toxicant? What is a Toxin?

Toxic substances that are produced by or are a byproduct of human-made activities.

Toxic substances that are produced naturally.

There is no confines between toxic & nontoxic.

1.6 Contributors to the "Pollution"

- Chemical　化学性的
  - Air pollutants, toxic wastes, pesticides, VOCs…
- Biological　生物性的
  - Disease organisms present in food and water…
  - Insect and animal allergens…
- Physical　物理性的
  - Noise, particulates, radiation…
- Socioeconomic　社会经济性的
  - Access to safe and sufficient services, i.e., water, sewerage, health care…

Part 2

2 Toxic Effect/Responses 毒性作用

- A result produced by the ingestion（吸入，摄取）or contact of poisonous materials.
- The physiologic（生理）, physical or laboratory manifestations（现象） or derangement（紊乱） that can be attributed to the presence of a substance within the body.
- 毒性作用，又称为毒效应，是化学物质对机体所致的不良或有害的生物学改变，故又可称为不良效应、损伤作用或损害作用。
- 是化学物质本身或其代谢产物在作用部位达到一定数量并停留一定时间，与组织大分子成分互相作用的结果。

2.1 Types of Toxic Responses

- Local（局部）.
  - Effect at site of contact.
  - Skin, lungs.

- Systemic（全身作用）.
  - Effect distant from exposure site.
  - kidney, lungs.

2.2 Types of Toxic Responses

- Immediate（速发性）.
  - Minutes to hours after a single exposure.
- Delayed（迟发性）.
  - Days to years after a or continues exposure.
- Some both.

2.3 Types of Toxic Responses

- Reversible (可逆)- rapidly regenerating tissue.
  - Liver, blood cells.
- Irreversible (不可逆)
  - Nerve center
  - Carcinogenesis（致癌作用）, Mutagenesis（致突变作用）, Teratagenesis（致畸作用-胚胎）.
- Largely determined by
  - Tissue involved, length of exposure and magnitude（量级） of toxic insult.

2.4 Types of Toxic Responses

- Hypersensitivity（过敏性反应）or
  Allergic Reaction（变态反应）

是机体对外源化学物产生的一种病理学免疫反应，是机体生命不需要的一种有害反应，有时仅有皮肤症状，有时可引起严重的过敏性休克，甚至死亡。

2.5 Types of Toxic Responses

- Idiosyncratic Reaction （特异体质反应）

  Largely determined by GENE（基因）

Part 3

3 Intensity of Toxic Response

- Acute（急性）
- Subchronic（亚慢性）
- Chronic（慢性）

3.1 Acute Toxicity

- Involves harmful effects to an organism through a single or short-term exposure.

  机体一次或在24小时内多次接触外来化学污染物之后所引起的中毒效应。

  – Occurs soon after exposure
    - In laboratory: within 24 hours
    - In 'real life'
      – Within 14 days

      (from IUPAC -- Int'l Union of Pure and Applied Chemistry)

3.2 Subchronic Toxicity

- The ability of a toxic substance to cause effects for more than one year but less than the lifetime of the exposed organism.

机体连续一年以上，但短于一生的时间接触外来化学污染物之后所引起的中毒效应。

3.3 Chronic Toxicity

- The ability of a substance or mixture of substances to cause harmful effects over an extended period, usually upon repeated or continuous exposure, sometimes lasting for the entire life of the exposed organism.

Part 4

4 General Factors Affecting Toxicity

- Structure & Property of Pollutant
  - Chemical Structure and Toxicity
  - Physical Structure and Toxicity
- Condition of Organism
- Condition of Exposure
- Environmental Factors

4.1.1 Chemical Structure and Toxicity

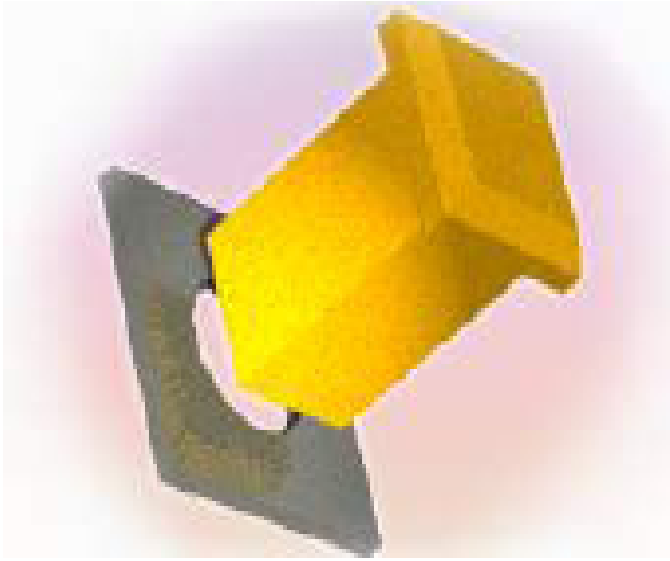
- 同系物的碳原子数
  - 一般碳原子数愈多，毒性愈大
- 分子饱和度
  - 分子不饱和键增多，毒性增强，如：乙炔＞乙烯＞乙烷
- 卤素取代
  - 卤素原子增加，毒性增强，如CCL_4 ＞ $CHCl_3$ ＞ CH_2Cl_2 ＞ CH_3Cl ＞ CH_4
- 构型
  - 同分异构体的毒性一般为：对位＞邻位＞间位

4.1.2 Physical Structure and Toxicity

- Lipid/Water Partition Coefficient
  - 脂溶性高毒性大
- Volatility
  - 挥发性大毒性大
- Dispersity
  - 分散度大毒性大
- Solubility
  - 溶解度大毒性大
- Purity

4.2 Condition of Organism

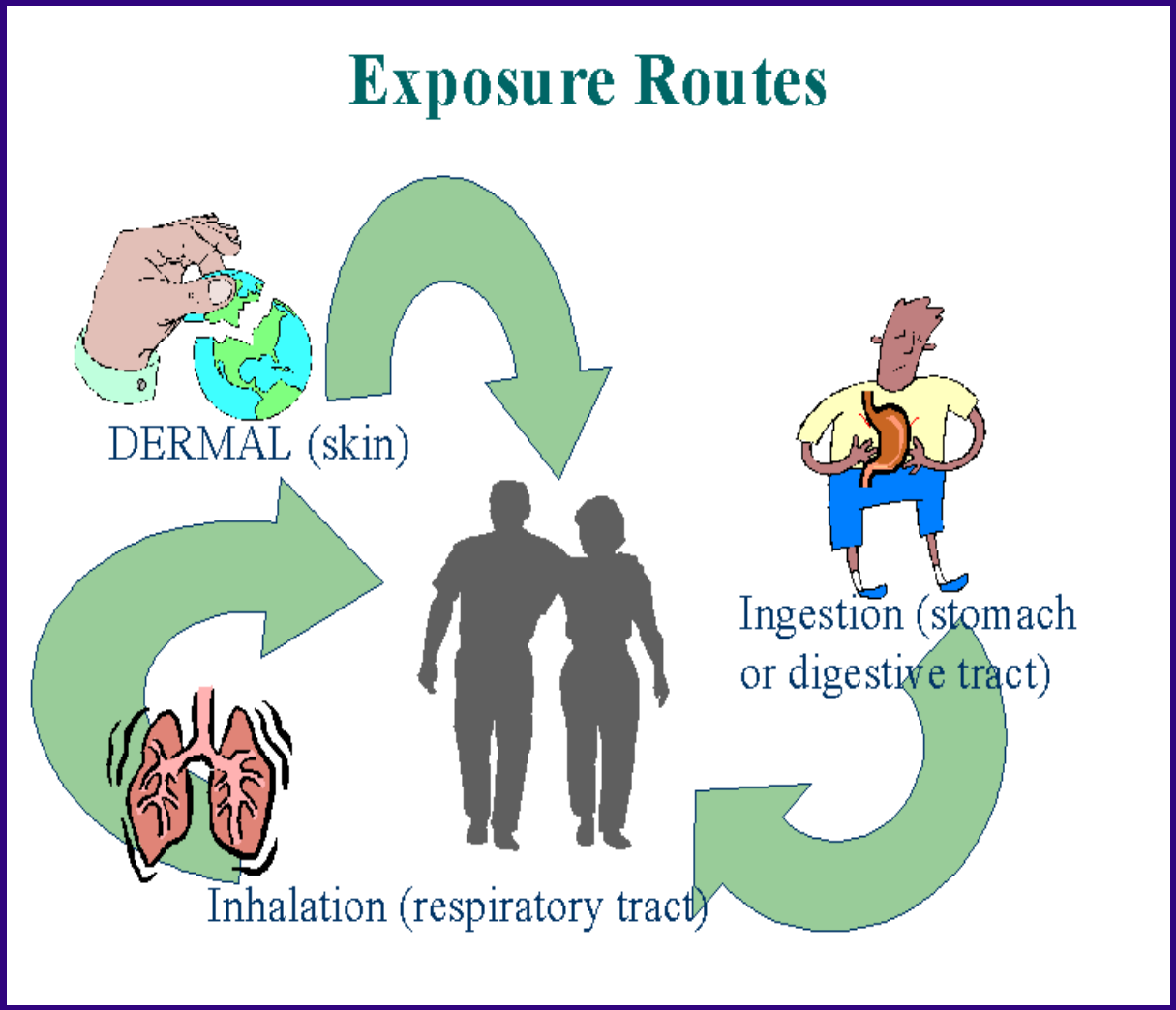
- Species
  - Absorption, distribution, biotransformation, elimination, storage differences
- Gender
  - Biotransformation differences
- Age
  - Metabolic/developmental differences
- Nutritional Status
  - Impaired cellular function
- Disease State
  - Affect interaction with toxicant
- Time of Day
  - Hormone/enzyme fluctuations



4.3 Condition of Exposure

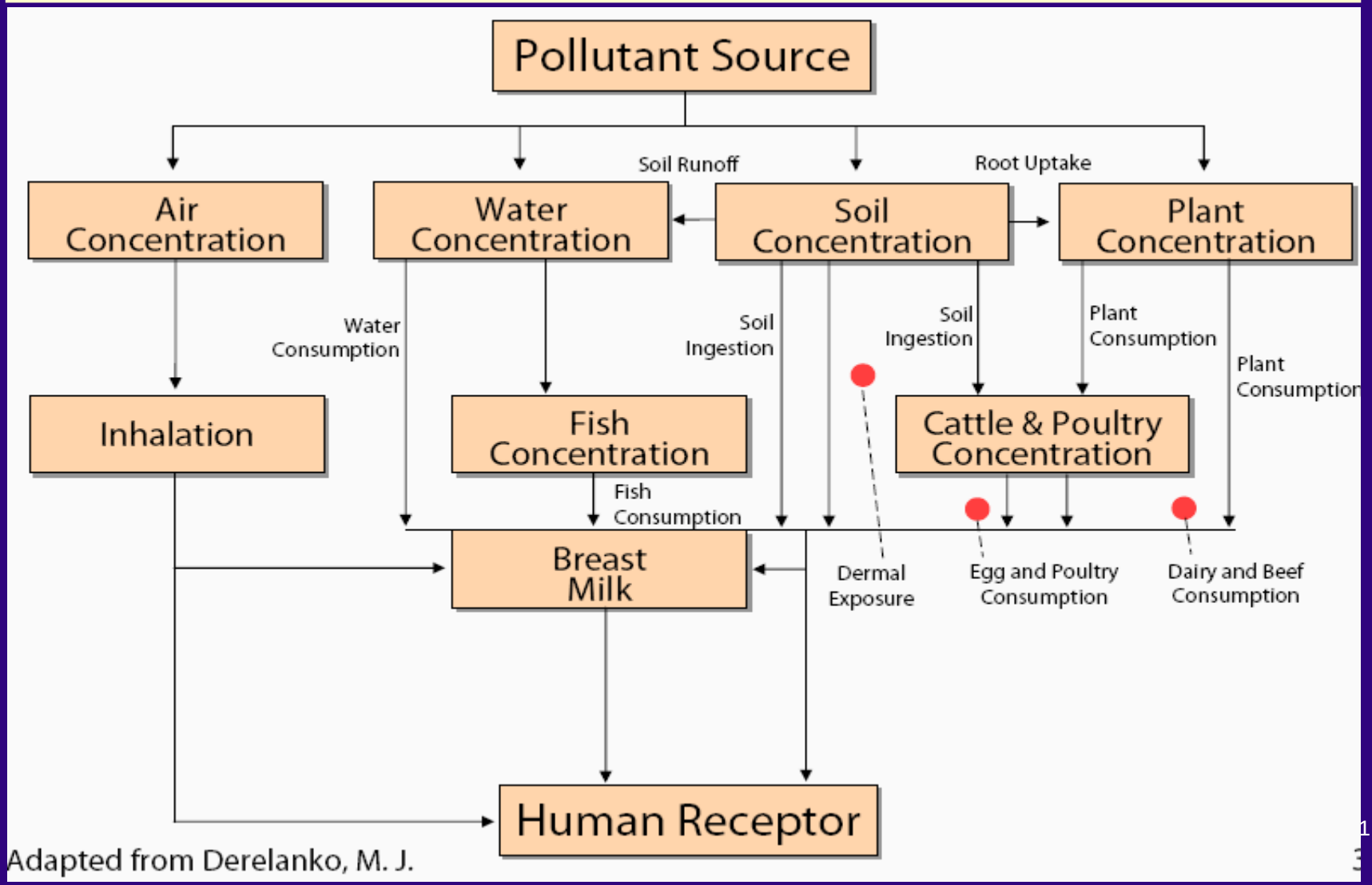
- Exposure pathways.
  接触途径（经静脉、经口、经皮肤等）.
- Dose.
  剂量.
- Exposure time, speed, frequency.
  接触期限、接触速率和接触频率.

4.3.1 Exposure Pathways



Before toxicity can develop, a substance must come into contact with a body surface such as skin, eye or mucosa of the alimentary or respiratory tract. Poisonous or deadly effect on the body.

4.3.2 Pollutant Source Pathways



4.4 Environmental Factors

- Temperature
- Humidity
- Atmospheric pressure
- Seasons and Diurnal rhythm

Part 5

Toxic effects are related to age of life.

5.1 The risk to the next generation

- First period of risk: embryo（胚胎）
  - peak period of risk is first trimester, first ten weeks, during organogenesis（器官形成）
  - severe damage is likely to result in spontaneous abortion（自然流产）

5.2 The risk to the next generation

- Second period of risk: fetal（胎儿）development
  - some late developing organs
  - Neurological（神经学上的） development and behaviour
  - cancer risk

5.3 The risk to the next generation

- After birth:
  - Lactation（哺乳期） and exposure through breast milk
  - environmental exposure

5.4 The risk to the next generation

- Toddlers and young children
  - accidental exposures
  - Inquisitive（好奇的）behaviour
  - Compulsive（禁不住的）ingestion

Who is Responsible?