

Occupational Toxicology (1)

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Objective

- What is Occupational Toxicology
- Spectrum of ill-effects
- Toxicokinetics
- Risk assessment
- Methods of Estimation of Risk
- Dose-response relationship

What is Toxicology?

- Science of poisons
- Study harmful effects of physical or chemical agents on living organisms
- Assess probability of hazards caused by such effects
- Studies the quantitative effect of chemicals on biological tissues

Toxicologic Evaluation

- “All substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy.”
 - *Paracelsus (1493-1541)*

- How much is too much?

Spectrum of Ill-effects

- Allergic reactions
- Idiosyncratic reactions
- Immediate vs. Delayed toxicity
- Reversible versus irreversible effects
- Local versus systemic effects
- Interactions of toxins
- Carcinogenicity
- Mutagenicity
- Teratogenicity

Toxicokinetics

- Study of the
 - Absorptions (route of entry)
 - Distribution (transportation)
 - Metabolism
 - Excretion
- of substances

Toxicokinetics: Absorption

- Inhalation
- Ingestions
- Topical/Transdermal
- Transplacental
- Indicator for method of
 - Monitoring and
 - Control

Toxicokinetics: Distribution

- Refer to the transportation of the substance within the body
- Depends on the Target organs
- Retained if lipophilic or are complex structures resistant to metabolism and excretion
 - Polychlorinated biphenyls (PCB)

Toxicokinetics: Metabolism

- The substance go through
 - Biotransformation or
 - Unchanged before it is excreted
- Biotransformation – two outcome
 - Bioactivation
 - Detoxification
- Toxicity occur if detoxification pathway fails or becomes saturated

Toxicokinetics: Excretion

- The substance is excreted through
 - Kidneys (polar compounds/water solouble)
 - Feces (bile),
 - Expired air,
 - Milk,
 - Tears,
 - Sweat and/or
 - Hair

What Influences the Toxicity of a substance

- Factors related to
 - Toxic agent
 - Exposure situation
 - Environmental factors relate the subject
 - Inherent factors related to the subject

Factors related to toxic agent

- Chemical composition
 - e.g. pH, choice of anion
- Physical characteristics
 - e.g. particle size, method of formulation
- Presences of impurities
- Stability and storage characteristics
- Solubility in biologic fluids

Factors Related to Exposure Situation

- Dose, concentration and volume
- Route, rate and site of administration
- Duration and frequency of exposure
- Time of administration

Environmental Factors Related to the Subject

- Temperature and humidity
- Atmospheric pressure
- Light and other radiation
- Housing and caging effects
- Noise and other Geographic influences
- Social factors
- Chemical factors

Inherent factors related to the subject

- Species and strain
- Genetic status
- Immunologic status
- Nutritional status
- Hormonal status
- Age, sex, body weight and maturity
- Presence of disease or organ pathology

Aim of toxicology

- Clinical, Epidemiological and Experimental studies in toxicology
 - To define the capacity of substances to produce harmful effects
 - Measure and analyse the doses at which toxicity occurs
 - Assess the probability that injury or illness will occur under specified conditions of use

Classification of toxic agents

- Physical State of the Agent
- Chemical Structure of the Agent
- Medium of the Agent
- Site of Injury by the Agent
- Mechanism of Action of the Agent
- Clinical Effects of the Agent

Toxicodynamics

- The study of the relationship between the dose that enters the body and the measured response

Risk Assessment

- Process of describing and quantifying the risk, enable decisions about
 - control measures,
 - training,
 - monitoring and
 - health surveillance to protect the health of workers/community from a hazard

Steps in risk assessment

- Hazard Identification
 - Population at risk
 - Adverse Health effects
- Dose-response assessment
 - Epidemiology
 - Experimental
- Exposure assessment
- Risk Characterisation

Methods in Estimation of Risk

- **Threshold Method**
 - For all noncarcinogenic responses
 - Risk is express in safety factor – allowable daily intake for humans and threshold dose in animals
 - NOAEL/NOEL – no observed adverse effect level
 - MOAEL/MOEL – minimum observed adverse effect level
- **No-Threshold Method**
 - For carcinogens

What is Acceptable Risk

- Judgment requiring a balance of risk and benefit
 - What need is met by the substance
 - Any safer alternative
 - Extent of public use
 - Economic consideration
 - Effect on environment
 - Attitude of society

Carcinogens

- “no detectable exposure levels for proven carcinogenic substances”
 - carcinogen policy published in 1976 by Edward J. Fairchild, II, Associate Director for Cincinnati Operations, (Annals of the New York Academy of Sciences, 271:200-207, 1976).

Dose-response relationship

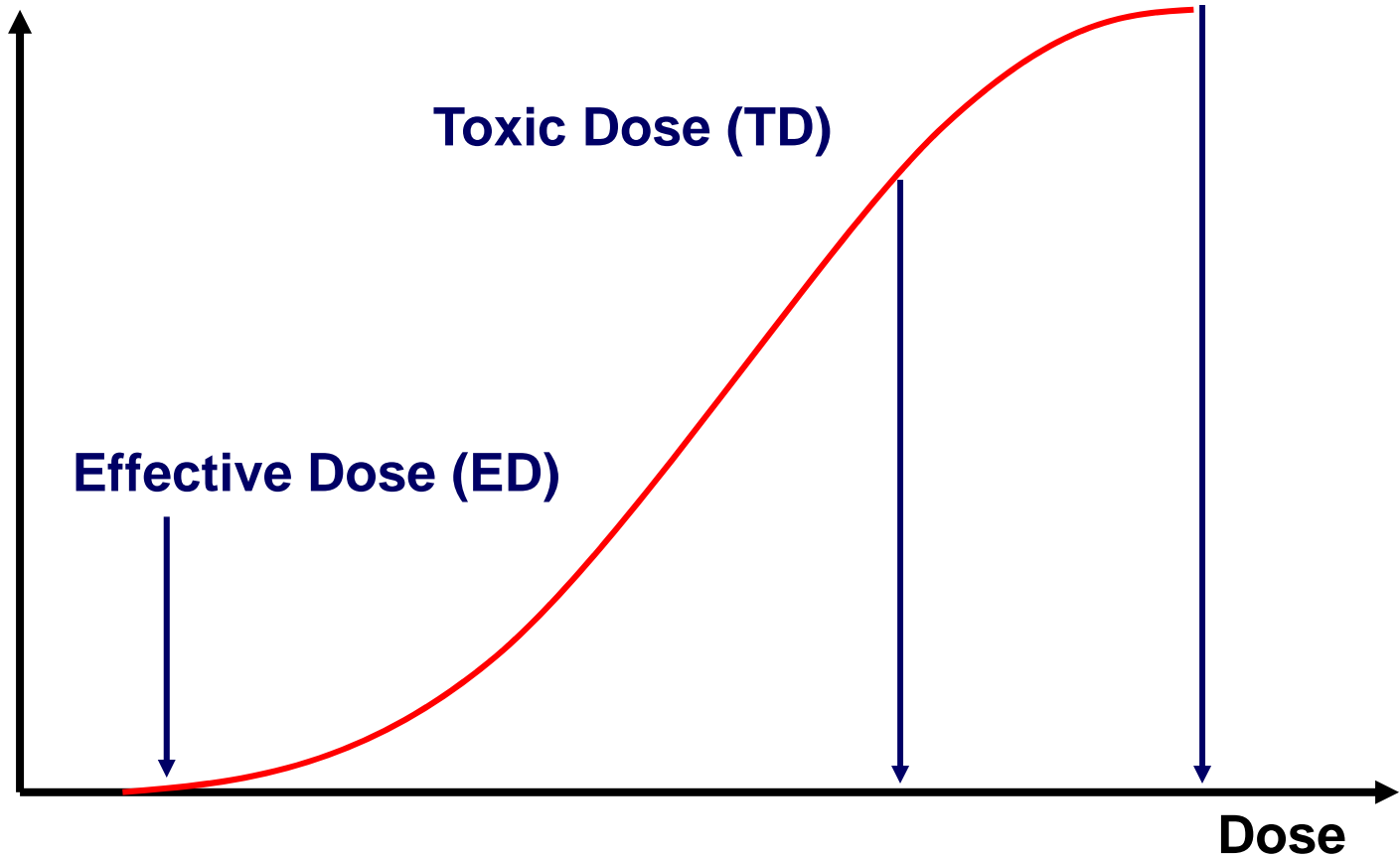
- Refers to relationship between the dose of a chemical and the response it elicits
- Response :
 - severity of effects
 - percentage population affected

Severity of effects

Lethal Dose (LD)

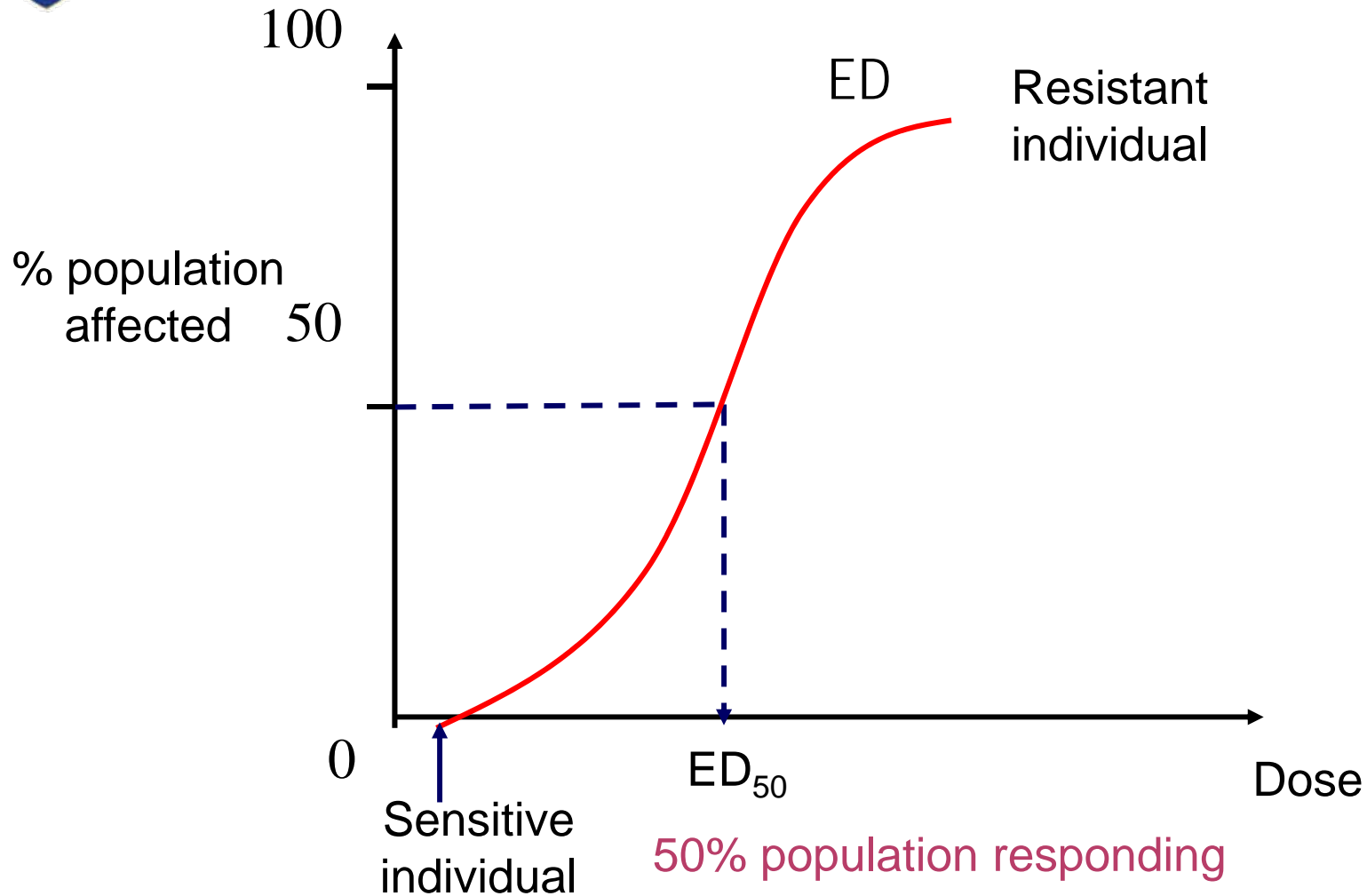
Toxic Dose (TD)

Effective Dose (ED)



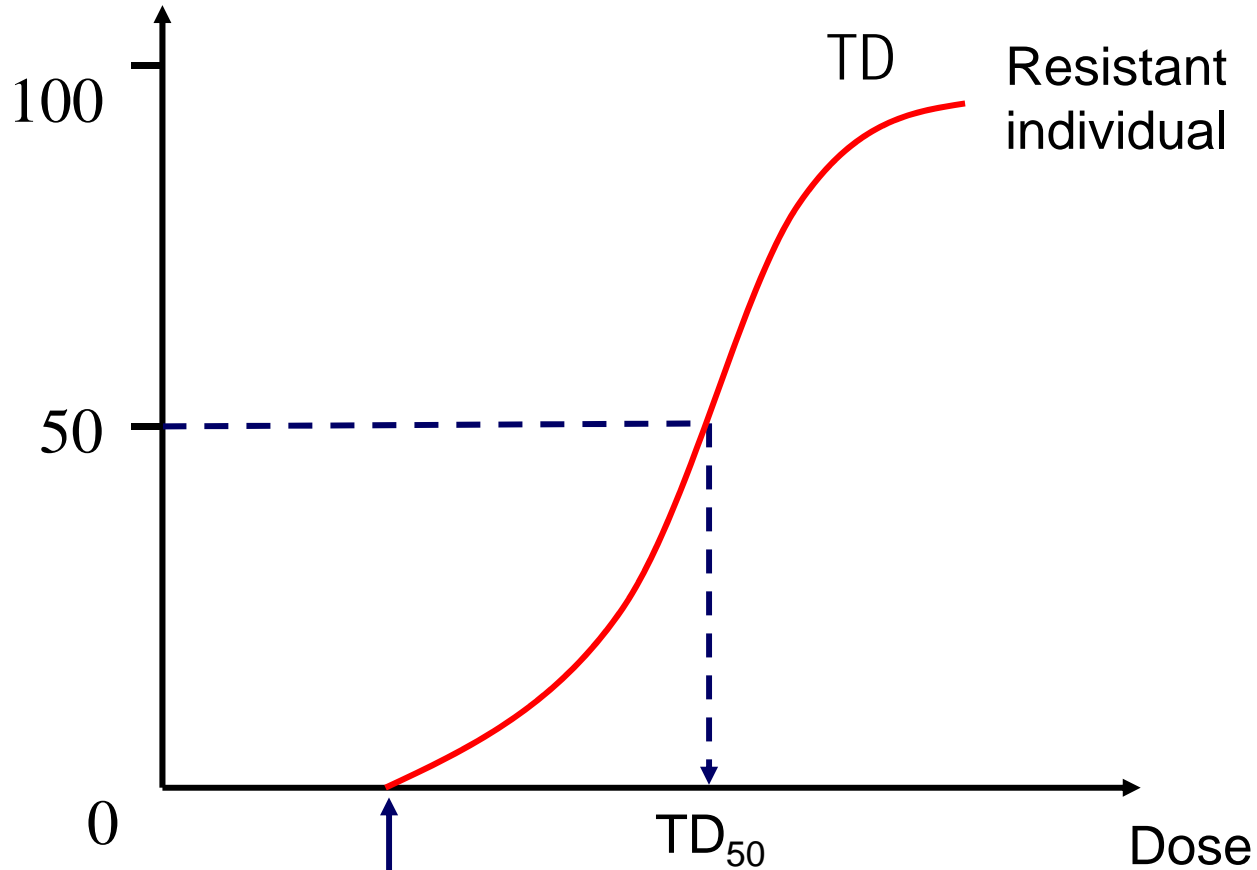
Uses of dose-response curve

- Toxicity rating
 - comparing toxicity between chemical for the same response
- Prevent overexposure and toxic outcome
 - by knowing ED
- Calculation of threshold dose
 - NOAEL (No Observable Adverse Effect Level)
- Calculation on the margin of safety
 - TD50/ED50



Effective Dose

% population affected

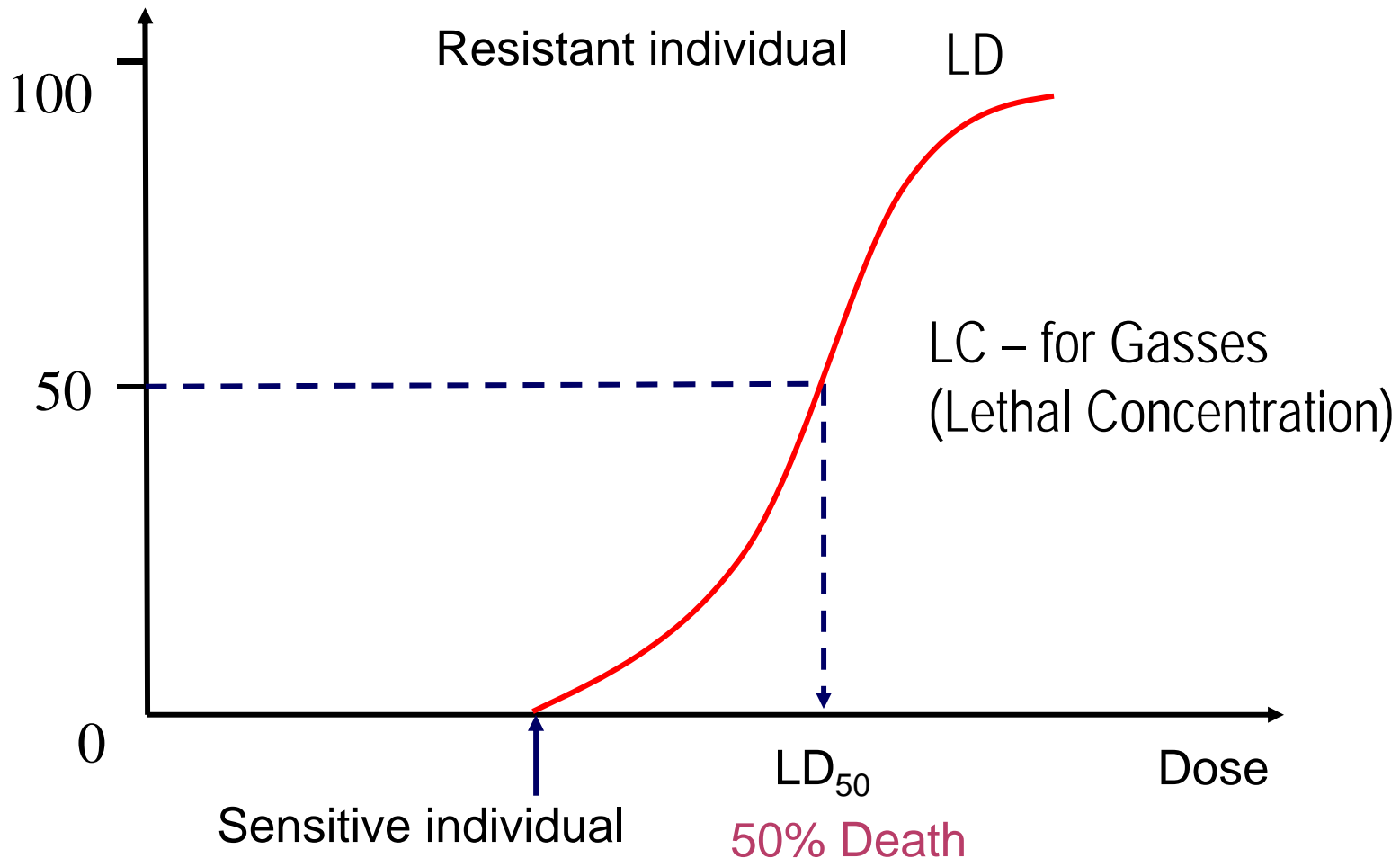


Sensitive individual

50% population Toxic

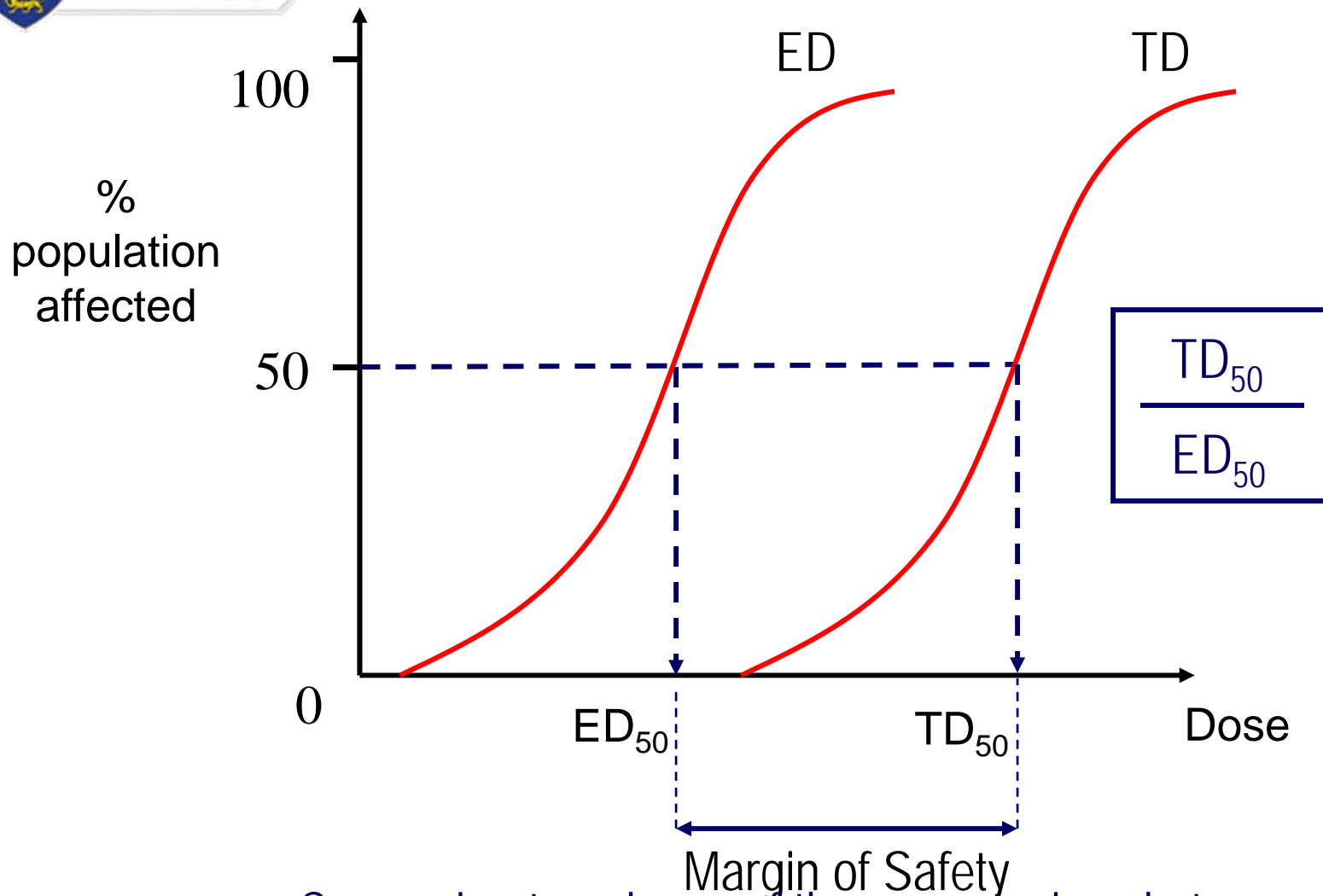
Toxic Dose

% population affected

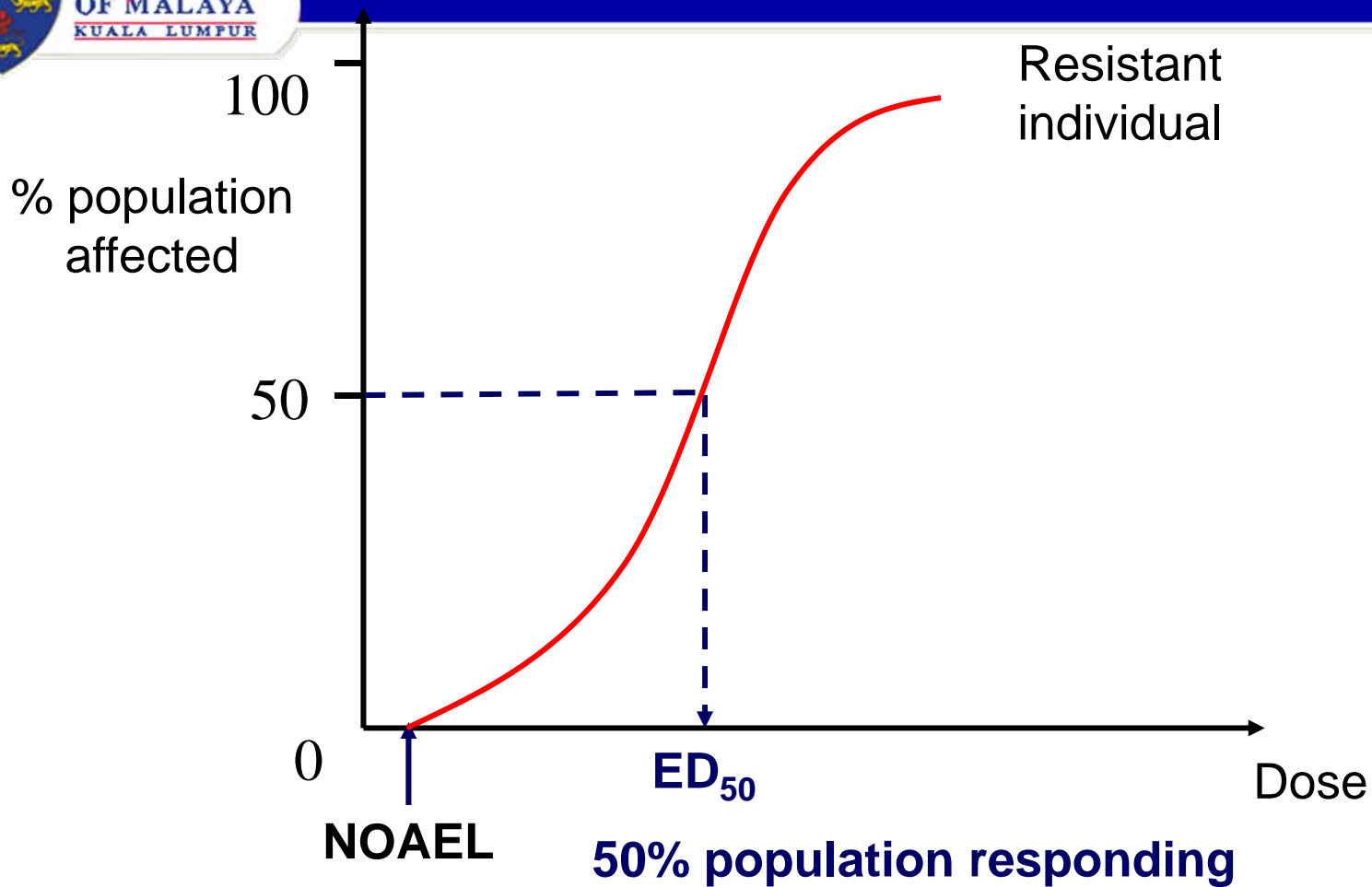


Lethal Dose (Use in chemical and pesticide toxicity rating)

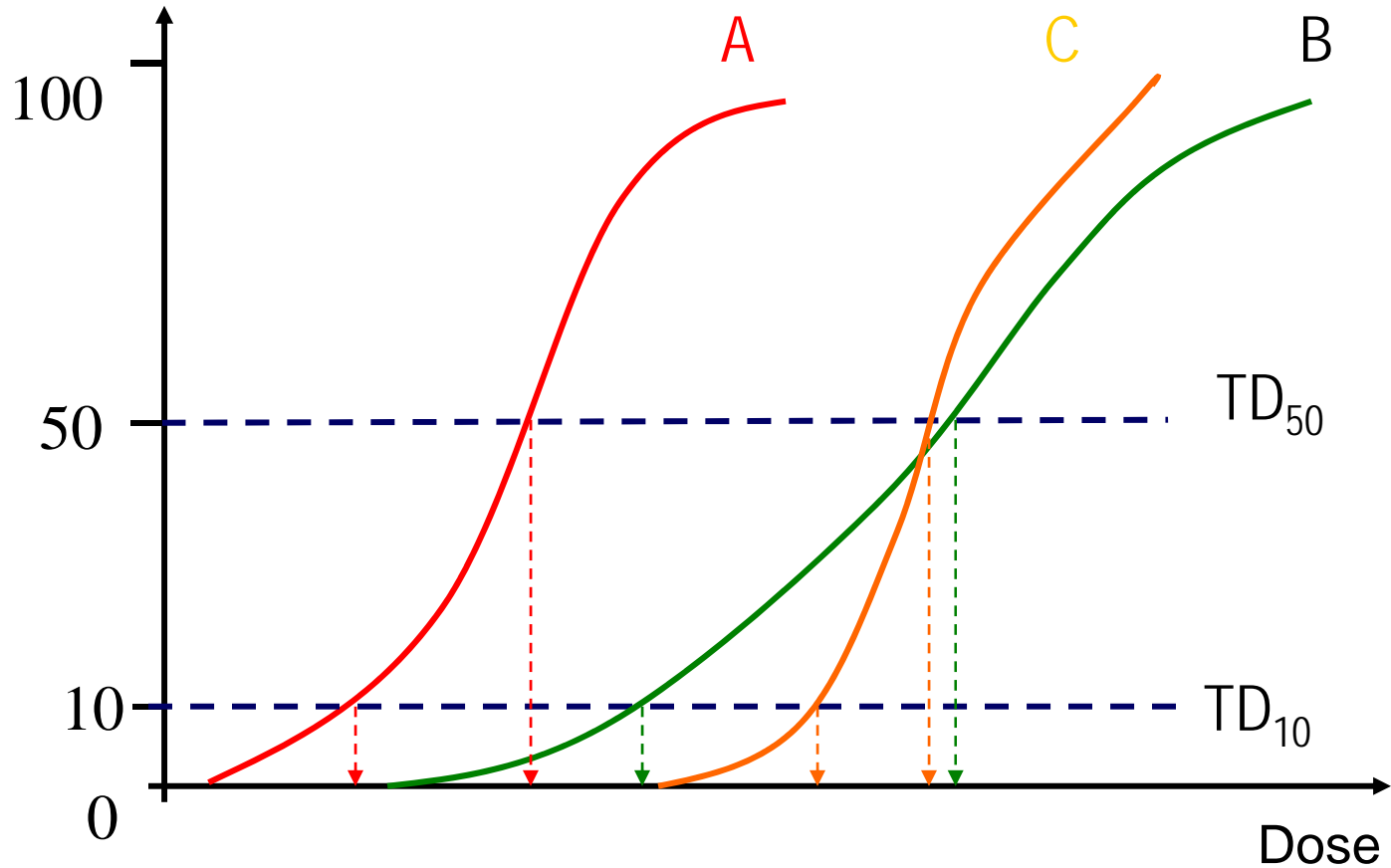




Comparing two doses of the same toxic substance



% population affected



Comparing the doses at which the same toxic effect of 3 toxin