

# **Valutazione del rischio chimico**

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# Valutazione della tossicità per la valutazione del rischio per la salute umana (RAoC cap.6)

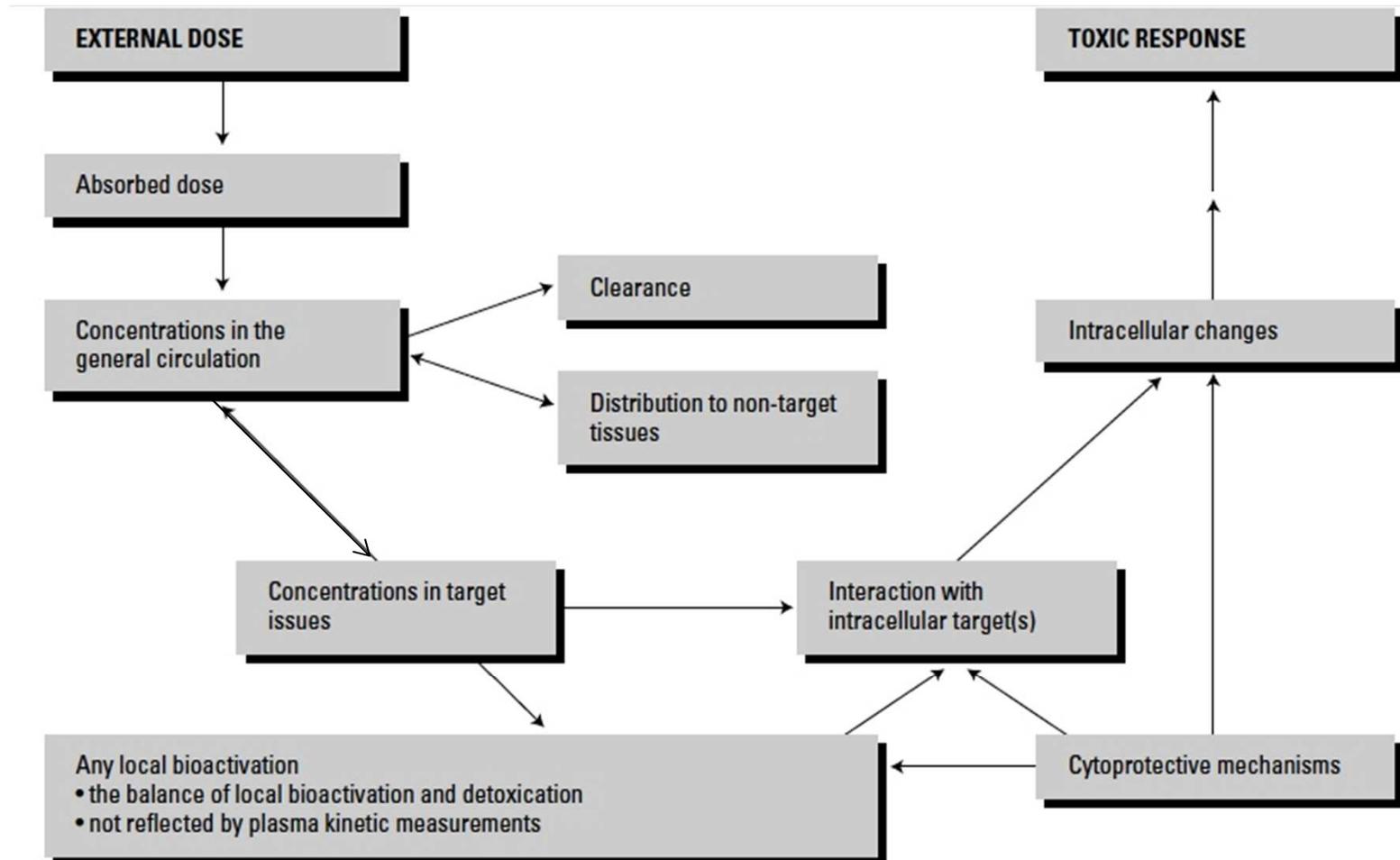


Figure 6.1. Processes leading to the generation of a toxic response [2].

Note: "Concentrations" refers to the relevant active form delivered by the general circulation and may be the parent compound or an active metabolite produced in another tissue and delivered to the target tissue or organ

Table 6.1 Ranking of physiological and pathological effects in order of severity

Effect	Severity
Biochemical/haematological change with no pathological change and no change in organ weight; or a change in organ weight with no pathological and biochemical/haematological change	least severe
Biochemical/haematological change with no pathological change and with a change in organ weight	
Enzyme induction and subcellular proliferation or other changes in organelles but no other apparent effects	
Biochemical/haematological change with slight pathological changes	
Hyperplasia, hypertrophy or atrophy with change in organ weight	
Reversible cellular changes: cloudy swelling, hydropic change or fatty changes	
Necrosis, or metaplasia with no apparent reduction in organ functions; any neuropathy without apparent behavioral, sensory, or physiological changes	
Necrosis, atrophy, hypertrophy, or metaplasia with a detectable reduction in organ functions; any neuropathy with a measurable change in behavioral, sensory, or physiological activity; reduced body weight gain; clinical symptoms	
Necrosis, atrophy, hypertrophy, or metaplasia with definitive organ dysfunction; any neuropathy with gross changes in behavioral, sensory, or motor performance	
Pronounced pathological changes with severe organ dysfunction; any neuropathy with loss of behavioral or motor control or loss of sensory ability	
Death or pronounced life-shortening	most severe



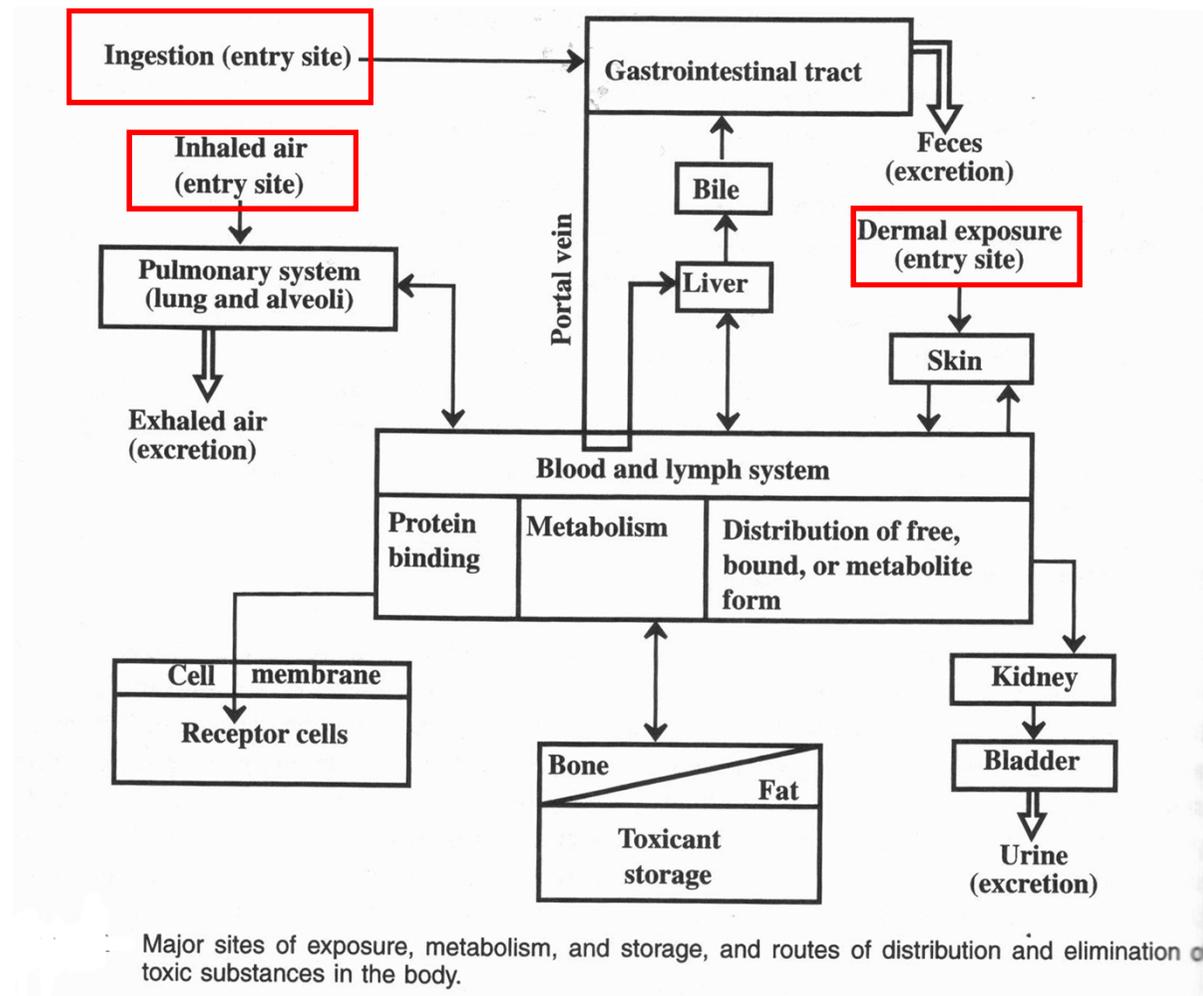
valutazione di fisiologo o tossicologo esperto per stabilire se c'è "serio danno alla salute"

# **Tossicologia – esposizione alle sostanze tossiche**

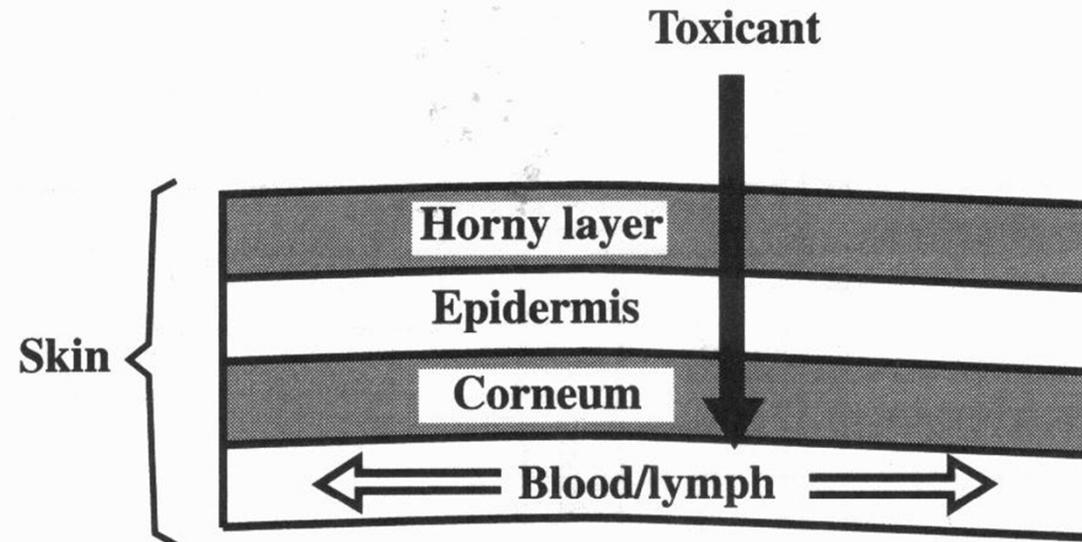
Esposizione:

- percutanea
- polmonare
- tratto gastro-intestinale
  - bocca / esofago / stomaco
  - intestini
  - tratto intestinale e fegato

# Tossicologia – esposizione alle sostanze tossiche

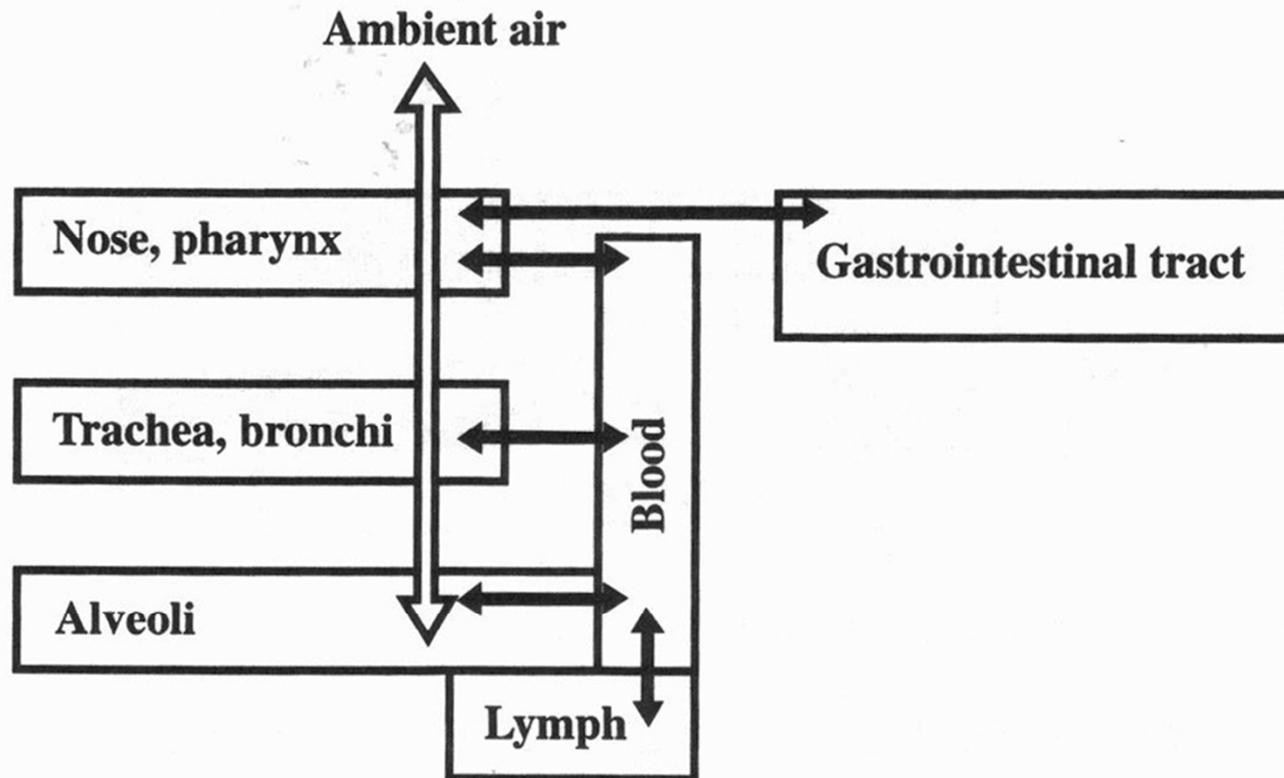


# Tossicologia – esposizione alle sostanze tossiche percutanea



Absorption of a toxic substance through the skin.

## Tossicologia – esposizione alle sostanze tossiche



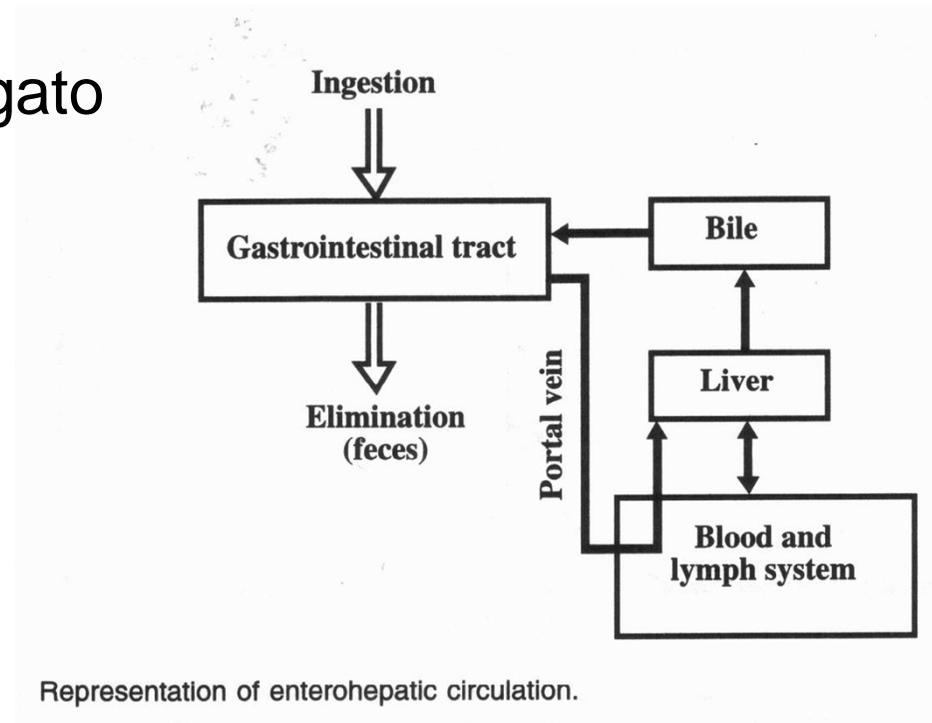
Pathways of toxicants in the respiratory system.

# Tossicologia – esposizione alle sostanze tossiche tratto gastrointestinale

bocca esofago stomaco

intestini

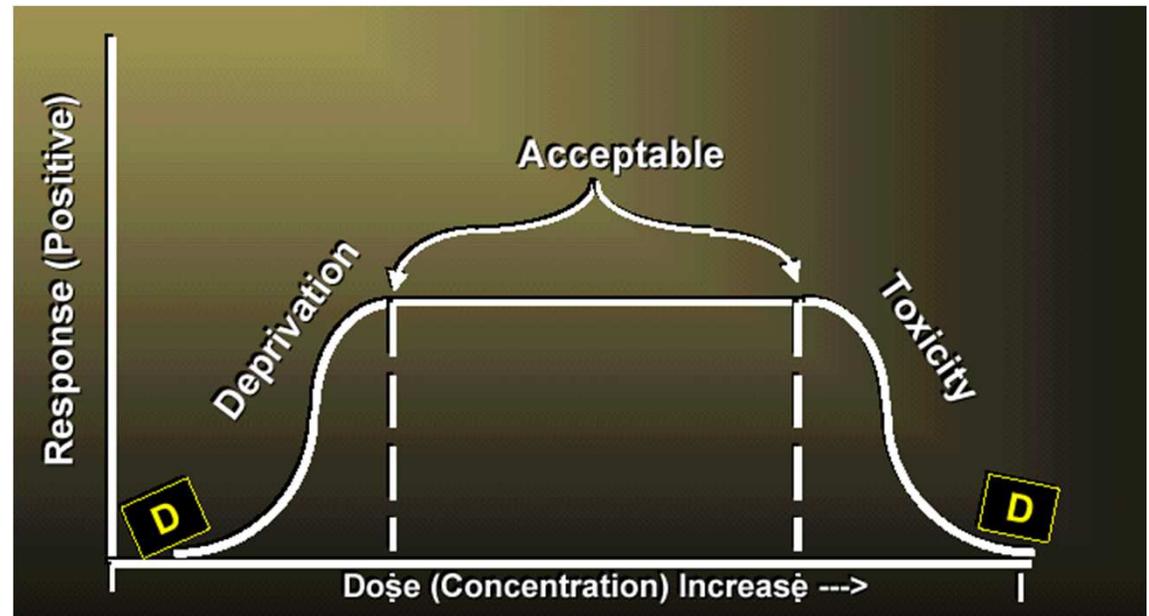
tratto intestinale e fegato



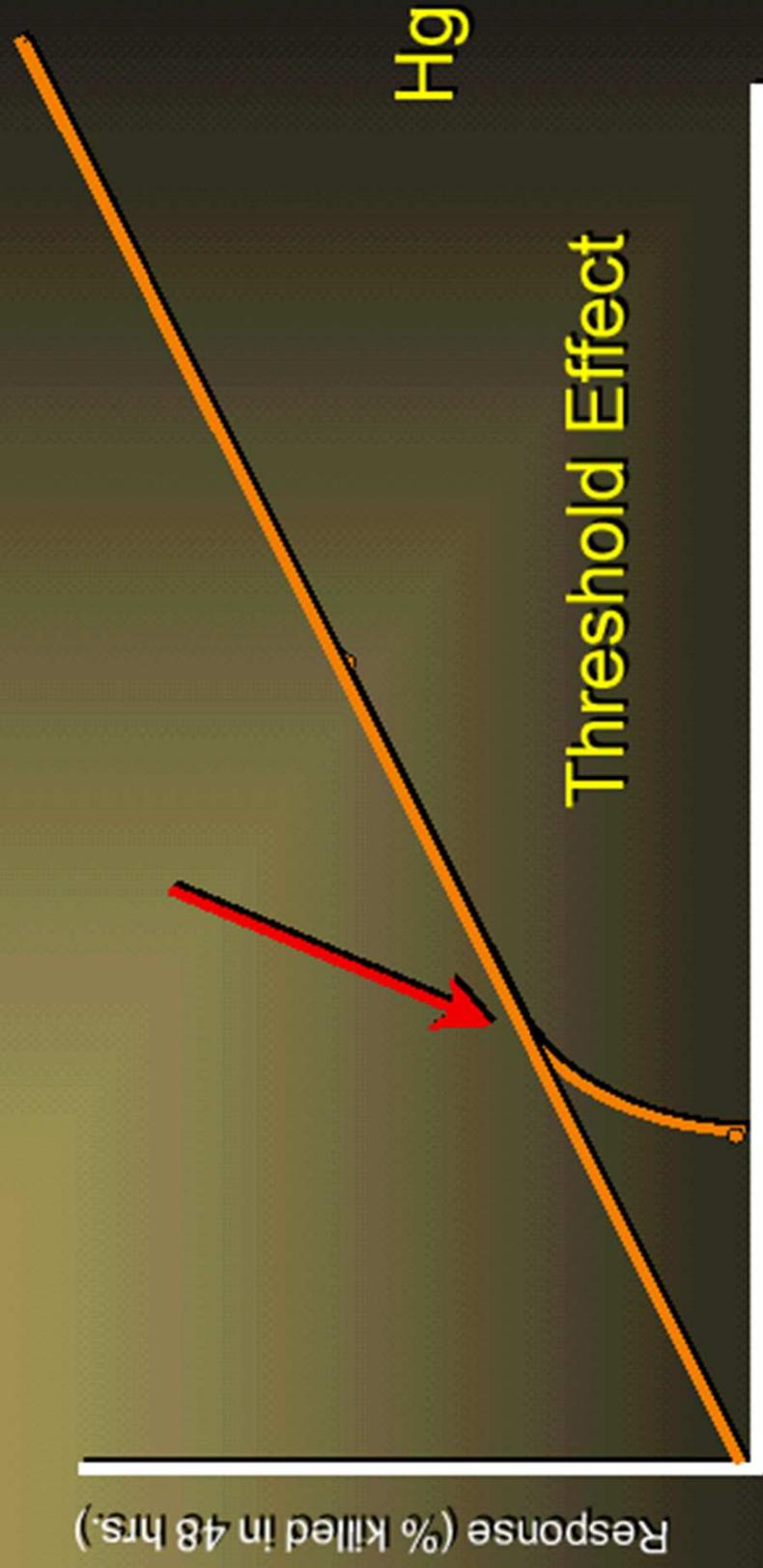
## Tossicologia – relazioni dose risposta

- a) Livello minimo d'effetto,
- b) sensibilità di organismo a incrementi di tossico e
- c) livelli per cui effetto definitivo (morte) accade per la maggior parte di organismi esposti.

Per nutrienti minerali esistono range ottimali



# Pieces of the Total Dose Response Curve



Dose (mg/kg body weight)

# Tossicologia – relazioni dose risposta

## Relazioni dose-risposta

*Risposta fisiologica rilevata*

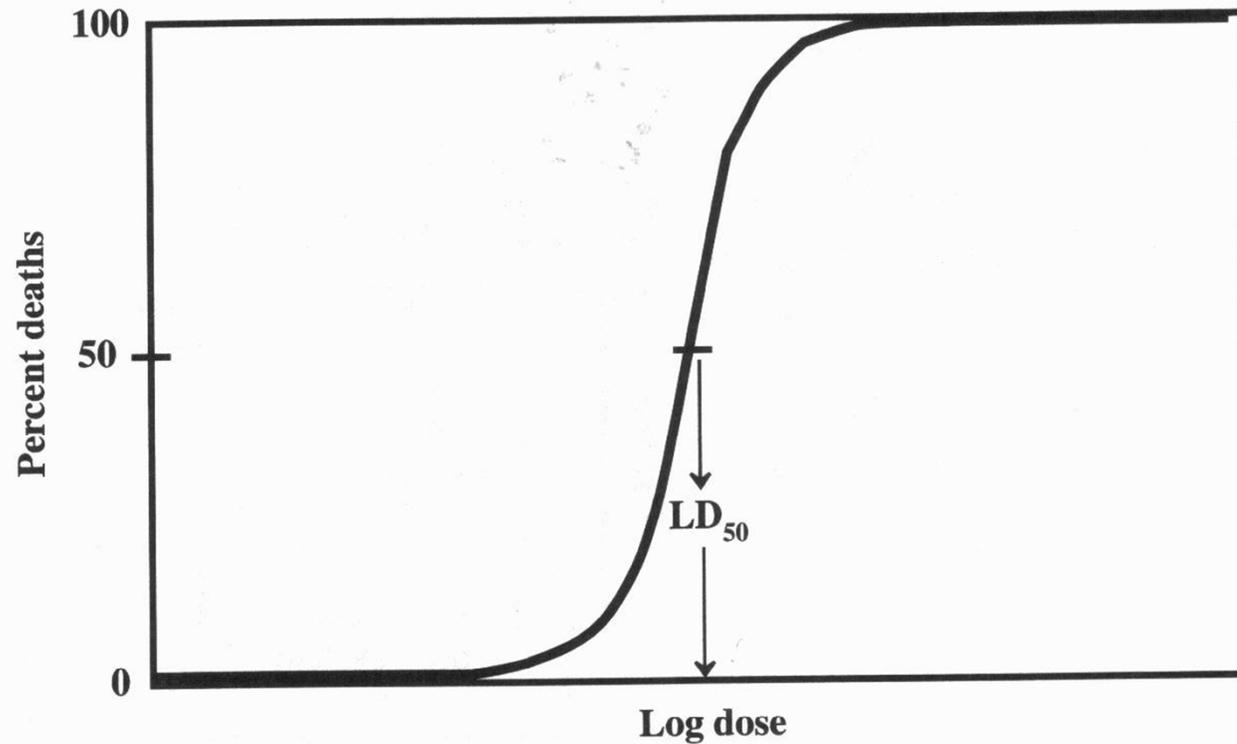


Illustration of a dose–response curve in which the response is the death of the organism. The cumulative percentage of deaths of organisms is plotted on the y axis. Although plotting log dose usually gives a better curve, with some toxic substances it is better to plot dose.

# Tossicologia – tossicità relative

## Effetti non letali

Table 6.1 Toxicity Scale with Example Substances<sup>a</sup>

Toxic Substance	Approximate LD <sub>50</sub>	Toxicity Rating
DEHP <sup>b</sup>	→ — 10 <sup>5</sup>	1. Practically nontoxic, > 1.5 × 10 <sup>4</sup> mg/kg
Ethanol	→ — 10 <sup>4</sup>	
Sodium chloride	→ —	2. Slightly toxic 5 × 10 <sup>3</sup> – 1.5 × 10 <sup>4</sup> mg/kg
Malathion	→ — 10 <sup>3</sup>	
Chlorane	→ —	3. Moderately toxic 500–5000 mg/kg
Heptachlor	→ — 10 <sup>2</sup>	
Parathion	→ — 10	4. Very toxic 50–500 mg/kg
TEPP <sup>c</sup>	→ —	
Nicotine	→ — 1	5. Extremely toxic 5–50 mg/kg
Tetrodotoxin <sup>d</sup>	→ — 10 <sup>-1</sup>	
	→ — 10 <sup>-2</sup>	6. Supertoxic <5 mg/kg
TCDD <sup>e</sup>	→ — 10 <sup>-3</sup>	
	→ — 10 <sup>-4</sup>	
Botulinus toxin	→ — 10 <sup>-5</sup>	

<sup>a</sup> Doses are in units of mg of toxicant per kg of body mass. Toxicity ratings on the right are given as numbers ranging from 1 (practically nontoxic) to 6 (supertoxic), along with estimated lethal oral doses for humans in mg/kg. Estimated LD<sub>50</sub> values for substances on the left have been measured in test animals, usually rats, and apply to oral doses.

<sup>b</sup> Bis(2-ethylhexyl)phthalate.

<sup>c</sup> Tetraethylpyrophosphate.

<sup>d</sup> Toxin from pufferfish.

<sup>e</sup> TCDD represents 2,3,7,8-tetrachlorodibenzodioxin, commonly called “dioxin.”

# Tossicologia – tossicità relativa

## Tossicità acuta

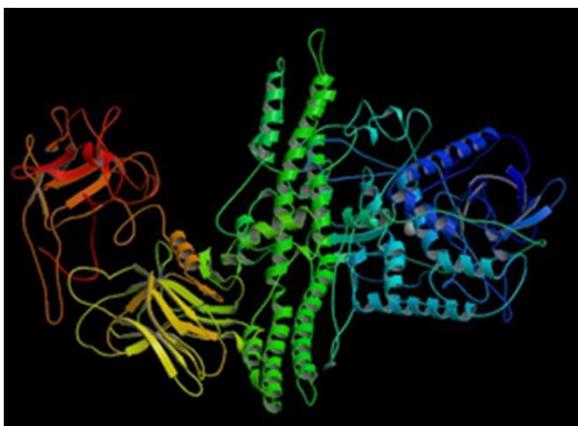


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# Tossicologia – tossicità relative

paragone tra criteri di tossicità acuta

*La tossicità acuta si riferisce agli effetti avversi che si verificano in breve tempo (di solito entro 14 giorni) dopo la somministrazione di una singola dose (o esposizione a un determinato dose o concentrazione) di una sostanza di prova, o più dosi date entro 24 ore.*

*La DL50 è definita come l'espressione derivata statisticamente di una dose singola che si prevede sia letale per il 50% degli animali testati*

Table 6.3. Some criteria for the classification of chemicals on the basis of LD50 values from acute oral toxicity data expressed as mg/kg<sub>bw</sub>

<i>United Nations</i>	toxic 1	toxic 2	toxic 3		
Solids	< 5	< 50	< 500		
Liquids	< 5	< 50	< 2000		
<i>World Health Organization</i>	extremely hazardous	highly hazardous	moderately toxic	slightly toxic	
Solids	< 5	< 50	< 500	< 5000	
Liquids	< 20	< 200	< 2000	< 2000	
<i>European Communities</i>	very toxic	toxic	harmful		
	< 25	< 200	< 2000		
<i>USA</i>	supertoxic	highly toxic	very toxic	moderately toxic	slightly toxic
	< 5	< 50	< 500	< 5000	< 15000

*Le  $DL_{50}$  hanno un valore limitato nell'esprimere i pericoli per l'uomo.*

*Questo è perché la morte a seguito dell'esposizione (ambientale) ad una sostanza tossica è un effetto irreversibile relativamente raro.*

*Maggiormente preoccupanti sono gli effetti subletali che sono spesso reversibili, come le allergie e difetti congeniti, o effetti che possono essere letali ma che non sono acuti come la cancerogenesi.*