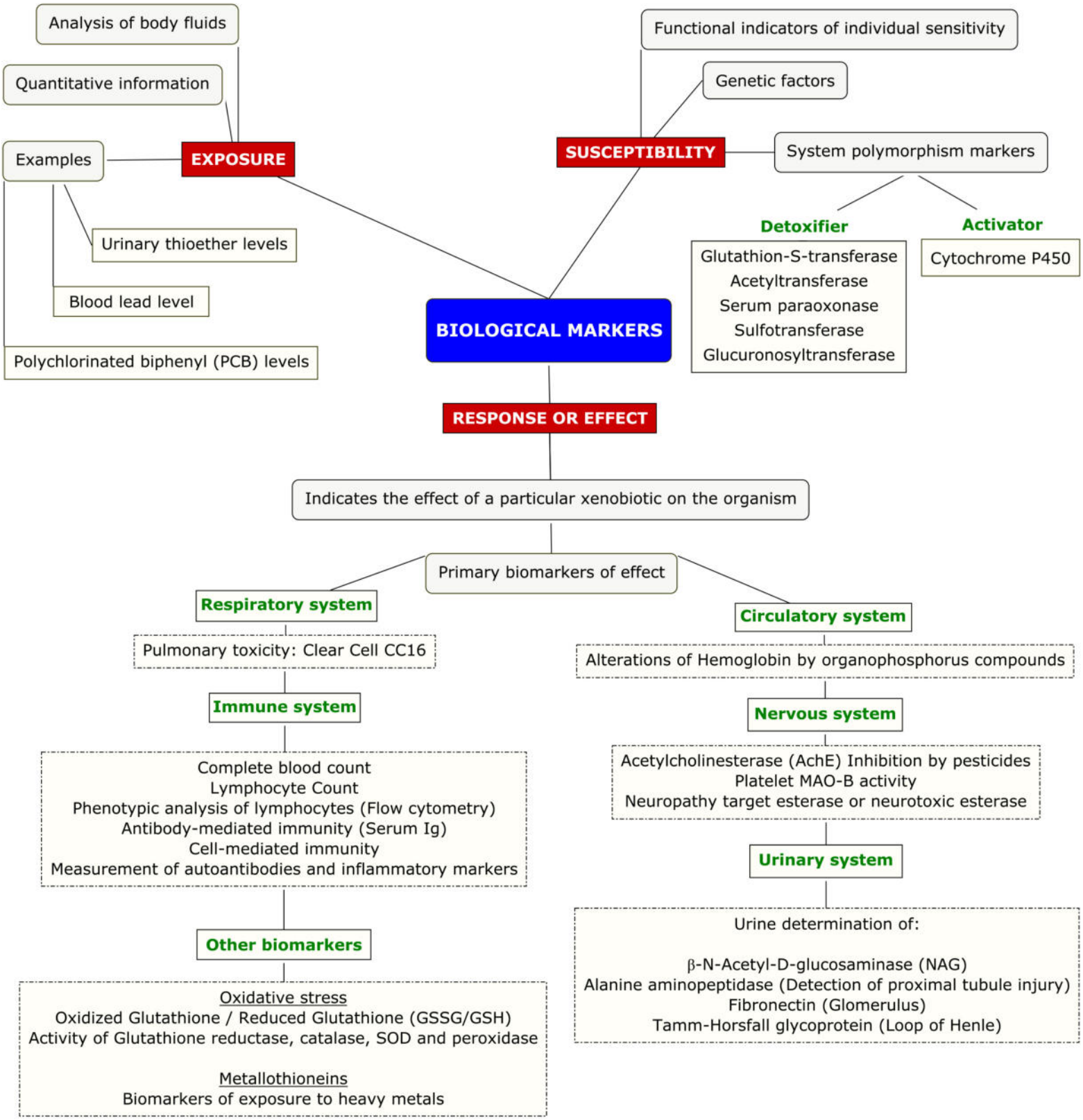
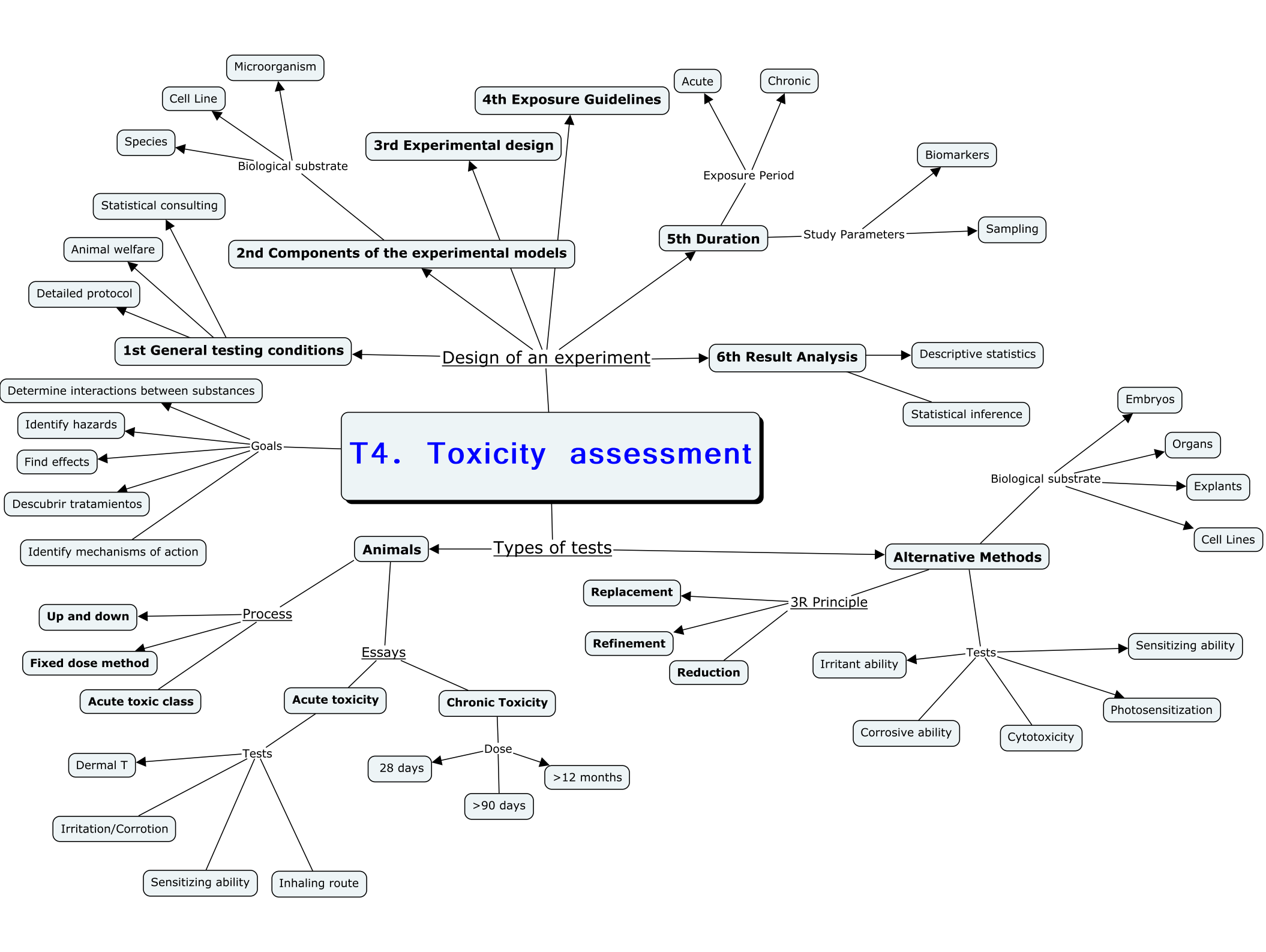
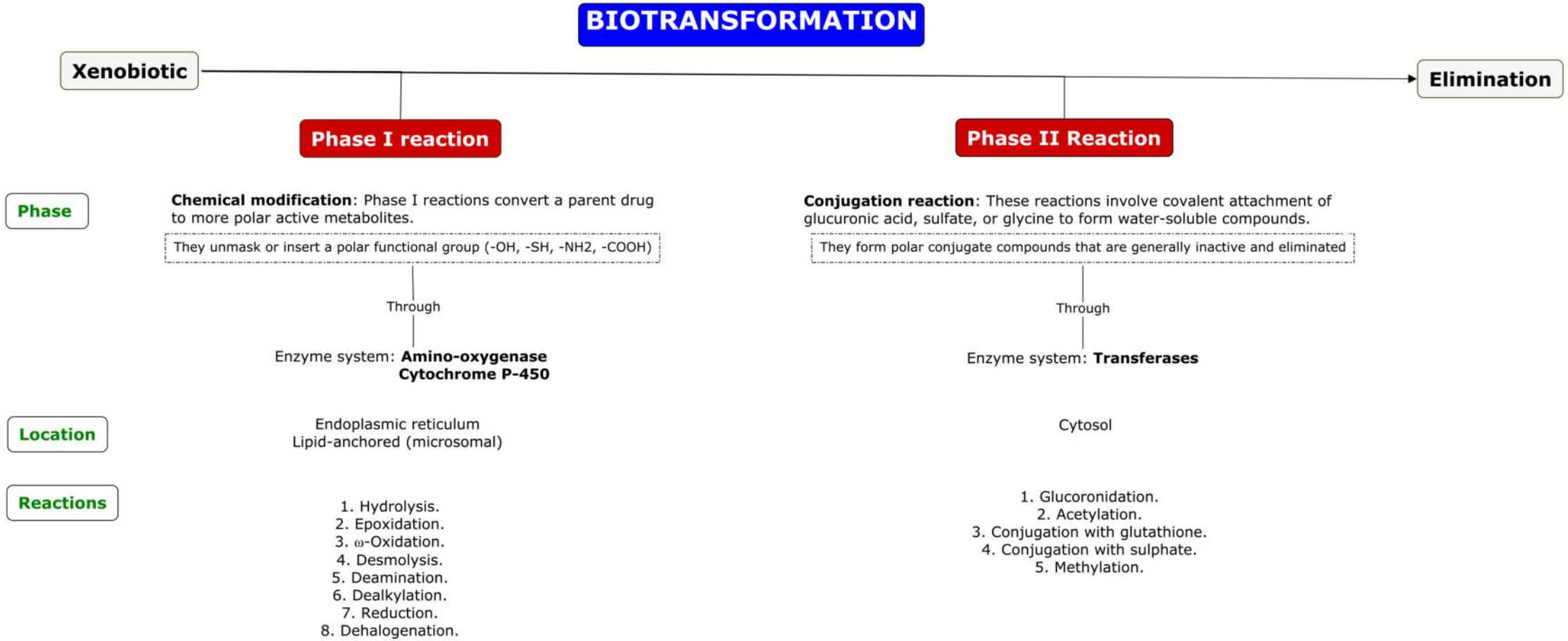
UNIT 3. APPLICATIONS OF BIOCHEMICAL TOXICOLOGY TO DIAGNOSIS AND TO THE TREATMENT OF POISONING

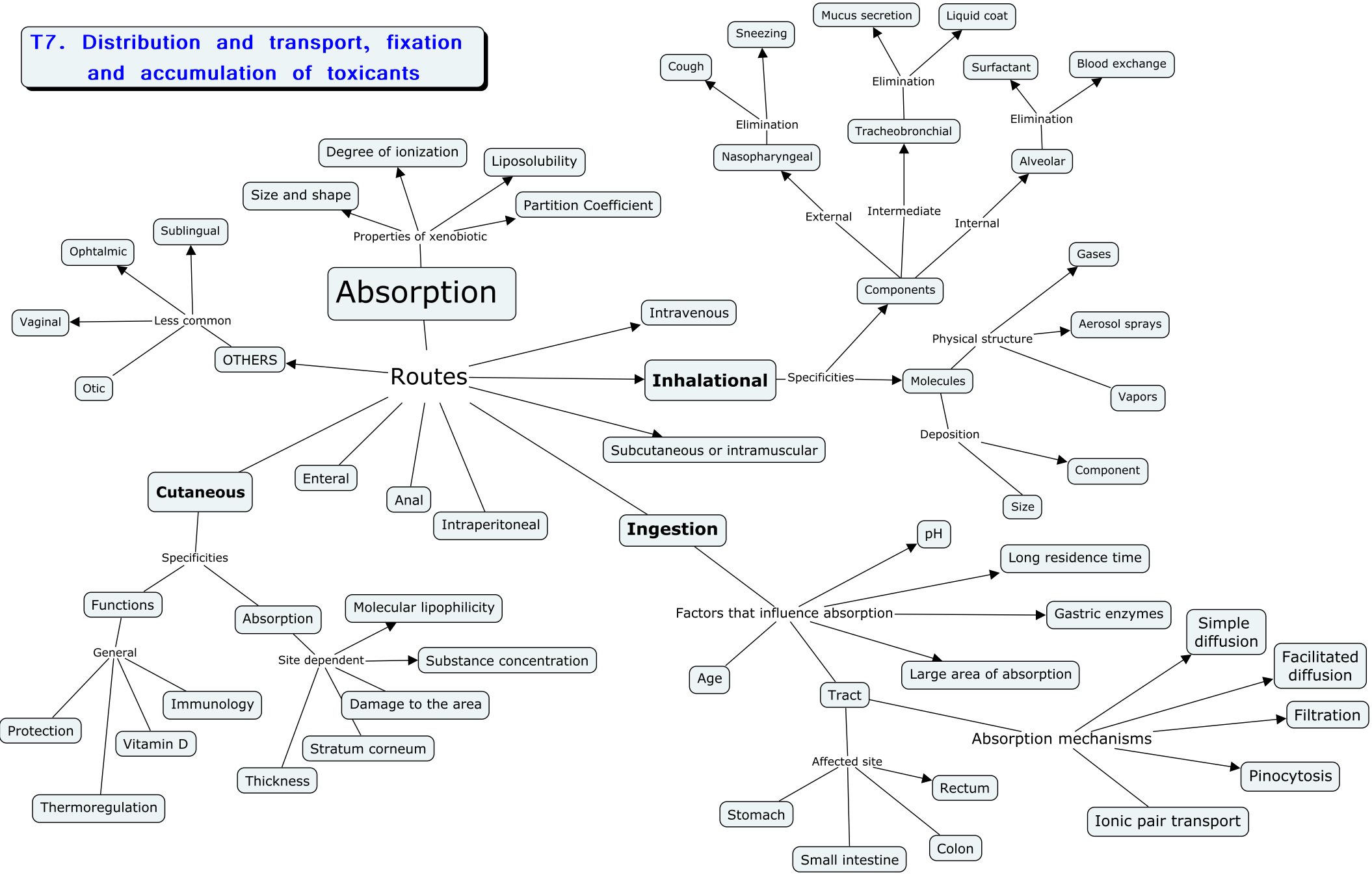



T4. Toxicity assessment
Design of an experiment
Types of tests
Goals
Determine interactions between substances
Identify hazards
Find effects
Descubrir tratamientos
Identify mechanisms of action
1st General testing conditions
Statistical consulting
Animal welfare
Detailed protocol
2nd Components of the experimental models
Biological substrate
Microorganism
Cell Line
Species
3rd Experimental design
4th Exposure Guidelines
5th Duration
Exposure Period
Acute
Chronic
Study Parameters
Biomarkers
Sampling
6th Result Analysis
Descriptive statistics
Statistical inference
Animals
Process
Up and down
Fixed dose method
Acute toxic class
Essays
Acute toxicity
Tests
Dermal T
Irritation/Corrotion
Sensitizing ability
Inhaling route
Chronic Toxicity
Dose
28 days
>12 months
>90 days
Alternative Methods
3R Principle
Replacement
Refinement
Reduction
Biological substrate
Embryos
Organs
Explants
Cell Lines
Tests
Irritant ability
Sensitizing ability
Photosensitization
Corrosive ability
Cytotoxicity

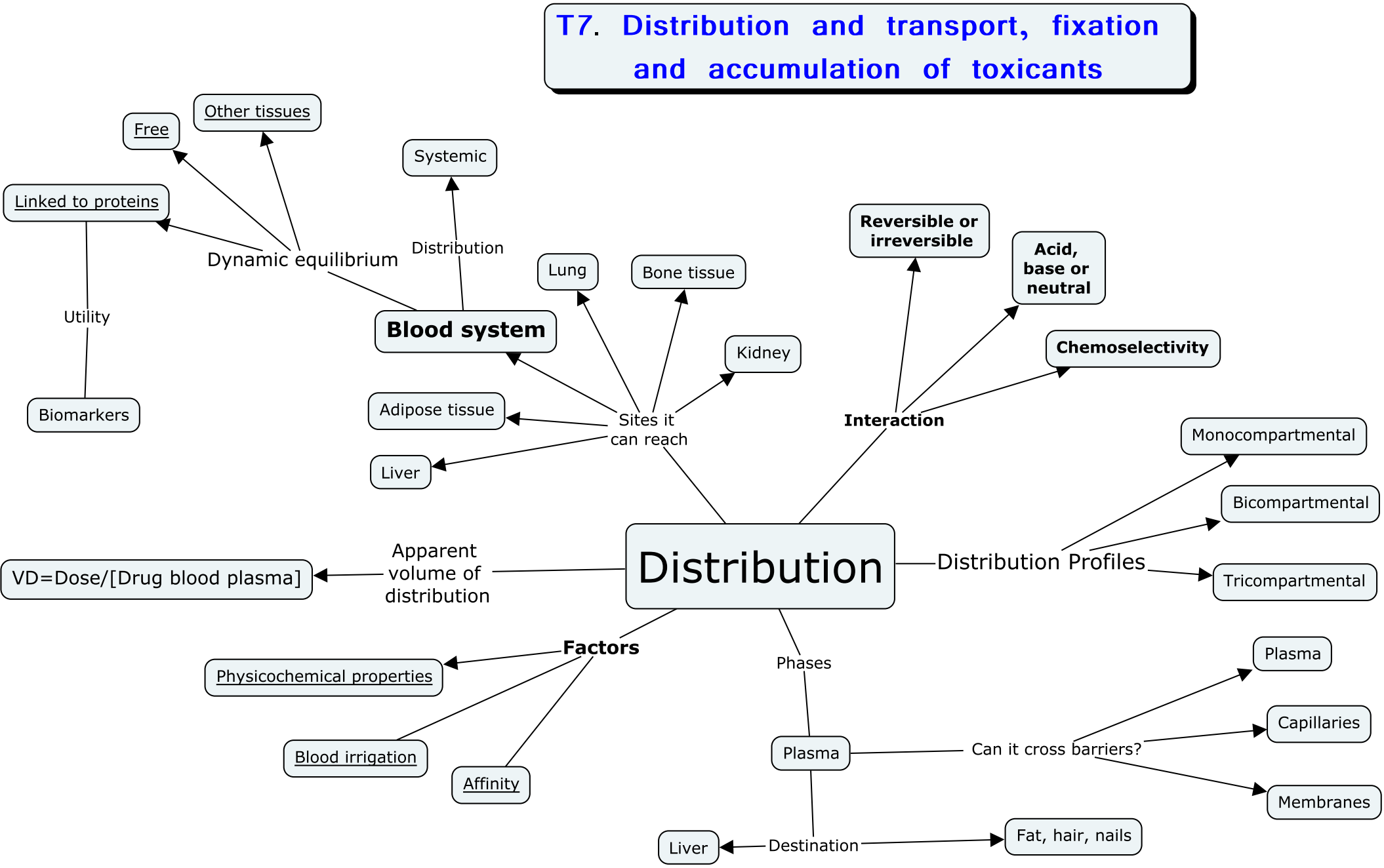
UNIT 6. BIOTRANSFORMATION OF TOXICS.

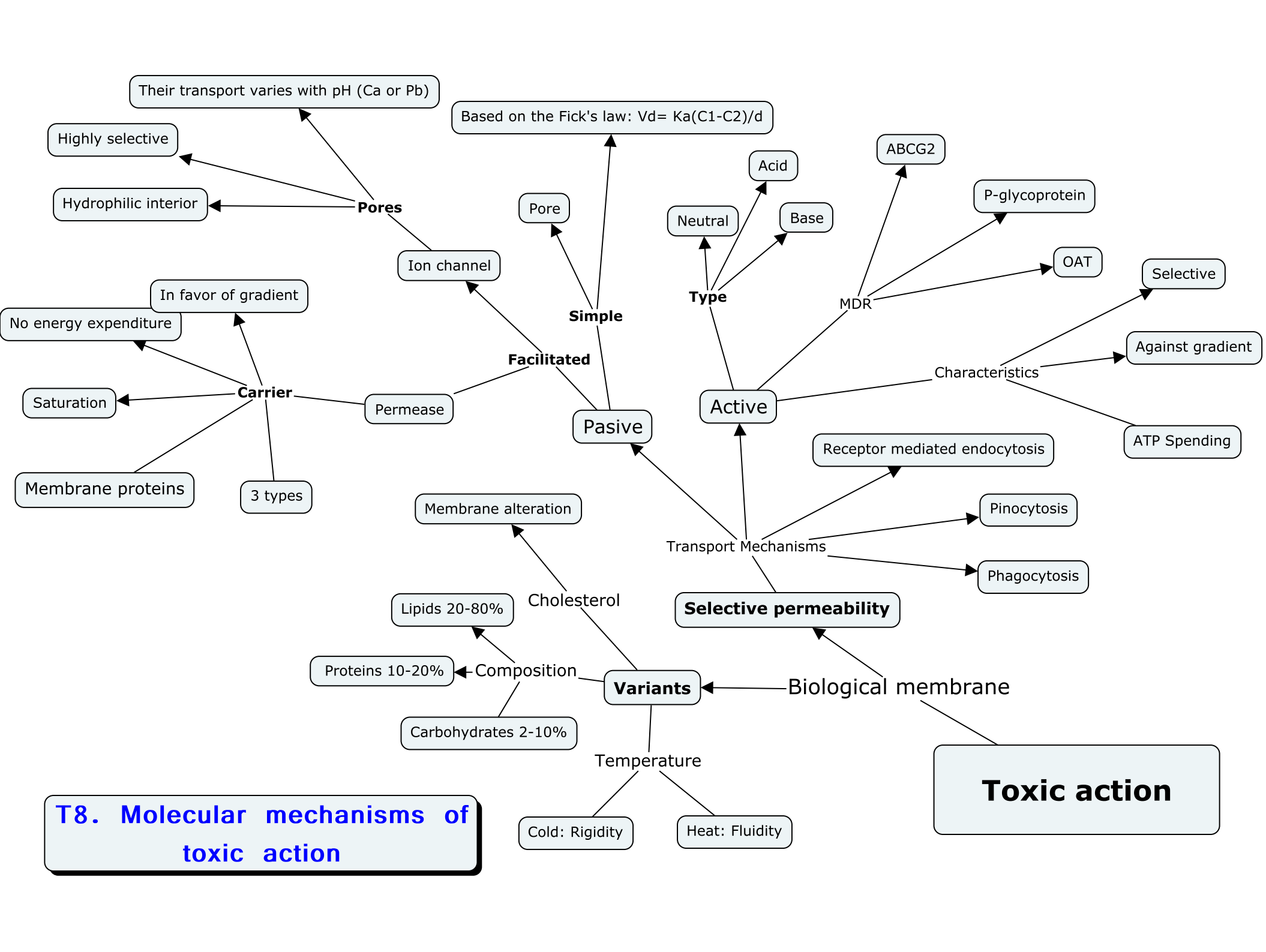


T7. Distribution and transport, fixation and accumulation of toxicants

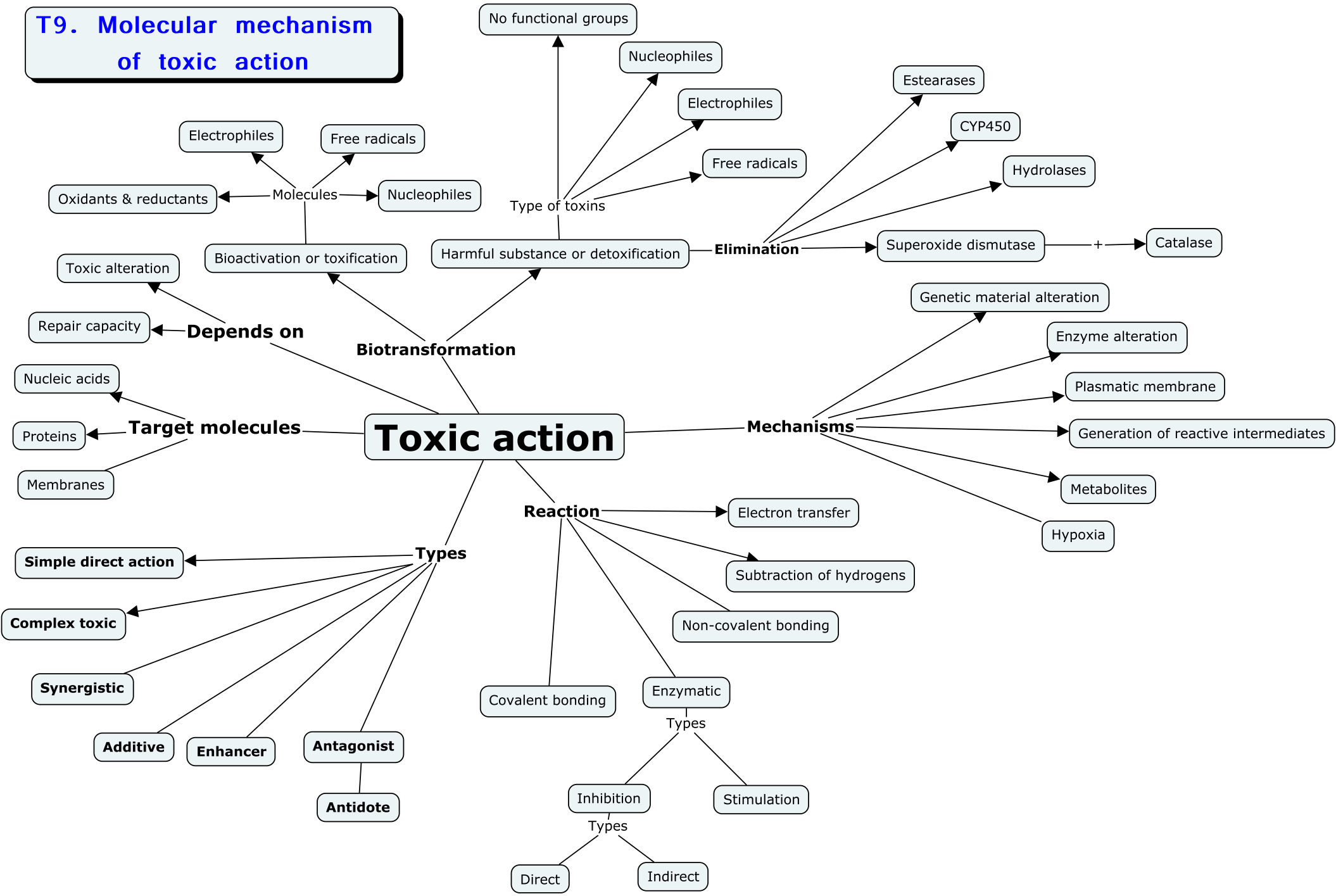


T7. Distribution and transport, fixation and accumulation of toxicants

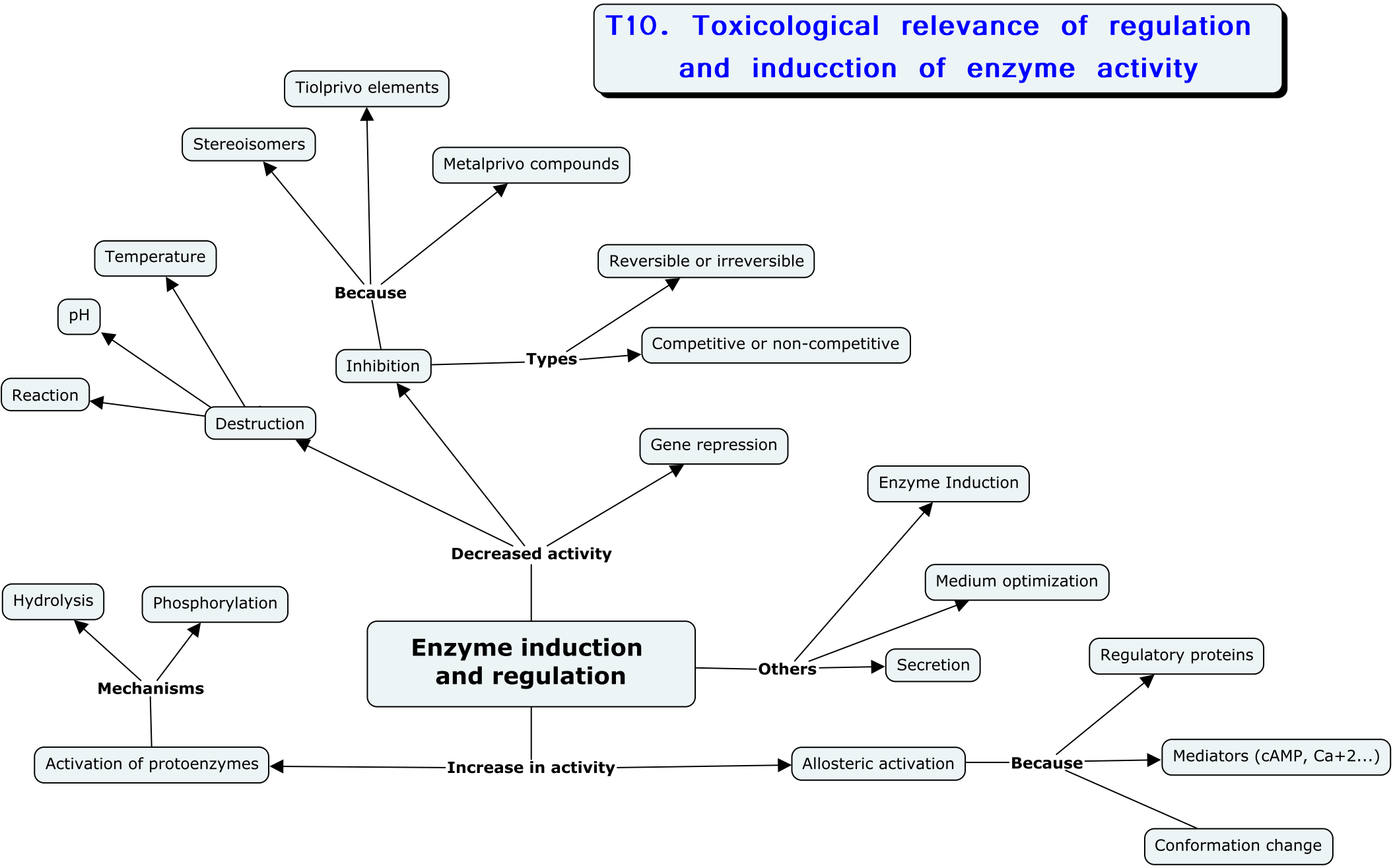



T8. Molecular mechanisms of toxic action
Toxic action
Biological membrane
Selective permeability
Variants
Composition
Lipids 20-80%
Proteins 10-20%
Carbohydrates 2-10%
Cholesterol
Membrane alteration
Temperature
Cold: Rigidity
Heat: Fluidity
Transport Mechanisms
Receptor mediated endocytosis
Pinocytosis
Phagocytosis
Active
Pasive
Characteristics
Selective
Against gradient
ATP Spending
Type
Neutral
Acid
Base
MDR
ABCG2
P-glycoprotein
OAT
Facilitated
Simple
Pore
Carrier
Permease
Saturation
Membrane proteins
3 types
No energy expenditure
In favor of gradient
Ion channel
Pores
Their transport varies with pH (Ca or Pb)
Highly selective
Hydrophilic interior
Based on the Fick's law: Vd= Ka(C1-C2)/d

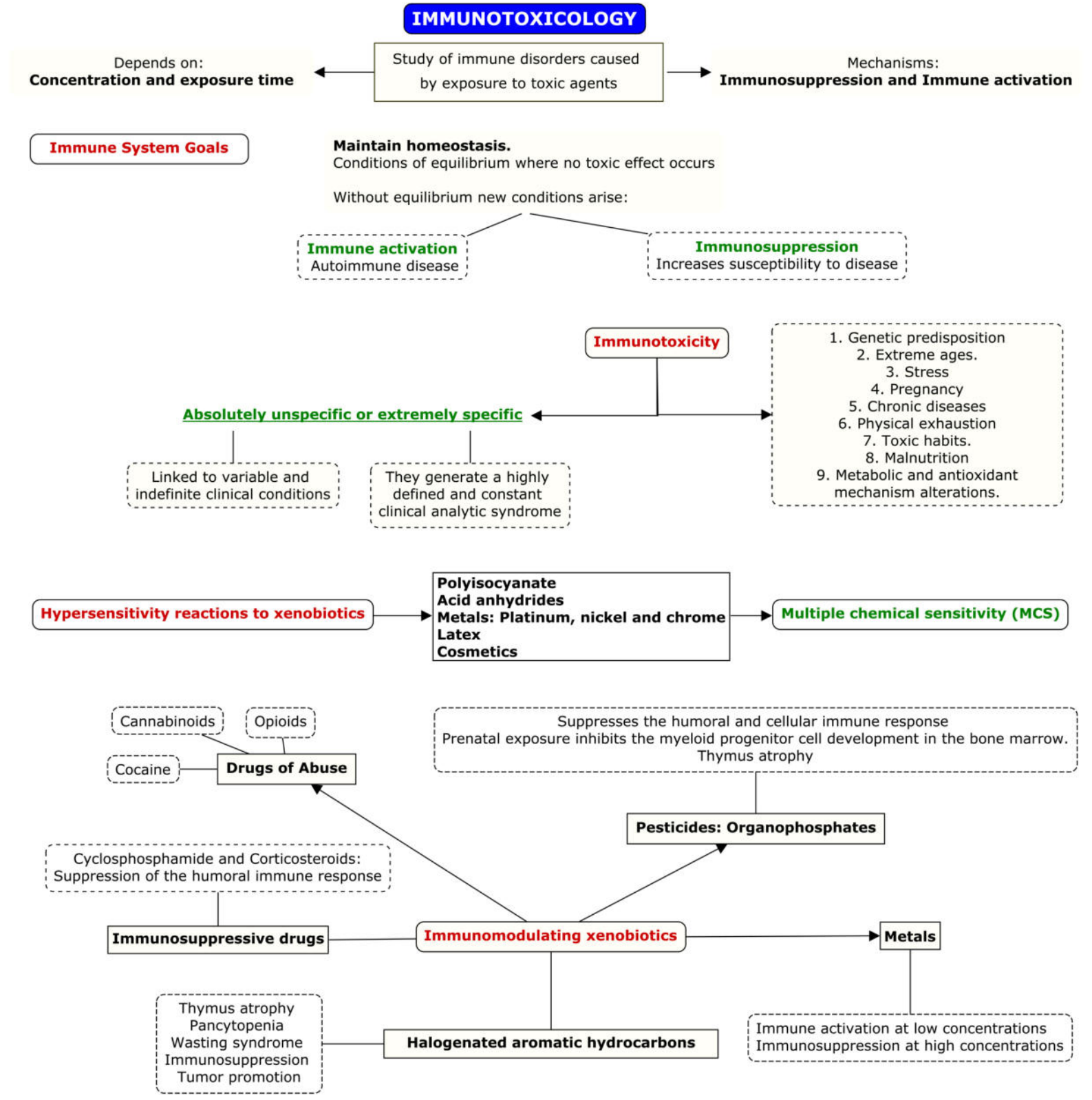
T9. Molecular mechanism of toxic action



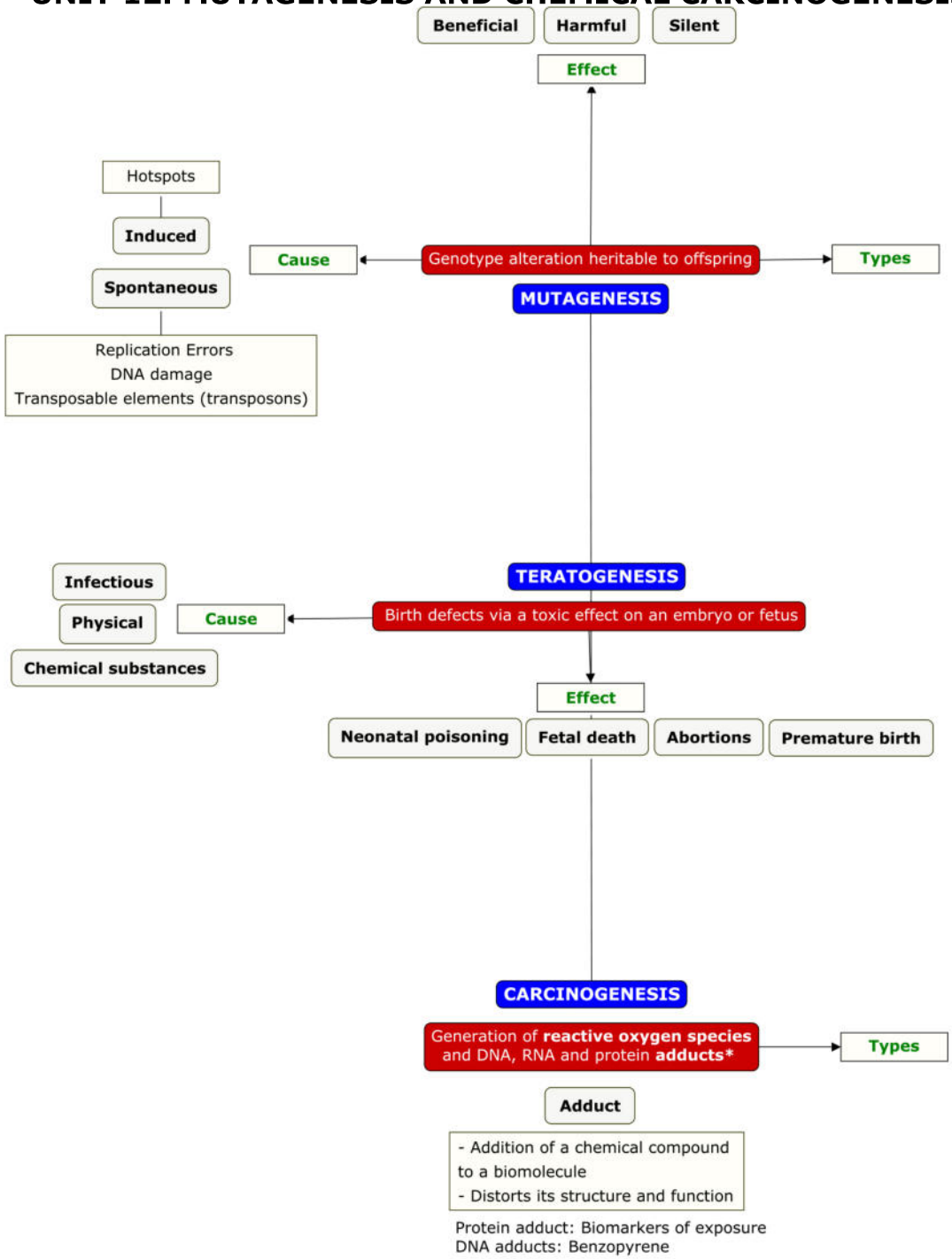
T10. Toxicological relevance of regulation and inducction of enzyme activity

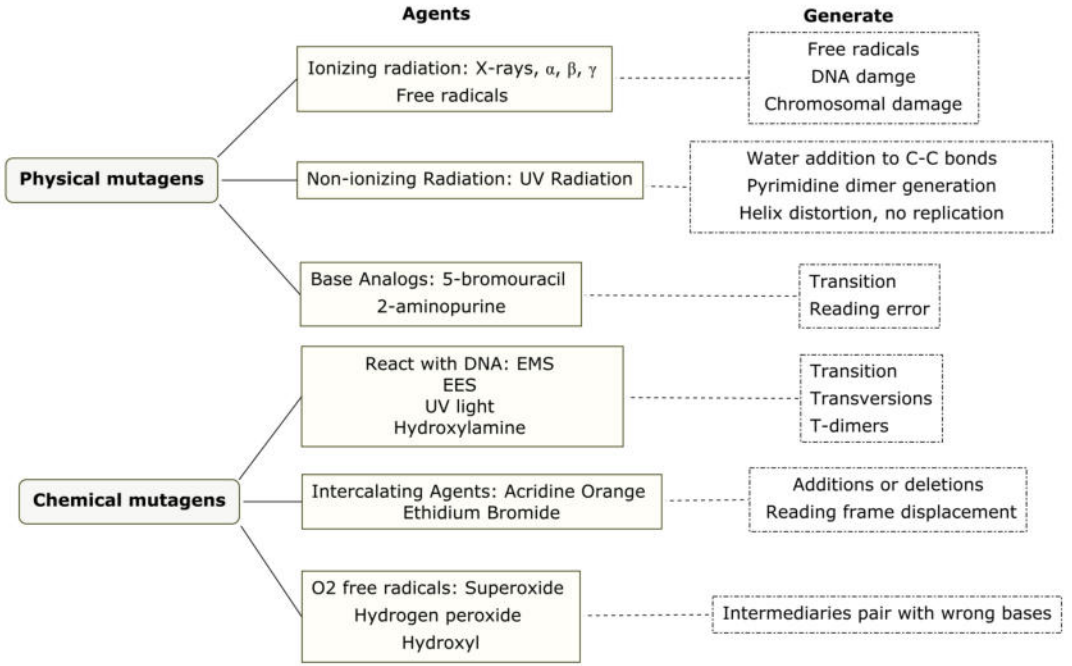


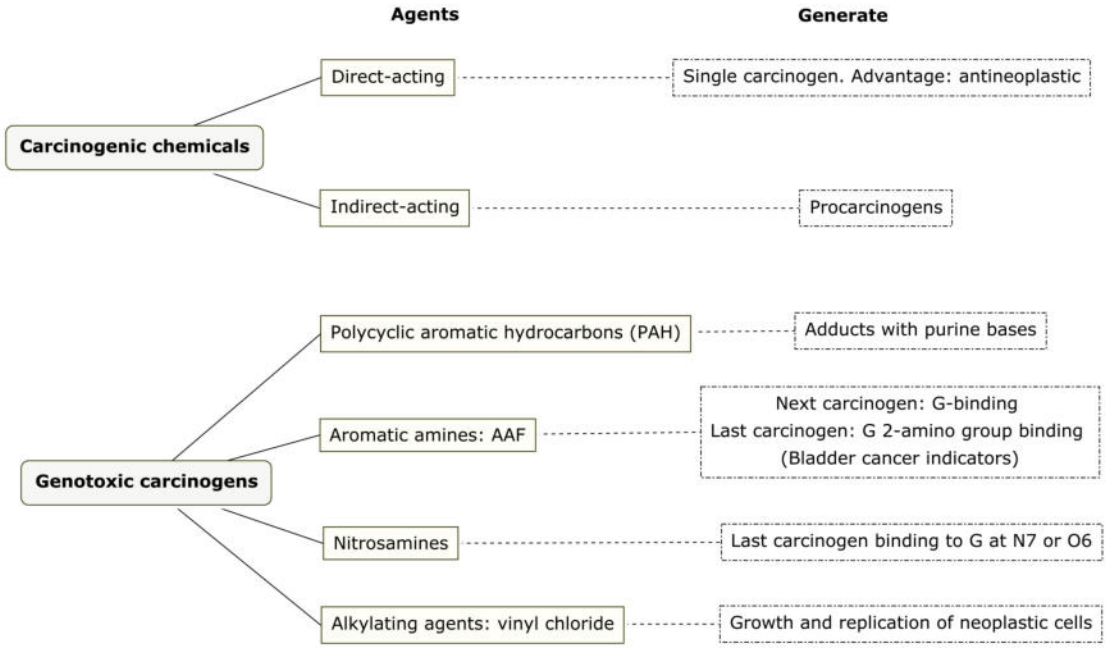
UNIT 11. INMUNOTOXICOLOGY



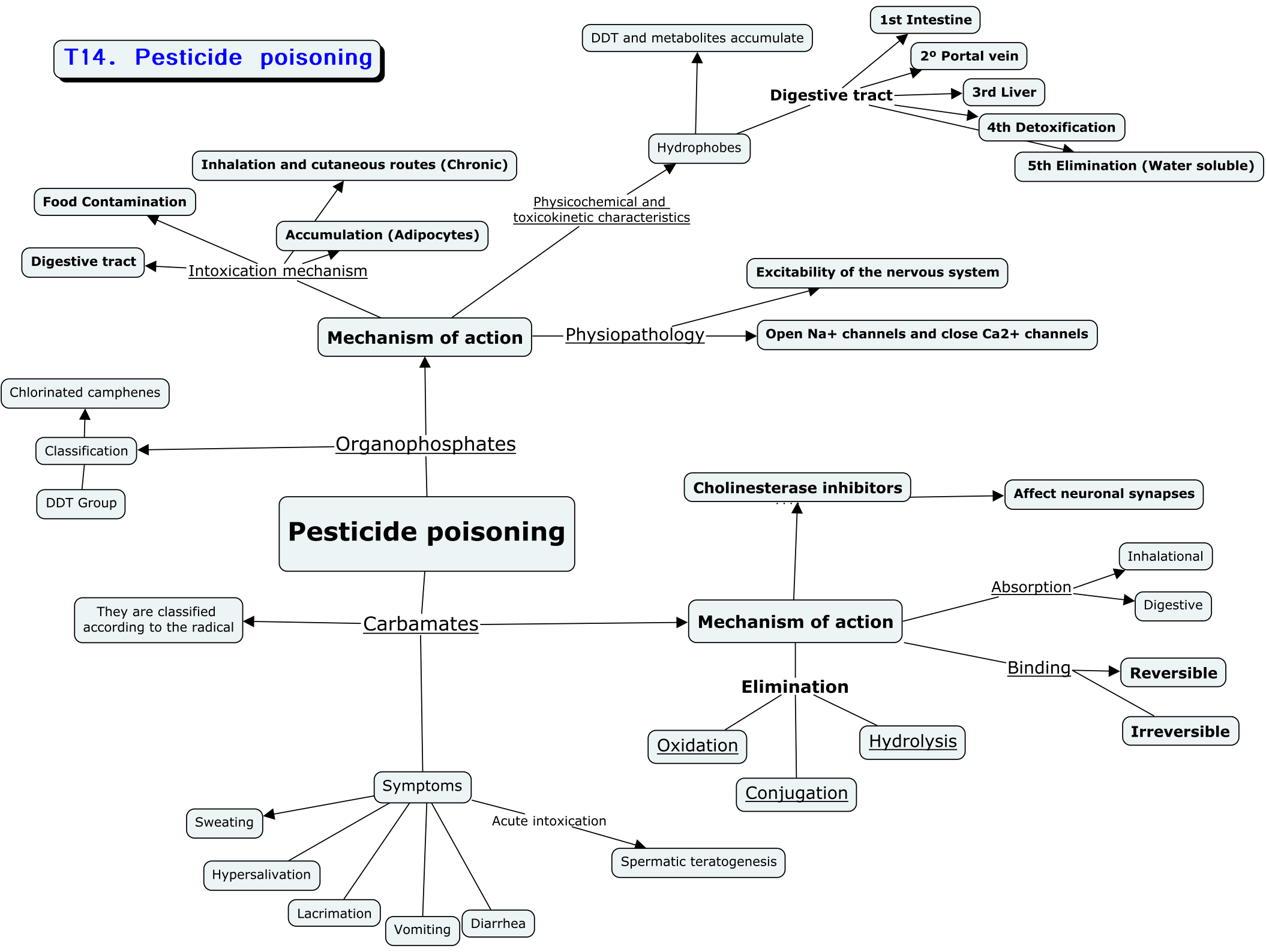
UNIT 12. MUTAGENESIS AND CHEMICAL CARCINOGENESIS

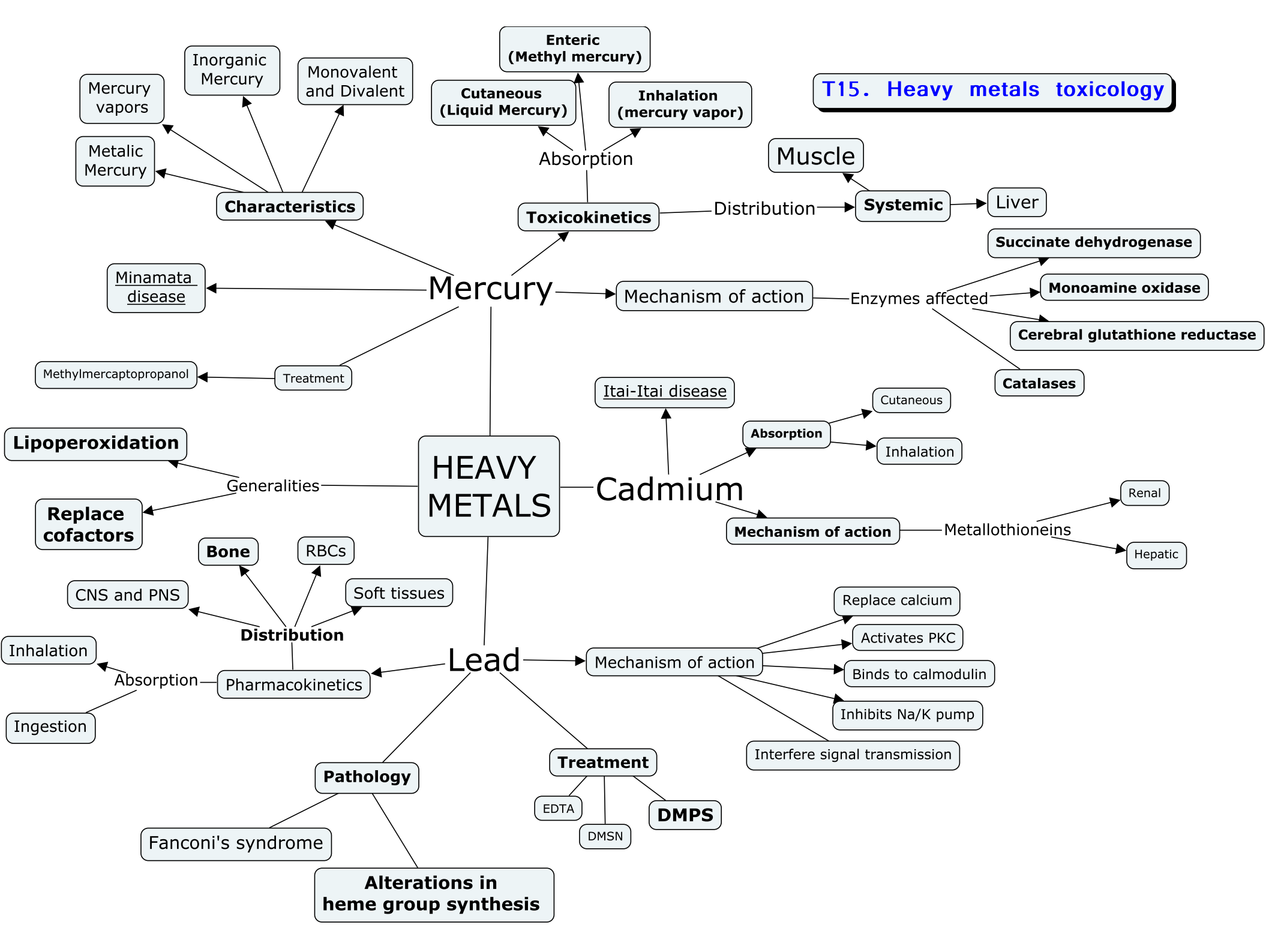


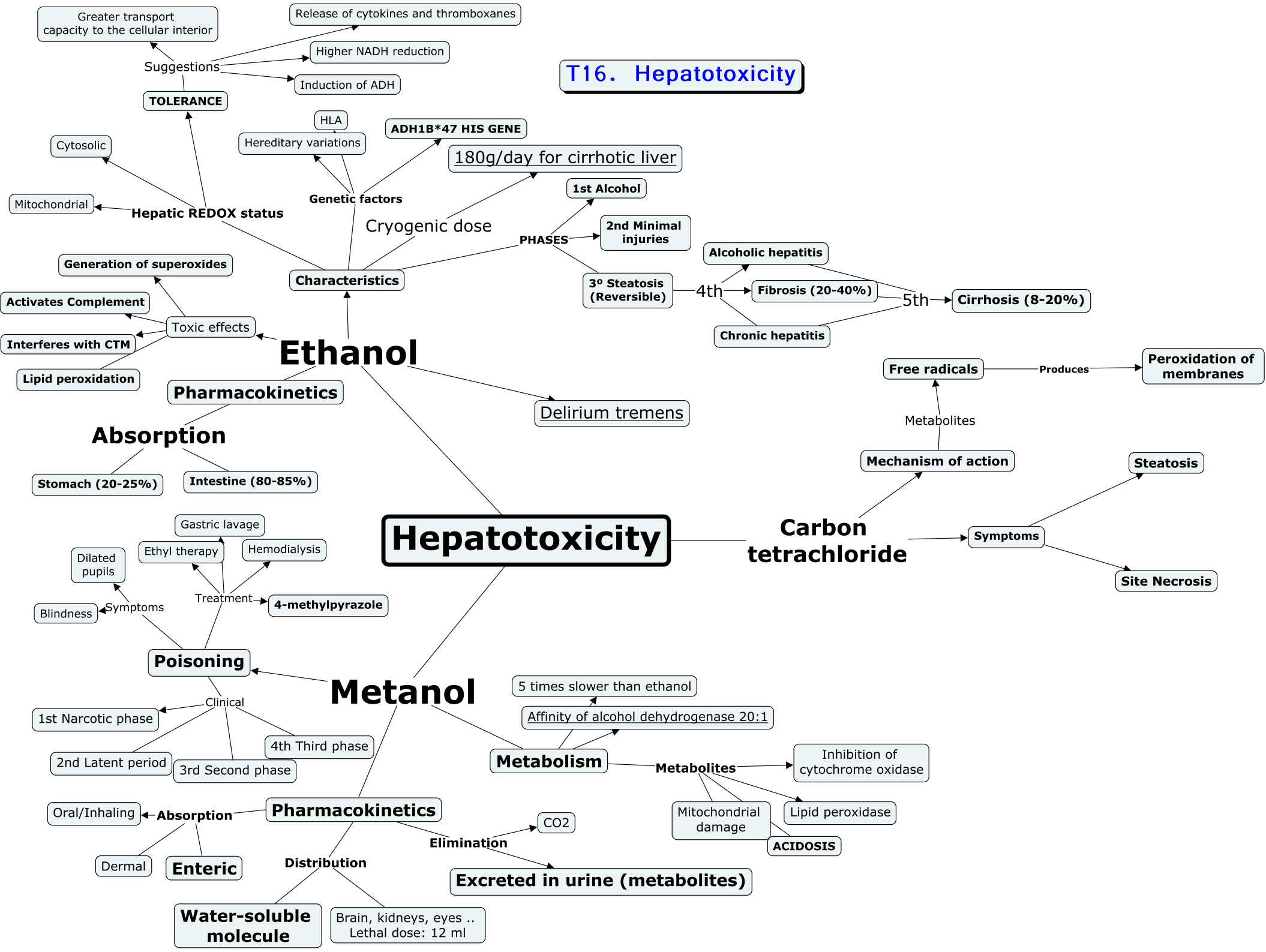




T14. Pesticide poisoning




T15. Heavy metals toxicology
HEAVY METALS
Mercury
Inorganic Mercury
Mercury vapors
Metalic Mercury
Monovalent and Divalent
Characteristics
Enteric (Methyl mercury)
Cutaneous (Liquid Mercury)
Inhalation (mercury vapor)
Absorption
Toxicokinetics
Distribution
Muscle
Systemic
Liver
Minamata disease
Mechanism of action
Enzymes affected
Succinate dehydrogenase
Monoamine oxidase
Cerebral glutathione reductase
Catalases
Treatment
Methylmercaptopropanol
Cadmium
Itai-Itai disease
Absorption
Cutaneous
Inhalation
Mechanism of action
Metallothioneins
Renal
Hepatic
Generalities
Lipoperoxidation
Replace cofactors
Lead
Distribution
Bone
RBCs
Soft tissues
CNS and PNS
Pharmacokinetics
Absorption
Inhalation
Ingestion
Mechanism of action
Replace calcium
Activates PKC
Binds to calmodulin
Inhibits Na/K pump
Interfere signal transmission
Pathology
Fanconi's syndrome
Alterations in heme group synthesis
Treatment
EDTA
DMSN
DMPS


T16. Hepatotoxicity
Hepatotoxicity
Ethanol
Pharmacokinetics
Absorption
Stomach (20-25%)
Intestine (80-85%)
Delirium tremens
Characteristics
Hepatic REDOX status
Cytosolic
Mitochondrial
Genetic factors
HLA
Hereditary variations
ADH1B*47 HIS GENE
Cryogenic dose
180g/day for cirrhotic liver
PHASES
1st Alcohol
2nd Minimal injuries
3º Steatosis (Reversible)
4th
Alcoholic hepatitis
Fibrosis (20-40%)
Chronic hepatitis
5th
Cirrhosis (8-20%)
Toxic effects
Generation of superoxides
Activates Complement
Interferes with CTM
Lipid peroxidation
TOLERANCE
Suggestions
Greater transport capacity to the cellular interior
Release of cytokines and thromboxanes
Higher NADH reduction
Induction of ADH
Carbon tetrachloride
Mechanism of action
Free radicals
Produces
Peroxidation of membranes
Metabolites
Symptoms
Steatosis
Site Necrosis
Metanol
Poisoning
Clinical
1st Narcotic phase
2nd Latent period
3rd Second phase
4th Third phase
Symptoms
Blindness
Dilated pupils
Treatment
Gastric lavage
Ethyl therapy
Hemodialysis
4-methylpyrazole
Metabolism
5 times slower than ethanol
Affinity of alcohol dehydrogenase 20:1
Metabolites
Inhibition of cytochrome oxidase
Mitochondrial damage
Lipid peroxidase
ACIDOSIS
Pharmacokinetics
Oral/Inhaling
Absorption
Dermal
Enteric
Distribution
Water-soluble molecule
Brain, kidneys, eyes .. Lethal dose: 12 ml
Elimination
CO2
Excreted in urine (metabolites)

T20. Cocaine, cannabis, amphetamine-type compounds intoxication. Emerging drugs