INTRODUCTION TO TOXICOLOGY

The meaning of the term ***toxicology*** is " the study of poisons." The root word toxic entered the English language around 1655 from the Late Latin word *toxicus* (which meant poisonous), itself derived from *n*, an ancient Greek term for poisons into which arrows were *ótoxik* dipped. The early history of toxicology focused on the understanding and uses of different poisons, and even today most people tend to think of poisons as a deadly potion that when ingested causes almost immediate harm or death. As toxicology has evolved into a modern science, however, it has expanded to all forms of adverse health effects that substances might produce, not just acutely harmful or lethal effects. The following definitions reflect this expanded scope of the science of toxicology:

Toxicology

the science that deals with the study of the adverse effects (toxicities) may produce in living organisms under specific conditions of exposure to chemicals or physical agents. It is a science that attempts to qualitatively identify all the hazards associated with a substance, as well as to quantitatively determine the exposure conditions under which those hazards/toxicities are induced. that experimentally investigates the occurrence, nature, incidence, mechanism, and risk factors for the adverse effects of toxic substances

Toxic

having the characteristic of producing an undesirable or adverse health effect.

Toxicant

any substance that causes a harmful (or adverse) effect when in contact with a living organism at a sufficiently high concentration.

Toxin

any toxicant produced by an organism

Exposure

to cause an adverse effect, a toxicant must first come in contact with an organism. The means by which an organism comes in contact with the substance is the route of exposure (e.g., in the air, water, soil, food, medication) for that chemical

Acute exposure

exposure over a brief period of time (generally less than 24 h). Often it is considered to be a single exposure (or dose) but may consist of repeated exposures within a short time period.

Subacute exposure

resembles acute exposure except that the exposure duration is greater, from several days to one month.

Subchronic exposure

exposures repeated or spread over an intermediate time range 1–3 months.

Chronic exposure

exposures (either repeated or continuous) over a long (greater than 3 months) period of time

Hazard

the qualitative nature of the adverse or undesirable effect resulting from exposure to a particular toxicant or physical agent. For example, asphyxiation is the hazard from acute exposures to carbon monoxide (CO).

Risk

the measure or probability that a specific exposure situation or dose will produce a toxic effect.

Risk assessment

the process by which the potential (or probability of) adverse health effects of exposure are characterized.

Safety

the measure or mathematical probability that a specific exposure situation or dose will not produce a toxic effect.

Toxicity

any toxic (adverse) effect that a chemical or physical agent might produce within a living organism

Toxic Symptom

any feeling or sign indicating the presence of a poison in the system

Selective Toxicity

means that a chemical will produce injury to one kind of living matter without harming another form of life, even though the two may exist close together

Acute toxicity

an adverse or undesirable effect that is manifested within a relatively short time interval ranging from almost immediately to within several days following exposure

Chronic toxicity

a permanent or lasting adverse effect that is manifested after exposure to a toxicant..

Delayed or latent toxicity

an adverse or undesirable effect appearing long after the initiation of exposure to the toxicant.

Local toxicity

an adverse or undesirable effect that is manifested at the toxicant's site of contact with the organism. Examples include an acid's ability to cause burning of the eyes, upper respiratory tract irritation, and skin burns.

Systemic toxicity

an adverse or undesirable effect that can be seen throughout the organism or in an organ with distant from the point of entry of the toxicant. Examples would be adverse effects on the kidney or central nervous system resulting from the chronic ingestion of mercury.

Reversible toxicity

an adverse or undesirable effect that can be reversed once exposure is stopped. Reversibility of toxicity depends on a number of factors, including the **extent of exposure** (time and amount of toxicant) ,ability of the affected tissue **to repair or regenerate**.

Allergic reaction

a reaction to a toxicant caused by an altered state of the normal immune response. The outcome of the exposure can be immediate (anaphylaxis) or delayed (cell-mediated).

Idiosyncratic reaction

a response to a toxicant occurring at exposure levels much lower than those generally required to cause the same effect in most individuals within the population. This response is genetically determined,

.

Dose

the total amount of a toxicant administered to an organism at specific time intervals. The quantity can be further defined in terms of quantity per unit body weight or per body surface area.

Dose response

is a relationship between exposure and effect, that can be established by measuring the response relative to an increasing dose. This relationship is important in determining the toxicity of a particular substance

WHAT TOXICOLOGISTS DO

- Recognition, identification, and quantitation of hazard
-Develops standards and regulations to protect health and the environment
- Involved in safety assessment and use of data as basis for regulatory control of hazards
- Determines risk associated with use of chemicals

Divisions of toxicology

Descriptive concerned directly with toxicity testing, to evaluate the risk of exposure to specific chemicals.

Mechanistic concerned with the mechanisms by which chemicals exert their toxic effects on living organisms .

Regulatory. establishment of standards for the amount of chemicals permitted in air, in the environment, in the workplace, or in drinking water

Other divisions of toxicology may be based on the classes of chemicals or application of knowledge from toxicology for a specific field

Forensic toxicology.

It is concerned with the legal aspects
of the harmful effects of chemicals on humans, establishing the cause of death and elucidating its circumstances in a postmortem investigation.

Clinical toxicology

recognizes and treats poisoning, and development of new techniques to treat these intoxications.

Environmental toxicology

is a relatively new area that studies the effects of chemicals on wildlife
.

Drug toxicology.

Drug toxicology o elucidates the mechanisms of side effects observed during clinical application.

Occupational toxicology studies toxicity of chemicals encountered in the occupational environment.

Pesticide toxicology is involved in the development of new pesticides and the safety of pesticide formulations.

Classification of Toxic Agents

: There are many types of Classification according to their

Effect on target organs (liver, kidney, hematopoietic system),

Use (pesticide, solvent, food additive),

Source of the agent (animal and plant toxins),

Effects (cancer mutation, liver injury,,,,,,,),

Physical state (gas, dust, liquid),

Labeling requirements (explosive, flammable, oxidizer),

Chemistry (aromatic amine, halogenated hydrocarbon),

Poisoning potential (extremely toxic, very toxic, slightly toxic)

Toxic substances are classified into the following

1- Heavy Metals differ from other toxic substances in that they are neither created nor destroyed by humans..

2- Solvents and Vapors.

3- Radiation and Radioactive Materials

4- Pesticides

5- Plant Toxins

6-Animal Toxins

Interaction of chemical

Antagonism : antagonist desirable in toxicology (antidote) . There are 4 types of antagonist :

A – functional : 2 chemicals counter balance each other by producing opposite effect on the same physiological function

B- Chemical reaction between 2 compound produce less toxic effect

C- Dispositional when that the absorption , distribution , biotransformation or excretion is altered so that the concentration and or duration are diminish

D- Receptor antagonist Occur when 2 chemical that bind to the same receptor produce less effect than give each one alone

MAJOR FACTORS THAT INFLUENCE TOXICITY

1-Route of administration:

2- Duration and frequency of exposure

3- Dose or concentration

DOSE RESPONSE RELATIONSHIP

it's the relation between the degree of response of biological system and the amount of toxicant administration . is related to

1- the dose

2- there is a receptor site with which the chemical interacts

3-the concentration at the site (related to dose administered)

Measures of Toxicity

Mortality (death)◆

Teratogenicity (ability to cause birth defects)◆

Carcinogenicity (ability to cause cancer), and,◆

Mutagenicity (ability to cause heritable change in the DNA)◆

The Median Lethal Dose LD_{50}

The amount (dose) of a chemical which produces death in 50% of a population of test animals **mg/kg** Normally expressed as milligrams of substance per kilogram of animal body weight

The Median Lethal Concentration LC_{50}

The concentration of a chemical in an environment (generally air or water) which produces death in 50% of an exposed population of test animals **mg/L** .Normally expressed as milligrams of substance per liter of air or water (or as ppm)

Signal Words The three possible signal words

CAUTION

WARNING

DANGER

CAUTION

"Caution" reflects the lowest degree of relative toxicity

All pesticides with an LD_{50} of greater than 500 mg/kg must display this word on their label

WARNING

"Warning" reflects an intermediate degree of relative toxicity

All pesticides with an LD_{50} of greater than 50 and less than 500 mg/kg must display this word on their label

DANGER

"Danger" reflects the highest degree of relative toxicity

All pesticides with an LD_{50} of less than 50 mg/kg must display this word on their label

POISON!!!

Legally defined term – not just anything you don't like

Any pesticide with an LD_{50} of 50 mg/kg or less

Labels must reflect this classification

Label must have the signal word "DANGER" plus the word ■ "POISON"

Units Used to Measure Chemicals in the Environment

PPM – Parts per million■

PPB – Parts per billion■

PPT – Parts per trillion■

One part per million is PPM

1 minute in two years■

1 cent in $10,000■

1 g of salt in 1 tons of potato chips■

■

One part per billion is PPB

1 second in 32 years■

1 cent in $10,000,000■

1 g of salt in 1000 tons of potato chips■

One part per trillion is PPT

1 second in 320 centuries■

1 mg of salt in 1000 tons of potato chips■

1 part per trillion is 1000 smaller than 1 part per billion◆

1 part per billion is1000 smaller than 1 part per million◆

1 part per million 1000 smaller than 1 part per thousand◆

The term **toxicokinetics** (the absorption, distribution, excretion, and metabolism of toxins, toxic doses of therapeutic agents, and their metabolites).

The term **toxicodynamics** is (the injurious effects of these substances on vital function.)

How Does Toxicity Develop

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

Step 1 Delivery from the site of exposure to the target

The intensity of toxic effect depend on **concentration** and **persistence** • of the toxicant at the site of action . After absorption of toxicant the rate is related to the **concentration** at the absorbing surface , of absorption **lipid soluble**(lipid soluble more absorb than water soluble)

Step 2 : Reaction of toxicant with target molecule

Types of reaction :

1- Noncovalent binding :

2- Covalent binding :

3- Hydrogen abstraction

4- Electron transfer

5- Enzyme reaction :

Step 3- Cellular dysfunction and result toxicity

1- Dysfunction of target molecules

2- Destruction of target molecules

3- New antigen formation

Step 4- Inappropriate repair and adaptation

HOW DOES THE POISONED PATIENT DIE?

. Many toxins depress **CNS** resulting in coma. Comatose patients frequently lose their airway protective reflexes and their respiratory drive. Thus, they may die as a result of airway obstruction, respiratory arrest. These are the most common causes of death due to overdoses of narcotics and sedative-hypnotic drugs

Seizures, muscular hyperactivity, and rigidity may result in death

Cardiovascular toxicity is also frequently. Hypotension may be due to depression of cardiac contractility; **hypovolemia** resulting from vomiting, diarrhea, **Lethal arrhythmias** can occur with overdoses of cardioactive drugs such as ephedrine, amphetamines, cocaine, digitalis, and theophylline;

Other organ system damage may occur after poisoning and is sometimes delayed in onset. lung tissue, resulting in **pulmonary fibrosis**, beginning several days after ingestion. **Massive hepatic necrosis** due to poisoning by acetaminophen or certain mushrooms results in hepatic encephalopathy and death 48-72 hours or longer after ingestion.

Management of the Poisoned Patient

Over a million cases of acute poisoning occur in the would each year, although only a small fraction are fatal. Most deaths are due to suicidal overdose by an adolescent or adult. Childhood deaths due to accidental ingestion of a drug or toxic household product
Even with a serious exposure, poisoning is rarely fatal if the victim receives prompt medical attention and good supportive care.

Attempting to the application of supportive measures that form the basis **("ABCDs")** of poisoning treatment.

Airway should be cleared of vomitus or any other obstruction and an oral airway or endotracheal tube inserted if needed.

Breathing. Patients with respiratory insufficiency should be intubated and mechanically ventilated.

Circulation continuous monitoring of pulse rate, blood pressure, urinary output, and evaluation of peripheral perfusion. An intravenous line should be placed and blood drawn for serum glucose and other routine determinations.At this point, every patient with altered mental status should receive a **Dextrose**, unless blood glucose test demonstrates that the patient is not hypoglycemic.

. HISTORY,

Family members, police, and fire department or paramedical personnel should be asked to describe the environment in which the toxic emergency occurred and should bring to the emergency department any syringes, empty bottles, household products, or over-the-counter medications in the possibly poisoned patient

. **PHYSICAL EXAMINATION**

1. Vital signs Careful evaluation of vital signs (blood pressure, pulse, respirations, and temperature)

2. Eyes Constriction of the pupils (miosis) is typical of opioids, cholinesterase inhibitors (eg, organophosphate insecticides),

. Dilation of the pupils (mydriasis) is common with amphetamines, cocaine and atropine and other anticholinergic drugs..

3. Mouth The mouth may show signs of burns due to corrosive substances,. Typical odors of alcohol, hydrocarbon solvents, or ammonia may be noted..

4. Skin The skin often appears flushed, hot, and dry in poisoning with atropine and other antimuscarinics. Excessive sweating occurs with organophosphates, nicotine.

5. Abdomen abdominal cramping, and diarrhea are common in poisoning with organophosphates, iron, arsenic, theophylline,.

6. Nervous system A careful neurologic examination is essential.

Decontamination

involves removing toxins from the skin or gastrointestinal tract.

SKIN Contaminated clothing should be completely removed and double-bagged to prevent illness in health care providers and for laboratory analysis. Wash contaminated skin with soap and water.

GASTROINTESTINAL TRACT

1. Emesis **2. Gastric lavage**

3. Activated charcoal." **4. Cathartics**

SPECIFIC ANTIDOTES

Specific antidotes reduce or abolish the effects of poisons through a variety of mechanisms, which may be categorised as follows:

• receptors, which may be activated, blocked or by passed

• enzymes, which may be inhibited or reactivated

• displacement from tissue binding sites

• exchanging with the poison

• replenishment of an essential substance

• binding to the poison (including chelating).

Methods of Enhancing Elimination of Toxins

it is important to consider whether measures for enhancing elimination, such as hemodialysis, Peritoneal dialysis or urinary alkalinization, forced diuretics can improve clinical outcome

TABLE 9.1 Some specific antidotes, indications and modes of action (see Index for a fuller account of individual drugs)

Antidote	Indication	Mode of action
acetylcysteine	paracetamol, chloroform, carbon tetrachloride	Replenishes depleted glutathione stores
atropine	cholinesterase inhibitors, e.g. organophosphorus insecticides	Blocks muscarinic cholinoceptors
	β-blocker poisoning	Vagal block accelerates heart rate
benzatropine	drug-induced movement disorders	Blocks muscarinic cholinoceptors
calcium gluconate	hydrofluoric acid, fluorides	Binds or precipitates fluoride ions
desferrioxamine	iron	Chelates ferrous ions
dicobalt edetate	cyanide and derivatives, e.g. acrylonitrile	Chelates to form nontoxic cobalti-and cobalto-cyanides
digoxin-specific antibody fragments (FAB)	digitalis glycosides	Binds free glycoside in plasma, complex excreted in urine
dimercaprol (BAL)	arsenic, copper, gold, lead, inorganic mercury	Chelates metal ions
ethanol	ethylene glycol, methanol	Competes for alcohol and acetaldehyde dehydrogenases, preventing formation of toxic metabolites
flumazenil	benzodiazepines	Competes for benzodiazepine receptors
folinic acid	folic acid antagonists e.g. methotrexate, trimethoprim	Bypasses block in folate metabolism
glucagon	β-adrenoceptor antagonists	Bypasses blockade of the β-adrenoceptor; stimulates cyclic AMP formation with positive cardiac inotropic effect
isoprenaline	β-adrenoceptor antagonists	Competes for β-adrenoceptors
methionine	paracetamol	Replenishes depleted glutathione stores
naloxone	opioids	Competes for opioid receptors
neostigmine	antimuscarinic drugs	Inhibits acetylcholinesterase, causing acetylcholine to accumulate at cholinoceptors
oxygen	carbon monoxide	Competitively displaces carbonmonoxide from binding sites on haemoglobin
penicillamine	copper, gold, lead, elemental mercury (vapour), zinc	Chelates metal ions
phenoxybenzamine	hypertension due to α-adrenoceptor agonists, e.g. with MAOI, clonidine, ergotamine	Competes for α-adrenoceptors (long-acting)
phentolamine	as above	Competes for α-adrenoceptors (short-acting)
phytomenadione (vitamine K_1)	coumarin (warfarin) and indandione anticoagulants	Replenishes vitamin K
pralidoxime	cholinesterase inhibitors, e.g. organophosphorus insecticides	Competitively reactivates cholinesterase
propranolol	β-adrenoceptor agonists, ephedrine, theophylline, thyroxine	Blocks β-adrenoceptors
protamine	heparin	Binds ionically to neutralise
Prussian blue (potassium ferric hexacyanoferrate)	thallium (in rodenticides)	Potassium exchanges for thallium
sodium calciumedetate	lead	Chelates lead ions
unithiol	lead, elemental and organic mercury	Chelates metal ions

Toxicokinetics

Is the quantitative study of uptake and movement of an chemical from site of entry into the body , through its uptake , distribution to organ and tissue by the blood circulation and its final disposition by way of biotransformation Sequestration and excretion

.

Uptake

Transport

Metabolism & transformation

Sequestration

Excretion

Uptake routes

Ingestion Respiration Body surface ◆

◆

Uptake Barriers

toxicant must cross one or several of barriers to produce toxic effect

Cell membrane –

Epithelial cells of GI tract –

Respiratory surface –

Body surface–

Uptake of Toxicants

Passive diffusion .1

Facilitated transport .2

Active transport .3

Pinocytosis .4

Uptake by Passive diffusion

molecules may diffuse along conc. gradient until equilibrium is reached . which depends on:

1-Concentration gradient

2-Surface area

3-Thickness

4-Lipid solubility & ionization

5-Molecular size

Uptake by Facilitated Transport

Carried by trans-membrane carrier along conc. Gradient .Energy ◆ independent . limited number of substance similar chemical structure , these substance can compete of the binding site and may be inhibit the binding of another ,. This called competitive inhibition which could be used to prevent uptake of toxicant .

Uptake by Active Transport

Independent of or against conc. Gradient .Require energy (ATP)◆

Substrate –specific◆

◆

Uptake by Pinocytosis

Pinocytosis: contribute to the transport of substance across the ◆

intestinal wall .For large molecules

Infolding of cell membrane Outside:◆

release of molecules Inside: ◆

Transport & Deposition

Transport Blood Lymph, Water ◆

Deposition_◆

Bone, teeth, brain Pb

Nervous tissue OP

Metabolism & Transformation

Convert toxicants into more water soluble form (more polar & – hydrophilic)Dissolve in aqueous phases and eliminate by excretion

Phase I Transformation

Oxidation, Reduction or Hydrolysis

Phase II transformation

-Covalent conjugation to water soluble endogenous metabloites (e.g. sugars, , glucuronic acid, glutathione, phosphates & sulphate) .Further increase hydrophilicity for excretion in bile, urine and sweat

Important Phase II enzymes

Glutathion S-transferases (GST)◆

UDP-glucuronosyltransferase (UDP-GTS) ◆

Sulfotransferase (ST).◆

Sequestration

Animals store toxicants (e.g. bone, fat, hair, nail) to reduce toxicity◆

Plants may store toxicants in bark, leaves, ◆

Lipophilic toxicants (e.g. DDT,) may be stored in milk at high conc ◆ and pass to the young

Excretion routes ◆

1- in urine depend on GFR , lipid soluble , pH◆

2- bile◆

3- expired air ◆

4-sweat ◆

5-milk (lipid soluble toxicant)◆

6-saliva ◆

7- GIT secretion ◆

8- genital secretion ◆

skin (arsenic and mercury) 9- by normal turnover of hair ◆

Excretion process

Gas (e.g. ammonia) and volatile (e.g. alcohol) toxicants may be ◆ excreted from the lung by simple diffusion

Water soluble toxicants excreted through the kidney by active or ◆ passive transport

Conjugates with high molecular wt. may be excreted into bile through ◆ active transport

Lipid soluble and non-ionised toxicants may be reabsorbed (systematic ◆ toxicity)

INTRODUCTION TO TOXICOLOGY TERMS CLASSIFICATION OF TOXIC MATERIALS

The meaning of the term ***toxicology*** is " the study of poisons." The root word toxic entered the English language around 1655 from the Late Latin word *toxicus* (which meant poisonous), itself derived from *toxikón*, an ancient Greek term for poisons into which arrows were dipped. The early history of toxicology focused on the understanding and uses of different poisons, and even today most people tend to think of poisons as a deadly potion that when ingested causes almost immediate harm
or death.

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MECHANISM OF TOXICOLOGY, PRINCIPLES OF TREATMENT OF POISINING TYPE OF ANTIDOTES

TOXICOKINETICS & TOXICODYNAMICS

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atropine	cholinesterase inhibitors, e.g. organophosphorus insecticides	Blocks muscarinic cholinoceptors
	β-blocker poisoning	Vagal block accelerates heart rate
benzatropine	drug-induced movement disorders	Blocks muscarinic cholinoceptors
calcium gluconate	hydrofluoric acid, fluorides	Binds or precipitates fluoride ions
desferrioxamine	iron	Chelates ferrous ions
dicobalt edetate	cyanide and derivatives, e.g. acrylonitrile	Chelates to form nontoxic cobalti-and cobalto-cyanides
digoxin-specific antibody fragments (FAB)	digitalis glycosides	Binds free glycoside in plasma, complex excreted in urine
dimercaprol (BAL)	arsenic, copper, gold, lead, inorganic mercury	Chelates metal ions
ethanol	ethylene glycol, methanol	Competes for alcohol and acetaldehyde dehydrogenases, preventing formation of toxic metabolites
flumazenil	benzodiazepines	Competes for benzodiazepine receptors
folinic acid	folic acid antagonists e.g. methotrexate, trimethoprim	Bypasses block in folate metabolism
glucagon	β-adrenoceptor antagonists	Bypasses blockade of the β-adrenoceptor; stimulates cyclic AMP formation with positive cardiac inotropic effect
isoprenaline	β-adrenoceptor antagonists	Competes for β-adrenoceptors
methionine	paracetamol	Replenishes depleted glutathione stores
naloxone	opioids	Competes for opioid receptors
neostigmine	antimuscarinic drugs	Inhibits acetylcholinesterase, causing acetylcholine to accumulate at cholinoceptors
oxygen	carbon monoxide	Competitively displaces carbonmonoxide from binding sites on haemoglobin
penicillamine	copper, gold, lead, elemental mercury (vapour), zinc	Chelates metal ions
phenoxybenzamine	hypertension due to α-adrenoceptor agonists, e.g. with MAOI, clonidine, ergotamine	Competes for α-adrenoceptors (long-acting)
phentolamine	as above	Competes for α-adrenoceptors (short-acting)
phytomenadione (vitamine K_1)	coumarin (warfarin) and indandione anticoagulants	Replenishes vitamin K
pralidoxime	cholinesterase inhibitors, e.g. organophosphorus insecticides	Competitively reactivates cholinesterase
propranolol	β-adrenoceptor agonists, ephedrine, theophylline, thyroxine	Blocks β-adrenoceptors
protamine	heparin	Binds ionically to neutralise
Prussian blue (potassium ferric hexacyanoferrate)	thallium (in rodenticides)	Potassium exchanges for thallium
sodium calciumedetate	lead	Chelates lead ions
unithiol	lead, elemental and organic mercury	Chelates metal ions

MECHANISM OF TOXICOLOGY, PRINCIPLES OF TREATMENT OF POISINING TYPE OF ANTIDOTES

Toxicokinetics

Is the quantitative study of uptake and movement of an chemical from site of entry into the body , through its uptake , distribution to organ and tissue by the blood circulation and its final disposition by way of biotransformation Sequestration and excretion

.

Uptake

Transport

Metabolism & transformation

Sequestration

Excretion

Uptake routes

- Ingestion Respiration Body surface

Uptake Barriers

toxicant must cross one or several of barriers to produce toxic effect

- Cell membrane
- Epithelial cells of GI tract
- Respiratory surface
- Body surface

Uptake of Toxicants

1. Passive diffusion
2. Facilitated transport
3. Active transport
4. Pinocytosis

Uptake by Passive diffusion

molecules may diffuse along conc. gradient until equilibrium is reached . which depends on:

1-Concentration gradient

2-Surface area

3-Thickness

4-Lipid solubility & ionization

5-Molecular size

Uptake by Facilitated Transport

- Carried by trans-membrane carrier along conc. Gradient .Energy independent . limited number of substance similar chemical structure , these substance can compete of the binding site and may be inhibit the binding of another ,. This called competitive inhibition which could be used to prevent uptake of toxicant .

Uptake by Active Transport

- Independent of or against conc. Gradient .Require energy (ATP)
- Substrate – specific

Uptake by Pinocytosis

- Pinocytosis: contribute to the transport of substance across the intestinal wall .For large molecules
- Outside: Infolding of cell membrane
- Inside: release of molecules

Transport & Deposition

- **Transport** Blood Lymph, Water

- **Deposition**

Pb	Bone, teeth, brain
OP	Nervous tissue

Metabolism & Transformation

–Convert toxicants into more water soluble form (more polar & hydrophilic)Dissolve in aqueous phases and eliminate by excretion

Phase I Transformation

Oxidation, Reduction or Hydrolysis

Phase II transformation

-Covalent conjugation to water soluble endogenous metabloites (e.g. sugars, , glucuronic acid, glutathione, phosphates & sulphate) .Further increase hydrophilicity for excretion in bile, urine and sweat

Important Phase II enzymes

- Glutathion S-transferases (GST)
- UDP-glucuronosyltransferase (UDP-GTS)
- Sulfotransferase (ST).

Sequestration

- Animals store toxicants (e.g. bone, fat, hair, nail) to reduce toxicity
- Plants may store toxicants in bark, leaves,
- Lipophilic toxicants (e.g. DDT,) may be stored in milk at high conc and pass to the young

Excretion

- 1- in urine depend on GFR , lipid soluble , pH
- 2- bile
- 3- expired air
- 4-sweat
- 5-milk (lipid soluble toxicant)
- 6-saliva
- 7- GIT secretion
- 8- genital secretion
- 9- by normal turnover of hair skin (arsenic and mercury)

Excretion

- Gas (e.g. ammonia) and volatile (e.g. alcohol) toxicants may be excreted from the lung by simple diffusion
- Water soluble toxicants excreted through the kidney by active or passive transport
- Conjugates with high molecular wt. may be excreted into bile through active transport
- Lipid soluble and non-ionised toxicants may be reabsorbed (systematic toxicity)

PHYSICAL EXAMINATION

1. Vital signs Careful evaluation of vital signs (blood pressure, pulse, respirations, and temperature)

2. Eyes Constriction of the pupils (miosis) is typical of opioids, cholinesterase inhibitors (eg, organophosphate insecticides),

. Dilation of the pupils (mydriasis) is common with amphetamines, cocaine and atropine and other anticholinergic drugs..

3. Mouth The mouth may show signs of burns due to corrosive substances,. Typical odors of alcohol, hydrocarbon solvents, or ammonia may be noted..

4. Skin The skin often appears flushed, hot, and dry in poisoning with atropine and other antimuscarinics. Excessive sweating occurs with organophosphates, nicotine.

5. Abdomen abdominal cramping, and diarrhea are common in poisoning with organophosphates, iron, arsenic, theophylline,.

6. Nervous system A careful neurologic examination is essential.

Antidotes

مطلوب حفظ الجدول

SOLVENTS

1. Halogenated Aliphatic Hydrocarbons

The substances include carbon tetrachloride, chloroform, trichloroethylene, tetrachloroethylene.

These substances are depressants of the CNS in humans,. Chronic exposure to tetrachloroethylene can cause impaired memory and peripheral neuropathy.. Hepatotoxicity ,Nephrotoxicity also a common toxic effect .

Treatment

There is no specific treatment for acute intoxication. Management depends on the organ system involved.

2. Aromatic Hydrocarbons

Benzene is widely used for its solvent properties and as an intermediate in the synthesis of other chemicals..

The acute toxic effect of benzene is depression of the central nervous system. Exposure to 7500 ppm for 30 minutes can be fatal. euphoria, nausea, , and coma; vertigo, drowsiness, headache, and nausea may occur at concentrations ranging from 250 to 500 ppm. No specific treatment exists for the acute toxic effect of benzene

INSECTICIDES

1. Organochlorine Insecticides

These agents are usually classified in four groups:

DDT (chlorophenothane) and its analogs,

Benzene hexachlorides,

Cyclodienes,

Toxaphenes

. The major effect is central nervous system stimulation. There is no specific treatment for the acute intoxicated state, management being symptomatic.

2. Organophosphorus Insecticides

These agents, are utilized to large variety of pests.. Some of these agents are used in human and veterinary medicine as local or systemic antiparasitics, or to reduced IOP .

Anticholinesterase poisoning

The anticholinesterases used in therapeutics are Reversibly inactivate cholinesterase only for a few hours. Poisoning with reversible anticholinesterases is appropriately treated by atropine and the necessary general support; it lasts only hours. In poisoning with irreversible agents the organophosphate insecticide irreversibly inactivate cholinesterase which used in agricultural, industrial, also used in war called nerve 'gas'

Features of acute poisoning

involve the gastrointestinal tract (salivation, vomiting, abdominal cramps, diarrhea, involuntary defecation), the respiratory system (bronchorrhoea, bronchoconstriction, cough, wheezing, dyspnoea), the cardiovascular system (bradycardia), the genitourinary system (involuntary micturition). Death is due to a respiratory failure

Treatment.

contaminated clothing should be removed and the skin washed. Gastric lavage is needed if any of the substance has been ingested. Atropine; 2 mg is given i.m. or i.v. as soon as possible and repeated every 15-60 min. Enzyme reactivation pralidoxime, 1 g of which should be given 4-hourly i.m. or (diluted) by slow i.v infusion.

3. Carbamate Insecticides

4. Botanical Insecticides

Insecticides derived from natural sources include nicotine, rotenone, and pyrethrum.

HERBICIDES

1. Chlorophenoxy Herbicides 2. Bipyridyl Herbicides

Heavy Metal Intoxication and Chelators

Some metals such as iron are essential for life, while others such as lead are present in all organisms but serve no useful biologic purpose.When intoxication occurs, chelator molecules may be used to bind the metal and facilitate its excretion from the body.

LEAD

widespread commercial application, including production of storage batteries, glass, plastics and ceramics. Environmental lead exposure, declined considerably in the past 3 decades as a result of diminished use of lead in gasoline and other applications.

Toxicodynamics:

Lead exerts multisystemic toxic effects that are mediated by multiple modes of action, including **inhibition of enzymatic function**; **interference with the action of essential cations**, particularly calcium, iron, and zinc; **disturbance of cellular redox status**; and alteration of the structure of cell membranes and **receptors**.

A. NERVOUS SYSTEM

fatigue, decreased libido, anorexia, sleep disturbance,. Headache, arthralgias, and myalgias are also frequent complaints. europathy may present with painless weakness of the extensors, resulting in classic **wrist-drop**.

B. BLOOD: interferes with heme synthesiscan induce an anemia .

C. KIDNEYS:renal interstitial fibrosis and nephrosclerosis.. may alter uric acid excretion by the kidney, resulting gouty arthritis .

D. REPRODUCTIVE ORGANS :stillbirth or spontaneous abortion.

E. GIT :loss of appetite, constipation, and, less commonly, diarrhea. At high dosage, colicky abdominal pain ("**lead colic**") may occur.

F. CARDIOVASCULAR SYSTEM

lead exposure elevates blood pressure in susceptible individuals.

Treatment of Major Forms of Lead Intoxication

A. INORGANIC LEAD POISONING)

Treatment of inorganic lead poisoning involves immediate termination of exposure, supportive care, and the use of chelation.

B. ORGANIC LEAD POISONING

Initial treatment consists of decontaminating the skin and preventing further exposure. Treatment of seizures requires appropriate use of anticonvulsants. Empiric chelation may be attempted if high blood lead concentrations are present.

ARSENIC

Use in the manufacture of semiconductors, , glass, and. Arsenic trioxide was reintroduced into the United States Pharmacopeia in 2000 as an orphan drug for the treatment of **relapsed acute promyelocytic leukemia** and is finding expanded use in experimental cancer treatment protocols

Melarsoprol, another trivalent arsenical, is used in the treatment of **advanced African trypanosomiasis**

Arsenic compounds are thought to exert their toxic effects by **Interference with enzymatic function** ,may induce **oxidative stress**, **alter gene expression**, and **interfere with cell signal transduction** , it also **disrupts cellular respiration in other tissues**.

Treatment of major Forms of Arsenic Intoxication

A. ACUTE INORGANIC ARSENIC POISONING

based on appropriate gut decontamination, intensive supportive care, and prompt chelation with unithiol, or dimercaprol,.

B. CHRONIC INORGANIC ARSENIC POISONING

C. ARSINE GAS POISONING

. Intensive supportive care,including exchange transfusion, vigorous hydration, and, in the case of acute renal failure, hemodialysis,is the mainstay of therapy. Currently available chelating agents have not been demonstrated to be of clinical value in arsine poisoning.

MERCURY

Metallic mercury the only metal that is liquid under ordinary conditions. industrial and commercial applications found in the electrolytic production of chlorine and caustic soda; the manufacture of electrical equipment, **thermometers**, fluorescent lamps; **dental amalgam**; and gold production. Use in pharmaceuticals and in biocides has declined, but occasional use in **antiseptics** is still encountered..

Mercury **interacts with sulfhydryl groups in vivo**, **inhibiting enzymes and altering cell membranes.**.

Treatment

A. ACUTE EXPOSURE

In addition to intensive supportive care, prompt chelation with oral or intravenous unithiol, intramuscular dimercaprol, or oral succimer may be of value in diminishing nephrotoxicity after acute exposure to inorganic mercury salts.

B. CHRONIC EXPOSURE

. Dimercaprol has been shown to redistribute mercury to the central nervous system from other tissue sites, and since the brain is a key target organ, dimercaprol should not be used in treatment of exposure to elemental or organic mercury. Limited data suggest that succimer, unithiol, and N-acetyl-L-cysteine (NAC) may enhance body clearance of methylmercury.

PHARMACOLOGY OF CHELATORS

Chelating agents are drugs used to prevent or reverse the toxic effects of a heavy metal on an enzyme or other cellular target, to accelerate the elimination of the metal from the body.

SUCCIMER	**DIMERCAPROL**
EDETATE CALCIUM DISODIUM	**DEFEROXAMINE**
PENICILLAMINE	**UNITHIOL**

Toxic Potential of Over-the-Counter Agents

Drugs are divided by law into two classes: those restricted to sale by prescription only and those for directions for safe use by the public (nonprescription) or over-the-counter (OTC) drugs,

There are over 100 different products, The selection of one ingredient over another may be important in patients with certain medical conditions or in patients taking other medications.
The recommendations listed in are based on the efficacy of the ingredients

(1) Select the product that is simplest in formulation In general, single-ingredient products are preferred. Although some combination products contain effective doses of all ingredients,. Acetaminophen, for example, is in many cough and cold preparations; a patient unaware of this may take separate doses of analgesic in addition to that contained in the cold preparation, potentially leading to toxicity.

(2) Select a product contains a therapeutically effective dose.

(3) Carefully read the product labeling to determine which ingredients are appropriate based on the patient's symptoms and underlying health conditions.

(4) For children, the dose, dosage form, and palatability of the product are prime considerations.

. Although OTC medications have standardized indications for use, dosage, warnings, and active and inactive ingredients contained in the product, many consumers do not carefully read this information. Lack of awareness of the ingredients in OTC products and the belief by many physicians that OTC products are ineffective and harmless may cause diagnostic confusion and perhaps toxicity .

Overuse or misuse of OTC products may induce significant medical problems.
Rebound congestion from the regular use of decongestant nasal sprays for more than 3 days.
The long-term use of some antacids (eg, aluminum hydroxide) may cause constipation and even impaction in elderly
Laxative abuse can result in abdominal cramping and fluid and electrolyte disturbances.
Insomnia, nervousness, and restlessness can result from the use of sympathomimetics or caffeine hidden in many OTC products

Antihistamines may cause sedation or drowsiness, especially when taken concurrently with sedative-hypnotics, tranquilizers, alcohol, or other central nervous system depressants.

For example, OTC products, including allergy, cough, and cold preparations, contain sympathomimetics. These agents should be avoided or used cautiously by type 1 diabetics and patients with hypertension, angina, or hyperthyroidism.

Aspirin and other NSAIDs should be avoided by individuals with active peptic ulcer disease, certain platelet disorders, and patients taking oral anticoagulants.
OTC products containing aspirin, , acetaminophen, ibuprofen, naproxen, or ketoprofen may increase the risk of hepatotoxicity and gastrointestinal hemorrhage in individuals who alcoholic drinks daily
Recent evidence suggests the long-term use of NSAIDs may increase the risk of heart attack or stroke. Furthermore, acute ingestion of large amounts of acetaminophen by adults or children can cause serious, and often fatal, hepatotoxicity.

ASPIRIN (SALICYLATE)

Salicylate poisoning is a much less common cause of childhood poisoning deaths since the introduction of child-resistant containers and the reduced use of children's aspirin. It still accounts for numerous suicidal and accidental poisonings. Acute ingestion of more than 200 mg/kg is likely to produce intoxication. Poisoning can also result from chronic over medication; this occurs most commonly in elderly patients using salicylates for chronic pain who become confused about their dosing.

The first sign of salicylate toxicity is often hyperventilation . Body temperature may be elevated due to uncoupling of oxidative phosphorylation. Severe hyperthermia may occur in serious cases. Vomiting and hyperpnea as well as hyperthermia contribute to fluid loss and dehydration. Tinnitus (Salicylism) & hearing loss. The hearing loss resolves 2-3 days after withdrawal of the drug. With very severe poisoning seizures, coma, pulmonary edema, and cardiovascular collapse may occur.

Absorption of salicylate and signs of toxicity may be delayed after very large overdoses or ingestion of enteric-coated tablets.

Treatment

General supportive care as described earlier is essential. After massive aspirin ingestions (more than 100 tablets), aggressive gut decontamination is advisable, including gastric lavage, repeated doses of activated charcoal ,consideration of whole bowel irrigation. Intravenous fluids are used to replace fluid losses caused by tachypnea, vomiting, and fever.

For moderate intoxications, intravenous sodium bicarbonate is given to alkalinize the urine and promote salicylate excretion

For severe poisoning emergency hemodialysis is performed to remove the salicylate more quickly and restore acid-base balance and fluid status.

ACETAMINOPHEN

Acetaminophen is one of the drugs most commonly involved in suicide attempts and accidental poisonings, both as agent and in combination with other drugs. Acute ingestion of more than 150-200 mg/kg (children) or 7 gram total (adults) is considered potentially toxic. In severe cases hepatic encephalopathy. Renal failure and death may also occur.

Signs and Symptoms of Overdose

The acute symptomatic presentation of acetaminophen toxicity can be divided into 3 phases:

Phase I (up to 1 day): Gastrointestinal irritability predominates with nausea, vomiting, and sweating.. Cardiac effects (arrhythmias, bradycardia) may develop.

Phase II (1-3 days): Hepatic toxicity develops with elevation of hepatic enzymes, prothrombin time, and bilirubin. Amylase elevation..

Phase III (3-5 days): Hepatic necrosis continues with disseminated intravascular coagulation, hepatic encephalopathy, and portal hypertension, The patient is at risk for hypoglycemia. Renal insufficiency may also be present.

The severity of poisoning estimated from a serum acetaminophen concentration measurement. If the level is greater than 150-200 mg/L approximately 4 hours after ingestion, the patient is at risk for liver injury.

Treatment

The antidote acetylcysteine acts as a glutathione substitute, binding the toxic metabolite as it is being produced. It is most effective when given early and should be started within 8-10 hours if possible.

A liver transplant may be required for patients with sever hepatic failure.

Barbiturates

Barbiturate abuse is a major addiction problem for many people. overdose occurs when someone accidentally or intentionally takes more than the normal or recommended amount of this medication. This is life threatening..

Symptoms

- Difficulty in thinking
- Drowsiness
- Incoordination
- Shallow breathing
- Slowness of speech
- Slurred speech
- Changes in alertness
- Decreased functioning
- Irritability
- Memory loss
- Altered level of consciousness
- Coma
- Death

Treatment

About 1 in 10 people who have a barbiturate overdose or mixture overdose will die. They usually die from heart and lung problems

There is no direct antidote for this type of overdose Supportive measures with i.v. fluid to restore central venous pressure and so cardiac output and, if that fails, using a drug with cardiac inotropic effect A good urine volume (e.g. 200 ml/h) promotes elimination of the drug. Urine alkalinisation accelerates removal of phenobarbital as do repeated doses of activated charcoal. Active elimination by hemoperfusion or hemodialysis may be needed in particularly

Benzodiazepine

Benzodiazepine have a wide therapeutic index and in over dose rarely cause severe complications or fatalities .

Patients initially present with Gastrointestinal symptoms such as nausea and vomiting also mild to moderate impairment of CNS function. include impaired balance, impaired motor function, and slurred speech, ataxia ,amnesia

Severe overdose symptoms include hypothermia, hypotension, bradycardia, prolonged deep coma, Hypoxia and, cardiac arrest with the possibility of death due to respiratory depression.

Treatment

Medical observation and supportive care are the mainstay of treatment of benzodiazepine overdose include observation of vital signs and airway patency. IV fluid replacement to correct Hypotension. intubation and artificial ventilation may be required if respiratory depression or pulmonary aspiration occurs.

Flumazenil is a competitive benzodiazepine antagonist that can be used as an antidote for benzodiazepine overdose .very effective at reversing the CNS depression associated with benzodiazepines but is less effective at reversing respiratory depression

ANTIDEPRESSANTS

Tricyclic antidepressants

are among the most common prescription drugs involved in life-threatening drug overdose. Ingestion of more than 500 mg of a tricyclic (or about 10 mg/kg) is considered potentially lethal.

Tricyclic antidepressants are competitive antagonists at muscarinic cholinergic receptors, and anticholinergic findings (tachycardia, dilated pupils, dry mouth) are common even at moderate doses.. Centrally mediated agitation and seizures may be followed by depression and hypotension. Most importantly effects that cause slowed conduction and depressed cardiac contractility. serious arrhythmias including ventricular conduction block and ventricular tachycardia.

Treatment of tricyclic antidepressant overdose

General supportive care. Endotracheal intubation and assisted ventilation may be needed. Intravenous fluids are given for hypotension, and dopamine or norepinephrine is added if necessary. Many toxicologists recommend norepinephrine as the initial drug of choice for tricyclic-induced hypotension. The antidote for cardiac toxicity is sodium bicarbonate:

Monoamine oxidase inhibitors. They can cause severe hypertensive reactions when interacting foods or drugs are taken; and they can interact with the selective serotonin reuptake inhibitors (SSRIs).

Newer antidepressants SSRIs are generally safer than the tricyclic antidepressants and monoamine oxidase inhibitors, although they can cause seizures. Some antidepressants have been associated with arrhythmia. The SSRIs may interact with each other or especially with monoamine oxidase inhibitors to cause the **serotonin syndrome**, characterized by agitation, muscle hyperactivity, and hyperthermia

ETHANOL

Over dosage with ethanol occurs frequently because of common availability and drink .individual with ethanol overdose may be euphoric in a state of stupor or coma. Comatose patients often have depressed respiratory drive. Depression of protective airway reflexes may result in aspiration of gastric contents. Hypothermia may be present because of environmental exposure and depressed shivering. Ethanol blood levels greater than 300 mg/dL usually cause deep coma, but regular users are often tolerant to the effects of even higher levels.

General supportive care should be provided. With careful attention to protecting the airway (including endotracheal intubation) and assisting ventilation, most patients will recover as the effects wear off. Hypotension usually responds to body warming if cold, intravenous fluids and, if needed, dopamine.

ETHYLENE GLYCOL & METHANOL

. They are causing CNS depression similar to ethanol overdose. However, their products of metabolism formic acid (from methanol) or oxalic, and glycolic acids (from ethylene glycol) cause a blindness (in the case of formic acid) or renal failure (from oxalic acid and glycolic acid). Initially, the patient accompanied by hyperventilation and altered mental status. Patients with methanol poisoning may have visual disturbances ranging from blurred vision to blindness.

Metabolism of ethylene glycol and methanol to their toxic products can be blocked by inhibiting the enzyme alcohol dehydrogenase with a competing drug. Ethanol is metabolized by alcohol dehydrogenase, so ethanol can be given orally or intravenously (5% pharmaceutical grade) to a level of approximately 100 mg/dL. Alternatively, the antidote Fomepizole an effective blocker of alcohol dehydrogenase that does not induce ethanol intoxicationcan be used.

ANTICHOLINERGIC AGENTS

A large number of prescription and nonprescription drugs, as well as a variety of plants can inhibit the effects of acetylcholine. Many drugs used for other purposes (eg, antihistamines) also have anticholinergic effects. such as Diphenhydramine . Tricyclic antidepressants, which have anticholinergic, effects, can cause severe cardiovascular toxicity.

The classic anticholinergic syndrome is remembered as

"Red as a beet" (skin flushed), "Hot as a hare" (hyperthermia), "Dry as a bone" (dry mucous membranes, no sweating), "Blind as a bat" (blurred vision, cycloplegia), and "Mad as a hatter" (confusion, delirium).

Pupils are usually dilated. Agitated delirium or coma may be present. Muscle twitching is common, but seizures are unusual unless the patient has ingested an antihistamine or a tricyclic antidepressant. Urinary retention is common, especially in older men.

Treatment is largely supportive. Agitated patients may require sedation with a benzodiazepine The specific antidote for peripheral and central anticholinergic syndrome **Neostigmine, physostigmine,** which has a dramatic effect and is especially useful for patients who are very agitated. It is given in small intravenous doses (0.5-1 mg), with careful monitoring, because it can cause bradycardia and seizures if given too rapidly. **Neostigmine, physostigmine,** should not be given to a patient with suspected tricyclic antidepressant overdose because it can aggravate cardiotoxicity, resulting in heart block or asystole. Catheterization may be needed to prevent excessive distention of the bladder

Cyanide poisoning

occurs when a living organism is exposed to a compound that produces cyanide ions (CN^-) when dissolved in water.

Acute poisoning

Cyanide poisoning is a form of hypoxia , primarily through the **inhibition cellular respiration**

Inhaled cyanide it causes a coma with seizures ,apnea , and cardiac arrest, with death following in a matter of minutes. At lower doses, ,general weakness, , headaches ,vertigo , confusion, and perceived difficulty in breathing loss of consciousness. At the first stages of unconsciousness, breathing is often sufficient or even rapid, although the state of the victim progresses towards a deep coma, sometimes accompanied by pulmonary edema and finally cardiac arrest. A fatal dose for humans can be as low as 1.5 mg/kg body weight.

Chronic exposure

In addition to insecticide, cyanide is contained in tobacco smoke, smoke from building fires and some foods, Exposure to lower levels of cyanide over a long period results in increased blood cyanide levels, which can result in weakness and a variety of symptoms, including permanent paralysis nervous lesions, hypothyroidism, and Other effects include mild liver and kidney damage.

Treatment of poisoning and antidotes

Treatment is largely supportive. The antidote first uses a small inhaled dose of **Amyl nitrate** followed by **intravenous sodium nitrate** followed by intravenous **sodium thiosulfate**, , , detoxifies cyanide and converts the cyanide into thiocyanate; a less toxic substance. vitamin B12 in the form of **hydroxycobalamin**, , may reduce the negative effects of chronic exposure.

Carbon monoxide poisoning

Carbon monoxide is a toxic gas, colorless, odorless, tasteless, and initially non-irritating, it is very difficult for people to detect. Carbon monoxide is a product of incomplete combustion of organic matter due to insufficient oxygen supply to enable complete oxidation to carbon dioxide (CO_2). It is often produced in by older motor vehicles and other gasoline-powered tools, heaters, and cooking equipment.

Carbon monoxide poisoning is the most common type of fatal poisoning in many countries. it was also commonly used as a method to suicide usually by inhaling the exhaust fumes of a running car engine. Modern automobiles, even with electronically-controlled combustion, can still produce levels of carbon monoxide which will kill if enclosed within a garage. Exposures at 100 PPM or greater can be dangerous to human health

Signs and symptoms

CO mainly causes combining with hemoglobin to form carboxy hemoglobin (HbCO) in the blood. This reducing the oxygen-carrying capacity of the blood, leading to hypoxia .
The main manifestations of carbon monoxide poisoning develop in the CNS and the heart include headache ,nausea , malaise , and fatigue These symptoms are often mistaken for a influenza or other illnesses such as food poisoning or gastroenteritis Increasing exposure produces cardiac abnormalities including fast heart rate, low blood pressure , and arrhythmia ,CNS symptoms include delirium ,hallucinations dizziness, unsteady gait , confusion, seizures, unconsciousness asphyxia,respiratory arrest and finally death

Treatment of poisoning

Treatment is supportive, consists of administering 100% oxygen. Oxygen works as an antidote as it increases the removal of carbon monoxide from hemoglobin, in turn providing the body with normal levels of oxygen.

Carbon Dioxide Poisoning

Individual are exposed to carbon dioxide every day in the air breathe and in household products, .At ordinary levels, carbon dioxide or CO2 is non toxic it's a normal component of air. When you use baking soda or baking powder, you are purposely introducing carbon dioxide bubbles into your food to make it rise. Carbon dioxide is as safe a chemical as any you'll ever encounter.

.

It is possible to suffer anoxia or asphyxiation from breathing carbon dioxide, because increased levels of carbon dioxide may be related to decreased concentration of oxygen, which you need in order to live.

.

Carbon Dioxide Poisoning Treatment

Treatment of carbon dioxide intoxication involves getting carbon dioxide levels back to normal in the patient's bloodstream and tissues. A person suffering from carbon dioxide intoxication typically can recover simply by breathing normal air. administering of oxygen

Nicotine Poisoning

There are more than 4,000 chemicals in tobacco smoke Nicotine is the addictive drug that keeps you coming back for more.
Some of the other chemicals found in cigarettes

•Tar Carbon monoxide
• ammonia (household cleaning agent)
• acetone (nail polish remover)
• naphthalene (mothballs)
• methanol (rocket fuel)
• formaldehyde (which preserves the dead)
• phenol (disinfectant)
• hydrogen cyanide
• metals (76 metals including arsenic, cadmium, nickel)
• radioactive compounds (polonium-210)
• acetic acid (vinegar)
• toluene (industrial solvent)

From the moment that inhale tobacco smoke, it takes four seconds for the nicotine to reach blood stream and about ten seconds to reach the brain. Once the nicotine has attached itself to special sites in the brain, many relaxing chemicals are released. But this effect only lasts for a short time and then the addicted smoker needs to ‘top up’ their nicotine. One of the reasons people continue to smoke is because they enjoy the effect of these relaxing chemicals being released by the brain.

The worst problem for tobacco smoke on health caused is that it is so addictive. include increased heart rate and blood pressure and constriction of blood
vessels. Over time, ingestion of nicotine damage the lining of blood vessels and make blood platelets stickier. In combination these effects contribute to the development of heart disease.

Before developing a tolerance to nicotine, the smoker may experience mild effects of nicotine toxicity..

The average dose of nicotine from Nicotine Replacement Therapy (NRT is about one third to one half of that obtained from smoking. A person who is dependent on nicotine is extremely unlikely to experience any toxic effect from using NRT.

Most of the nicotine (80 per cent) is broken down in the liver. Nicotine is also filtered from the blood by the kidneys and removed in urine.

The nicotine in NRT) products, such as the patch, gum, lozenge, sublingual tablet or inhaler is safe if used according to the product directions