Forensic toxicology

General notions about intoxications

Clinical toxicology is the science that studies the identification, isolation, quantitative evaluation and the effects of toxic substances on the human body.

Intoxications are specific pathological states that onset as a result of the action of various substances that reach inside the human body by different ways and induce functional and organic changes.

Intoxications can often be the result of administrating large quantities of a substance that is frequently used in small doses, but induces toxic manifestations in high concentrations. The limit between the therapeutic and the toxic doses can be very fine for some substances.

Other substances are used as “poisons” because they are noxious in small or very small doses. Plutonium is probably the most toxic substance, but the castor-oil toxin is also an extremely powerful toxic.

Accidental intoxications are the most frequent. The situations can vary from a child that ingests various drugs instead of sweets, to veritable industrial mass disasters, with thousands of victims. Manny accidental intoxications occur in agriculture (paraquat, organophosphorus substances etc.). The history of toxicology offers many examples of such tragedies, such as leakages from contaminated wheat sacks, accidental ingestion of ethylene glycol mistook for comestible beverages, carbon monoxide intoxications due to defective heating devices that can even lead to the death of entire families, mainly during their sleep.

Suicide by intoxication is one of the most common self-destructive methods, especially in societies with high living standards, where various drugs with potentially lethal effect in high doses, are easy to obtain.

In Great Britain, for example, the preference for Paracetamol has lately exceeded barbiturics and aspirin (Knight). In Asia, the most frequently chosen are various substances used in agriculture (paraquat, parathion) or in the rubber industry (acetic acid). The use of corrosive agents decreased significantly in the last half-century, probably because less painful methods (substances) are now available.

Homicidal intoxications are less frequent then in the last century. It is still practiced in less developed societies, where all types of inorganic and vegetal toxins are used. Most toxic substances can easily be detected in the body of the victim with modern techniques; this is probably why they are only rarely used as homicidal means.

. Toxic substance, toxicity, dose

There is a wrong opinion according to which for each drug or toxic substance, there is a certain fix, small dose that determines certain symptoms and consequences, and a bigger, lethal dose. This simplistic image is incomplete, because different individuals present different sensitivity or resistance to certain substances; even in the same person, these effects can differ in time.

- The *toxic substance* is a substance that, introduced in the body in small quantities, induces functional alterations or lesions that determine a pathological state called intoxication (Banciu).
- *Toxicity* is the response reaction of the organism at the action of a toxic substance. It is in direct relation with factors like:

1. The properties of the toxic substance

- the dispersion degree: the higher the dispersion degree, the higher the toxicity;
- volatility: a higher volatility increases the risk of intoxication; the respiratory absorption is in direct relation with volatility;
- solubility: the toxicity of water-soluble substances depends on their solubility in water. Fat-soluble substances are easily absorbed through the skin.

2. The dose

The dose is the most important determinant for the toxicity of a substance; it represents the quantity of exogenous toxic substance that, introduced in the organism, determines a certain visible effect. Hodge and Gleason classified toxicity according to the doses as follows:

Toxicity degree	Dose
6 = super-toxic	5 mg/kg
5 = extremely toxic	5-50 mg/kg
4 = very toxic	50-500 mg/kg
3 = moderately toxic	0,5-5 g/kg
2 = mildly toxic	5-15 g/kg
1 = practically non-toxic	15 g/kg

Toxicity scale; the lethal oral dose in humans

The toxicity of a substance after oral or parenteral administration is determined through experimental studies on animals; the main purpose is to establish the lethal dose (LD):

- *the 0 lethal dose (LD-0)* is the quantity of substance that induces severe toxic phenomena but is not lethal;
- *the lethal dose (LD)* is the smallest quantity of substance that provokes death in an adult;
- *the 50 lethal dose (LD-50)* is the quantity of toxic substance that determines the death of 50% of the animals in the study group within 24 hours;
- *the minimum lethal dose (MLD)* is the smallest quantity of toxic substance that determines the death of a healthy adult;
- *the child minimum lethal dose (CMLD)* is calculated according to the Young formula (Age = years):

$$CMLD = Age / Age + 12$$

- LD-50 represents the dose that is expected to kill over one half of the tested animals. Still, some animals can survive, with no apparent problems, even at doses higher then LD-50, while others die after much smaller doses. So this concept cannot always be used for the prediction of the toxic effects in humans or in a single experimental animal, because the vulnerability to toxic substances varies within large limits.

So, it is difficult to establish the lethal dose of a substance. Still after studies on thousands of animals, the limits within which most severe toxic effects and deaths occur can be established. Many of these data come from studies on autopsy sampling; the validity of these results has been questioned, because it has been proven that, unlike in live humans, the distribution of toxic substances in cadavers is uneven, due to the circulatory arrest.

The concentration, the administration way and the speed

- The concentration of a toxic substance plays a very important role in the determining its toxicity.
- In every activity domain in which the use of toxic substances is involved, there are maximal admitted concentrations (MAC) for each toxic substance. MAC represents the average concentration in the air that does not determine any symptoms or changes that can be determined with the most sensitive tests (except hyper-sensitivity).
- The toxicity is higher if the substance is administered orally or respiratory, and usually smaller for the digestive way. In some cases the toxicity is annulled by the digestive passage (snake venom, curare, heparin). The presence of lipids in the digestive tract can enhance the toxicity (the absorption speed) of fat-soluble toxic substances.

Age and gender

The toxicity of some substances (e.g. barbiturics) is higher in children then in adults, because in children the brain and spinal cord are proportionally more developed then the rest of the body. Women are less resistant to the effects of toxic substances then men, especially during pregnancy, breast-feeding and menstruation. Adverse reactions at various drugs are more frequent in women, probably due to a weaker metabolism for toxic substances.

The body weight

Toxicity is not in direct relation with the body weight or the dimensions of the body. MLD is not proportional with the body weight because the surface/volume report is correlated with the metabolism and the elimination of the toxic substance: the smaller the volume of the body, the larger the body surface in comparison with the body weight and thus the more increased the metabolism.

Habit and reactivity

- One of the main problems raised by the toxic and lethal doses is that not only different subjects have different susceptibilities, but the substance itself can determine a certain degree of tolerance, so the administration of larger doses will not produce the same effect as initially (e.g. painkillers, especially opiates are needed in increasing doses for the same therapeutic effect).
- So, in the evaluation of toxicological result, tolerance has to be taken in consideration, because it can determine normal, clinical effects at high doses (e.g. amphetamines, barbiturics, benzodiazepines, the morphine-heroin-methadone group)
- Drugs that create dependence (heroin) can be lethal at the first administration; the victim can be found dead with the needle still in the arm, while another person that uses daily a dose even 10 times higher can survive with no immediate negative effects.
- Likewise, some persons can survive the ingestion of as much as 200 aspirin tablets, with no apparent negative effect, while others can die after 2 tablets, due to idiosyncrasy or hyper-sensitivity.
- Other drugs like penicillin, cocaine and heroin can also determine idiosyncrasy – a particular response to certain substances administered in small or very small doses, determined by individual susceptibility and various constitutional particularities.
- Other particular reactions are:
    - the allergy or specific sensitivity appears if the organism had a previous contact with the substance for which it developed antibodies;
    - anaphylaxis is an inverse exaggerated reaction to foreign proteins, after a previous contact;
    - the anaphylactic shock is the fastest and most dangerous allergic reaction, frequently leading to collapse and death.

The interaction of toxic substances

- The interaction of more or less toxic substances can manifest as synergism or antagonism.
- Synergism can manifest as addition, summation or potentiation of the effects of the interacting substances. Some synergic substances are: dichloretan and carbon tetrachloride, scopolamine and morphine, adrenalin and nor-adrenalin. Antagonism is represented by the contrary action of two substances. The antagonistic substances diminish, annul or reverse each other’s effects.

The classification of toxic substances

- The large extremely large number of toxic or potentially toxic substances and the variety of their effects renders their classification difficult. Scripcaru proposes the following criteria:

a. *origin:* mineral, vegetal and animal toxic substances

b. *physical and analytical characteristics*: gas, volatile, fix substances;

c. *source*: organic and inorganic substances;

d. *biological criteria*: haematic, nervous, neuro-muscular, muscular, corrosive;

e. *pharmaco-dynamic criteria*:

- simpatico-mimetic (adrenalin, ephedrine)
- parasimpatico-mimetic (muscarine, pilocarpine)
- simpatico-lithic (ergotamine)
- parasimpatico-lithic (atropine, scopolamine)

f. *source*: domestic, industrial, agricultural, alimentary;

g. *morpho-pathology*:

- substances that produce specific lesions at the entrance gate;
- substances that produce major post-resorption lesions or lesions at the elimination gate;
- substances that produce minor, insignificant alterations

h. *juridical criteria*:

- executions (death sentences by lethal injection)
- suicides
- accidents
- criminal intoxications

The entrance gates of toxic substances in the body

The digestive gate

Most liquid and solid toxic substances enter the body through the digestive gate. They can be absorbed at any level of the digestive tract, mostly in the small intestine.

The bucal mucous membrane can absorb any water-soluble substance in the superior cava system. The contact period with the bucal mucous membrane is short, so the absorbed quantity will be small. The bucal absorption of hyper-toxic substances (cyanide) can ensure lethal concentrations. Ethylic alcohol can easily be absorbed through the bucal membrane.

The absorption through the oesophagian mucous membrane is reduced, practically negligible, because the oesophagian passage is rapid so the contact with the mucous membrane is short. Caustic substances are not absorbed in the oesophagus but can produce specific, often severe, local lesions.

Water-soluble toxic substances or substances that determine prolonged pyloric spasm are easily absorbed through the gastric mucous membrane. The gastric absorption is limited by the structure of the mucous membrane, not adapted for absorption and with high cholesterol content. Some toxic substances can irritate the gastric membrane and provoke vomiting, with consequent elimination of a part of the ingested toxic substance.

The preferential absorption organ is the small intestine; its mucous membrane presents finger-like villi – “the absorption organ”. Most ingested toxic substances (except the corrosive ones) are absorbed here.

The absorption through the colon and rectum is generally much more reduced then in the small intestine.

The respiratory gate

Toxic gases are absorbed through the alveolo-capillary membrane, due to mechanisms similar to haematosis. Some liquids with high vapour tension (organic solvents) can also be absorbed this way, as can fine liquid or solid particles (1-10 mμ) in stabile suspension in the air. Chemically active gases and vapours (acids, bases, and irritant gases) act mainly on the pulmonary structures, so their absorption in the blood stream is reduced.

The entrance gates of toxic substances in the body

The trans-cutaneous gate

The skin is an important gate for some toxic substances. Water-soluble toxic substances penetrate in small quantities, because of the lipid, sebaceous layer. Fat-soluble substances penetrate much easier because they dissolve in the lipid layer. The penetration of some substances through the skin can be enhanced by using ointments or creams. The skin humidity and temperature, the contact with contaminated clothing and the presence of skin discontinuities (abrasions, wounds) influence the trans-cutaneous passage.

The parenteral gate

Toxic substances can be injected in the body (subcutaneous, intramuscular, intravenous). The incidence of this type of intoxications is low.

The trans-placental gate

Various toxic substances can be carried in the maternal blood, across the placental barrier, from the mother to the foetus. The most frequent situation is the passage of ethylic alcohol. Repeated alcohol consumption while breast-feeding leads to the “foetal alcoholism syndrome”, with delayed intrauterine development and congenital malformations. Other substances like the chlorinated hydrocarbons (DDT) can even be found in the fecundated egg; they can determine various teratogenic effects.

The utero-vaginal gate

This gate is rarely used in cases of illegal abortion by injecting various substances with abortive reputation in the uterus (saline or alcoholic solutions, soap solution, permanganate, physiologic saline).

The absorption of toxic substances

The absorption of toxic substances is a complex process. In general, a toxic substance has to be dissolved in a solution in order to be absorbed. The absorption implies transportation through membranes, either by simple diffusion or passive transportation, or by active transportation. Any membranous crossing is in relation with various factors like the physical and chemical nature of the membrane, of the substance and of the environmental molecules.

- *Simple (passive) diffusion* is a simple, passive crossing of the toxic substance from a medium with higher concentration to another medium with lower concentration, until the chemical balance between the two mediums is reached. This process is based on the selective permeability of membranes and it usually not energy consuming. The determinant elements of passive diffusion are the fat-solubility and the size of the molecules; fat-soluble, small molecules can easily cross various membranes.
- *Active diffusion* is represented by the passage of a ionic flux from a medium with lower concentration to a medium with higher concentration, against the concentration gradient. The active transport, characteristic for mineral ions, for which biological membranes are less permeable, takes place with energy consumption and requires special mechanisms. This kind of transportation is also highly selective, because the transporters or vectors are specific for certain molecules.
- The transporters (enzymes or other protein components of the membranes) form compounds with the transported substances before crossing the membranes. The role of the transporters is to render a polar (ionised) molecule temporally fat-soluble, in order to permit its crossing through a biological membrane. After crossing, the compounds unbind, the toxic substance is released and the vector restores.

The absorption of toxic substances

Absorption is in direct relation with various factors that depend on the entrance gate. The digestive absorption depends on:

- the water- and fat-solubility of the toxic substance
- the degree of dissociation of the substance
- its stability in the digestive tract
- the size if its molecules
- the type of absorption (passive, active)
- the duration of the evacuation from the digestive tract
- the intestinal motility
- the interaction with various components from the digestive tract

The trans-cutaneous absorption depends on characteristics of the skin, the toxic substance and the environment:

- the lipid layer on the skin
- the width of the cornified layer
- the presence of hair follicles (entrance gate)
- the molecular weight of the toxic substance
- the presence of skin discontinuities
- UV radiations (they increase the absorption)
- the external temperature
- the presence of organic solvents, kerato-lithic substances, detergents

For solid toxic substances, the absorption through the lungs is in relation with the size of the particles and the presence of mucus in the air passages. For gas toxic substances the absorption is determined by their partial pressure and fat-solubility, and by the respiratory frequency.

The effects on the human body

The effects of toxic substances in the human body can be local or general. They are in relation with the molecular activity and with the chemical bonds between the biological molecules and the toxic substance. With the exception of substances absorbed in the stomach and intestine, which reach the liver through the vena porta, the toxic substances absorbed through other gates will reach the whole body through the systemic circulation and the lymphatic system. From the blood flow, the toxic substances reach into the tissular fluids, the systems and organs, where they undergo a process of distribution, sometimes associated with depositing and accumulation. In other cases, toxic substances can be conjugated in the blood flow with serum albumins and thus inactivated.

After passing from the blood and lymph into the interstitial fluid, the toxic substances undergo three major processes:

- *The distribution of toxic substances* is generally an uneven process - transport or transfer of the substances from the blood flow into the tissues. It mostly depends on the fat- or water-solubility of the toxic substance. Fat-soluble substances are distributed mostly in the cerebral matter (sedatives, hypnotics, organo-chlorinated substances), while water-soluble substances are distributed in to the liver and kidney.
- *The depositing of toxic substances* is an elective fixation process in various tissues and organs. The depositing mostly depends on the elective distribution, so toxic substance will deposit in preferential areas of the body: the adipose tissue (organic solvents, nitroderivates, chlorinated compounds), the bony tissue (Pb, Ba, F), in hair and nails (Ar) etc.
- *The accumulation of toxic substances* is characteristic for less toxic substances, administered in small, repeated doses. Once the toxic concentration is reached, specific intoxication signs manifest.

The metabolism (biotransformation) of toxic substances is represented by the transformations they undergo in the human body. For ingested substances, the changes can start before they reach into the blood stream, because of the digestive enzymes and local flora. The toxic substances that penetrate through the air passages can combine with the water and carbon dioxide in the pulmonary medium, before they enter the blood stream.

Immediately after absorption, some toxic substances undergo hydrolysis processes under the influence of plasmatic enzymes; others (metals) can combine with plasmatic proteins. The main organ for the biotransformation of toxic substances is the liver, where toxic substances are transported with the blood flow and will be transformed in less toxic compounds. Besides the liver, metabolism can also take place in the kidneys, skin, lungs, spleen, gastro-intestinal mucous membrane. It is to be noted that the organ in which the biotransformation processes take place is not necessarily the main target for the toxic effects of a substance.

The metabolism usually takes place in two phases:

- In the first phase, a biologically active or inactive compound is transformed through oxido-reduction or hydrolysis reactions. The newly formed metabolites can either be biologically more or less active then the initial substance.
- In the second phase of biotransformation, synthesis reactions usually take place. The result is a biologically inactive compound. The resulting substances are water-soluble and non-toxic and can be eliminated in urine.

The elimination of toxic substances

The elimination of toxic substances represents the natural removal of administered toxic substance, after their diffusion through the bodily cells, tissues and fluids. Only a small part of the toxic substance is eliminated in the initial form; most of the introduced quantity is eliminated as metabolites. The degree, speed and length of the elimination are conditioned by various factors like: the elimination way, the properties of the toxic substance, the entrance gate, the administered dose, the physiological and pathological conditions of the body.

- *The renal elimination* is the most important because the kidney is the main elimination organ for toxic substances. The degree of elimination depends on: the molecular weight, the type of metabolites, the urine flow and pH, the integrity of the renal function and various interactions with other toxic substances. The smaller is the molecular weight, the easier the elimination. The renal elimination is also influenced by: the glomerular filtration, the fat-solubility, the ionisation and the polarity of the toxic substance. The urine pH plays a very important role in elimination: the ionised form of the toxic substances and their metabolites is less reabsorbed in the renal tubes, so it will be eliminated in larger quantities. Substances that behave like weak acids and are better eliminated when the tubular urine is alkaline; weak bases are better eliminated when the tubular urine is acid. Exogenous toxins that behave like strong electrolytes are rapidly eliminated, regardless of the urine pH, because they are completely dissociated. This information is very important for the administration of medication to patients with renal failure. The interactions of substances that are eliminated through active tubular secretion are very important; one of the substances can compete for the tubular secretion, thus decreasing the elimination of the other.
- *The digestive elimination* is used by toxic substances that are eliminated through the digestive fluids, especially through the bile, so the gall bladder plays an important role. This type of elimination depends on: the molecular weight of the substance, the sex and age of the subject, the heredity, the type of biotransformation, the degree of protein bonding.
- As a general rule, substances with small molecular weight are eliminated through urine, those with big molecular weight through the bile and those with medium molecular weight through both ways.
- *The pulmonary elimination* is the main way type of elimination for gas and volatile toxic substances; they have high vapour pressure at body temperature so they can easily cross the alveolo-capillary membrane into the alveoli from where they are eliminated during expiring.
- *The trans-cutaneous elimination* takes place mainly through the sweat glands. It is specific for toxic compounds of arsenic, bromine, iodine, quinine and volatile substances (camphor). The trans-cutaneous elimination takes place in small amounts, practically negligible in acute intoxications.

- *The elimination through the mammary glands* is specific for some exogenous toxic substances. Milk is an important vehicle for toxic substances from mother to suckling but also from animals to humans (children). The ethanol intoxication of the suckling via maternal milk is one of the most severe problems. Because of the alcohol-dehydrogenase deficit, the alcohol accumulates in the suckling’s body.

The morpho-pathology of intoxications

The macroscopic changes determined by various toxic substances are generally non-specific: congestion, stasis, haematic suffusions, hepatic steatosis, nephrosis etc.

Depending on the morphological aspect of the lesions, toxic substances can be divided in to the following categories:

a. Toxic substances (a few) that produce typical lesions

- carbon monoxide determined the reddish discoloration of the skin (lividities) and blood;

- sublimate determines nephrosis;

- formaldehyde determines an in vivo fixation of the stomach;

- acids and bases determine erosions around the mouth and chin, and sores: yellowish (HNO_3), blackish (H_2SO_4) or whitish (HCl).

b. Toxic substances (the big majority) that determine non-specific lesions like stasis, oedema, and haemorrhages.

c. Toxic substances that do not determine any lesions; death onsets rapidly due to the big quantity or high concentration of toxic substance. There are some toxic substances that induce rapid metabolic paralysis and quick death, before any other lesion can onset (alkaloids).

Although most of them determine non-specific and inconstant morpho-pathological lesions, toxic substances can act somewhat preferentially, due to certain affinities for various tissues and organs:

- The digestive tract can present direct lesions, localised at the entrance gate (congestive, caustic, necrotic lesions) and/or lesions caused by the action of digestive ferments, sometimes associated with the effects of microbial flora on the already compromised digestive membrane (e.g. mercurial stomatitis). In most cases, the intoxications involve important organs (liver, kidneys), implicated in the methablisation and elimination of toxic substances. Toxic hepato-nephrites are frequent, with the predominance of hepatitis (in intoxications with phosphorus) or nephritis (intoxications with carbon tetrachloride).
- The respiratory system can present pulmonary oedema caused by the action of volatile toxic substances (chlorine, bromine, nitrous vapours). The oedema can be the background for secondary broncho-pneumonia.
- The heart can be affected by phosphorus or arsenic intoxications that can determine fatty myocardial dystrophy. Some toxic substances determine typical sanguine changes: carbon monoxide forms carboxyhemoglobin, aniline forms methemoglobin, hydrogen arsenide produces haemolysis.
- The nervous system (brain and spinal cord) is affected by toxic substances. Alcohol, chloroform, benzol determine agitation and delirium, followed by depression and coma. Mercury can induce chronic Parkinson-like syndromes. Strychnine and cantharidine determine spinal excitation, while alcohol and lead generate polyneuritis.

Sample collecting for toxicological analysis

In all cases of intoxication or suspected intoxication, samples for toxicological analysis must be carefully collected, regardless if the victim is alive or dead. It is imperative that the samples are introduced in adequate recipients and correctly labelled, with the name of the victim, the name of the physician that collected the samples and the hospital/institute where the sampling was performed. For protection reasons, the tubes or flacons with blood should be introduced in another recipient. Samples must be delivered to the toxicological laboratories as soon as possible.

Blood sampling

- In live victims, venous blood can be collected from any bodily region. The post-mortem distribution of toxic substances in the blood is not uniform and there is the danger of blood contamination with other bodily fluids or extraneous materials.
- The blood from the abdominal cavity can be contaminated with intestinal content, urine, faeces. The blood from the heart and pulmonary vessels can be contaminated with gastric content (vomit) aspirated in the air passages. Moreover, alcohol and Paracetamol ingested shortly before death can diffuse through the gastric wall, leading to high concentrations in the heart and large blood vessels. Even the jugular vessels can be contaminated due to the reflux in the superior thorax.
- The best sampling areas are the femoral, iliac and axillary veins
- For most toxicological analysis, 25-30 ml of blood is sufficient. The sample must be divided in two recipients: one in which it can coagulate and one containing an anticoagulant (EDTA, potassium oxalate, heparin). For determining the blood alcohol level, 10-15 ml blood must be introduced in a recipient with sodium fluoride, in order to prevent the production or destruction of alcohol by some micro-organisms.

Urine sampling

- The urine sample must amount to 20-30 ml, introduced in a clean recipient. Usually, no conservative substance is needed, except the situations when the toxicological examination is delayed. In these cases a small quantity of sodium nitrite must be added and the sample must be kept in a freezer.
- The toxicological analyses of urine can unravel the presence of toxic substances or of their metabolites.

Vomit and gastric content

- Vomit and gastric content must be introduced in a clean glass jar or a plastic recipient with lid. The recipients must not be washed with detergents or disinfectants because these compounds can influence the outcome of the chemical analysis.
- During the autopsy, the gastric content can be collected by opening the inferior gastric curve with a pair of scissors and letting the gastric content flow into a container. Some laboratories require the whole stomach, because the mucous membrane can retain traces of powdery material or fragments of tablets.

Sample collecting for toxicological analysis

Faeces sampling

- The rectal content can be useful in intoxications with heavy metals like arsenic, mercury or lead. The 20-30 g sample must be introduced in a jar with a lid or a hermetic plastic container.

Organ fragments sampling

- Organ fragments are usually introduced in clean recipients or plastic bags that can be closed hermetically.
- The most important organ is the *liver*, because it concentrates most toxic substances that enter the body; they can be identified in the liver even if the blood and urine concentrations are low. It is recommended that the liver fragment is of at least 100 g; if necessary the entire organ can be collected. Sometimes the bile can prove useful because it concentrates morphine and chlorpromazine.
- Samples of *lungs* can be useful in intoxications with solvents, although these substances can usually be identified in the blood
- Given the fact that most toxic substances are eliminated through the renal way, collecting *kidney* fragments is useful.
- Depending on the type of intoxication, samples of *brain* (one hemisphere), *heart* (half), *spleen*, *small intestine* (1 m) and *large intestine* (0.5 m) and their content can also be collected.
- The organ fragments must not be washed with water and no fixative or other foreign substance is to be used.

Hair and nails sampling

- Hair and nail samples are necessary in suspicions of intoxication with heavy metals like stibium, arsenic, thallium. The hair samples can either be cut or torn together with the root. It is known that these elements are deposited in keratin, in layers that can indicate the length of the chronic administration. Methods that use neutron activation on hair samples indicate that the most recent doses are deposited closer to the root of the hair.

The principles of forensic expertise in intoxications

The objective of the forensic expertise in all intoxication cases are:

- establishing the nature, the quantity and the entrance gate of the toxic substance (clinical, anatomo-pathological and toxicological examinations);
- establishing the approximate time of the toxic input (by evaluating the chronology of events, the length of the free interval, the severity and the duration of the symptoms and the terminal syndrome in comparison with the theoretical data);
- determining the favouring factors;
- finding elements for sustaining the juridical type of intoxication (accident, suicide, homicide)
- the positive diagnosis of death

The crime scene investigation must be extremely rigorous; the following aspects must be analysed:

- sources of toxic gases;
- sources of industrial or domestic toxic substances;
- the presence of drugs or medication;
- the presence of toxic substances in food;
- various materials with toxic traces;
- excretions with toxic content (vomit, urine, faeces)

The anamnesis and the medical documents (patient's chart) are also very important; they can provide information regarding the latent period, the moment and the characteristics of the debut, the symptoms, their duration and evolution.

Besides corroborating all available information, the forensic expertise must not neglect possible errors due to the intra-vitam or post-mortem transformations of the toxic substance (specific reactions, treatments, losses during extraction, the presence of impurities, changes due to putrefaction etc.)