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Review Article

A Few Words about Toxicology

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Abstract

Toxicology is the science of the effects of toxic substances on the body. Toxic substances are medicines, chemicals from everyday life or industry, and food additives. Toxicology is also a branch of pharmacology that is scientifically researching the prevention, diagnosis and treatment of poisoning. Toxin is a poisonous substance that forms in living cells of organisms and acts in very low concentrations. Toxins can be small molecules, peptides, proteins that cause disease by absorption or contact with tissues. Toxins react with biological macromolecules, such as enzymes and cellular receptors. The effects of toxins vary from minimal to lethal. Toxicity is the degree to which a substance can cause damage to the body, caused by a toxin. Toxicity can refer to the whole organism, such as a human, animal, plant or bacterium, and also to substructures, eg cells, organs, etc. By extension, the word toxicity can also be described as a toxic effect on larger and more complex groups, such as family and social groups. The central concept of toxicology is dose-dependent toxicity; even harmless substances such as water can lead to water poisoning if consumed in high enough doses, while taking a sufficiently small amount of highly toxic substances such as snake venom can occur without any consequences or effects of toxicity.

Keywords: Substance; Poison; Poisoning; Testing

Introduction

Biology and social environment always work together and they do so in complex, subtle, nuanced ways [1]. Almost all the research that indicates genetic or biological influences on criminal behavior also shows strong environmental components. But this is the beauty and challenge of most biological studies. By their nature, they must take into account both the genes and the environment. In trying to distinguish the effects of biology from those of the environment, scientists must study both; they thus accept both. Biological studies never exist in a vacuum. Much sociological research, on the other hand, does not take biology into account at all. Biological studies of crime must look at both environment and physiochemistry in order to compare the two and determine the effect of one versus the other. All biological studies fully recognize the importance of the environment and use it as a comparable variable. In fact, biological studies have done more to prove the existence of an environmental influence, particularly as an ameliorating effect, than sociological studies ever have.

In assessing the potential danger of drugs, society has become particularly conscious of their effects on human behavior [2]. In fact, the first drugs to be regulated by law in the early years of the 20th century were those deemed to have "habit-forming" properties. The early laws were aimed primarily at controlling opium and its derivatives, cocaine, and later marijuana. Today, it is known that the ability of a drug to induce dependence after repeated use is submerged in a complex array of physiological and social factors.

Dependence on drugs exists in numerous patterns and in all degrees of intensity, depending on the nature of the drug, the route of administration, the dose, the frequency of administration, and the individual's rate of metabolism. Furthermore, nondrug factors play an equally crucial role in determining the behavioral patterns associated with drug use. The personal characteristics of the user, his or her expectations about the drug experience, society's attitudes and possible responses, and the setting in which the drug is used are all major determinants of drug dependence.

The question of how to define and measure a drug's influence on the individual and its danger to society is difficult to assess. To this end, the nature and significance of drug dependence must be considered from two overlapping points of view: the interaction of the drug with the individual, and the drug's impact on society. It will be useful when discussing the nature of the drug experience

to approach the problem from two distinctly different aspects of human behavior—psychological dependence and physical dependence.

The number of drug users grows every year [3]. There is more and more opportunities for people to find a company where someone will offer "grass" or at least stimulate curiosity. Simply curiosity can only be the first step leading to addiction. People are sometimes unaware of the fact that every beginning, as it has done simply and harmlessly, can end tragically. The drug is every psychoactive substance of a natural or synthetic origin that a person takes to achieve a desired change in the mental or physical condition that may become addictive. Dependence is defined as a periodic or permanent drug taking, characterized by an insuperable need for drug, a tendency to increase the amount of the drug, and the harmful consequences for addicts (physical, psychological, economic, social), as well as its environment.

Pharmacokinetics

An important part of any investigation involving drugs or poisons is the interpretation of toxicological data [4]. The onset, duration and intensity of action of a drug after administration are controlled by the rate at which the drug reaches its site of action, by the concentration of the drug and by the sensitivity of the individual to the drug. Hence, a good understanding of the basic concepts of pharmacokinetics and metabolism is essential to enable an informed comment to be made on the approximate amount and timing of the exposure, and a likely response to the substance(s) under question. These answers are always predicated on the amount of information available to the toxicologist (the route of administration, age, sex, presence of disease and whether exposure was acute or chronic are important factors).

The disposition of a drug includes the following processes:

- Absorption
- Distribution
- Metabolism
- Excretion.

The processes of metabolism and excretion are often referred to as elimination because they function together to eliminate poisons from the body.

Pharmacokinetics describes the time course of the blood and tissue concentration profile, while pharmacodynamics refers to the relationship between dose and the intended pharmacological response.

The absorption phase relates to the entry of drug from the absorption site. This may be relatively slow, as from the gastrointestinal tract for oral absorption, or rapid if given intravenously.

Substance

With any substance (drug, poison) that is present in a person's body, there are a variety of terms that are used to describe processes involving that substance [5]. The "route" of exposure or administration describes how the substance gets into a person's blood stream. Common routes are ingestion (through the GI tract), injection (via a needle intravenously (into a vein), intramuscularly (into a muscle), or subcutaneously (under the skin)), inhalation (breathing it in, either directly or via burning or smoking it), and insufflation (snorting). The term "metabolism" describes how the human body breaks down the substance. Two common locations for drug/toxin metabolism are the liver and the bloodstream itself, where various enzymes can break down certain substances. A substance that is formed by the breakdown of a "parent" substance is referred to as a "metabolite," or a "breakdown product." With certain drugs, a metabolite might be "active," meaning it has pharmacological properties, often similar to the parent drug/toxin. Many other metabolites are "inactive," meaning that they do not have pharmacological properties. How the body actually gets rid of a drug, usually via metabolism and excretion (often via the kidneys), is referred to as "elimination." The "half-life" (designated as t1/2) of a drug/toxin is the length of time it takes for the body to eliminate half of the substance that was originally present. There are certain drugs that have very short half-lives. With some of these, postmortem (after death) metabolism can continue to occur, using blood enzymes that remain partially active after death. As such, pathologists often rely on toxicology tests identifying a metabolite in order to establish that a death was related to a particular drug's toxicity.

Substance abuse

The term substance abuse is most simply defined as the excessive use of one or numerous drugs [6]. In general, most people typically have some level of access to several types of drugs, including legitimately prescribed medications, and on average, will benefit from their appropriate use. However, the term substance abuse can be applied to a variety of situations or circumstances. For example, one person may intentionally be abusing a multitude of substances including illicit drugs, prescribed medications, and over-the-counter remedies (i.e., supplements, herbals, diet aids, etc.). This is in direct contrast to another individual who may be taking only a single medication, but deliberately using it in a manner that is not consistent with normal therapeutic use. It stands to reason that when individuals begin to abuse one or more substances, and use them in an uncontrolled manner without the appropriate oversight, that they place themselves in a potentially harmful or lethal situation.

In a forensic or medicolegal setting it often becomes a matter of necessity to interpret drug findings and render an opinion regarding the toxicological, physiological, and pathological impact the drugs may have had upon an individual. To this end, it is important to evaluate and consider a host of factors. These factors are not al-

ways straightforward or quantifiable, but nevertheless include the drug's inherent physical and chemical properties, the dosage of the drug used, the frequency of the drug intake, the route of drug administration, the concentration of drug and drug metabolite found, the person's tolerance level to the drug and any medical conditions or disease states the person may have experienced.

It is important to recognize that for a particular drug to ultimately produce a toxic or lethal effect, it must be present in an individual at a sufficient concentration for a sufficient length of time. However, while references and other texts are available that help to classify drug concentrations as "therapeutic," "toxic," or "lethal," interpretation is often not so simple. For example, postmortem methadone concentrations are often challenging to interpret because the range of blood concentrations detected in people enrolled in narcotic maintenance programs may overlap the blood concentrations found in overdose or lethal situations.

Poisons

Poisons are chemical substances that are capable of causing illness or death [7]. Excessive amounts of almost any substance can be poisonous. This would include therapeutic agents, drugs of abuse, industrial chemicals, botanical substances, venoms, and pesticides in addition to notorious poisons such as arsenic, strychnine, and cyanide. It is the amount (dose) of a substance that makes it a poison. Most often, the term poison is applied to substances that can be lethal to humans in relatively small doses. In forensics, poisons are considered in an expanded context that includes chemicals that can be used to modify behavior to achieve criminal goals. More formal definitions for a poison can be found in various statutes and regulations that deal with the use, labeling, and other issues relative to the availability of potentially toxic substances and public health.

The ingestion of liquid poisons is sometimes clear from outward signs on the body [8]. Powerful caustic lyes or acids may produce vomiting once the liquid reaches the digestive tract. There is considerable damage to lips, tongue, and mouth, and there may be blood in the vomitus, along with pieces of the esophagus and stomach. Usually, death does not occur rapidly, and victims may employ another means of suicide to stop the excruciating pain.

Cases of suspected poisoning frequently pose very difficult problems to the police investigator and to the medical examiner. Many poisons produce symptoms similar to those of certain diseases, a fact that can complicate determination of whether a crime has been committed. However, if there is any reason to suspect poisoning, the investigation must proceed along the lines of a possible homicide, suicide, or accidental death until death due to natural causes is established. To compound the problem, suicides and accidental deaths by poisoning are sometimes very difficult to distinguish from homicide. Alcohol, when consumed with certain medications, may result in an accidental (possibly suicidal) death by respiratory failure. An example is the combination of barbiturates and alcohol; when the alcohol level in the blood reaches about half the lethal dose, most individuals lose consciousness and thus stop breathing. But with the addition of a stimulant, such as an amphetamine, this effect may not occur, and individuals may drink a lethal dose of alcohol before they fall into a coma.

General principles in pharmacology and toxicology also play an important role in forensic alcohol analyses [9]. When applied to forensic alcohol test evidence, these principles allow for accurate estimates of blood alcohol concentrations and how much alcohol was consumed, determining the distribution and elimination of alcohol and bringing objectivity to the often variable evidence that comes from subjective reporting. In recent years, training in toxicology has included topics such as "performance toxicology", incorporating findings from other disciplines (e.g., psychology) to relate behavior to objective chemical or toxicological test results.

In the last few decades our understanding of the mechanisms through which the drug alcohol changes the brain to change behavior has come largely from neuroscience and neuropharmacological research. Thus, it is apparent that understanding and interpreting alcohol intoxication evidence involves education and training in a number of overlapping disciplines, not one specific field. When possible, practical clinical experience combined with laboratory training will be particularly useful in the forensic examination of alcohol intoxication evidence.

Being under the influence of alcohol, or of any other mind-altering drug, may mean that the defendant cannot think clearly enough to form some types of criminal states of mind [10].

While intoxication may mean that the defendant does not have the ability to reach the "intent" and "knowledge" levels of mens rea, the law normally finds that he or she may still reach the "recklessness" and "negligence" levels. Negligence holds a defendant not only to what he or she knows but to what a reasonable person knows, and intoxication does not change this standard. (One might say that a reasonable person would not be intoxicated.) Likewise, in the case of recklessness, many courts hold that using mind-altering drugs to the point of intoxication is in itself reckless behavior that makes a person liable for the reckless acts he or she commits while intoxicated.

Poisoning

Poisoning, one of the oldest methods of murder, can occur from an overwhelming dose that causes immediate death or from small doses that accumulate over time and cause death [11]. Poisons can be injected into the blood or muscles, inhaled as gases, absorbed through the skin surface, taken in foods or liquids or inserted into the rectum or vagina.

Homicidal poisoning can be accomplished with any one of thousands of substances, but some are far more common that others. Among the most commonly used is arsenic, known as the King of Poisons and the Poison of Kings. Cyanide, also commonly used, is a favorite in mass homicides, suicides and politically motivated killings. Strychnine, given in large enough doses, produces "a dramatic and horrifying death with the victim's body frozen in mid-convulsion, eyes wide open". Experts in toxicology (the study of poisons) can determine the type of poison, the amount ingested, the approximate time ingested and the effect on the body.

Investigators should ask the following questions to help determine if a homicidal poisoning has occurred:

- Was the death sudden?
- Has the caregiver been associated with other illnesses or death?
- Did the victim receive medical treatment and appear to recover, only to die later?
- Did the caregiver have access to restricted drugs or other chemicals?
- Was the victim isolated by the caregiver? Did the caregiver position himself or herself to be the only one with access to the victim's food or medications?
- Was there a history of infi delity of either the victim or spouse?
- Is there a history of the deaths of more than one child?

If a child is poisoned by accidentally ingesting cleaning fluid, detergents, pills or other such substances, the parents are sometimes charged with manslaughter or negligent homicide.

An overdose death is not necessarily a suicide. It might have been accidental—a result of the person's not knowing when medication was last taken or being in a semi-stupor and taking more pills than intended. If a prescription bottle is found, determine from family members how many pills were in the bottle before the death. Check with the issuing pharmacist to determine whether it was a legal prescription, how many pills were prescribed and the date the prescription was last filled. Preserve all evidence until the coroner's office rules the death accidental or a suicide. Other important evidence includes the medicine cabinet's contents, any excretions or vomit at the scene and any food the victim recently ate.

Testing

Analytical methodologies used by forensic laboratories vary, but most use a combination of immunoassay and chromatographic methods to identify and quantify drugs and poisons [12]. Alcohol is routinely analyzed in forensic laboratories by gas chromatography. Enzymatic and colorimetric methods are occasionally used as an initial or screening test. Carbon monoxide testing can be tested by spectrophotometric differentiation between oxyhemoglobin, reduced hemoglobin, methemoglobin, and carboxyhemoglobin. Carbon monoxide analysis is also done by a diffusion and colorimetric method, and by gas chromatography. Cyanide testing is done by diffusion and by colorimetric quantitation. Immunoassay testing can be used for screening both blood and urine specimens for a variety of drugs and drug classes. Opiates, amphetamines, barbiturates, benzodiazepines, and cocaine metabolites are examples of immunoassay testing. Chromatographic methods such as thin layer chromatography (TLC), gas chromatography (GC), high performance liquid chromatography (HPLC), and chromatography interfaced with mass spectrometry (GC/MS, GC/MS/MS, LC/MS, LC/MS/MS) are used for qualitative analysis and quantitative testing of specimens for drugs and poisons. For heavy metal poisoning, specimens of arsenic, mercury, cadmium, lead, and so on can be analyzed by atomic absorption spectrophotometry.

For the results of toxicology testing to be scientifically valid, the methods and procedures used for analyzing specimens must be validated to ensure the accuracy, precision, and specificity of the method. The process includes identifying limits of detection and lower and upper limits of quantitation. The method of validation tests for possible interfering substances, evaluates carryover from previously tested samples. The method must be able to provide accurate results for reference specimens. The forensic toxicologist must understand the importance of validation and be able to evaluate the effectiveness of the process. Results from scientifically valid methods are necessary to support medico-legal circumstances of criminal or civil cases.

Management

Many individuals who are detained in custody have underlying chronic illness for which they take regular medication [13]. The aim of the forensic practitioner is to continue regular medication and to quickly identify and treat any acute problems as they arise. Often, the period of detention is so short that no regular medication needs to be prescribed/administered. When a longer period of detention (e.g. overnight) is planned, it is usually appropriate to arrange for usual medication to be continued. In many instances, detainees bring their own medication to the police station and this can be prescribed and administered at the usual times. On occasions when detainees do not have their usual medication with them, the best options are either to arrange for this medication to be brought to custody or for alternative medication to be provided from custody. In order to achieve the latter option, depending upon local arrangements and the contents of the custody medicines cabinet, it may be necessary to obtain drugs via a private prescription from a local pharmacy. Many detainees may be non-compliant or not have access to medication. Common chronic illnesses encountered in everyday custody practice include chronic heart disease, hypertension, asthma, epilepsy, diabetes, epilepsy, alcoholism, drug misuse, and mental health issues.

Conclusion

Toxicology is the science of the adverse effects of chemicals on living organisms. Toxicology studies the symptoms, mechanisms, treatment and detection of biological poisoning - especially human poisoning. The main criterion for a chemical's toxicity is dose, apropos the degree of exposure to the substance. It can be said that almost all substances are toxic under certain conditions. Toxicity is a condition caused by poisoning or excessive ingestion of normally harmless substances. The most common intoxication in humans is intoxication with psychoactive drugs, alcohol, caffeine, water, etc. The term xenobiotic is often mentioned in relation to poisons. A xenobiotic is any substance found inside an organism that is not normally produced within the body or expected to be present within it. Ecotoxicology is the science that studies the direct or indirect impact of xenobiotics on the ecosystem, on all living organisms and their organization, on the relationship to non-living matter, on their relationships with each other and on their relationship to humans.

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