

# PHYSIOLOGY, PHARMACOLOGY, AND TOXICOLOGY OF ALCOHOL

## Glossary of Terms

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For many years this glossary has been used as part of the handout materials for my lectures on the Borkenstein ALCOHOL course (Indiana University). The content of the glossary has been continually updated and improved and contains acronyms, words, concepts and phrases often encountered in articles and books dealing with the physiology, pharmacology and toxicology of alcohol. Like the Borkenstein course itself, the main focus of the glossary is on forensic aspects of alcohol and questions that arise during the prosecution and defense of drunken driving offences. Some of the material in this A-Z glossary is explained in more detail than others, although this was done intentional to aid in the learning process.

### A

**Absorption.** This refers to the uptake of a drug or poison (e.g. alcohol) from outside of the body into the bloodstream. For small molecules unionized at physiological pH, absorption occurs by passive diffusion through cell membranes. For all practical purposes alcoholic beverages are consumed by mouth and unlike other drugs the ethanol they contain starts to become absorbed into the blood from the stomach. However, the rate of absorption is much faster from the upper part of the small intestine (duodenum and jejunum), owing to the larger absorption surface area provided by the villi and microvilli. The speed of ethanol absorption thus depends on factors that influence gastric emptying, e.g. food in the stomach, type of beverage consumed, dilution and alcohol content (beer, wine or spirits), anatomy or surgery on the gut, concomitant drug intake, smoking, time of day etc.

**Absorption deficit.** This term is often encountered in the older German literature and refers to the observation that when blood-alcohol concentration is extrapolated back to time of starting to drink ( $C_0$ ) the BAC is less than expected for dose of ethanol (g/kg) ingested and body weight of the individual. The deficit was found to be about 10-15% of the dose of ethanol administered. This amount of alcohol did not seem to have reached the systemic circulation. The volume of distribution of ethanol (dose/ $C_0$ ) was higher than expected for the actual dose given. When alcohol was consumed together with or after a meal the deficit was larger compared with drinking on an empty stomach. The reason for the deficit is often ascribed to appreciable first-pass metabolism occurring in the liver or the gastric mucosa before ethanol reach the systemic circulation. Another mechanism is food-induced increases in liver blood flow. The research done by Widmark considered that molecules of ethanol became bound to constituents of the meal (e.g., amino acids) and were not absorbed into the bloodstream. Otherwise the bound ethanol was released very slowly into the blood over several hours and metabolized without increasing the BAC in the post-absorptive phase.

**Absorption half-life.** For orally administered drugs, the rate of absorption is expressed in units of time by calculating the absorption half-life. The absorption rate constant ( $k_{abs}$ ) has units of reciprocal time ( $\text{min}^{-1}$  or  $\text{h}^{-1}$ ) and substances with high  $k_{abs}$  (short half-life) are rapidly absorbed, which results in higher and earlier occurring  $C_{max}$  in blood. During one half-life 50% of the drug is absorbed from the site of administration and 90% is absorbed after about four half-lives. Pharmacokinetic modeling of the absorption phase of the blood-alcohol curve is complicated because rate of uptake into the blood occurs from both the stomach and the proximal part of the intestine (duodenum and jejunum). Accordingly, the rate of absorption depends on factors that influence gastric emptying. A simpler and more pragmatic way to obtain information about the rate of ethanol absorption is to calculate the ratio of  $C_{max}/t_{max}$  in units of g/L/h or g% per h.

**Absorption lag-time.** For most orally administered drug some time elapses before the active substance is

measurable in the systemic circulation e.g. venous blood. This time is referred to as absorption lag-time and differs for different drugs depending on, among other things, the dose and dosage form (liquid or solid), pKa of active substance,  $k_m$  of hepatic metabolizing enzymes, extent of first-pass metabolism etc and sensitivity of the analytical method used. Because ethanol is taken in liquid form, the absorption into the blood starts immediately and lag-time is therefore negligible.

**Abstinence.** The state or condition of remaining free of alcohol or other drugs (abstainers).

**Accreditation.** The accreditation of e.g. a laboratory represents a formal recognition by an authorized agency that the work done meets high standards and that the management and laboratory staff have the appropriate qualifications and training and are competent to perform the tasks required.

**Accuracy.** A statistical measure of the closeness of agreement between the result of an analysis and the true (known or assigned) value of the quantity (e.g. concentration of a drug). The discrepancy or difference between the true value and the result obtained is often referred to as analytical bias.

**Acetaldehyde.** The first metabolite of ethanol produced by various enzymatic oxidations that take place mainly in the liver. Acetaldehyde is a toxic substance and elevated concentrations in blood trigger a range of unpleasant effects on the individual including facial flushing, rapid heartbeat, nausea etc.

**Acidosis.** Too much acid (low pH) in the blood and body fluids (opposite = alkalosis).

**Acute tolerance.** This refers to the development of tolerance to the effects of alcohol and/or other psychoactive drugs during a single exposure. Sometimes referred to as the Mellanby effect, named after a British pharmacologist Sir Edward Mellanby (1884-1955), who first observed the phenomenon when doing research on impairment effects of alcohol in dogs.

**Addictive drug.** The name given to a drug, medication or chemical agent often self-administered usually without a medical prescription, repeatedly and compulsively.

**ADME.** An acronym widely used in pharmacology and toxicology that stands for **A**bsorption, **D**istribution, **M**etabolism and **E**xcretion of drugs in the body.

**Adulterate.** This refers to the contamination of a pure substance with another substance of the same appearance as the original. In connection with the illegal manufacture and sale of drugs like cocaine or heroin, these are blended with other inert substances in a process known as "cutting" before the product is packaged and sold to illicit drug users.

**Aphrodisiac.** A term derived from Aphrodite, the Greek goddess of love. An aphrodisiac is often considered a food, drink, drug, scent or device that arouses or increases sexual desire or libido. In short anything that improves sexual performance.

**Agonist.** An agonist drug is a chemical substance that binds to a receptor to produce an effect or start a sequence of events leading to a physiological response.

**Agreement.** The extent to which two different tests or analytical results agree, sometimes referred to as degree of concordance. The closeness of agreement of two different observers when assessing the same thing.

**Alcohol abuse disorder.** This is a pattern of alcohol consumption leading to clinically significant impairment or distress, such as failure to fulfill major commitments related to work, school or the family. Those who suffer from alcohol abuse disorder tend to show disregard for others, they exhibit poor judgment and self-control and are often apprehended for driving under the influence of alcohol. Relationships with friends and family are worsened because of the continuous heavy drinking.

**Alcoholism.** Alcoholism or alcohol dependence is a chronic relapsing condition depending on genetic,

psychosocial, and environmental control factors. Symptoms of the disease include craving and urge to continue drinking despite experiencing physical, mental and/or social harm. Alcoholics are unable to stop drinking once they start and start to drink alcohol in the morning, often to relieve a hangover, reduce feelings of anxiety or to counteract withdrawal symptoms as blood-alcohol concentration reaches zero.

**Alcohol tolerance (acute).** This refers to a progressive adaptation to the effects of alcohol during a single exposure to the drug. This adaptation includes both subjective and objective tests of alcohol-influence. The signs and symptoms of intoxication are more pronounced on the rising limb of the blood-alcohol curve compared with the declining limb. Another name for acute alcohol tolerance is the Mellanby effect (see later).

**Alcohol tolerance (chronic).** This refers to a decrease in response to a specified dose of alcohol after repeated exposure. The person needs to consume more alcohol on each occasion to achieve the same desired state or feelings as was originally produced by lower doses when first starting to drink.

**Alcohols.** A collective name for a class of organic compounds containing carbon, hydrogen and oxygen and one or more hydroxyl (-OH) groups. Alcohols are often classified as mono-hydroxy (e.g. methanol), di-hydroxy (e.g. ethylene glycol), tri-hydroxy alcohols (e.g. glycerol) and poly-hydroxy (e.g. mannitol).

**Alcohol dehydrogenase (ADH).** The liver enzyme catalyzing conversion of primary alcohols into aldehydes and secondary alcohols into ketones. Thus, ethanol is oxidized into acetaldehyde and isopropanol is converted to acetone.

**Alcohol withdrawal.** Alcohol withdrawal refers to a spectrum of unpleasant symptoms that occur when an alcoholic suddenly stops drinking. These symptoms can develop into life-threatening physiological and psychological disturbances of body functions if a long period of heavy drinking ends abruptly.

**Aldehyde dehydrogenase (ALDH).** An oxidative enzyme mainly located in mitochondria and cytosol of the liver with the major function of converting acetaldehyde to acetate. There are two polymorphic forms of ALDH with low  $K_m$  (high functional activity) and high  $k_m$  (low functional activity). A mutant form of ALDH is inherited by 30-50% of people of Asian descent. This makes them less capable of oxidizing the acetaldehyde derived from ethanol. These individuals react by flushing in the face and they suffer palpitations, tachycardia and nausea after drinking small amounts of alcohol. This genetic trait protects them from becoming alcohol abusers and alcoholics.

**Aliquot.** The portion of the sample that is actually used for analysis.

**Alkaloid.** A word coined by a German chemist Wilhelm Meissner in 1819 to denote a naturally occurring organic compound produced by plants or shrubs that contain one or more nitrogen atoms in the molecule and have a basic (alkaline) character. Many alkaloids are pharmacologically active with important medicinal applications - atropine, cocaine, strychnine, nicotine, morphine to name just a few examples.

**Allele.** One or two or more variants of a gene or other DNA sequence. Different alleles of a gene generally serve the same function e.g. code for proteins that determine eye color, but may produce different phenotypes (e.g. blue, green or brown eyes). Some alleles may be defective and produce a protein (e.g. an enzyme) that has no function at all or an abnormal function.

**Alveolar.** Pertaining to the alveolar sac - the air cells - the site of gas exchange in the lungs.

**Alveoli.** Plural of alveolus the extreme ends of the branches of the bronchial tree, the air sacs at the base of the bronchioles where gases and volatile substances, such as oxygen, carbon dioxide and ethanol, can enter and leave the pulmonary circulation.

**Alveolar air.** Alveolar air is end-expired air representing that fraction of the exhaled breath remaining after air from the dead-space region of the lungs (mainly nose and upper airway) has been ventilated out. For determination of alcohol in breath at least 1.5 liters of a prolonged exhalation should be discarded

prior to sampling and analysis of the alcohol content.

**Amino acids.** Organic compounds containing both an acid and amino group, e.g. carboxylic acid (-COOH) and amine (-NH<sub>2</sub>) groups. Twenty amino acids are important in human nutrition and biology and they are the building blocks of proteins.

**Amylase.** An enzyme produced in the pancreas to catalyze the digestion of carbohydrates (sugars).

**Analgesic.** A term derived from the Greek word *algos* which means pain and is the ability of a drug or other treatment to deaden or alleviate pain.

**Analyte.** The specific component or substance measured in a chemical analysis.

**Analytical specificity.** The property of a method to determine solely the desired compound it purports to measure and without responding to any other substances that might be present in the specimen received for analysis.

**Analytical sensitivity.** The ability of a method or instrument to discriminate between samples with different concentrations or containing different amounts of the analyte. The slope of the analytical calibration function (plot) is one index of a method's sensitivity, the steeper the slope the more sensitive is the method.

**Analytical toxicology.** This entails extraction, detection, identification and quantitative analysis of drugs and poisons (xenobiotics) and their metabolites in biological fluids and tissues.

**Analytical wavelength.** Any wavelength at which an absorbance measurement (UV or IR) is made to determine any of a constituent of the specimen by a photometric method of analysis.

**Analytical run.** A set or series of measurements carried out successively by one analyst using the same measuring system, at the same location, under the same conditions, and during the same period of time, usually the same day.

**Anaerobic.** A biological process not requiring oxygen.

**Anemia.** A deficiency of hemoglobin in the blood resulting from a decrease in the proportion of erythrocytes - an abnormally low number of red blood cells.

**Anorexia nervosa.** A serious mental illness associated with a diminished appetite for food in a relentless pursuit for thinness. Usually shows itself during adolescence primarily in women with sometimes fatal consequences. The disorder is associated with substantial psychological disturbances and symptoms overlap with other psychiatric illnesses – mood and anxiety disorders.

**Antabuse:** The proprietary name for a drug developed in the late 1940s and used to treat alcoholism. Antabuse (disulfiram) works by blocking the action of hepatic aldehyde dehydrogenase enzyme, which leads to higher concentrations of acetaldehyde in peripheral blood after people consume alcoholic beverages. The elevated concentrations of acetaldehyde triggers unpleasant effects (facial flushing, nausea, tachycardia), which hopefully will scare the person from continuing to drink alcohol, hence this treatment is referred to as aversion therapy.

**Antagonist.** A chemical substance (drug) that binds to a receptor to block or reverse the action of another drug or chemical substance; Naloxone is an opiate antagonist that blocks the action of morphine at its receptor.

**Anthropometric data.** Measurements of body height, weight, age, and skin-fold thickness to provide an indirect assessment of body composition, body size and development.

**Antibody.** An antibody is a large protein molecule produced by the body's immune system to recognise and bind foreign molecules such as viruses.

**Anticoagulants.** These are drugs or chemicals that delay or stop blood from clotting either in-vivo or in-vitro in the evacuated tubes used to draw blood. Heparin is a natural anticoagulant in the body and the drug warfarin is also used to counteract thrombosis. Typical in-vitro anticoagulants include potassium oxalate, citrate, EDTA, and sodium fluoride, substances that prevent clotting by binding calcium ions or blocking an enzyme needed for the clot reaction.

**Antidiuretic hormone (ADH).** A hormone (arginine vasopressin) produced in the hypothalamus and released from the posterior pituitary gland, that regulates the reabsorption of water by the collecting tubules of the kidneys. Without adequate amounts of hormone water is not reabsorbed and the person produces excessive urine (diuresis).

**Antigen.** A molecule that binds to an antibody.

**Antipyretic.** A word derived from the Greek word *pyresis*, which means fire so antipyretic is often used to characterize a drug that reduces fever by lowering body temperature (e.g. paracetamol).

**Anuria.** The absence or cessation of urine secretion, a life-threatening event.

**Apnea.** A word derived from Greek "to breathe" and means suspension of external breathing. Apnea can be produced voluntarily by holding one's breath or induced by drugs such as opiates, mechanically induced e.g. by strangulation or choking or through brain trauma. Prolonged apnea leads to severe lack of oxygen and permanent brain damage death occurring after ~3 minutes duration unless ventilation is restored.

**Apoptosis.** A word derived from Greek language referring to a series of biochemical reactions that occur within living cells leading to a process of self-destruction also known as programmed cell death.

**Area under the Curve (AUC).** AUC refers to area under the concentration-time curve of the drug in blood or some other body fluid. For drugs metabolized by first-order kinetics the AUC is directly proportional to the dose administered. When bioavailability of a drug after different routes of administration or in different dosage forms is of interest, then AUC is the parameter to measure and compare. However, for drugs metabolized by saturation kinetics (e.g. ethanol, aspirin, GHB and phenytoin) the AUC increases disproportionately with increase in dose. Under these circumstances bioavailability cannot be calculated by comparing AUC after oral and intravenous administration of the same dose of the drug.

**Artery.** An artery is a blood vessel that carries oxygenated blood from the heart and lungs to the rest of the body.

**Artifact.** A term used in conjunction with chemical analysis to indicate an artificial (false) result, such as something introduced during processing the tissue specimen. In analytical toxicology this implies a substance not naturally present in biological specimens but which was an impurity in the reagents used in the analysis or produced by some metabolic process after sampling or after death in medical examiner cases.

**Ascites.** This is a pathological condition involving accumulation of fluid in the peritoneal cavity or abdomen. This medical condition is often associated with portal hypertension as a consequence of liver cirrhosis resulting from chronic heavy drinking and alcoholism. The volume of ascites fluid might reach 10 liters or more in some individuals.

**Asthma.** A common respiratory disease manifested in difficulties breathing, owing to narrowing of the airways. Asthma is a chronic inflammatory disorder, which causes obstruction of airflow and a marked reduction in a person's forced expiratory volume. Those suffering from asthma might not be able to fulfill the sampling requirements (time-pressure-volume) of some breath-alcohol analyzers.

**Ataxia.** This is the inability to coordinate voluntary muscle movements, owing to various influences (drugs or diseases) acting on the cerebellum.

**Atrophy.** Is the wasting away or shrinkage of tissue caused by cell-death.

**Auto-brewery syndrome.** Also known as gut fermentation syndrome, this refers to endogenous synthesis of ethanol in the gut by fermentation of dietary carbohydrates. This fermentation process is alleged to occur in people also suffering from an intestinal overgrowth of yeast, often several species of *Candida*, such as *Candida albicans*. This is a rare condition best documented in Japan but used recently as a drunk-driving defense argument in USA and UK with some success. Medical and expert testimony is necessary to document candida infections etc.

**Autopsy.** The word autopsy comes from a Greek word *autopsia*, meaning "to see for oneself" (*autos* = oneself and *opsis* = eye). In Great Britain the term necropsy is used as an alternative word to autopsy, which also comes from the Greek "seeing a dead body." In USA autopsy is synonymous with postmortem examination done by a medical examiner.

**Aversion therapy:** A treatment for alcoholics based on administration of enzyme inhibitor antabuse® so that the unpleasant effects of elevated blood acetaldehyde are intended to scare patients from continuing to drink.

## B

**Bariatric surgery.** Bariatric comes from the Greek words *baros*, which means weight and *iatic* which means treatment. Hence bariatric surgery is an operation for treatment of being severely overweight (obesity) and usually involves making the stomach smaller by gastric banding or a gastric bypass operation.

**Basal metabolism.** The total energy output of the body at rest after a 12 h fast is approximately 1.0 kcal/kg/h for men (0.9 for women). For a 150 lb (68 kg) man the energy requirement for basal metabolism is therefore 1632 kcal/day.

**Baseline measure.** An observation made or a quantitative measurement before administration of any experimental treatment or procedure, such as alcohol or a drug. When results of the experiment are evaluated, the post-treatment measures are compared with the baseline measures.

**Beer's law.** States that the absorbance of a homogeneous sample containing an absorbing substance is directly proportional to the concentration of the absorbing substance.

**Bias.** Refers to a more or less persistent tendency for the measurements as a group to be too large or too small and is therefore a systematic error of measurement often expressed as the difference between the expected result of a measurement and a true value (compare with accuracy).

**Bibliometrics.** The quantitative study of published articles and books and their evaluation in terms of authorship, readership and number of times cited.

**Bile.** A greenish-yellow liquid secretion made in the liver and collected and stored in the gallbladder and used in digestion. Bile is an emulsifier, which promotes mixing and digestion of fatty foods.

**Binge drinking.** Two definitions of binge drinking are in current use. One considers a binge as the consumption of sufficient alcohol within 2 hours to reach a blood alcohol concentration of 0.08 g% or more. This requires consumption of 4 standard drinks for women or 5 drinks for men, where one standard drink contains ~16 g ethanol. Another older definition of a binge is continuous heavy drinking over several days, during which time the individual fails to fulfill other commitments or activities because of irresponsible drinking.

**Bioavailability.** This expression refers to the fraction of drug that reached the systemic circulation after a particular route of administration, usually oral intake. The bioavailability is usually expressed as a percentage and after the intravenous route of administration the drug is bio-available to 100%. But after oral intake, especially after eating a meal, the percentage availability might be appreciable less owing to degradation (metabolism) occurring in the gut or liver before the blood reaches the heart and the systemic circulation.

**Biological specimen.** Material from a living or deceased person needed for identification purposes (e.g. DNA) or to determine if a person has been exposed to drugs (licit or illicit). The specimens most often submitted for drug analysis are blood, urine, saliva or hair strands.

**Biomarker.** This refers to the analysis of an endogenous substance that can be used to measure the prognosis of developing a disease, exposure to a chemical or the effect of a treatment. An alcohol biomarker refers to a chemical or physiological indicator of acute or chronic exposure to alcohol. Elevated levels of certain enzymes in the blood are indicative of liver damage caused by long-term over-consumption of alcohol.

**Biopsy.** Removal and laboratory examination of tissue from a living body, e.g. liver biopsy is the gold standard for investigating liver cirrhosis.

**Biotransformation.** This refers to the chemical conversion of a drug into its metabolites, either by oxidation, reduction, hydrolysis (phase I reactions) or acetylation, sulfation or glucuronidation (phase II reactions). In general, lipid soluble drugs are converted into more polar molecules by the action of enzyme-catalyzed biochemical reactions mainly taking place in the liver and in this way facilitating removal by renal excretion.

**Bipolar disorder.** A psychiatric disorder formally referred to as manic depression. Today this ailment is known as bipolar disorder, because the illness involves two phases, an “up” or manic phase and a “down” or depressive phase. Lithium as its carbonate salt is a common treatment for this disorder.

**Bladder.** A muscular sac that serves as a reservoir for the accumulation of urine.

**Bland-Altman plot.** Martin Bland and Douglas Altman two British statisticians, who published a simple and intuitive way of comparing the results of two methods of clinical measurement. This entailed plotting the individual differences ( $x_1 - x_2$ ), which is a measure of bias, against the mean result of the two methods  $(x_1 + x_2)/2$ . The resulting Bland and Altman plot shows the magnitude of bias and the degree of scatter. A multiple of the standard deviation of the differences ( $\pm 2 \times SD$ ) is a parameter that reflects the 95% limits of agreement between the methods.

**Blind (masked) sample.** A test of proficiency in which the analyst or participating laboratory is unaware of the origin of the test sample at the time of the analysis. An undeclared proficiency trial entails submitting samples for analysis blinded or masked.

**Blinding.** A term often used in connection with clinical trials of drug treatments in which knowledge of intervention assignments is hidden from participants and investigators, or outcome assessors. The term “double blinding” denotes a trial in which participants, investigators, and assessors are aware of the intervention assignments or treatment given throughout the trial. The term “single blind” denotes a trial in which the participant but not the investigator remains ignorant about the treatment received, whether placebo or active substance.

**Blood-brain barrier.** A permeable barrier consisting of cells and small blood vessels with the important task of controlling passage of endogenous and exogenous substances from the bloodstream into the brain and cerebrospinal fluid.

**BMI.** Is an acronym for body mass index and has been found to provide a useful measure of the degree of obesity. BMI is derived by dividing the person’s weight in kg by height in meters squared, hence the

units ( $\text{kg}/\text{m}^2$ ). Normal BMI ranges from 18.5 to 24.9, overweight spans from 25-29.9, grade 1 obesity is from 30-34.9, grade II obesity is from 35-39.9 and morbid obesity (grade III) is  $> 40$ . BMI furnishes a simple clinical tool for use by health care professionals to demonstrate obesity and the risk for certain diseases, such as diabetes type II and cardiovascular disease.

**Body alcohol turnover ( $B_{60}$ ).** This represents the rate of elimination of ethanol from the entire body and is usually expressed per unit of total body mass ( $\text{g}/\text{kg}/\text{h}$ ) or the entire body weight ( $\text{g}/\text{h}$ ). The turnover rate depends on the mass and metabolic capacity of the liver. Ethanol clearance rate from the whole body is calculated as the product of volume of distribution ( $V_d$ ), in units of liters/kg, and elimination rate of alcohol from blood ( $\beta$ ) in units of  $\text{g}/\text{L}$  per hour. This rate of body clearance can also be calculated by dividing the dose administered ( $\text{g}/\text{kg}$ ) by the extrapolated time to reach zero BAC ( $\text{min}_0$ ). A good rule of thumb is that a person can eliminate 0.1  $\text{g}/\text{kg}$  body weight per h or 7-8  $\text{g}$  per h for a person with a weight of 70-80 kg. This parameter seems to be the same for males and females, but varies between different animal species.

**Bolus.** The amount of drug swallowed at one time.

**Box plot.** A box plot is an increasingly common way to display information about the shape of a distribution, without showing individual values. For example, the box might extend from the 25<sup>th</sup> to 75<sup>th</sup> centiles of the frequency distribution and contain a line representing the median value. Lines projecting from the box (whiskers) are often added to show the extreme values of the distribution.

**Bronchi.** The large air-tubes or conducting airways of the lungs (one such tube is a bronchus).

**Bronchioles.** Small subdivisions and tiny branches of air tubes within the bronchi of the lungs.

**Bruise.** A bruise is a focal discoloration of the skin caused by an extra-vascular collection of blood under the intact epidermis. A bruise erupts after trauma to the body by the impact of a blunt instrument. Examination of bruises in the living and the dead to determine their age and cause is an important investigation in forensic medicine.

## C

**Calibrant.** A chemical substance obtained from a reliable and traceable source then used to calibrate an instrument to determining the analytical response as a function of concentration.

**Calibration.** A process or sequence of steps in which an analytical instrument or method is standardized to allow quantitative or semi-quantitative measurements. This is usually done by analysis of known strength standards prepared from pure substance and used to establish response of the instrument at increasing concentrations of the target analyte. The resulting calibration curve and appropriate response factors are then used for determining the concentration of the same substance in the unknown specimens.

**Candida Albicans.** A type of yeast or fungus sometimes found in living humans (skin, mouth, gut, vagina), that can utilize glucose to produce ethanol.

**Capillary.** A small blood vessel that branches from an artery; capillaries connect arteries to veins. Exchange of oxygen, nutrients and waste material takes place across capillary walls.

**Carbohydrates.** Organic compounds containing carbon, hydrogen and oxygen atoms in the molecule. Simple carbohydrates are sugars that are generally classified as monosaccharides, disaccharides and polysaccharides depending on the number of molecules in the chain. Examples of more complex carbohydrates are starch and fiber (cellulose). Carbohydrates are important nutrients that supply energy to the body actually 4  $\text{kcal}/\text{g}$ .

**Carbohydrate Deficient Transferrin (CDT).** Transferrin is a glycoprotein normally present in serum which helps to transport and deliver iron to the body. The analysis of CDT (a carbohydrate deficient form)



has proven to be a sensitive and specific biological marker of heavy continuous drinking. After drinking about 80 g ethanol per day for men and 60 g per day for women for 7 continuous days CDT levels are elevated.

**Case-control study.** This represents a powerful experimental design in which individuals having a certain disease or condition (the cases) are selected and compared to a control or reference group of individuals without the same condition or disease. The Grand Rapids study evaluated the risk of a motor-vehicle crash as a function of the driver's blood-alcohol concentration serves as a useful example of a case-control study. Those drivers involved in a traffic crash were cases and their BAC was compared to drivers not involved in a crash but who were driving close to where the crash occurred on the same weekday and at the same time of day.

**CEDIA.** This is an acronym for Cloned Enzyme Donor ImmunoAssay, which has become a widely used analytical technique in clinical and forensic laboratories. CEDIA is a rapid and fairly cheap method of analysis often applied to the determination of drugs of abuse in urine and other biofluids. The results serve as a preliminary screening analysis although positive test results need to be verified by more specific methods, such as GC-MS.

**Central nervous system (CNS).** The part of the nervous system consisting of the brain and spinal cord.

**Cerebellum.** The structure at the base of the brain involved in the control of muscle tone, balance, and sensorimotor coordination.

**Cerebral cortex.** This is the outer layer of gray matter covering the cerebellum. The cerebral cortex processes sensory information for the control of motor functions, speech, higher cognitive functions, emotions, behavior, and memory.

**Cerebrospinal fluid.** The clear fluid that fills the cavities (ventricles) that surround the brain and spinal cord.

**Certification.** A written document or declaration that a particular product or service complies with stated criteria.

**Chain-of-custody.** The procedure used to document how laboratories receive and handle specimens from the moment of collection, during transport, arrival at the laboratory, and during the testing process.

**Chromatography.** A widely used method of analysis that is able to separate compounds in a mixture based on their differential rates of movement through a two-phase system (e.g. gas-liquid, liquid-liquid, solid-liquid). The rate of movement of the molecules is determined by various physicochemical properties, such as size, solubility, boiling point, electric charge and functional groups present in the molecules.

**Chromosomes.** Microscopic rod-shaped structures composed of double stranded DNA and proteins and located within the cell nucleus. There are normally 46 chromosomes 23 inherited from each parent.

**Chronic tolerance.** The gradual decrease in degree of intoxication at the same blood alcohol level in the course of repeated exposures.

**Cirrhosis.** A type of chronic progressive liver disease in which the liver cells are replaced by scar tissue, they have hardened and turned an orange color – cirrhosis comes from the Greek word for orange-yellow.

**Clandestine Laboratory.** A clandestine laboratory is a secret and unlawful facility for production of narcotic drugs. These labs take many forms and might be a kitchen, garage, bathroom, or out-house equipped with the necessary glassware, apparatus, chemicals, organic solvents, and other materials necessary for the synthesis, isolation, or purification of drugs of abuse.

**Clinical laboratory science.** This entails examination of some part of the living patient – his excreta, or blood or secretions – to help the physician reach a diagnosis or provide a better treatment.

**Clinical Pharmacology.** The word pharmacology derives from a Greek word for drug (*pharmakon*) and discourse or reasoning (logos). Clinical pharmacology is concerned with the safe and effective therapeutic management of a patient with medicines. This is tightly linked to the concentrations of drugs determined in blood or plasma in relation to their therapeutic efficacy - hence the emergence of therapeutic drug monitoring (TDM) programs.

**Cognition.** The term cognition involves all the mental functions through which information and knowledge is processed. It includes global functions such as consciousness, drive and attention as well as specific functions like memory, language and calculations.

**Collagen.** The major protein of fibrous connective tissue e.g. tendons and ligament involved in the production of scar tissue produced in the liver.

**Coma.** A state of profound unresponsiveness, usually the result a blow or injury to the skull and brain. However, a person might become unconscious for other reasons, such as from overconsumption of alcohol or taking other psychoactive drugs. A comatose patient typically has closed eyes, cannot be roused and fails to respond to active “painful” stimuli, such as a pin-prick (see Glasgow Coma Scale).

**Compartment modeling.** A pharmacokinetic compartment represents a hypothetical space within the body having a certain volume and concentration of the drug. This hypothetical compartment is part of the overall pharmacokinetic model and is used to account for the observed changes in drug concentration as a function of time. A one-compartment model assumes instantaneous mixing of the administered drug in all body fluids and tissues. A two compartment model assumes two distinct spaces within the body - a central compartment into which drug initially distributes and a peripheral compartment that reaches concentration equilibrium with the administered drug more slowly.

**Compliance.** This refers to adherence to a prescribed regime of medication and taking the prescribed dose in accordance with the physician’s ordination

**Concentration.** The quantity of substance contained in a unit quantity of sample. When working with solutions, the recommended unit of concentration is grams of solute per liter of solution.

**Confidence interval.** In descriptive statistics this is the interval (range) within which the true value of a summary statistic (e.g. median or mean) is contained with a given probability.

**Confirmatory tests.** Such tests are used to verify (confirm) the presence of a particular compound in a biological specimen and usually involve some type of chromatography to separate closely related substances followed by detection and quantitation of a target analyte by mass spectrometry or other highly sensitive and selective conclusive method.

**Confounding.** Extraneous variables causing effects that obscure or exaggerate the “true” effect of an intervention or treatment.

**Congeners.** Substance or thing of the same kind or form, e.g. the other constituents of alcoholic beverages besides ethanol and water, such as other alcohols, aldehydes and esters.

**Correlation coefficient.** This is a statistic that measures the strength of the relationship between two variables, such as that between the analytical results using two methods of analysis on the same specimen. Correlation means degree of association but not necessarily good agreement. The correlation is usually depicted as a x-y scatter plot and Pearson correlation coefficient “r” is often given as r<sup>2</sup> meaning the proportion of the variation in y that is explained or predicted by variation in x.

**Controls.** Tests performed in parallel with experimental samples and designed to demonstrate that a

procedure worked correctly.

**COPD.** Is an acronym for **Chronic Obstructive Pulmonary Disease**, one of the most common lung disorders in adults world-wide and can lead to sudden death. COPD is characterized by limitations in air-flow caused by chronic bronchitis and emphysema owing to inflammation and excess mucus that decreases airflow. Those suffering from COPD have reduced forced expiratory volumes and might be unable to satisfy the breath-sampling requirements with some breath-alcohol analyzers. COPD ranks as one of the leading causes of death in developed nations in both men and women and smoking is one of the primary causes.

**Craving.** This refers to an intense desire to re-experience the effects of a psychoactive substance and represents the principal reason that people relapse to abuse of drugs after a period of abstinence.

**Creatinine.** Is a waste product of the body derived from creatine, which is a substance synthesized in muscles from amino acids. Creatinine is excreted in the urine and there is no reabsorption in the kidney. Creatinine is measure in blood to determine renal function. Creatinine content is also used as an indicator of the dilution of a urine specimen in connection with drug testing programs. A U-creatinine concentration below 0.2 g/L (20 mg/100 mL) indicates a dilute specimen and possible manipulation by adding water post-sampling or drinking water before voiding. However, urine specimens with U-creatinine < 0.2 g/L are not unusual when people consume alcohol, owing to the well-known alcohol-induced diuresis.

**Cross-over design.** This refers to a repeated measurement experimental design whereby the same subject or patient serves as his or her own control. The patient or test subject crosses-over from one treatment to another on the second measurement or test occasion, thus removing between subject sources of variation. Such designs are common in pharmacology testing and bioequivalence studies.

**Cross reactivity.** This refers to the response in an assay method caused by a substance other than the target drug intended to be analysed. Usually an antibody for an immunoassay recognises only a part of the target drug by binding to a specific functional group or structure in the molecule.

**Cross tolerance.** A physiological condition in which tolerance to the effects of one drug results in a diminished response to the effects of another substance.

**Cutaneous.** Associated with the skin – subcutaneous = beneath the skin.

**Cytochrome P450.** A family of enzymes found in animals, plants and bacteria that play an important role in drug metabolism. P450 enzymes metabolize (detoxify) foreign chemical substances that enter the body as well as many endogenous species. The P450 enzymes are found in the microsome fraction of cells especially liver cells (hepatocytes). The particular P-450 enzyme that metabolizes ethanol is denoted CYP2E1 or P450IIE1.

**Cytoplasm.** Or cytosol is the soluble fraction, the fluid or jelly-like substance within cells and outside the nucleus and is where many biochemical reactions take place.

## D

**Delirium.** Is a word used to describe shifting mental states, as reflected in altered cognition and perception and behavior, sometimes with hallucinations and an abnormal speech pattern.

**Delirium Tremens (DTs).** Is the syndrome described above that occurs after a period of chronic binge drinking, usually starting 1-2 days after last drink when the blood-alcohol concentration reaches zero. Often a drug such as lorazepam or diazepam is administered to the patient to counteract the worst withdrawal symptoms.

**Dementia.** This refers to a clinical syndrome characterized by a cluster of signs and symptoms manifested by difficulties in memory, disturbances in language and articulation, psychological and

psychiatric changes and impairment in the normal activities of daily life. Dementia is a consequence of Alzheimer's disease, which affects about 6% of the population aged over 65 y and increases with incidence during aging.

**Depressants.** These represent a class of psychoactive drugs, both licit and illicit, that relieve anxiety by depressing the central nervous system (CNS). Such drugs have a high abuse potential and ethyl alcohol is the prime example along with barbiturates and the sedative hypnotic chloral hydrate.

**DFSA.** An acronym for *drug facilitated sexual assault*, which conjures up the image of someone (a perpetrator) adding a substance (knock-out drug) to a person's drink with the intention of incapacitating an individual for the purposes of performing some illicit sexual act. Drugs often associated with date rape are rohypnol (flunitrazepam), GHB or z-hypnotics. However many studies show that the legal drug ethanol is the number one drug identified in blood samples from victims of DFSA.

**Diabetes.** A medical condition related to impaired metabolism of glucose owing to a deficiency in the production of insulin. This leads to increases in concentrations of sugar (glucose) in the blood (see hyperglycemia). Severe complications from diabetes might include heart disease, vascular disease and neurological disorders. There is no known cure for diabetes, but the disease can be managed by careful control of blood sugar level (see type I and type II diabetes).

**Diffusion plunge:** This refers to the sharp drop in BAC that occurs immediately after reaching  $C_{max}$  as often happens after ethanol is taken as a bolus dose on an empty stomach or after rapid intravenous infusion. During the diffusion plunge ethanol equilibrates between the blood and the rest of the body water. For some time after reaching  $C_{max}$  the concentration of ethanol in the blood is higher than expected for the person's body weight, volume of distribution and dose administered. Studies have shown that the half-life of the diffusion plunge for ethanol is about 5-10 min.

**Digestive system.** The organs responsible for getting food into and out of the body comprising the esophagus, stomach, liver, gallbladder, pancreas, small intestine, colon and rectum.

**Disposition.** This refers to the sum of all pharmacokinetics processes after a drug reaches the blood circulation, including distribution and elimination (metabolism and excretion) but excluding absorption and other pre-systemic processes.

**Distribution.** The transport of absorbed drug or alcohol by the blood-stream to all parts of the body. The distribution of alcohol follows the distribution of body water and the rate of distribution depends on the rate of flow of blood to various organs and tissue.

**Diuretic.** A drug (e.g. mannitol) that promotes water excretion by increasing the volume of urine produced.

**DNA.** Acronym for deoxyribonucleic acid, a family of large molecules located within the nucleus of a cell that contains genetic information by specifying the amino-acid sequence and hence the structure of proteins. DNA is a double-stranded helical molecule that encodes genetic information and is composed of the sugar deoxyribose, phosphate groups and the bases adenine (A), thymine (T), guanine (G) and cytosine (C). A run of three nucleotides called a triplet encodes one amino acid.

**Dopamine.** An important catecholamine neurotransmitter mainly found in basal ganglia of the central nervous system. Major physiological functions include inhibition and excitation of peripheral muscles, cardiac excitation and metabolic, endocrine and central nervous system actions such as pleasure and well-being. An underproduction of dopamine is seen in people suffering from Parkinson's disease and a common treatment is to administer the amino acid L-DOPA, a dopamine precursor. An overproduction of dopamine is seen in conditions such as schizophrenia.

**Dosage form.** The dosage form of a drug refers to the actual physical form in which the drug is given to the patient. This might be a liquid, tablet, capsule, coated tablets, spray or syrup. The particular dosage form of a

drug can markedly influence rate of absorption of active substance into the blood. For ethanol, the type of alcoholic beverage, whether beer (5% v/v ethanol), wine (12% v/v), spirits (40% v/v), cocktails (15% v/v) or simply pure ethanol solvent diluted with water or tonic can be considered dosage forms. Many alcoholic drinks contain sugars and other constituents that might delay rate of absorption by slowing gastric emptying.

**Drug.** Any chemical substance that influences body functioning.

**Drug Addiction.** A chronic relapsing disorder in which compulsive drug-seeking and drug-taking behavior persists despite serious negative consequences for the individual and his or her family and friends.

**Dubowski chart:** A chart or table originally produced by Professor KM Dubowski (Oklahoma City, USA) that displays well-known symptoms of drunkenness in relation to a person's blood-alcohol concentration (BAC). Originally called "Stages of acute alcohol influence/intoxication" the first chart appeared in 1954 but has been continually updated and the most recent version dates from 2012.

**DUI.** Acronym for driving under the influence (usually under the influence of alcohol DUIA).

**DUID.** Acronym for driving under the influence of drugs.

**Duodenum.** The first part (~12 inches) of the small intestine extending from the pylorus to the jejunum.

**DWI.** Acronym for driving while impaired (usually taken to mean impairment caused by alcohol).

**Dystonia.** A disorder of the central nervous system leading to altered muscle tone and recurrent spasms. Some patients experience sustained muscle contractions, repetitive twisting movements, and abnormal postures of the trunk, neck, face, arms or legs.

## E

**Ecstasy.** The popular name for a recreational drug of abuse 3,4-methylenedioxyamphetamine (MDMA). Like amphetamine and methamphetamine, MDMA acts as a central nervous stimulant.

**Edema.** Excess accumulation of fluid in extracellular body tissue spaces usually resulting in swelling.

**EIA** = Acronym for Enzyme ImmunoAssay.

**Electromagnetic spectrum.** This constitutes the range of all possible frequencies of electromagnetic radiation or energy from very high energy (short wavelength) such as gamma rays to very low energy (long wavelength) such as radio waves. Other examples of electromagnetic radiation include X-rays (0.5-1.5 angstroms), ultraviolet, visible (4000-7000 angstroms), infrared, and microwaves. Note that 10 billion angstroms = 1 meter.

**Elimination.** The term used to denote removal of a drug (e.g. alcohol) from the body. The process of elimination involves both metabolic breakdown (biotransformation) and removal in an unchanged form, such as in breath, urine, and sweat (excretion).

**Elimination rate constant.** For drugs that obey first-order kinetics, the elimination rate constant ( $k_{el}$ ) corresponds to the slope of concentration-time curve plotted on log-linear coordinates. The units of  $k$  are reciprocal time ( $h^{-1}$  or  $min^{-1}$ ). For drugs eliminated by zero-order kinetics a constant amount of drug is eliminated independent of the concentration in the blood. The slope of the pseudolinear phase of the C-T curve for ethanol is commonly denoted by the Greek letter  $\beta$  or  $k_o$ .

**ELISA** Is an acronym for Enzyme Linked ImmunoSorbent Assay a method of analysis of widely used as a preliminary screening test for drugs of abuse testing in urine or other body fluid.

**EMIT.** Is an acronym for Enzyme Multiplied Immunoassay Technique, which is widely used in analytical toxicology as a preliminary screening tests, such as during urine drug testing programs. EMIT is a homogenous assay and a major advantage is that a prior clean-up or extraction of analyte from the biological matrix prior to analysis is not necessary. EMIT involves an antibody-antigen reaction where a candidate drug in the biological specimen (urine or blood) and the same drug labelled with the enzyme glucose-6-phosphate dehydrogenase compete for binding sites on the antibody.

**Endocrinology.** This is the study of hormones and their effects and the system of organs or glands that produce hormones.

**Endocrine glands.** Glands that secrete hormones (chemicals) directly into the bloodstream, such as pituitary glands, adrenal glands, and thyroid glands.

**Endogenous.** Substances produced or originating within the body by natural processes, such as normal metabolic processes.

**Endoplasmic reticulum.** This is a type of organelle within the cytoplasm of cells. There are two types of endoplasmic reticulum, rough and smooth. It is the smooth endoplasmic reticulum that contains the detoxification P450 enzymes.

**Enzymes.** Protein molecules that serve to speed-up chemical reactions in the body - An enzyme acts as a catalyst for promoting biochemical reactions.

**Epidemiology.** Derived from the Greek *epidemia* or prevalence of disease. The branch of medical science concerned with the incidence and distribution of disease.

**Epilepsy.** The term epilepsy applies to a group of central nervous system disorders characterized by recurrent seizures, which are sometimes called convulsions. Seizures can affect vision, speech or movement.

**Erythrocytes.** The name given to the red blood cells.

**Error.** The word error comes from a Latin root for wander or stray, although in the field of metrology a measurement "error" does not mean a mistake was made. Instead, error is a technical term denoting deviation of the measured value from an average or some assigned or computed quantity. Such deviations are considered to be either "random" or involve the notion of a "constant error" or a bias (see accuracy and precision).

**Esophagus.** A tube-like structure connecting the pharynx with the stomach.

**Ethyl glucuronide.** Abbreviated EtG is a non-oxidative metabolite of ethanol formed in the liver by a phase II enzyme catalyzed reaction involving glucuronic acid (glucuronidase). EtG is eliminated from the body more slowly than ethanol itself, which makes it useful to analyze as a biomarker of recent drinking. EtG analysis has found applications when people, for various reasons, are not permitted to drink alcohol, such as in safety-sensitive work, military or surgical operations, or in recovering alcoholics. Great care is needed when concentrations of EtG are interpretation and appropriate cut-off levels need (e.g. >0.5 mg/L in urine) because everyday materials contain alcohol, such as cough medicines, shampoos, hand-rubs, mouth-wash etc.

**Ethyl sulfate.** Often abbreviated EtS is a non-oxidative metabolite of ethanol formed in the liver by a phase II enzyme catalyzed reaction involving sulfatase and ethanol. EtS is also eliminated in the urine over a much longer time than ethanol itself serves as a biomarker of recent drinking. EtS appears to be a more specific test for recent drinking than EtG.

**Excretion.** This refers to removal of a drug or alcohol in an unchanged form in body excreta - urine,

breath, sweat, stools, and saliva (if the latter is ejected as oral fluid).

**Exogenous.** Produced or originating outside the body.

**Exsanguination.** From Latin ex = out of, and sanguine = blood. Hence to be drained of blood. Extensive loss of blood, owing to internal or external hemorrhage, is a major cause of death after trauma.

**External proficiency tests.** These are designed to test the proficiency of work done at analytical laboratories. A good track record in such tests has become an important element in laboratory accreditation. Aliquots of the same specimen (spiked samples) containing known concentration of the analytes are sent for analysis to participating laboratories, e.g. clinical chemistry or toxicological laboratories. Most proficiency tests are “declared trials” that is the participating laboratories know that they are being evaluated. In a blind proficiency trial, that test specimens are masked and the laboratory is unaware it is being evaluated. The results from blinded trials are considered much more informative, but such trials are more difficult to organize.

**Extravascular.** Outside of the blood stream.

**Extracellular fluid.** Fluid outside the cells (interstitial fluid and plasma) amounting to about 20% of body weight.

**Exocrine glands.** These are glands that secrete their product out of the gland through a duct and into a cavity; the enzyme producing glands of the pancreas are typical examples.

## F

**False positive rate.** This represents the proportion of healthy subjects who give a positive test result when screened for a certain disease state.

**False negative rate.** This is the proportion of subjects with the disease but who give a negative test result.

**Fatty liver.** An accumulation of fat in the liver (steatosis) represents the first stage of deterioration of this important body organ often the result of a period of heavy drinking. Fatty liver is reversible on termination of drinking and a period of abstinence.

**Fatty acid.** A compound made up of a hydrocarbon chain (either saturated or unsaturated) terminating in a carboxylic acid group.

**Fatty acid ethyl ester (FAEE).** These are compounds formed in the body in enzyme catalyzed reactions between ethanol and short chain fatty acids, such as ethyl palmitate, stearate, oleate, linoleate and arachidonate. Analysis and identification of FAEE have been suggested as biomarkers of heavy drinking and organ damage.

**Fermentation.** An enzymatically controlled anaerobic decomposition of carbohydrates to produce ethanol and liberate carbon dioxide.

**Fibrosis.** The formation of fibrous (scar) tissue another intermediate stage of liver deterioration.

**First-order kinetics.** In a first-order reaction, the change in drug concentration at any time ( $-dC/dt$ ) is proportional to the concentration in blood or plasma at that time. Proportionally more of the drug is eliminated at high concentrations in blood than at low concentrations. The C-T plot for a drug that is metabolized by first-order kinetics is an exponential function when plotted on Cartesian graph paper. The C-T profile becomes a straight line after making a logarithmic transformation. The meaning of  $k_1$  is not easy to conceptualize so elimination rate is mostly expressed as an elimination half-life (see below), which is independent of drug concentration.

**First-pass metabolism.** This refers to the metabolism (removal) of part of the dose of a drug such as alcohol when administered orally and before it reaches the systemic circulation. First-pass metabolism can occur either in the stomach or in the liver and for some substances also in the lung.

**Forensic.** From the Latin word *forensis* meaning of the forum. In ancient Rome the forum was where debates took place and as such served as the courtroom.

**Forensic toxicology.** A scientific subject closely related to analytical chemistry that deals with the isolation, identification and quantitative analysis of drugs, poisons and their metabolites in biological specimens and the interpretation of the analytical results in a legal or medico-legal context.

**Forced vital capacity (FCV).** This is the maximum volume of air exhaled from full inspiration to forced maximum expiration. The values are usually expressed as a percentage of the normal predicted value for healthy individuals.

**Forced expiratory volume in one second (FVC<sub>1sec</sub>).** This represents the volume of exhaled air in the first second of a forced exhalation. The result is usually expressed as a percentage of the expected value for healthy individuals.

**FPIA** Acronym for Fluorescence Polarization ImmunoAssay an analytical method used to determine drugs in body fluids such as in urine-drug testing laboratories

**Free radicals.** Molecular intermediates that have a single unpaired electron often produced during oxidation reactions. They are highly reactive and readily attack other molecules.

**Fuel cell.** A fuel cell is a device that converts energy from a chemical reaction into electricity through a chemical reaction with oxygen. Such electrochemical detectors are widely used in instruments for breath-alcohol analysis.

## G

**GABA.** This is an acronym for gamma-aminobutyric acid. GABA is the major inhibitory neurotransmitter in the brain and activation of GABA receptors lowers activity of nerve cells - applies brakes on the brain. There are two main types of GABA receptor denoted type A and type B. The GABA-A receptor is a so-called ligand-gated ion channel and when an agonist drug binds this facilitates binding of GABA increasing the flow of chloride ions into the adjacent cell. Depressants of the central nervous system, such as ethanol, barbiturates, and benzodiazepines, have binding sites on the GABA-A receptor and work via an allosteric regulation, that is an interaction with areas of the receptor protein away from the site that binds the natural ligand.

**Gas Chromatography.** An analytical technique widely used for separating volatile substances on the basis of their solubility and partition between a gas and a liquid phase (GLC) or a gas and solid phase (GSC).

**Gastrectomy.** Surgery to remove part of the stomach.

**Gastric bypass.** A surgical procedure used in the treatment of morbid obesity that involves bypassing the duodenum and other segments of the small intestine. The operation involves dramatically reducing the size of the stomach and is the most effective way to restrict food intake and to go down in weight.

**Gastroparesis.** Gastro means pertaining to the stomach and *paresis* means paralysis, hence paralysis of the stomach or a condition that results in delayed emptying. A meal might be retained in the stomach for much longer than normal in people who suffer gastroparesis. A delayed gastric emptying is common in type I and type II diabetes, owing to elevated levels of sugar in blood, which influence the vagus nerve controlling contractions of the stomach and the passage of food into the intestines.

**General anesthetic.** An agent (drug) that renders a person unconscious and oblivious to pain, examples



include nitrous oxide, chloroform diethyl ether and halothane.

**General anesthesia.** This refers to a drug-induced reversible condition that includes specific behavioral and physiological traits – unconsciousness, amnesia, analgesia, and akinesia.

**GERD.** Abbreviation for gastroesophageal reflux disease which is a clinical syndrome that manifests as heartburn and regurgitation, owing to reflux of gastric contents into the esophagus.

**Gene.** A sequence or segment of DNA consisting of a series of paired nucleotides at a particular location on a chromosome that together constitute a unit capable of expressing the amino-acid sequence required to synthesize a protein. A mutation in a gene can alter the functioning of the encoded protein.

**Generic.** A nonproprietary drug name usually describing the drug's chemical structure and not protected by a trademark.

**Genotype.** The entire genetic makeup of an individual. The fundamental constituents of an organism in terms of its hereditary factors.

**Gestational diabetes.** A medical state characterized by glucose intolerance of variable severity that begins or is first diagnosed during pregnancy and usually resolves not long after delivery. A smell of acetone on the breath might be evident in women with this condition. It is important to distinguish this condition from type 2 diabetes

**Glasgow Coma Scale (GCS).** A clinically useful neurological scale originally developed by neurosurgeons working in Glasgow, Scotland. The scale was initially developed and intended to provide an objective way to evaluate and record the conscious state of trauma patients. The GCS is a way to document the level of consciousness before various treatment options are considered. Use of the scale has been extended to other clinical situations, such as drug-related intoxicated state and coma. Individual elements of the scale include assessment of eyes, verbal communication and motor responses and perception of pain (pin-prick). The three elements separately and their sum are considered in the final diagnosis. The lowest possible GCS score is 3 (deep coma or death), while the highest is 15 (fully awake).

**GLP.** Stands for **Good Laboratory Practice**, which implies high quality work performed analytical service laboratories. An important element of GLP is the proper training of staff, who are expected to be familiar with and adhere to standard operating procedures (SOPs), which are written instructions specifying use of approved materials, reagents and equipment. All records of analytical results including chromatograms and spreadsheets must be retained for later verification, authenticated and inspection. Quality assurance personnel are responsible for ensuring that the laboratory work is done in accordance with acceptable procedures and according to current SOPs.

**Glucagon.** A hormone secreted by cells of the pancreas in response to low blood sugar. This hormone promotes an increase in blood sugar levels by initiating the breakdown of liver glycogen to produce glucose.

**Gluconeogenesis.** Synthesis of glucose from non-carbohydrate precursors, such as protein and fat. This process begins when blood glucose levels are abnormally low and cellular levels of carbohydrates, such as liver glycogen stores are depleted.

**Glutamate.** An amino acid that serves as the major excitatory neurotransmitter in the brain.

**Glutathione (GSH).** An antioxidant molecule found naturally in the body, composed of three amino acids, glutamate, cysteine and glycine.

**Glycogen.** A polysaccharide and the principle carbohydrate reserve in the body. Excess glucose is converted to glycogen and is stored in the liver and muscle. Glycogen can be converted easily into

glucose when more energy is required, however these reserves are short-lived and glucose then needs to be synthesized from endogenous substances such as proteins.

**Glycogenesis.** Formation of glycogen from glucose molecules.

**Glycogenolysis.** Hydrolysis of glycogen to glucose.

**Glycolysis.** A sequence of biochemical reactions involved in the metabolic breakdown of glucose, which is converted to either lactate or pyruvic acid.

**Gout.** The clinical syndrome of gout arises from deposition of urate crystals (salt of uric acid) in joints, where they cause an inflammatory response. One of the factors that increase serum urate levels leading to attacks of gout is heavy drinking. During metabolism of alcohol one of the metabolic disturbances is a preferential conversion of pyruvate to lactate and lactacidosis. The lactate competes in the kidney for excretion with ureate and this causes an elevation of serum urate concentrations.

**G-Proteins.** G-proteins are involved in neural signal transduction through the cell membrane and have the ability to activate different cellular amplifier systems. They get their name because they bind guanosine triphosphate (GTP). Various aspects of alcohol addiction, such as development of tolerance and dependence, may depend on altered signaling via G-proteins. Credit for the discovery of G-proteins and elucidation of their function was recognized in 1994 when Alfred Gilman and Martin Rodbell shared a Nobel Prize in Medicine or Physiology.

## H

**Half-life:** The elimination half-life ( $t_{1/2}$ ) of a drug is an important concept in clinical pharmacology because it expresses the rate of change in concentration in blood or plasma in units of time. For drugs metabolized by first-order kinetics, the half-life expresses the time required for the concentration of active substance in blood or plasma or amount of drug in the body to decrease by half or 50%. After five half-lives, ~97% of the drug is eliminated from the body. For a drug metabolized according to first-order kinetics, the important relationship  $t_{1/2} = 0.693/k_1$  operates where 0.693 = natural logarithm (Ln) of two.

**Halitosis.** Halitosis comes from the Latin word *halitus* meaning breath and describes any unpleasant breath odor. Halitosis is usually known as bad breath and is a common complaint in adults and children caused by poor oral hygiene, ulcers and infections in the mouth. Some cases of halitosis are the result of gastrointestinal conditions or respiratory tract infections or metabolic diseases.

**Hallucinogens.** Are drugs or naturally occurring substances that bring about a state of dreaming or wandering of the mind characterized by an altered perception of sights and sound. The classic hallucinogenic drug is LSD (lysergic acid diethylamide) as well as psychoactive substances occurring naturally in various plants or fungi.

**Headspace.** Headspace is the gaseous phase above a sample (e.g. blood or urine) of a liquid or solid material that contains volatile or semi-volatile compounds that are released from the liquid or solid material. Headspace gas chromatography is the accepted "gold-standard method" for the analysis of ethanol and other volatiles in forensic toxicology.

**Helicobacter pylori.** *H Pylori* is a common bacterium found in the mucous lining of the stomach in millions of people worldwide (50% of people over 60 y in USA). *H Pylori* is the primary cause of gastric ulcers and also duodenal ulcers. The discovery of *H Pylori* by two Australian scientists was rewarded with a Nobel Prize in Physiology or Medicine in 2005. Previously ulcers were thought to be the result of stress or poor diet such as by eating foods high in acid content.

**Hematocrit.** The percentage of blood volume occupied by erythrocytes; normal values often cited are 44-54% for men and 38-48% for women. Blood with a lower hematocrit contains more plasma and accordingly a higher percentage of water per unit volume blood.

**Hemolysis.** This term is used to describe the bursting or breakage of red blood cell (RBC) membranes, causing the release of hemoglobin and other constituents into the surrounding fluid. A reddish coloration of the serum or plasma fraction gives evidence that a blood specimen has undergone hemolysis.

**Henry's law.** This refers to a scientific principle discovered by William Henry (1774-1836) that teaches us about the solubility of gases. The concentration of a volatile substance dissolved in a liquid in a closed container and kept at a constant temperature and pressure is directly proportional to the concentration of that substance in the air phase in equilibrium with the liquid.

**Hepatic vein.** This is the vein that receives blood after it passes through the central veins of the liver transporting blood into the inferior vena cava of the heart.

**Hepatitis.** Generalized inflammation of the liver and characterized by jaundice, fever, liver enlargement and abdominal pains. Hepatitis is often accompanied by tissue death and fibrosis (scar tissue). The name derives from *hepat* the Greek word for liver and *itis* the Greek word meaning inflammation. Many different chemical agents, including drugs and alcohol, can cause inflammation of the liver. Alcoholic hepatitis can prove fatal but is usually reversible on abstinence.

**Hepatocyte.** The name of the principal cells within the liver responsible for most of the metabolic activity.

**Heritability.** The proportion of observed variation in a particular trait that can be attributed to inherited genetic factors as opposed to changes brought about by environmental factors.

**Histogram.** A histogram is a graphical method used to display the frequency of continuous data, such as a person's height, age or concentration of a substance in blood, divided into suitable intervals. The horizontal axis displays the limits that are used for each interval and above these a rectangular column rises from the mid-point. The vertical axis measures the number of values (frequency) that fall within each interval or if desired the percentage thus giving a relative frequency distribution.

**Homeostasis.** The maintenance of a relatively constant internal body condition; a state of equilibrium within the body with respect to functions and chemical composition of body fluids and tissues.

**Hormone.** A chemical messenger produced in an organ or tissue and transported to another part of the organism where it produces a behavioral or physiological response (effect).

**HPLC** Acronym for High Performance Liquid Chromatography a widely used analytical technique in forensic and other laboratories for separation and quantification of chemical substances such as drugs of abuse in bio-fluids. The liquid chromatography part (LC) is often used in combination with mass spectrometry (MS) to give hyphenated LC-MS a very powerful analytical combination.

**Hydrophilic.** Attracts water - water liking

**Hydrocarbon.** A class of organic compounds with only hydrogen and carbon atoms in the molecule.

**Hyperglycemia.** Means high blood glucose and is a medical condition when there is an excessive amount of glucose in the bloodstream. Normal blood glucose is between 70-110 mg/100 mL. People get most of the glucose they need after digestion of the food they eat. Hyperglycemia can occur when production of insulin is insufficient or that produced cannot be properly utilized. Onset of hyperglycemia is fairly slow and people tend to feel thirsty, they produce large volumes of urine, are hungry and have a dry mouth. High levels of blood glucose are not associated with behavioral impairment, such as occurs in states of hypoglycemia. Untreated hyperglycemia leads to a dangerous condition known as ketoacidosis and diabetic coma. Under these circumstances there is usually a fruity acetone-like smell on the person's breath.

**Hypertension.** High blood pressure measured as a ratio of systolic (100-140 mm Hg) to diastolic (60-90

mm Hg). High blood pressure is defined as a persistent ratio of systolic/diastolic of 140/90 mm Hg.

**Hypoglycemia.** Low blood glucose is a potentially dangerous medical condition characterized by an abnormally low concentration of glucose in the blood. The body either has too much insulin or a person does not eat any food for considerable time (starvation) or after strenuous physical activity or exercise. Low blood sugar can arise if a diabetic injects too much insulin, and the resulting is an insulin shock reaction. Some of the symptoms of hypoglycemia resemble those associated with alcohol impairment, such as slurred speech, dizziness, disorientation etc. Onset of hypoglycemia is fairly rapid and if left untreated can lead to loss of consciousness or produce seizures.

**Hypoventilation.** The term hypoventilation defines a condition in which alveolar ventilation is insufficient to meet the metabolic demands of the individual and carbon dioxide content in blood is too high.

**Hypoxia.** A lower than normal level of oxygen in the blood or tissue.

## I

**Impairment.** A condition associated with certain medical conditions and particularly after use of psychoactive drugs. Impairment is manifested by the person's decreased ability to perform skilled tasks, such as driving.

**Incidence.** The number of new cases of a variable (condition, symptoms, disease, or trait) occurring during a particular period of time. Incidence is the measure of new cases in a given time period (rate) and has the units of cases per population at risk per unit time (i.e. the number of new cases of a specific disease occurring during a certain period).

**Inflammation.** A defensive response to local tissue injury or infection, serving to prevent the spread of injury and activate the immune system.

**Infrared.** Pertaining to the region of the electromagnetic spectrum from approximately 0.78 to 300 microns.

**Insulin.** A hormone produced in the islets of Langerhans special cells within the pancreas and which is released in response to elevated blood sugar levels. The hormone permits the metabolism and utilization of glucose. Insulin in fairly pure form was prepared first at the University of Toronto and led to successful treatment of diabetes. Two of the scientists involved (Banting and Macleod) shared a Nobel Prize for their work in 1923.

**Interfering substance.** A chemical compound or substance other than the substance of interest (e.g. ethanol) to which the measuring instrument responds to give a falsely elevated result.

**Inter-individual variation.** The distribution of a measurement or a quantity in a given sample of individuals.

**Intra-individual variation.** The distribution of measured values of a quantity in a given individual over time.

**Intravascular.** Within the blood vessels.

**Intracellular fluid.** Fluid within the cells making up about 40% of body weight.

**Interstitial fluid.** Fluid between the cells.

**In-vivo.** From the Latin meaning *in the living body* a term commonly used to signify tests made with living subjects (humans or animals).

**In-vitro.** From the Latin meaning *in glass* a term commonly used to signify experiments done in a test tube or flask as opposed to in the living organism.

**Ischemia.** A condition in which blood flow to a body organ or tissue is restricted.

**Isozyme or isoenzyme.** This is a form of an enzyme (protein), which serves the same function as another enzyme, but has a slightly different composition and arrangement of the amino- composition and shows different kinetic properties.

**Isotopes.** Are different forms of a chemical element that differ in atomic mass. Isotopes contain the same number of protons in the nucleus but a differing number of neutrons hence a different mass number. Drugs labeled with isotopes of hydrogen or carbon are widely used in clinical and biomedical research as biomarkers or tracers. Examples include deuterium oxide  $^2\text{H}_2\text{O}$ , which contains a stable isotope of hydrogen (deuterium) and tritiated water  $^3\text{H}_2\text{O}$ , which contains the radioactive isotope of hydrogen or tritium.

## J

**Jejunum.** Pertaining to the second part of the small intestine from the duodenum to the ileum.

## K

**Ketogenesis.** The production or synthesis of ketone bodies consisting of acetone, acetoacetate, beta-hydroxybutyrate.

**Ketosis.** A condition characterized by the enhanced production of ketone bodies, e.g. during starvation or in disease states such as diabetes mellitus.

**Ketonuria.** Excess ketone bodies in the urine

**Ketonemia.** Excess ketone bodies (acetone, acetoacetate and  $\beta$ -hydroxybutyrate) in the blood.

**Ketone bodies.** These are the end-products of lipid (fat) metabolism whereby triglycerides are transformed to free fatty acids and then acetylCoA, which functions as precursor of acetoacetate. This compound either undergoes non-enzymatic decarboxylated to give acetone or is reduced enzymatically in a NAD-NADH reaction to give beta-hydroxybutyrate.

**Kidneys.** These are two bean-shaped organs about the size of a clenched fist located near the middle of the back and below the rib cage. The main function of the kidneys is to filter blood a process that takes about 30 min. Components that are useful are retained and waste products of metabolism and excess fluid are removed and transported to the bladder for excretion. Another function of the kidneys is to regulate blood pressure and the number of red blood cells.

**Kinetic properties.** Characteristics of an enzyme including rate of reaction ( $V_m$ ) and affinity for substrates ( $K_m$ ).

## L

**Lactic acid.** An organic acid produced from pyruvate during anaerobic metabolism.

**Licit.** Means lawful or permitted and describes pharmaceutical preparations obtainable on prescription or over-the-counter as opposed to illicit or unlawful drugs classified as controlled (scheduled) substance, such as heroin, methamphetamine and cannabis.

**Lipase.** A pancreatic enzyme that facilitates the digestion of fats.

**Lipids.** Fatty substances - a class of organic compounds that include fats, waxes, oils, (triglycerides)

phospholipid and sterols (cholesterol) consisting largely of esters formed by combining fatty acids with alcohols or other molecules.

**Lipogenesis.** The synthesis of lipids from glucose and amino acids.

**Lipid peroxidation.** The destructive metabolism of lipids (fatty substances) within cells by chemical oxidation leading eventually to the destruction of cell membranes.

**Limit of detection (LOD).** The smallest result obtainable by a given measurement procedure that can be accepted with a stated level of confidence as being different from the value of the measurable quantity obtained on blank material; by convention  $LOD = 3 \times s_0$  where  $s_0$  is the standard deviation of measurements without the analyte present, e.g. blanks.

**Limit of Quantitation (LOQ).** The lower limit of concentration or amount of substance that must be present before a method is considered to provide quantitative results. By convention,  $LOQ = 10 \times SD_0$ , where  $SD_0$  = the estimate of standard deviation at the lowest level of concentration measurable.

**Linear regression.** A mathematical method to describe the relationship between two or more variables and which entails calculating a best-fitting straight line to a set of data points, the x-variable is denoted as the independent and the y-variable the dependent.

**Lipophilic:** Lipid-liking, the propensity of a chemical substance to dissolve in fats in preference to water.

**Liver steatosis:** Another name for fatty liver and implies an accumulation of lipids in the liver cells (hepatocytes) contributing to ~5% of liver weight.

**Local anesthesia.** In contrast to general anesthesia, local anesthesia refers to a deadening of pain at a specific area of the body by injecting an anesthetic agent. This permits a medical procedure being performed without the patient feeling any pain e.g. dental operation, taking a biopsy, stitching a wound etc. The patient is awake and can speak to the physician during the procedure.

**Lumen.** In biology, a lumen is the inside space of a tubular structure, such as an artery or vein or the stomach or intestine. The gastric lumen is the inside space of the stomach.

## M

**Macronutrients.** Refers to dietary nutrients as sources of energy and are required in large quantities, namely protein (4 Kcal per g), fat (9 Kcal per g) and carbohydrate (4 kcal per g).

**Micronutrients.** Refers to the vitamin and mineral constituents of the diet.

**Malnutrition.** A deficiency in protein and energy, a complication often seen in alcoholics, who get most of their daily calories from combustion of alcohol.

**Matrix.** The material that contains the analyte of interest, e.g. blood, urine or tissue.

**Matrix Effects.** Influence of a component in the analytical sample other than the component being investigated and how this impacts on the accuracy and precision of the measurements being made.

**Mean corpuscular volume (MCV).** Refers to the average size of a red blood cell. MCV is a crude biomarker of heavy drinking with abnormally high MCV being one indication of over consumption.

**Median.** The middle value of a ranked set of measurement data. For skewed data the median is a better measure of central tendency than the arithmetic mean and is always lower than the mean. In a normal distribution the mean and median are the same.

**Medical eponym.** This is the name of a disease or condition based on the name of a person or place when the condition was first described. Eponyms have by tradition been used to honor the research scientist or physician who first discovered or documented the disease or condition. Examples include Parkinson's disease, Alzheimer's disease etc

**Mellanby effect.** Named after Sir Edward Mellanby (1884-1955) a British pharmacologist who investigated the fate and actions of alcohol. Based on animal studies he found that impairment effects after a given dose were more pronounced on the ascending limb of the blood alcohol curve (absorption phase) compared with the descending limb (post-absorptive phase). The pharmacological response to a given dose of alcohol was more marked when the BAC was rising compared with the same concentration when BAC is falling. Another term for the Mellanby effect is acute tolerance developing during a single exposure to the drug.

**MEOS.** An acronym for **M**icrosomal **E**thanol **O**xidizing **S**ystem, which refers to a family of oxidative enzymes located mainly in a subcellular component of liver cells (hepatocytes). The MEOS enzymes can metabolize drugs and other foreign chemicals as well as endogenous substrates. The particular MEOS enzyme involved in oxidative metabolism of ethanol to acetaldehyde is denoted CYP2E1 where CYP stands for cytochrome.

**Meta-analysis.** A statistical method used to combine the results of different studies. A common application of meta-analysis is the pooling of results from a set of randomized controlled trials, none of which alone was powerful enough to demonstrate statistical significance.

**Metabolism.** The name given to various chemical reactions occurring in a cell, an organ, or the body as a whole. The term is sometimes applied more narrowly to the breakdown of a particular substance e.g. the degradation of ethanol or some other drug by specific enzymes.

**Metabolite.** A compound produced by a chemical reaction taking place in the body, such as the metabolism of a drug or chemical substance; acetaldehyde is a metabolite of ethanol.

**Metrology.** The science of measurement.

**Mitochondria.** Are observed as subcellular fraction of liver cells often obtained by differential centrifugation of liver homogenates and are contained in fragments of the endoplasmic reticulum. The enzyme contained in liver mitochondria are denoted (e.g., CYP2E1, CYP2D6, CYP2C19) where CYP stands for cytochrome and these are responsible for metabolism of many types of drugs.

**Microsomal enzymes.** Detoxifying enzymes (cytochrome P450) associated with certain membranes (microsomes) within the liver cells.

**Microvilli.** Plural of villus, referring to small vascular protrusions growing on a mucous surface. The intestinal villi are the microscopic thread-like or finger-like projections covering the mucosa of the small intestine with main function to increase the absorption surface area of the cell.

**Micturition.** Medical term for the passing of urine.

**Mitochondria.** Small spherical rod-shaped structures within the cytoplasm that generate most of the cell's energy through the production of adenosine triphosphate (ATP).

**Michaelis-Menten (M-M):** A German Leonor Michaelis (1875-1949) and a Canadian Maud Menten (1879-1960) collaborated to develop an equation to describe the kinetics of biochemical reactions in terms of a capacity limited process (saturation kinetics), often associated with enzymatic reactions. The parameter  $V_{max}$  defines the maximum velocity of the reaction and  $k_m$  is the Michaelis constant, which characterizes the affinity of the enzyme for a particular substrate. The  $k_m$  for ethanol in human liver alcohol dehydrogenase (class I) is about 0.1 g/L and  $V_{max}$  is about 0.22 g/L/h.

**Mode.** The most frequently occurring value in a set of numbers.

**Motor function.** This is a general term and refers to movement, mobility and behavior.

**MS** Short for mass Spectrometry a powerful analytical technique used to identify compounds based on their mass to charge ratios. After separation from the biological matrix by chromatography drugs are commonly identified by mass spectrometry. This entails bombarding the molecules with electrons thus causing them to disintegrate into characteristic mass fragments, which are collected amplified and displayed in the form of a mass spectrum.

## N

**NAD.** Acronym for nicotinamide adenine dinucleotide (NAD), which is an important cellular coenzyme that accepts a hydrogen atom during biochemical reactions, such as the oxidative metabolism of ethanol. NAD<sup>+</sup> is simultaneously reduced to NADH when ethanol is oxidized to acetaldehyde. The function of the NAD-NADH redox couple is to move hydrogen atoms back and forth between various oxidation-reduction reactions within the cell.

**NAFLD.** Acronym for non-alcohol fatty liver disease, which refers to development of a fatty liver that by mechanisms other than chronic heavy drinking. Excessive fat can deposit in the liver by inappropriate dietary intake, e.g. eating junk food or some metabolic disorder, such a type II diabetes or obesity.

**Necrosis.** Cell death that occurs in response to adverse conditions in the cell's environment.

**Neoformation:** Means new formation or generation and is used in forensic medicine and toxicology to signify formation of ethanol in bodies after death.

**Nephron.** From Greek nephros = kidney is the anatomical and functional unit of the kidney. Each kidney contains about 1.3 million nephrons. The nephron consists of five distinct functional parts, including the glomerulus, the proximal tubule, the loop of Henle, the distal tubule, and the collecting duct.

**Neurotransmitters.** These are brain chemicals that transmit messages from one nerve cell (neuron) to another. They are located and released in the brain and the impulse travels through the axon and can activate or inhibit an adjacent neuron.

**Neuron.** A nerve cell - the functional unit of the nervous system consisting of the nerve cell body, the dendrites and the axon.

**NMDA.** N-methyl-D-aspartate, a synthetic amino acid capable of activating certain glutamate receptors.

**Nystagmus.** Rhythmical oscillation (bouncing or jerking movement) of the eyeballs often involuntary. Gaze nystagmus occurs when the eyes gaze or move to the side along a horizontal plane.

## O

**Obesity.** The word obesity is derived from the Latin word meaning "to overeat". A person is considered obese if they have a body mass index (BMI) over 30 kg/m<sup>2</sup>. BMI is calculated by dividing weight in kilograms by square of the height in meters and the healthy range is from 18.5 to 25. Although BMI provides a useful clinical guide of obesity it does not allow for variations in build and body composition. For example athletes with an excess of muscle mass would be considered overweight based on a BMI calculation.

**Oedema:** An excessive accumulation of fluid (serum), which is retained in tissue spaces of the body resulting in swelling. In US the term used more commonly is edema.

**Oliguria.** A significant decrease in the volume of urine excreted (< 400 mL/day).



**Ordinal scale.** Ordered set of measurements consisting of words and or numbers indicating the magnitude of the possible values that a type-of-quantity can take.

**Osmolality.** Is used in clinical chemistry as an expression of the concentration of a biological fluid, e.g. serum or urine. It is expressed in terms of the total number of solute particles present per kilogram solvent (water). A random urine void might have an osmolality ranging from 50 to 1400 mOsmol/kg

**Outlier.** One value in a series of measurements so distant from the other data points as to suggest that it may come have some unusually large error of measurement involved.

**OUI.** Acronym for operating a motor vehicle under the influence of alcohol, which is an alternative term used in some US states for driving a motor vehicle when under the influence of alcohol (DUI) or driving while intoxicated (DWI).

**Overdose deaths.** This refers to deaths caused directly by the consumption of one or more drugs commonly referred to as poisonings or drug-induced deaths. Such deaths might be accidental or intentional as with self-intoxication in connection with suicide. Note that drug-related deaths are deaths indirectly related to drug use, such as AIDS or hepatitis or road-traffic crashes among drivers taking alcohol or drugs.

**Overshoot peak.** An overshoot peak reflects a situation when the observed  $C_{max}$  exceeds the expected  $C_{max}$  based on dose of ethanol and time of its occurrence. The magnitude of an overshoot effect (or deficit) is calculated as  $(Peak_{obs} - Peak_{exp})/Peak_{exp}$  and is usually expressed as a percentage. The overshoot BAC is followed by a diffusion plunge, as excess ethanol in the blood stream equilibrates with the total body water.

**Oxidation.** A chemical reaction that results in the loss of negatively charged electrons and often involves removal of a hydrogen atom from a molecule or adding an oxygen atom, or both.

## P

**Palcohol.** Brand name for powdered alcohol that is alcohol (ethanol) that has been absorbed into a carbohydrate, such as dextrin to produce a dry state instead of a liquid. Powdered alcohol is 50% alcohol by weight and if mixed according to instructions on the packaging yields a liquid that is 10 vol% ethanol.

**Pancreas.** Abdominal gland located behind the stomach that secretes pancreatic juice into the intestine and also manufactures the hormones insulin and glucagon that are released into the blood stream.

**Pancreatitis.** Pancreatitis is an inflammation of the pancreas and is a painful condition including nausea and vomiting. Chronic pancreatitis is often caused by excessive consumption of alcohol or gallstones.

**Parallel group design.** In a parallel group design experiment, patients or test subjects are randomized into two separate groups and each group receives one particular treatment throughout the study.

**Pathogenesis.** The physiological and biochemical mechanisms, by which diseases start, develop and progress.

**Pathology.** The word pathology comes from the Greek word *pathos*, suffering or distressed state or the disturbance of vital processes.

**PBT.** Acronym for preliminary breath test, which is usually done at the roadside often with the driver still sitting behind the wheel. PBTs are screening tests of alcohol influence and positive results are followed up with an evidential breath-alcohol test or a blood sample is taken for forensic analysis.

**Peptide.** A molecule that contains a smaller number of amino acids as opposed to a protein, which might contain several hundred amino acids linked together. The endogenous opiates were found to be penta-peptides (peptides comprising just 5 amino acids) and were named enkephalines.

**Per se.** This is a Latin expression for “in or by itself” and in forensics is used in connection with statutory concentration limits of alcohol in blood, breath, or urine above when a motorist is in violation of the law, hence a per se statute.

**Peer Review.** The judgment of something, usually a scientific article or study (manuscript), by individuals “peers” with documented expertise and experience in the same or a closely related area of research. Types of peer review include single-blind, double-blind and open depending on whether names of authors and reviewers are disclosed.

**Peroxisome.** Membrane bound body within the cell containing enzymes (catalase) that either synthesis or decompose hydrogen peroxide.

**Pharmaceutical drug:** A medicine based on a single bioactive compound approved by a government agency and available on a physician’s prescription or bought from a reputable source over-the-counter.

**Pharmacology.** The word pharmacology is derived from the Greek words *pharmakon* (drug or poison) and *logos* (word or discourse) and is therefore the science that deals with the disposition and fate of drugs in the body and how they act on body functioning.

**Pharmacokinetics (PK).** Derived the two Greek words *pharmacon* (drug or poison) and *kinesis* (movement) and concerns studies of the concentration-time course of drugs in the body including absorption, distribution, and elimination processes. The discipline of PK applies mathematical models to describe and predict the time course of drug concentrations and drug amounts in body fluids.

**Pharmacodynamics (PD).** Derived from the two Greek words *pharmacon* (drug or poison) and *dynamikos* (force or power) and this subject focuses on the time course of drug action in the body. In short quantitative studies of the dose of drug, the route of administration and the frequency of intake in relation to its pharmacologic or therapeutic effect.

**Pharmacogenetics.** Is from the Greek words *pharmacon* (drug or poison) and genetics and is the study of the role of inheritance on inter-individual variation in drug response. Pharmacogenetics entails studies of racial, ethnic, and genetic factors that alter kinetics and dynamics of drugs and related substances that could explain the observed variability in pharmacokinetic parameters.

**Phase I reactions.** This is a term used to describe various metabolic (detoxification) reactions whereby drugs and other chemical compounds foreign to the body are oxidized, reduced or hydrolyzed by the addition of polar groups rendering them less toxic and more soluble in water. However, some metabolic pathways produce a metabolite more toxic than the parent drug.

**Phase II reactions.** This is a term used to describe metabolic reactions whereby certain enzymes convert drugs or foreign chemicals entering the body into more water-soluble compounds to facilitate excretion in the urine. The main drug conjugates formed are glucuronide, sulfate, acetate, and reactions with various amino acids. A phase I reaction often precedes a phase II reaction

**Phenotype.** The observable properties, traits or physical appearance of an organism resulting from the interaction of the genotype with environmental factors.

**Phenylketonuria.** This represents the most prevalent disorder caused by an in-born error of amino-acid (AA) metabolism. Resulting from a point mutation in the phenylalanine hydroxylase gene so that dietary phenylalanine is not properly metabolized leading to elevated concentrations in plasma sometimes causing serious neurological effects and intellectual impairment.

**Phlebotomy.** This pertains to the process of making an incision in a vein with a needle, also known as venipuncture. The word phlebotomy derives from Greek *phlebo*, pertaining to a blood vessel and *tomy*, to make an incision. The person trained to draw blood is referred to as a phlebotomist.

**Phosphatidylethanol.** Abbreviated PEth is an abnormal phospholipid formed in cell membranes in the presence of ethanol in a reaction catalyzed by the enzyme phospholipase D. Methods such as HPLC or GC-MS are available for determine PEth in blood and other body organs. PEth serves as a biomarker of heavy drinking.

**Physical dependence.** After long term chronic exposure to a psychoactive drug the individual develops tolerance and in parallel a condition of physically dependent. This is revealed by the precipitation of physiological disturbances (abstinence) when intake of the drug is terminated.

**Physiology.** The scientific discipline that deals with the functions of the living body.

**Placebo.** Derived from the Latin "*I shall be acceptable or pleasing*" and is a treatment that lacks any known pharmacological effect. However, placebo might provide psychological relief or be perceived to have a beneficial effect. Placebo treatments are commonly included in experiments as control treatments, such as a tablet of the same color and shape as the active drug or a drink that might look, taste, and smell like ethanol.

**Plasma.** The yellowish clear liquid component of an anticoagulated blood specimen. The blood specimen is spun-down and the supernatant plasma is removed for analysis. Plasma contains fibrinogen. The plasma volume in an adult is approximately 4 liters.

**Polycythemia.** Also known as polycythemia vera or in UK erythrocytosis represents an increase in the number of red cells (erythrocytes) in whole blood, which leads to an increased viscosity of the blood. Clinical laboratory analysis showing an abnormally high hematocrit (>52%) and an excess of hemoglobin (>185 g/L) are indications of polycythemia.

**Polydipsia.** Intense and excessive thirst and a cardinal sign of diabetes.

**Polymorphism.** The presence of two or more alleles of a gene or other DNA sequence in a population. The existence of more than one form of a genetic trait,

**Polypharmacy.** This is defined as the chronic co-prescribing of several drugs and which can result in adverse drug-drug interactions and sometimes death.

**Polyuria.** The excretion of large volumes of urine, greater than 3 L per day, and one of the cardinal signs of diabetes.

**Portal vein.** A large blood vessel that collects blood from the stomach and intestine and transports nutrients to the liver.

**Postprandial.** The physiological condition or state after eating a meal.

**Potentiation.** The action of two drugs in which the combined effects are greater than the sum of the individual effects.

**Precision.** Closeness of agreement between results of independent measurements obtained by a procedure under prescribed conditions. Precision is a measure of the variation or scatter of the measurements about the mean and is expressed mathematically by the standard deviation of the measured values. Near synonyms for precision are repeatability, stability, consistency, and reproducibility.

**Presumptive tests.** These as preliminary analytical tests, mostly qualitative tests, often involving a color change of a chemical reagent after mixing with a test specimen. The main application of such tests is for broad screening analysis to identify a class of compounds, such as certain types of drugs and poisons. Enzyme immunoassays are widely used in the field of urine drug testing. Other classic screening tests

include Trinder's test for salicylic acid derivatives, the Fujiwara test for trichloro compounds (e.g. trichlorethanol) and the nitroprusside test for urinary ketones.

**Prevalence.** The frequency with which a variable (condition, symptom, disease, or trait) occurs in the population at a certain point in time. Prevalence is the measure of the number of cases at a single point in time and has no units.

**Proficiency test.** A test designed to evaluate the reliability of an analytical method or procedure and the overall quality performance of a laboratory.

**Prohibition.** This generally refers to alcohol prohibition in USA, which lasted from 1919-1933 after the passage of the Volstead act or 18<sup>th</sup> amendment to the US constitution. This act prohibited the production, sale and transportation of "alcoholic liquors" without further definition. Technically, this referred to any beverage containing more than 0.5% alcohol by volume.

**Propofol.** Discovered by the British drug firm Zeneca (now Astra-Zeneca), propofol is a widely used general anesthetic agent (trade name Diprivan®). The drug is suitable for short out-patient surgery lasting about 30 min at most. Propofol is not very soluble in water so is administered intravenously as a milky oil-in-water emulsion and is appropriate for induction and maintenance of anesthesia. Propofol hit the headlines internationally in 2009 when it was incriminated in the death of the pop icon Michael Jackson, whose personal physician used it to treat chronic insomnia.

**Proteins.** Large molecules composed of long chains of amino-acids. The shape and function of a protein is determined by the sequence of its amino-acids. Proteins help to maintain the structure of cells and also participate in many biological reactions as catalysts (enzymes).

**Protein binding (PB).** This refers to the reversible binding of a drug or endogenous substance to serum proteins, mainly albumin. The binding consists of weak ionic bonds, Van der Waals forces and hydrogen bonding. PB is an important concept for therapeutic drugs because only the free-fraction (non-bound) is pharmacologically active. An adverse drug-drug interaction might depend on competition between two drugs for binding sites on plasma proteins. Ethanol is generally considered to show negligible protein binding and concentration in blood and pharmacological effects of ethanol are not likely to depend on what other drugs if any were co-ingested.

**Proteinuria.** The presence of an increased amount of protein, usually albumin in the urine and associated with hyperglycemia and diabetes.

**Psychotropic drug.** A drug with its main site of action in the central nervous system (brain) often associated with altered mood, thought processes and behavior. Results in euphoria and tolerance and dependence.

**Psychomotor functions.** Motor functions as a consequence of mental activity.

**Pyruvic acid.** An endogenous substance produced from glucose as the end product of glycolysis.

**Pylorus.** The sphincter muscle separating the stomach from the small intestine also called *pyloric sphincter*.

## Q

**Quality assurance.** The planned and systematic actions taken to ensure that work done at a factory or at a laboratory are reliable and meet a given set of requirements and performance standards. As alternative definition could be use of an established protocol and procedures for analytical work necessary to ensure confidence in the results reported and at these are fir for purpose.

**Quality control.** Often abbreviated QC for short is a process by which the various stages involved in the

manufacture of a product or item are reviewed to ensure they meet pre-defined standards. In connection with laboratory analysis of a specimen, these pre-defined standards might involve accuracy, precision, specificity or other characteristics of the analytical method used.

## R

**Radioisotope.** The form of a chemical element that has radioactive properties. In medical diagnosis the three isotopes generally used in for example radioimmunoassay are tritium ( $^3\text{H}$ ), carbon-14 ( $^{14}\text{C}$ ), and iodine-125 ( $^{125}\text{I}$ ).

**Randomized controlled trials.** These are the mainstay of evaluating new medicines. In such trials, the participants who receive the treatment are assigned at random or by chance, which is essential to ensure that the outcomes are determined only by the treatment.

**Range.** The difference between the largest and smallest values in a collection of measurements.

**Reaction time.** The time interval between presentation of a stimulus and initiation of a response.

**Receptor.** A protein embedded in the wall of a neuron or other cell that recognizes and binds a neurotransmitter or other chemical messenger.

**Recovery.** A characteristic of an analytical method normally expressed as a percentage and refers to the amount of drug removed from the original sample, which reaches the end of the analytical procedure. Poor recovery can be compensated for by adding an internal standard to the bio-fluid before starting the analysis.

**Reduction.** This is a chemical reaction that involves removal of an oxygen atom from a molecule or adding a hydrogen atom or both.

**Relapse.** This refers to resumption of drug-seeking or drug-taking behavior after a period of abstinence. Often various environmental cues, such as people, places or things associated with past drug use (syringe and needle or other drug paraphernalia) trigger intense craving and a relapse to use of the drug.

**Response latency.** The time interval between presentation of a stimulus and making a response.

**Reference standard.** A sample prepared or purchased that has known properties in terms of identity, purity, chemical composition, and concentration. Reference standards are used for the purpose of calibrating analytical equipment and for use as a control in actual experiments.

**Repeatability.** The closeness of agreement between the results of successive measurements during a short time, defined as the within-run standard deviation).

**Reproducibility.** The closeness of agreement between the results of measurements of the same measurable quantity on different occasions (e.g. the between run standard deviation). Different observers, different calibrations, different locations, different times.

**Respiratory membrane.** The membrane within the lungs being only a few microns thick across which an exchange of gases takes place.

**Retrograde extrapolation.** The practice of estimating a person's blood or breath alcohol concentration at some time prior to the time of obtaining a specimen for analysis - back extrapolation, back-tracking.

**RIA.** Acronym for radioimmunoassay, which is a highly sensitive analytical method used to determine low concentrations of endogenous substances or various drug molecules in body fluids.

**Ribosome.** A small spherical body within cells where the synthesis of proteins occur.

**Robustness.** Robustness is the capacity of an analytical method to produce accurate and precise results despite small deliberate changes in test conditions and/or method parameters. In GC analysis of ethanol the addition of an internal standard helps to ensure the method is robust.

**Route of administration.** Defines the way a drug gets into the bloodstream. Although oral ingestion is the most convenient route, under some circumstances this might not be practical. For example, after swallowing a drug it has to pass the gastrointestinal canal and liver before the active substance reaches the systemic circulation and interacts with target organs or tissue. During passage through the gut and/or the liver some of the drug becomes metabolized (broken down) by enzymes, a process called first-pass metabolism, which lowers the therapeutic efficacy of the drug. After intravenous administration the drug reaches the systemic circulation more rapidly and its bioavailability is 100%.

**Ruggedness.** Ruggedness is a measure of the degree of reproducibility of the analytical results when performed under varying tests conditions, such as when different technicians, instruments, source of reagents, laboratories, or even different countries.

## S

**Saccadic eye movements.** Rapid conjugate movements of the eyes when a person is instructed to follow a target object.

**Scatter plot.** A scatter plot usually displays the relation between two continuous variables plotted on the x- and y-axes. A one-way or one-dimensional scatter plot may be used to display a single continuous variable.

**Screening device:** To improve traffic safety and apprehend drunken driver the police authorities in most nations use breath-alcohol screening devices, which are applied at the roadside to screen driver for excessive alcohol consumption. These device have evolved from the simple chemical tube and bag to sophisticated hand-held electronic instruments based on electrochemical oxidation of alcohol. The result might be displayed as pass or fail or as green, amber and red diodes, where green = pass, amber = borderline and red = above the alcohol limit for driving. Alternatively, these preliminary breath alcohol screeners display digitally the alcohol content of the person's breath or are calibrated to furnish an estimate the blood-alcohol concentration.

**Screening test.** In addiction medicine, a screening test is applied to a group of individuals or patients to diagnose the presence of a certain disease or condition, such as alcohol abuse and dependence.

**Second messenger.** A molecule produced within a cell that carries information to another site within the cell membrane eliciting a physiological response; an example is cyclic AMP.

**Sensitivity of an analytical method.** This is the measured detector signal per unit increase in the concentration of the analyte as reflected by the slope of the linear calibration plot.

**Sensitivity of a diagnostic test.** This is defined as the proportion of the patients having a disease and for whom the test results were positive.

**Sensorimotor functions.** Functions involving perception of information from the senses and the resulting physical reactions of muscles.

**Serotonin.** 5-hydroxytryptamine (5HT) an important neurotransmitter synthesized from the dietary amino acid L-tryptophan. 5HT is associated with mood, sleep, aggression, anger, and appetite and is the target for the mechanism of action of so-called SSRI drugs (selective serotonin reuptake inhibitors) exemplified by Prozac (fluoxetine) for treatment of major depression.

**Serotonin syndrome.** A potentially life-threatening adverse drug reaction by inadvertent combination of

therapeutic drugs or intentional self-poisoning. As the name implies the syndrome results from excessive serotonergic agonism of central nervous system receptors and peripheral receptors. The widespread prescribing of SSRI drugs in today's society, often in combination with other medications that might impact on serotonin neurotransmission, makes this syndrome clinically much more important and sometimes a life-threatening occurrence.

**Serum.** The clear fluid portion of blood remaining after coagulation (removal of fibrin and blood cells). If a chemical test requires serum then the blood sample must be drawn into a tube that will allow the sample to clot (red top evacuated tubes). The freshly drawn blood tube must be allowed to stand upright for 30 min while the clotting process occurs. Once the clot is formed, the tube must be centrifuged and the supernatant (liquid fraction) separated to give the serum. Serum does not contain any clotting factors.

**SFST.** Acronym for **Standardized Field Sobriety Tests** and refers to a set of tests done with people suspected of driving under the influence of alcohol (or drugs). Such tests are conducted by a trained police officer, usually at the roadside, with the aim of gathering probable cause to make an arrest for further more sophisticated testing. SFSTs comprise a battery of three tests involving including one-leg-stand, walk-and-turn and gaze nystagmus.

**Signs & Symptoms.** In medicine a symptom is generally a subjective observation, whereas a sign is objective. Observed flushing in the face, heavy breathing, high blood pressure, hypoglycemia etc are signs observed by a physician. By contrast, stomach aches, other types of pain and fatigue are symptoms reported by the patient.

**Slurred speech.** A typical clinical sign of intoxication e.g. after drinking alcohol or taking certain drugs resulting in imprecise speech articulation including deviation in rate, pitch and intensity and often an incorrect production of consonants and vowels.

**SOP.** This is an acronym for **Standard Operating Procedure** that refers to written instructions used by people working at a laboratory to perform a test or analysis a sample sent to the laboratory.

**Soporifics.** Substances that cause or induce profound sleep, opium being the first such substance since ancient times, until chloral hydrate was developed as a sedative-hypnotic in 1869 and the barbiturates in 1902.

**Specificity of a diagnostic test.** This is defined as the proportion of healthy subjects in whom the test results were negative.

**Spirometer.** A device for measuring the volume of respiratory gases.

**Spleen.** The spleen is an organ situated behind the stomach on the left side of the abdomen. Old red blood cells and platelets are stored in the spleen, which also serves to clear and fight bacteria.

**SSRI.** Acronym selective serotonin reuptake inhibitors and refers to a type of antidepressant drug, which is intended to increase the concentration of a neurotransmitter (serotonin) at receptor sites by blocking reuptake (a type of molecular pump), which otherwise returns the transmitter into the pre-synaptic neuron. Prozac® or fluoxetine was the first SSRI and a blockbuster drug, quickly followed by other SSRIs, e.g. citalopram (Cipramil®), paroxetine (Paxil®) and sertraline (Zoltoft®).

**Standard drink.** In the USA, one standard drink contains 14 gram ethanol, which corresponds to consumption of 5 oz (150 ml) table wine (12 vol%), 1½ oz (45 mL) spirits (40 vol%), 12 oz (360 mL) beer (5 vol%).

**Stasis.** A state in which the normal flow of some biological fluid stops, such as the flow of blood through vessels (hence hemostasis) or intestinal contents through the digestive tract.

**Steatosis.** Accumulation of fat in the liver, often caused by heavy consumption of alcohol, a condition

more commonly referred to as fatty liver.

**Stimulants.** Represent a class of drugs that stimulate the central nervous system (CNS) by interfering with the brain's neurotransmitters. CNS stimulants cause stimulation of the sympathetic nervous system by altering neurotransmission of catecholamine such as dopamine, norepinephrine and serotonin. The abused drugs cocaine and methamphetamine are the prototype central nervous system (CNS) stimulants.

**Stroke.** Any condition during which the blood supply to the brain or regions of the brain is suddenly interrupted.

**Student t-test.** This constitutes a widely used statistical test to compare variation between two groups of data. The name Student was a pseudonym for William Gossett who worked at the Guinness brewery in Ireland and was forbidden to publish under his real name and to give the address where he worked. There are two forms of the t-test called one-sample (paired) and two-sample (unpaired) test. When two measurements are made on the same person, the average difference is best assessed by a paired t-test (degrees of freedom one less than the number of differences). When the two sets of measurements are made on different people the variation between individuals cannot be eliminated and the means of the two independent groups are compared ( $n_1$  and  $n_2$  in each group). The ratio between the difference between the two means and a pooled estimate of the within group variance is used to make the test (degrees of freedom  $(n_1 + n_2 - 2)$ ).

**Substrate.** The substance (molecule) acted upon by an enzyme; its conversion to a particular product is catalyzed by a specific enzyme, e.g. ethanol is the substrate for alcohol dehydrogenase.

**Symptom.** Any subjective evidence of a disease or of a patient's condition.

**Synapse.** Region of a nerve-cell (neuron) from which nerve signals are transmitted to neighboring neurons. The synapse is a microscopic gap (or cleft) separating pre-synaptic and post-synaptic neurons.

**Synovial fluid.** The fluid within joint cavities formed by the ultra filtration of plasma across the synovial membrane and by secretions from certain cells.

## T

**Tardive dyskinesia.** This is an undesirable side effect of certain medication and is characterized by a movement disorder after long-term use (months or years) of taking antipsychotic drugs (neuroleptics). The condition usually worsens after discontinuation of the drugs.

**TDM** An acronym for Therapeutic Drug Monitoring, which refers to the analysis of a sample of blood or plasma for a specific drug at various times after dosing to control and maintain a constant concentration of the active substance in the bloodstream.

**Therapeutic agent.** A drug or chemical substance used to treat a disease or condition hence the term therapeutic drug monitoring (TDM) the science of analyzing the concentrations of drugs in blood or plasma to monitor patient compliance and to ensure that correct and appropriate concentrations are reached and maintained after treatment.

**Therapeutic drug monitoring.** The aim of therapeutic drug monitoring (TDM) is to ensure that the concentration of an active drug in blood or plasma is appropriate for a desired therapeutic effect and without any undesirable side effects or toxicity. The experience gained from TDM allows future predictions to be made when the same drug is administered to other patients under the same conditions of dosing. A delicate balance exists between the dose of a drug, the concentration in blood and the desired therapeutic effect on the individual.

**Therapeutic index (ratio).** Gives a way to express a drug's safety margin and is commonly defined as



the ratio between the dose producing toxicity in 50% of patients to the dose that produces the desired therapeutic response in 50% of patients ( $TI = TD_{50}/ED_{50}$ ). If a drug has a TI of 100, this means that the toxic dose is about 100 times larger than the effective dose and means that this particular drug has a wide safety margin.

**Therapeutic range.** This refers to the concentration range of a drug in blood or plasma that leads to the desired pharmacological or beneficial effect of the medication (the safe zone). At plasma concentrations below the minimum therapeutic level the drug fails to exert its effects and above the upper therapeutic level the drug causes undesired side-effects or toxicity.

**Tidal volume.** The volume of air inspired and expired in a single breath and this volume corresponds to approximately 500 ml in healthy adults.

**Tolerance.** A state that develops after long-term exposure to a drug. Metabolic tolerance infers a faster removal of the drug, e.g. by metabolic degradation in the liver. Functional tolerance infers a change in sensitivity of the brain to the effects of the drug after continual exposure.

**Tolerance Interval.** The range within which a specified percentage of individual values of a population are expected to fall with a stated level of confidence.

**Toxicity.** The ability of a substance to harm living organisms - all substances are toxic even water if ingested in large enough amounts.

**Toxicology.** The word toxicology derives from the Greek term "*toxon*", which meant a bow for shooting arrows. During antiquity poisons were often placed on the tips of arrows making them more deadly, giving rise to the word *toxicos* and *intoxicated*, which means made sick by poison. Hence toxicology is the study of how poisonous substances interact with living organisms.

**Traceability.** Traceability means that a result of measurement can be traced back, through an unbroken chain of comparisons, to a national or international standard value. The traceability of the ethanol standards used to calibrate the gas chromatography needs to be well documented.

**Tracking.** The name given to a laboratory test used to measure effects of alcohol on an individual and might involve adjusting an instrument to maintain a desired value (compensatory tracking) or to follow a moving reference marker or object (pursuit tracking).

**Transferrin.** A protein found in the blood that helps transport iron ( $Fe^{3+}$ ) to developing red blood cells.

**Triglycerides.** The chemical form in which fat molecules exist within the body comprising a glycerol backbone with each of the three hydroxyl groups replaced by fatty acids of varying carbon-chain length, branching and double bonds.

**Trypsin.** An enzyme in the small intestine produced in the pancreas that digests proteins.

**Type I diabetes.** Insulin-dependent diabetes also known as juvenile-onset diabetes and happens because the pancreas stops producing insulin. Often considered an auto-immune disease type-I diabetes is in part hereditary.

**Type II diabetes.** Non-insulin-dependent diabetes (the more common form) also called adult onset diabetes, which initially is treatable by careful control of the diet, exercise and certain medication. Obesity is a strong risk factor for development of this disease.

## U

**U-Creatinine.** The creatinine content of urine can span over a wide range depending on the relative concentration of water in the specimen. U-creatinine below 0.2 g/L (20 mg%) indicates a highly dilute

specimen, which might result from manipulation of the specimen by adding water in-vitro or by drinking large volumes of water or an alcoholic beverages before voiding.

**Ultraviolet.** Pertaining to the region of the electromagnetic spectrum from approximately 10 to 380 nm.

**Uncertainty.** The word uncertainty means doubt in something, such as the result of analysis. Analytical uncertainty is defined as a parameter associated with the result of a measurement, which characterizes the spread or dispersion of the results that could reasonably be attributed to the quantity being measured.

**Unit of alcohol.** In UK one unit of alcohol equals 10 mL ethanol (1 mL = 0.79 g) so ~8 gram ethanol.

**Upper respiratory tract.** Abbreviated URT, this part of the lungs comprises the nasal cavity, pharynx and its associated structures. The URT is covered with a watery mucous membrane.

**Urine.** The aqueous fluid secreted by the kidneys and stored in the bladder before being voided. Although urine is mainly water its chemical composition varies widely in health and disease and is also dependent on the quantity and type of food and drink consumed. The composition also reflects body metabolism and processes important for homeostasis. Urine is produced by the kidneys at a rate of approximately 1 mL per minute and urinary excretion is the primary means by which the body eliminates waste products and maintains homeostasis. Urine in healthy individuals has an amber (deep-yellow) color, a special aromatic odor and a bitter saline taste. The average quantity of urine secreted in 24 hours is 1200-1600 mL or on average 80 mL per hour. Urine is an ideal body fluid for use in analytical toxicology to screen for drug use during life. However urinary drug concentrations cannot be used to estimate concentrations in blood or the effects of drugs on the individual.

**Uroscopy.** This term refers to the examination of urine especially its volume, appearance, smell, color and taste for the purpose of making a medical diagnosis. The collection and examination of a person's urine is considered the oldest clinical test and furnishes information about what several metabolic processes occurring within the body.

## V

**Vasodilation.** Same as vasodilatation is a condition whereby there is an increase in the diameter of blood vessels - the opposite is vasoconstriction. These two conditions cause a decrease and increase in blood pressure, respectively.

**Vasopressin.** The antidiuretic hormone secreted from the pituitary gland in response to dehydration, which instructs the kidney to reduce urinary volume. Drinking alcohol inhibits the action of this hormone thereby resulting in an increased production of urine or alcohol-induced diuresis.

**Vein.** A vein is a blood vessel that carries blood back from body organs and tissue to the heart.

**Viscera.** Pertaining to the internal organs - the soft parts - the internal organs of the abdominal cavity.

**Visible light.** Pertaining to radiant energy in the electromagnetic spectral range that is visible to the human eye. This corresponds to light of wavelengths from approximately 380 to 780 nm.

**Vital Capacity (VC).** This is defined as the total volume of air that can be expelled from the lungs after a maximum inspiration to maximum expiration. A healthy adult person might have a vital capacity of approximately 4600 ml, being less in women compared with men and markedly diminished in heavy smokers and those with lung disease.

**Vitreous humor.** (VH) Means literally glassy fluid and refers to a transparent jelly-like substance that fills the space between the lens and the retina of the eye and is a fluid commonly sampled for forensic analysis of ethanol in postmortem toxicology. The major advantage of VH is that there is less risk for contamination by bacteria spreading from the gut.

**Volume of Distribution.** The volume of distribution of a drug ( $V_d$ ) is defined as the ratio between the amount of drug in the body (the dose) divided by the concentration in a reference compartment, usually blood, plasma or serum. Note that  $V_d$  does not necessarily represent the volume of any particular physiological compartment hence the term "apparent distribution volume" is often used to describe this important pharmacokinetic parameter.  $V_d$  gives an indication of how much of the drug is distributed to tissues outside of the vascular space (blood compartment). For any given amount of drug in the body, the lower the concentration in blood the more of the drug that is taken up into extravascular sites.  $V_d$  might vary from a few liters to several hundred liters. Drugs that bind tightly to plasma proteins tend to have lower  $V_d$  compared with highly fat soluble drugs that get localized in adipose tissue (high  $V_d$ ). In the case of ethanol the  $V_d$  is closely related to the proportion of water in the body (~60% for men and ~50% for women) and the amount of water in the blood (80%) or plasma (92%) specimen analyzed.

## W

**Wavelength.** A property of radiant energy, such as IR, visible or UV. The distance measured along the line of propagation, between two points that are in phase on adjacent waves.

**Whole blood.** This is an anticoagulated specimen where the cellular elements remain mixed with the plasma and this is necessary for testing purposes. Prior to removing an aliquot for analysis the tube of blood should be inverted several times to ensure that the plasma and red cells are thoroughly mixed together.

**Widmark.** Erik MP Widmark (1889-1945), was a pioneer in forensic research on alcohol, and is perhaps best known for his seminal work on ethanol pharmacokinetics as reported in his 1932 monograph. He introduced the factors beta and rho and reported a study of clinical signs and symptoms of intoxication in relation to the person's blood-alcohol concentration. He was appointed full professor in medicinal and physiological chemistry at the University of Lund in Sweden aged 31 y.

**Widmark's  $\beta$ -factor.** This denotes the slope of the post-absorptive elimination phase assuming zero-order kinetics. Hence the rate at which ethanol is eliminated from the blood stream per unit time, usually reported as g% per h or g/L per h. A slang term is the alcohol burn-off rate.

**Widmark equation.** A simple mathematic equation derived by Erik MP Widmark of Sweden that defines the relationship between the amount of ethanol absorbed and distributed in all body fluids and tissues (A) to and person's measured blood-alcohol concentration (BAC). Variables in the equation are body weight (BWt) and a distribution factor rho. The value of rho depends on a person's age, gender and amount of adipose tissue. The Widmark equation is often written  $A = BAC \times BWt \times \rho$ , where A is grams ethanol, BAC is in g/L, BWt is in kg and the rho factor has units of L/kg. Note that A is not the amount of alcohol consumed, but the amount absorbed and distributed in blood and all other body fluids at the time that the blood sample was taken. Any alcohol remaining unabsorbed in the stomach is not reflected in the BAC.

**Widmark's rho-factor.** This important pharmacokinetic parameter represents the distribution ratio of alcohol between the body (g/kg) and the bloodstream (mg/g). Because Widmark measured BAC in units of mg/g the rho-factor is a dimensionless ratio and denoted with the Greek letter  $\rho$  (rho). This parameter stands for "*die reduzierte Körpermasse*" (the reduced body mass). Rho is a factor (less than unity) by which a person's body weight must be multiplied (lowered or reduced) to obtain the body mass with the same concentration of alcohol as measured in the blood. The rho factor characterizes the distribution of alcohol in the body and is given by the quotient [alcohol in organism] to [alcohol in blood]. Modern books devoted to pharmacokinetics uses the term distribution volume ( $V_d$ ) for rho factor.

**Withdrawal syndrome.** This represents a constellation of signs and symptoms that occur after abrupt discontinuation or reduction in use of a psychoactive substance. Fear of the unpleasant and sometimes unbearable withdrawal symptoms makes an addict continue to use the drug. The withdrawal syndrome can also be elicited by administering an antagonist drug (e.g. naloxone in heroin addicts).

## X

**Xenobiotic.** From the Greek *xeno* (foreign) and usually refers to chemical substances (drugs or toxins) that enter the body from the environment or by ingestion. Xenobiotics are not normally present in the body and lack any physiological role or function, hence synthetic organic chemicals, environmental pollutants and drugs and solvents.

## Y

**Yeast infection.** Fungal infection, such as genital candidiasis, caused by proliferation of the yeast *Candida albicans*. This clinical condition is common in women suffering from type I diabetes.

## Z

**Z-score.** The Z-score is a mathematical device used to compare results of external proficiency tests regardless of concentration. It is calculated as a ratio [(laboratory result - assigned or target value)] divided by the standard deviation (SD) of results from all participants in the test. Note that before a between lab SD is computed outlying values must be eliminated and there are a number of statistical tests available to identify outliers (e.g. range test).

**Zero-order.** A term used to describe rates of chemical and biochemical reactions, such as zero-order kinetics, which means that the rate of elimination from blood or plasma is independent of the dose and starting concentration. Rate of decrease in concentration ( $-dC/dt$ ) represents a fixed amount of substance per unit time regardless of dose or starting concentration in blood. The units of  $k_0$  or  $\beta$  are g/L/h or g/h. In the post-absorptive phase when blood or plasma concentration is plotted against sampling time, one obtains a straight line with slope denoted  $k_0$  or  $\beta$ . A drug that follows zero-order process implies saturation of the metabolic pathway as substrate concentration (BAC) increases above a certain threshold value, such as 0.2 g/L. This concentration for ethanol is roughly ( $2 \times k_m$ ) of Class I hepatic ADH or 0.02 g% in blood.

**Zero-tolerance law.** Refers to a type of traffic-safety legislation whereby the presence of any amount of a controlled substance in the driver's blood is deemed a punishable offence. Zero-tolerance laws simplify the prosecution of drug-impaired drivers, because they avoid the need to produce clinical or other evidence of impairment by drugs. Another name for this type of legislation is zero-limit laws or limit of quantitation (LOQ) laws.