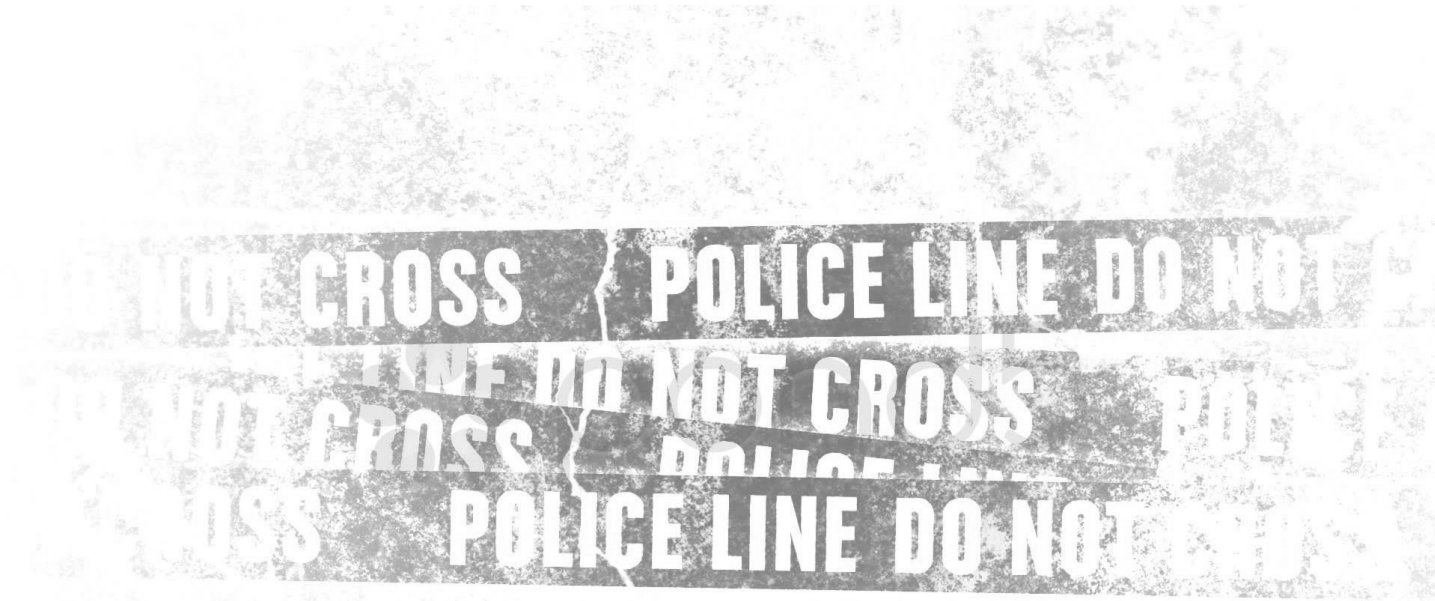

Toxicology

Chapters 18, 19, 20, 21, and 22

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Correction file

Chapter 18

Principles of Toxicology

Definitions

- **Toxic**: Some use the term toxic synonymously with 'poisonous', meaning to imply that ingestion of a particular substance will cause death or illness.
- **Lethal dose**: To understand the definition of 'lethal dose you need to know that drug sensitivity and resistance vary from individual to individual. A 'lethal dose' is said to represent the dose of that drug at which all subjects given the drug will die, and that dosage will be expressed in g, mg, mcg/kg.
- **LD50**: The dose at which 50% of those who take a particular dose would die. This partly depends on mode of drug administration (bioavailability)
- **Drug receptor physiology**: How well a particular drug will bind to a receptor determines how effectively it will act (or how toxic it will be). It is also important to know that receptors are capable of mutating.
- **Drug tolerance**: An individual is said to be tolerant when increasingly large doses of the drug produce less effect. It usually occurs after chronic exposure to a specific drug.
- **Drug dependence**: When an individual cannot function normally in the absence of a specific drug. It relates to tolerance which are both partly controlled by receptor distribution, density, and genetics.

DSM-IV recognizes the following substance dependencies

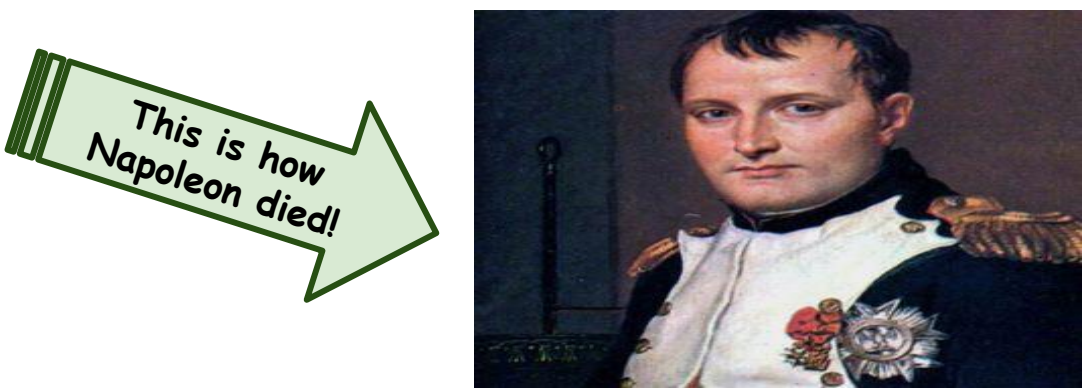
-Alcohol	-Nicotine	-Sedative, hypnotic, or anxiolytic
-Amphetamines	-Hallucinogens	-Polysubstance dependence
-Cannabis	-Opiods	-Phencyclidine
-Cocaine	-Inhalant	-Unknown substances

...Continue Definitions

- **Drug withdrawal:** The development of symptoms when a drug is abruptly discontinued. Only individuals who are already dependent on a drug and took the substance in large quantities for a long time can experience withdrawal symptoms. In simple withdrawal syndrome, such as seen after long-term cocaine or heroin abuse, individuals feel increasingly ill, but after a certain number of days recovery begins. However, withdrawal from drugs like benzodiazepines could cause uncontrollable seizures and death.

- **Drug Idiosyncrasies**: This term is used to describe **unanticipated** drug reactions. These reactions fall under the category of hypersensitivity reactions (allergies). Pathologists have been debating for more than half a century whether the pulmonary oedema associated with heroin abuse might be a type of hypersensitivity reaction, although this hypothesis **has never been convincingly proven.**

- **Drug Interactions:** Unanticipated symptoms and signs that result after two or more different drugs have been given. The most common cause of drug interactions is that those two drugs are metabolized by the same enzyme. Surprisingly, drugs can interact with the channels that control electrical conduction in the myocardium. The channel responsible for most unexpected drug reactions (arrhythmias and sudden death) is the one that conducts potassium back into the cell after depolarization (known as hERG and caused by combining with arsenic).



Principles of Testing Matrices

- It is extremely difficult to determine a death caused by drug overdose.
- Post-mortem drug concentrations almost always exceed those measured in the immediate ante-mortem period.
- The concept of 'therapeutic' drug concentration measurements made in the living does not have any relevance to the dead. Post-mortem detection of a drug proves that it was either ingested or exposure occurred, but that says nothing about the toxicity of it.
- The route of administration can never be determined by measuring the drug concentration in suspected areas (meaning that if cocaine was recovered from the vagina that does not necessarily mean that it was taken that way).
- After death, concentrations of weakly basic drugs (i.e. cocaine) are higher on the left side of the heart than anywhere else.

Testing Blood and Urine for Drugs

- Blood (particularly cardiac blood) is still the preferred testing matrix for drug concentration. This is because at autopsy, there is often no urine in the bladder.
- First, cardiac blood is screened with GC/MS and the findings are confirmed with a peripheral blood sample. The sample is collected into a sodium-fluoride-containing tube to prevent further drug degradation.
- There are differences between pre and post-mortem blood specimens:

In the living only the plasma is analysed, whereas in the dead the whole blood is analysed. This is because drugs concentrations (alcohol especially), are different in plasma and whole blood. Serum and plasma contain 10-15% more water than whole blood which is why ethanol concentrations are 10-15% higher in plasma.

Testing Vitreous Humor

- This is especially useful for the diagnosis of electrolyte disorders, renal failure, hyperglycemia, and ethyl alcohol ingestion.
- The vitreous humor is protected from the external environment which is why it may be the only reliable testing matrix when individuals drown or when bodies are found after an extended period of environmental exposure.
- Measuring alcohol concentrations in the vitreous humor may help distinguish between post-mortem alcohol formation and ante-mortem ingestion.

Testing Hair

- Measuring drug concentrations in hair can yield valuable information about drug exposure, compliance, and sometimes the presence of unexpected drugs.
- Once drugs are deposited in hair they are stable indefinitely. This is why we use it to determine prior drug use.

Testing the Liver and Stomach

- Liver analysis is valuable when drugs are either highly protein-bound (Tricyclic antidepressants) OR if it undergoes enterohepatic circulation (morphine). However, most drugs diffuse from the stomach to the right lobe of the liver so only the left lobe should be used for testing.
- Stomach content testing is only worthwhile if the volume of gastric contents is recorded, a homogenous specimen is analysed, and total drug content in the stomach is computed.
- It may also be possible to identify small pill fragments by microscopic examination of gastric fluid.
- Ion trapping may cause small amounts of some charged drugs to appear in gastric content. And large amounts may be artefacts caused by the enterohepatic circulation.

YAY chapter 18 done.. You got this!

Chapter 19

Alcohol

Ethanol sources and concentrations:

★ Alcohol (ethanol) may be ingested or presented by virtue of bacterial action after death.

Alcohol Concentration Formulas

Widmark's Formula: to calculate the amount and time of alcohol ingestion. Used for trials.

Winnek's Formula: (IMP.)
BAC = (150/bodyweight in pounds)x(%ethanol/50)x(ounces consumed)x(0.025)
-This equation provides a rough estimate and is easier-

Example

A 200-pound (90.7 kg) man drank five 12-ounce (354.9 mL) cans of beer, and the beer contained 4% ethanol. Calculate BAC.

Weight= 200 pound
Ethanol%= 4%
Ounces consumed= (5)(12)= 60 ounce * he consumed 5 cans
BAC= (150/200)(4/50)(60)(0.025) = 0.090% (90 mg%)

Ethanol Absorption

- Alcohol is absorbed from GI by diffusion mostly in the small intestine.
- The higher the alcohol concentration of the beverage, the faster the rate of absorption.
- Gastric absorption is 30% of ethanol or 10% of that consumed with food and water respectively which means that alcohol is more rapidly absorbed with water leading to higher blood levels of it.
- The maximum absorption rate occurs after consuming a beverage containing 20-25% alcohol on an empty stomach.
- The absorption rate slows when:

1. When alcohol is consumed with food.
2. When 40% alcohol solution is consumed on an empty stomach.
3. When consuming high fluid volume/low alcohol content beverages (beer).

Alcohol Elimination

- Ethanol is converted into acetaldehyde via alcohol dehydrogenase, leading to the production of acetic acid and then acetaldehyde which is responsible for most of the side-effects produced by alcohol.
- The measured alcohol concentration depends on both weight and sex as these two determines the total volume of body water (obese people will have a lower BAC).
- Alcohol is eliminated in a constant rate, the median rate of decrease in BAC is around 15 mg% per hour

Ethanol Measurement

- Breath test (Breathalyzer) is used by most enforcement agencies in most countries for road traffic offences. It is specific and reliable as it does NOT interact with acetone which is formed by uncontrolled diabetics.

Clinical Effects of Alcohol

- Ethanol is a potent CNS depressant.
- As the concentration rise initial feelings of relaxation and cheerfulness give way to blurred vision, loss of coordination and behavioral issues. Extreme level of consumptions may lead to unconsciousness, alcohol poisoning and death.
- Tolerance plays a role with alcohol. For example, a BAC exceeding 0.40% (400mg%) may be lethal in a non-drinker while producing few if any in a chronic alcoholic.

Blood alcohol concentration and general effects

10-50 mg%	Feeling of relaxation, well-being and increased sociability
50-100 mg%	Increased self-confidence, talkativeness, mild euphoria, reduced co-ordination. Legal driving limit is 80 mg%
100-150 mg%	Impaired balance, thickened speech, clumsiness, reduced alertness, lowered social reserve.
150-200 mg%	Drunkenness, slurred speech, glazed eyes, staggered gait, drowsiness, exaggerated emotional response, dizziness, nausea and disorientation.
200-250 mg%	Confusion, impaired co-ordination, vomiting, reduced awareness, impaired short-term memory.
250-300 mg%	Extreme drunkenness, stupor, impaired consciousness, reduced reflexes, depressed respiratory and incontinence.
300-400 mg%	Unconsciousness, absence of reflexes and coma
400 mg% and above	Possible death due to respiratory depression or cardiac arrest

Post-mortem Considerations

- Bacterial enzymes (predominantly alcohol dehydrogenase and acetaldehyde dehydrogenase) act upon carbohydrates within the cadaver. Glycogen or lactate is converted to pyruvate and then ethanol.
- The amount of alcohol produced depends on the amount of glycogen available.
- Factors accelerating alcohol production:

1. Hyperthermia
2. Sepsis
3. Storing a body at high temperatures
4. Bowel trauma or disruption
5. Aircraft accidents (or other causes of severe body disruption)

- How do we know whether alcohol was formed before or after death?
- We compare the ethanol content of urine (UAC) which should have no carbohydrates (unless the deceased was diabetic) and vitreous humor with the BAC.

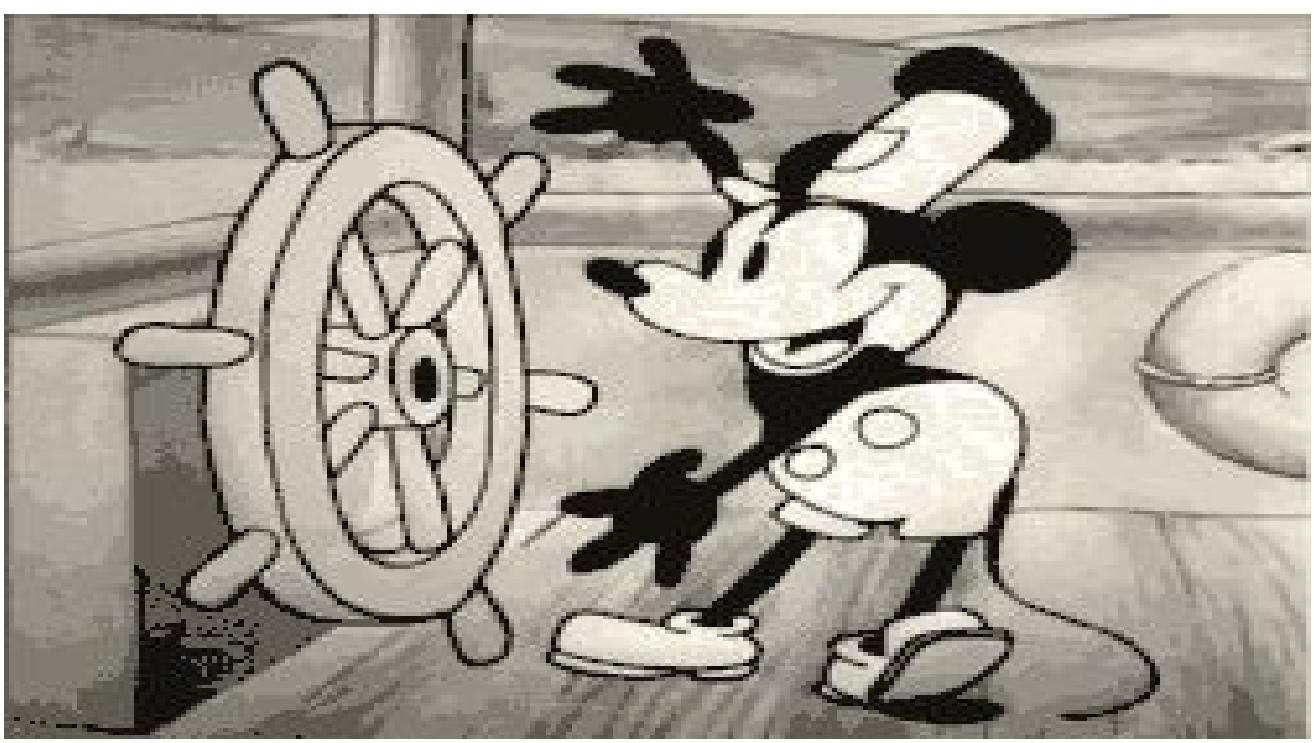
UAC:BAC Ratio (IMP.)

Less than 1:2 means ethanol concentrations were rising at time of death

More than 1:3 means that the decedent was in post-absorptive stage

Much much more than 1:3 means heavy consumption over a long period of time

Woah, look at you go! Tick off chapter 19!

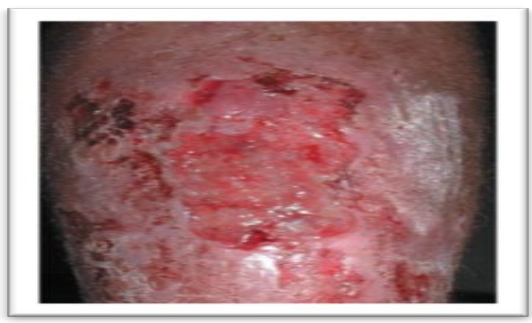


Chapter 20

Licit and Illicit Drugs

Harm Reduction

- Harm reduction (or harm minimization) refers to a range of public health policies designed to reduce the harmful consequences associated with drug use and other high-risk activities, and an essential part of the treatment of substance misuse.
- The area where complications of substance misuse have been substantially reduced is with regard to intravenous drug misusers. The most common complications are skin infections from unsafe injection practices.
- In some areas of the world essentially all injection drug users are infected with hepatitis C.



Legal Status of Drugs

- The penalties associated with crimes such as possession, possession with intent to supply, and importation may reflect the political, religious, cultural or social environment of the country in question.
- Drugs cost and availability **is influenced by demand and effect**.
- Increasingly 'legal highs' are being developed; these are often **synthetic drugs that mimic the effects of some illegal drugs**, and which may then be sold via the Internet. These are also considered illegal.

Commonly Misused Drugs

1)Stimulants:

★ All drugs in this group act by increasing concentrations of a neurotransmitter called dopamine which mediates the sense of pleasure.
★ When ingesting a moderate dose of stimulants it causes euphoria.
★ All stimulants -except khat- can be injected, snorted, or smoked.

Cocaine	Amphetamine
• Prevents the reuptake of dopamine, serotonin (which sometimes causes serotonin syndrome), and catecholamines (NE esp.) • Half-life = 1 hour. • Blood levels after smoking cocaine or injecting it are the same thing. • Heave users may manifest paranoid symptoms. When frank psychosis does occur it's in the form of Magnun Syndrome where users believe that bugs are crawling out of their skin (formication) and in extreme cases, this results in self-injury. • Blocks the Na and hERG K channels in the heart.	• Not only prevents the reuptake of dopamine but also causes presynaptic neurons to release extra. • Khat, fenethylline and captagon have almost the same structure as amphetamines • Half-life = 12 hours (meth). • Abusers can manifest florid paranoid psychosis. • Uniquely, psychosis may recur years after drug usage has been stopped which could be caused by damage to cortical white matter. • Interacts with the L-type Ca channels causing arrhythmias. •

Stimulants Continued:

- ★ Physical effects of stimulants include pupil dilation, increased heart rate, and raised bp.
- ★ The most feared consequence of stimulant abuse is excited delirium. The syndrome, often lethal, is notable for the acute onset of hyperthermia and agitated violent behavior that often culminates in sudden unexplained death.
- ★ Excess amounts of NE damage the walls of blood vessels potentially causing dissection, stroke, coronary artery spasm, and myocardial remodelling.
- ★ Stimulants also lead to prolonged repolarization of heart cells.

2)Opiates and Opioids:

- ★ "Opiates" refers to morphine, codeine, and compounds made by modification of the morphine molecule (tramadol, fentanyl, etc..).
- ★ They exert their effects by binding to the μ1 receptors located on neurons throughout the brain and intestines (this is why opiate users are almost always constipated) relieving pain, depressing respiration, and reducing gut motility.
- ★ The only important difference between different forms of opiates are their affinity for the μ1 receptor.
- ★ Complications of using opiates are often related to the process of injecting it.
- ★ Heroin smokers can develop a specific type of brain degeneration that is not different from mad cow diseases, but it is uncommon.
- ★ Tolerance to the pain relieving effects of morphine emerges quickly, but tolerance to respiratory depression is very slow.
- ★ The best known sign of acute opiate use are pinpoint pupils.
- ★ Withdrawal symptoms are: gooseflesh, rhinorrhea, lacrimation, yawning, abdominal pain, muscle pain, diarrhea, and vomiting.
- ★ Routine drug screening tests are antibody based and designed to attach to only morphine hence variants are hardly detected.

3)Sedative Hypnotics:

★ The drugs most frequently prescribed for insomnia are benzodiazepines (BZs), non-benzodiazepines (nonBZs), and anti-depressants (which are considered a third-line treatment and have not been authorized in most countries).
★ BZs increase the effect of a neurotransmitter known as GABA which is the major inhibitory neuron in the CNS. Any drug that can bind to the GABA A receptor is likely to exert sedative, anticonvulsant, and anxiolytic effects.
★ These drugs are usually very safe except when combined with other drugs such as alcohol, barbiturates, opiates, and TCAs which may cause coma and death mediated by respiratory depression. Flumazenil is an appropriate overdose reversal agent, but is unpredictable.
★ Supportive care in an appropriately monitored setting is usually sufficient treatment for those who have ingested sedatives.
★ Long-term usage of BZs leads to dependence and abrupt discontinuation may cause seizures. Non-BZs are effective and safer.

4)Hallucinogens:

★ All members are said to share five common properties:

1. Changes in mood and perception dominate;
2. There is minimal impairment of intellect or memory;
3. Use is not associated with agitation;
4. There are minimal side effects;
5. Craving and addiction do not occur.

★ Hallucinogens have been divided into two groups -the phenylalkylamines (mescaline) and indolealkylamines (psilocybin AKA magic mushrooms, LSD, and bufotenine)-
★ At worst, hallucinogen usage leads to behavioural toxicity.

5)Dissociative Anaesthetics:

- ★ Five drugs fall into this category: phencyclidine (PCP), ketamine, gamma-hydroxybutyrate, dextromethorphan, and Salvia divinorum. All are hallucinogens and the first four share the same MOA: blocking the NMDA receptor.
- ★ Salvia has no effect on the NMDA channel, instead it specifically blocks the K receptor. Drugs that bind to this receptor produce intense feelings of depression but has hallucinogenic effects.
- ★ There is evidence that stimulating the K receptor protects the neuron from damage by hypoxia/ischemia in particular.

6)Marijuana:

- ★ The body itself produces marijuana-like drugs called endocannabinoids that bind to receptors C1 and C2.
- ★ The active ingredient in marijuana (tetrahydrocannabinol AKA THC) binds to C1, C2, BZs, and opioid Rs.
- ★ THC increases pulse rate and may sometimes cause syncope.
- ★ THC remains in body fat stores for over a month. Hence, the interpretation of postmortem blood levels is almost impossible
- ★ There is no way to differentiate between THC ingested just before death or a month earlier.

7)Solvents:

- ★ Toluene volatizes at room temperature allowing users to inhale fumes. As opposed to the solvents found in glue or gas fuel, it is the most agent responsible for fatal intoxication by disrupting cardiac electrical activity. It is highly flammable so abusers may have burns.
- ★ Inhalation of any solvent will result in transient euphoria, headache, and ataxia. This selectively destroys brain white matter (seen on MRI).

8)New Synthetic Agents and Legal Highs:

- ★ Newly abused drugs belong to the class piperazines which were used to treat roundworms.
- ★ More than half of the cocaine sold in the USA is contaminated with an adulterant (renders something poorer in quality by adding another substance) known as levamisole inducing bone marrow suppression.
- ★ 1-Benzylpiperazine (BZP) is a legal alternative to amphetamine.
- ★ Trifluoromethylphenylpiperazine (TFMPP) is an alternative to MDMA.
- ★ Meta-chlorophenylpiperazine (MCPP) is a non selective serotonin receptor agonist.

Drug Facilitated Sexual Assault

- ★ Alcohol is the most important substance that facilitates sexual assault.
- ★ Gamma-hydroxybutyrate can also be used for sexual assault but it is produced as a post mortem artefact hence inferences about ingestion cannot be made.

You’re more than halfway through this! Chapter 20: check

Chapter 21

Medicinal Poisons

Introduction

Toxicity usually occurs as a result of the drug's ability to stimulate the same set of brain receptors as are stimulated by abused drugs. Analgesics such as oxycodone and hydrocodone bind to the same μ receptors as morphine. Antitussives, such as dextromethorphan, bind the same set of N-methyl-D-aspartate (NMDA) receptors as any other dissociative anesthetic. Barbiturate drugs are rarely the cause of death except possibly in epileptics, where death is more likely caused by the absence of the drug rather than any excess (sudden unexpected deaths in epileptics – SUDEP). Members of the benzodiazepine family (alprazolam, clonazepam, diazepam, zolpidem) bind the benzodiazepine receptor located on the γ-aminobutyric acid A (GABAA) receptor acting synergistically with opiates to depress respiration. When prescription medications are considered, two disorders have come to predominate most discussion: serotonin syndrome and QT interval prolongation.

Serotonin Syndrome

Serotonin syndrome is a potentially life-threatening adverse drug reaction caused by accumulation of serotonin within the synaptic cleft of neurons in the CNS. Second- and third-generation antidepressants are known to cause 'serotonin syndrome' in the same mechanism as that of cocaine. the antidepressants prevent the reuptake of serotonin leading to its accumulation. A spectrum of specific symptoms may occur. Full blown serotonin syndrome includes: cognitive (mental confusion, hypomania, hallucinations, agitation, headache and coma), autonomic (shivering, sweating, hyperthermia, hypertension, tachycardia, nausea and diarrhea) and somatic effects (myoclonus, hyperreflexia and tremor).

Drugs known to cause serotonin syndrome	
Antidepressants	-Monoamine oxidase inhibitors -Selective serotonin reuptake inhibitors -Tricyclic antidepressant -Bupropion -Trazodone
Opiates	- Buprenorphine -Fentanyl -Hydrocodone - Merperidine -Oxycodone -Pentazocine
Stimulate drugs	- Cocaine -All amphetamines -Methylphenidate
Migraine treatments	- All triptans (agents that bind type 1 serotonin receptors)
Psychedelics	- LSD (lysergic acid diethylamide) - MDMA (3,4-methylenedioxymethamphetamine, commonly known as ecstasy) - MDA (3,4-methylenedioxyamphetamine)
Miscellaneous agents	- Chlorpheniramine -Dextromethorphan -Lithium - Olanzapine -Risperidone -Ritonavir

QT Interval Prolongation

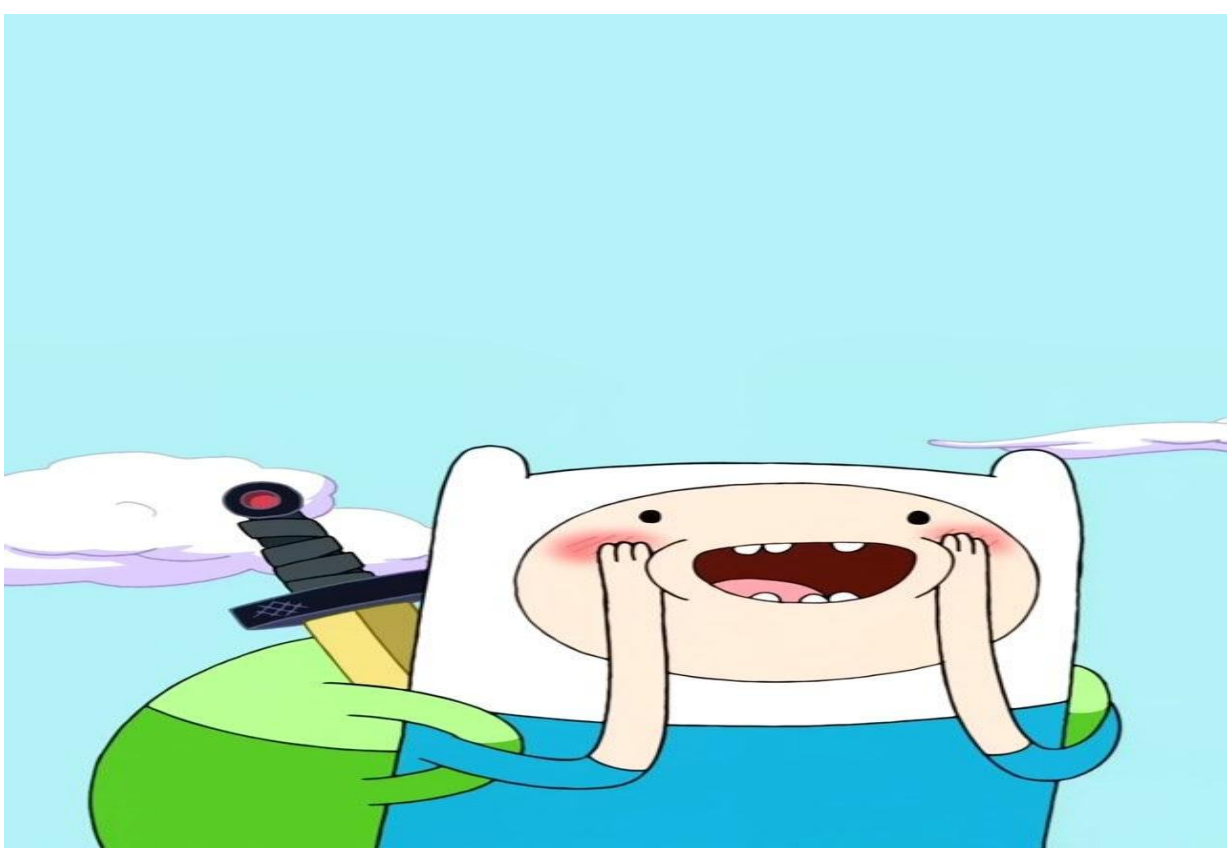
Abnormal prolongation on the ECG that represents repolarization of cardiomyocytes. The diagnosis of this syndrome cannot be made at autopsy except by DNA resequencing. The normal length for the QT interval is less than 440 milliseconds. A prolonged QT interval favors the occurrence of a lethal form of ventricular tachycardia known as torsades des pointes. Acquired LQTS is the result of an interaction between a drug and a 'rapid delayed repolarizing channel', abbreviated as hERG which is one of the channels that controls the orderly sequence of depolarization within the heart's individual cardiomyocytes causing QT prolongation, arrhythmia and death. Many drugs may cause this syndrome the most common is Methadone.

Drugs with Unique Modes of Action

They are three main drugs:

1. **Phenacetin**: poisoning with is is an exceedingly rare event because its proclivity to produce renal disease is well known. However, it is an effective pain reliever by virtue of its actions on the sensory tracts of the spinal cord.
2. **Lithium**: a mood stabilizer and its mode of action is not known with certainty. Most recently it has been proposed that lithium might restore normal brain function to those with bipolar disorder, and that it somehow does so by deactivating an enzyme called GSK-3B. Chronic lithium poisoning is associated with greater toxicity than acute ingestion, and is usually manifested by neurotoxicity of rapid onset. Another feature of lithium poisoning is delayed cardiotoxicity, usually bradycardia. Diagnosis of poisoning is by measurement of blood lithium concentrations.
3. **Insulin**: Insulin poisoning was once a popular means of homicide; now it is rare. Insulin overdose can cause fatal brain damage, and is confirmed by several different methods. C-Peptide is a peptide that is made when proinsulin is split into insulin and its C-peptide fragment. This event occurs just before release of insulin from the pancreas. If concentrations of the peptide are very low and insulin very high, this suggest that exogenous insulin had been administered. However, unless the blood specimen is frozen, levels of C-peptide may degrade rapidly. DNA analysis offers another possible approach. Biosynthetic ‘human’ insulin is now produced by genetic engineering which has a slightly different structure than human insulin and these differences can be detected. A friend, relative or caregiver is almost always the one who carries out homicide by insulin injection.

Just. One. More. Chapter. And. You'll. Be. Done. With. The. Longest. Session. We. Have.



Chapter 22

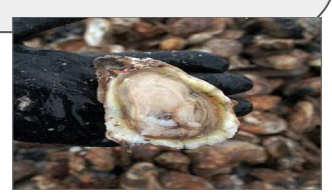
Miscellaneous Poisons

Arsenic

- The significance of its presence is difficult to determine, It may indicate acute poisoning or nothing at all. This because arsenic exists in two forms that we cannot differentiate post-mortem:

Organic: binds to another organic molecule to form arsenosugars or arsenobetaine and is unable to exert toxicity
E.g, coal

Inorganic: the arsenic atom is a salt that binds to another cation and when it dissociates from it that's when it is poisonous.
E.g. contaminated oysters



- The liver is capable of rapidly detoxifying free arsenic and excreting it unless it is overwhelmed.
- Poisoning is most likely to be seen in children who ingested arsenic pigments found in old lead-based paint.
- At any stage of arsenic poisoning the breath (and cadaver's tissues) may have garlic-like odor.

Three Forms of Arsenic Poisoning Exist

Acute	Subacute	Chronic
❖ When 1g or more of inorganic arsenic has been administered GI symptoms predominate with bloody vomiting and diarrhea. ❖ The diarrhea can cause shock and cardiorespiratory failure. ❖ If the victim dies quickly no abnormalities will evident at autopsy. ❖ If a few hours pass before death then the esophagus would be red and inflamed and sometimes the bowel will have a red velvet appearance. ❖ Bleeding of the left ventricular subendocardium is also a finding, but it's not specific.	Nothing remarkable	❖ It is sometimes diagnosed as gastroenteritis or neuropathy. ❖ Vague symptoms of leg and arm pain 2ry to arsenic-induced nerve damage. ❖ Skin may be overly dry and pigmented esp within the lines of the forehead and neck. ❖ Hair loss is common. ❖ The liver edges will contain fat. ❖ The kidneys and heart will be damaged but that would only show under a microscope. ❖ Nails may show 'Mee's Lines' which are transverse white bands.

Carbon Monoxide

- It is a colorless, odorless and non-irritant gas produced by the incomplete combustion of hydrocarbons and found whenever organic matter is burned in the presence of insufficient oxygen.
- Exposure occurs in two main ways:

1. Acute exposure where the effects are immediately obvious
2. Chronic exposure where the effects may be unrecognized.

- CO is absorbed through the lungs and binds to Hb forming COHb which causes a shift of the O-Hb dissociation curve to the left.
- CO causes cellular hypoxia and cardiac function becomes diminished.
- The amount of CO uptake is governed by a number of variables, all of which are interrelated and include: relative concentrations of CO and oxygen, alveolar ventilation, duration and intensity of exposure.
- the CH2OPD2 mnemonic is used to try to explore the source of environmental exposure (enquiring about Community, Home, Hobbies, Occupation, Personal, Diet and Drug issues).
- Classic acute CO intoxication is said to cause the triad of cherry-red lips, cyanosis and retinal haemorrhages, but this type is rare. It is described as the diseases with a thousand faces due to its clinical variance.
- Diagnosis is made by measurement of venous COHb levels; however, there is no absolute level that can confirm the presence or absence of poisoning. A level above 10 per cent is considered to confirm the diagnosis, unless the individual is a heavy smoker.

Cyanide

- Cyanide ions prevents cells from utilizing oxygen by inhibiting the enzyme cytochrome C oxidase.
- High concentrations of cyanide lead to cardiac arrest within minutes of exposure. Exposure to lower levels of cyanide over a long period for example after use of cassava roots as a primary food source will result in increased blood cyanide levels, which can cause weakness and a variety of symptoms including permanent paralysis.
- Cigarette smoking will increase blood cyanide levels but to modest levels.
- Large infusions of sodium nitroprusside, used to treat hypertensive emergencies, can lead to serious cyanide poisoning, but more commonly cyanide poisoning is encountered in fire survivors.
- Cyanide is said to have the smell of bitter almonds, but approximately 10 per cent of the general population are congenitally unable to perceive this smell.

Lead

- Routes of lead exposure include contaminated air, water, soil, food and certain lead-containing consumer products.
- In adults the most common cause of lead poisoning is occupational exposure, whereas in children it is the lead paint that exists in older homes.
- Lead is toxic because it can substitute for calcium in many fundamental cellular processes it can also cross red blood cell membranes as well as the blood–brain barrier and enter the neuroglia cells which support brain function.
- Symptoms of lead poisoning include abdominal pain, headache, anemia, irritability and, in severe cases, seizures, coma and death.

Lead Continued

- X-rays will expose dense lines in the long bones of children and red cells undergo a change known as basophilic stippling, where blue-staining remnants of destroyed DNA are seen lining the margins of the red cells. This change is diagnostic for lead poisoning.
- The main tool for diagnosis is measurement of the blood lead level. Treatment depends on the blood level and is designed to remove the lead from the body (chelation therapy).

Methanol

- Methanol can cause fatal central nervous system (CNS) depression, it is also toxic because it is metabolized to produce formic acid (present as the formate ion) via formaldehyde in a process initiated by the enzyme alcohol dehydrogenase (all of which occur in the liver).
- Formate inhibits mitochondrial cytochrome c oxidase, causing hypoxia at the cellular level and metabolic acidosis. It also may lead to blindness or even multi-organ system failure and death
- Methanol poisoning occurs after drinking windscreen-washer fluid or moonshine liquor.
- When pediatric poisoning occurs it is usually the result of having ingested methanol- containing household products.
- The initial symptoms of methanol intoxication include CNS depression, with headache, dizziness, nausea, lack of coordination and confusion. Large doses quickly lead to unconsciousness and death. Once the initial symptoms have passed, a second set of symptoms can be observed 10–30 hours after the ingestion. These include blindness and worsening acidosis. These secondary symptoms are caused by accumulating levels of formate in the bloodstream. The process may progress to death by respiratory failure.

Methanol Continued

- Methanol poisoning can be treated with the antidotes ethanol or fomepizole which compete with alcohol dehydrogenase so that the methanol is excreted by the kidneys instead of being converted into toxic metabolites. Supplemental treatment with sodium bicarbonate for metabolic acidosis and hemodialysis or even hemodiafiltration can be used to remove methanol and formate from the blood.
- Because of its toxic properties, methanol is frequently used as a denaturant additive for ethanol manufactured for industrial uses as this addition of methanol exempts industrial ethanol from liquor excise taxation. Methanol is often referred to as 'wood alcohol' because it was once produced chiefly as a by-product of the destructive distillation of wood.