PRINCIPLE OF TOXICOLOGY

Poison are substances which causes disturbance to organisms, usually by chemical reaction or other activity, therefore it is a substance that causes injury, illness or death of living organism, especially of chemical means.

Poisoning occurs when any substance interfere with normal body functions after iit is swallowed, inhaled, injected or adsorbed.

The branch of medicine that deals with the detection and treatment of poison is known as TOXICOLOGY.

REASON OR CAUSES OF POISON

1. Accidental
2. Incidental
3. Iatrogenic
4. Intentional

90% of all chemical- related deaths are due to –

1. Barbiturate
2. Salicylates
3. Ethanol
4. Carbon monoxide

TYPES OF POISONING SUBSTANCES

1. Pesticides- insecticide, fungicide, rodenticide, herbicide, fumigants
2. Based on route of entry- ingested, absorbed, inhaled, injected
3. Industrial pollutants
4. Automobile pollutants
5. Drug poisoning- opioids, sedatives, digoxin, alcohol, caffeine, cocaine, iron, NSAIDs
6. Nontoxic common households agents- shampoo, toothpaste, lipstick, creams, toilet soaps, cosmetics etc.

Classification of poison on the basis of symptoms-

1. Corrosive- strong acids, alkalides, metallic salts
2. Systemic- cerebral, spinal and peripheral.
3. Miscellaneous- food poisoning and botulism.

General principles of treatment of poisoning

History taking-

1. What and how?

2. How long, multiple? substances?
3. Treatment attempted
4. How? What advice?
5. History of suicide
6. Psychiatric history.

SIGN AND SYMPTOMS OF POISONING

Signs and symptoms of poisoning depend on the amount and type of toxin, the form of exposure (e.g., ingestion, skin absorption, inhalation), and the age and overall health of the person. In some cases, poisoning does not cause noticeable symptoms.

Signs that may indicate poisoning include the following:

- Drug or chemical containers that are open, spilled, or out of place
- Unusual odors (e.g., the breath or clothing, in the air)
- Spills and stains on clothing, skin, flooring, etc.
- Acute (sudden) or chronic (long-lasting) symptoms (e.g., behavior changes, drowsiness, heavy drooling, stomach pain, sweating, vomiting)

Symptoms can vary from mild to moderate to severe. Mild poisoning symptoms usually resolve quickly, are localized (i.e., affect one area of the body), and do not require medical treatment. Mild symptoms of poisoning may include the following:

1. Behavior changes (e.g., restlessness, crankiness)
2. Diarrhea
3. Dizziness
4. Drowsiness
5. Fatigue
6. Headache
7. Loss of appetite
8. Minor skin or eye irritation
9. Nausea or upset stomach
10. Passing cough (cough that comes and goes)
11. Soreness or stiffness in the joints

12. Thirst

Moderate symptoms of poisoning may be prolonged (i.e., long lasting) and systemic (i.e., affect more than one organ, organ system, or part of the body) and often require treatment. Moderate poisoning symptoms, which usually are not life threatening or permanent, may include the following:

1. Blurred vision
2. Confusion and disorientation
3. Difficulty breathing
4. Drooling
5. Excessive tearing
6. Fever
7. Low blood pressure (hypotension)
8. Loss of muscle control and muscle twitching
9. Paleness (pallor) or flushed or yellowish skin
10. Persistent cough
11. Rapid heart rate
12. Seizures
13. Severe diarrhea
14. Severe nausea
15. Stomach cramps
16. Sweating
17. Thirst
18. Trembling
19. Weakness

Severe poisoning symptoms are life threatening and can result in permanent brain damage, disability, or death. Major symptoms of poisoning include the following:

1. Cardiopulmonary arrest
2. Convulsions
3. Disseminated intravascular coagulation (condition that causes uncontrolled bleeding or blood clotting)

4. Esophageal stricture (narrowing of the organ that carries food from the mouth to the stomach)
5. Fever (often high)
6. Inability to breathe
7. Increased respiration (rapid breathing)
8. Loss of consciousness
9. Muscle twitching (uncontrolled and severe)
10. Rapid heart rate with low blood pressure
11. Respiratory distress that requires intubation (involves passing a tube down the trachea [windpipe] to the lungs to provide breathing assistance; mechanical respiration [i.e., a ventilator] may be necessary)
12. Seizures that do not respond to treatment (called status epilepticus)
13. Thirst (often extreme)

GENERAL TREATMENT OF POISONING

1. Identify the poison- first of all we have identified the type of poison based on symptoms and other factors.
2. Support vital function(ABC's)
    a. Secure airways
    b. Ensure adequate circulation
    c. Monitor ECG
    d. Obtain vascular access
    e. Manage hypotension
3. Keep patient calm and suppress convulsions- if convulsion provoked by the poison are not controlled by adequate ventilation, diazepam 10 mg i.v. should be administered in adults. Barbiturate must be avoided.
4. Maintain normal body temperature.
5. Fluid and electrolyte therapy- isotonic saline (0.9% w/v) or isotonic glucose (5% w/v) or plasma may be used.
6. Prevention of further absorption of poison.

Management

- Initial management for all poisonings includes ensuring adequate cardiopulmonary function and providing treatment for any symptoms such as seizures, shock, and pain.
- Injected poisons (e.g., from the sting of animals) can be treated by binding the affected body part with a pressure bandage and placing the affected body part in hot water (with a temperature of 50 °C). The pressure bandage prevents the poison being pumped throughout the body, and the hot water breaks it down. This treatment, however, only works with poisons composed of protein-molecules.
- In the majority of poisonings the mainstay of management is providing supportive care for the patient, i.e., treating the symptoms rather than the poison.

Decontamination

1. Treatment of a recently ingested poison may involve gastric decontamination to decrease absorption. Gastric decontamination can involve activated charcoal, gastric lavage, whole bowel irrigation, or nasogastric aspiration. Routine use of emetics (syrup of Ipecac), cathartics or laxatives are no longer recommended.
    a. Activated charcoal is the treatment of choice to prevent poison absorption. It is usually administered when the patient is in the emergency room or by a trained emergency healthcare provider such as a Paramedic or EMT. However, charcoal is ineffective against metals such as sodium, potassium, and lithium, and alcohols and glycols; it is also not recommended for ingestion of corrosive chemicals such as acids and alkalis.
    b. Cathartics were postulated to decrease absorption by increasing the expulsion of the poison from the gastrointestinal tract. There are two types of cathartics used in poisoned patients; saline cathartics (sodium sulfate, magnesium citrate, magnesium sulfate) and saccharide cathartics (sorbitol). They do not appear to improve patient outcome and are no longer recommended.
    c. Emesis (i.e. induced by ipecac) is no longer recommended in poisoning situations, because vomiting is ineffective at removing poisons.
    d. Gastric lavage, commonly known as a stomach pump, is the insertion of a tube into the stomach, followed by administration of water or saline down the tube. The liquid is then removed along with the contents of the stomach. Lavage has been used for many years as a common treatment for poisoned patients.

However, a recent review of the procedure in poisonings suggests no benefit. It is still sometimes used if it can be performed within 1 hour of ingestion and the exposure is potentially life-threatening.

e. Nasogastric aspiration involves the placement of a tube via the nose down into the stomach, the stomach contents are then removed by suction. This procedure is mainly used for liquid ingestions where activated charcoal is ineffective, e.g. ethylene glycol poisoning.
f. Whole bowel irrigation cleanses the bowel. This is achieved by giving the patient large amounts of a polyethylene glycol solution. The osmotically balanced polyethylene glycol solution is not absorbed into the body, having the effect of flushing out the entire gastrointestinal tract. Its major uses are to treat ingestion of sustained release drugs, toxins not absorbed by activated charcoal (e.g., lithium, iron), and for removal of ingested drug packets (body packing/smuggling).

Enhanced excretion

- In some situations elimination of the poison can be enhanced using diuresis, hemodialysis, hemoperfusion, hyperbaric medicine, peritoneal dialysis, exchange transfusion or chelation. However, this may actually worsen the poisoning in some cases, so it should always be verified based on what substances are involved.

Treatment for poisoning depends on the type of exposure (e.g., ingestion, inhalation), the specific toxin (poisonous substance), and the severity of the person's condition.

Initial Treatment for Poisoning-

In severe poisoning cases, the goal of initial treatment is basic life support (e.g., perform cardiopulmonary resuscitation [CPR], prevent or treat shock, treat serious burns). When the person is not breathing and is unresponsive following exposure to a toxic substance, **administer CPR (i.e., rescue breaths and chest compressions) and refer to the hospital,** where the some information required-

- Person's name, age, weight, address, telephone number
- Agent that was ingested (have the package with you when you call), inhaled, etc.

- Amount of the substance that was swallowed, spilled on the skin, etc.
- Person's condition and symptoms
- Amount of time that has passed since the agent was ingested, inhaled, etc.

Always **follow the advice of the Poison Control Center or a qualified health care provider** regarding treatment for poisoning. In some cases, the ingested poison should be diluted by drinking milk or water.

Using syrup of ipecac to induce vomiting (emesis) at home is **no longer recommended**. Activated charcoal, which binds ingested poisons so they are not easily absorbed, may be recommended instead. Administer syrup of ipecac or activated charcoal only as directed by the Poison Control Center or by a qualified health care provider.

If the person is in cardiopulmonary arrest, administer CPR. Do not return to any area where toxic fumes may be present.

If the child's skin or clothing has been exposed to a toxic substance, remove the clothing as quickly and carefully as possible and flush all exposed areas of skin with plenty of water.

If the child has gotten a poisonous substance in his or her eye, rinse the eye thoroughly with plain water that is room temperature for about 15 minutes. Then transport the child to the nearest emergency room. Bring all possible sources of the poisoning with you.

Medical Treatment for Poisoning

The goals of childhood poisoning treatment are to reduce absorption and increase elimination (excretion) of the toxin and provide supportive care. Medical treatment may include the following:

1. Activated charcoal (substance that binds ingested poisons and reduces absorption)
2. Induce vomiting (only under the supervision of a qualified health care provider)
3. Lavage (used only rarely in children; involves using a stomach tube to remove contents of the digestive tract)
4. Alkaline diuresis (involves using sodium bicarbonate to increase the alkalinity of the urine)

5. Dialysis (e.g., hemodialysis, peritoneal dialysis; used to remove toxins from the blood)
6. Intravenous (IV; administered through a vein) fluids

Medications may be used instead of or in addition to activated charcoal to treat certain types of poisoning. These drugs, which may be administered orally, intramuscularly (into muscle), or through an IV, include the following:

1. Acetylcysteine (e.g., to treat acetaminophen poisoning)
2. Diazepam (e.g., to treat amphetamine or antihistamine poisoning)
3. Dimercaprol (e.g., to treat arsenic, mercury, or lead poisoning)
4. Dexamethasone (e.g., to treat swelling in the brain [cerebral edema] caused by carbon monoxide poisoning)

Surgical Treatment for Poisoning

Childhood poisoning that involves a foreign object (e.g., small toy, battery) may require surgery to remove the object. In most cases, however, the object passes safely through the child's digestive tract. X-rays may be used to make sure that the object has not come apart of become trapped (e.g., in the esophagus). Sharp or caustic items may cause severe tissue damage and may be removed surgically.

BARBITURATE POISONING

A **barbiturate overdose** results when a person takes excessive doses of barbiturates. Symptoms of an overdose typically include sluggishness, incoordination, difficulty in thinking, slowness of speech, faulty judgment, drowsiness, shallow breaths, and staggering. In severe cases, coma and death can result. The lethal dosage of barbiturates varies greatly with tolerance and from one individual to another.

Sign and symptoms of barbiturate poisoning

This drug is normally abused to give a person a relaxed, sleepy feeling. They will lose their inhibitions and may walk unevenly and slur their speech as though drunk. Their blood pressure will drop and they will breathe more slowly. They will experience a lowering of anxiety.

If a person takes TOO much of this drug, the signs are striking.

Barbiturate Abuse causes-

1. Difficulty thinking
2. Poor judgment
3. Slow and shallow breathing
4. Slow talking
5. Lethargy
6. Extreme sleepiness or even coma
7. Poor coordination
8. Inability to walk properly, staggering or stumbling

If a person uses too much of this drug for too long, they can simply cease to function at an expected or efficient level. They can be irritable and have little memory. They will lack awareness of their surroundings, their problems and dangers.

Some young people who have been abusing stimulant drugs may seek barbiturates to help them come down from the high of the stimulant. Today's young drug abusers will not have experienced the heavier periods of barbiturate use and abuse that occurred in the 1960s and 1970s and so may abuse these dangerous drugs without realizing the problems that can occur, including overdose deaths. Miscarriages and birth defects are also signs of barbiturate abuse.

Barbiturate overdose with other CNS (central nervous system) depressants, such as alcohol, opiates or benzodiazepines, is even more dangerous due to additive CNS and respiratory depressant effects. In the case of benzodiazepines, barbiturates also increase the binding affinity of the benzodiazepine binding sites thus leading to an exaggerated benzodiazepine effect. This makes predicting the effect of combinations difficult and the same dose of the same drugs will not always produce the same degree of sedation and respiratory depression from one day to the next.

Benzodiazepines increase the frequency of chloride channel opening while barbiturates increase the duration that the chloride pore remains open. If a normal pore opened once every 30 seconds to pass one chloride ion, a benzodiazepine may cause it to open once every ten seconds while a barbiturate may cause it to remain open until three ions have passed through.

Separately, both of these increase the effect of the pore threefold, but together, the channel would allow three ions to pass every 10 seconds. This would exponentially increase the effect of the pore ninefold, greater than the sum of the two drugs effects.

The treatment of barbiturate abuse or overdose is generally supportive. The amount of support required depends on the person's symptoms. If the patient is drowsy but awake and can swallow and breathe without difficulty, the treatment can be as simple as monitoring the patient closely. If the patient is not breathing, it may involve mechanical ventilation until the drug has worn off.

Supportive treatment often includes the following:

1. Activated charcoal may be given via nasogastric tube.
2. Intravenous administration of saline, naloxone, thiamine, and/or glucose.
3. $NaHCO_3$ to alkalize the urine to increase rate of excretion.
4. Intubation and bemegride, or a hand-breather where these are not available until the patient can breathe under their own power.
5. Observation in the Emergency Department for a number of hours or admission to the hospital for several days of observation if symptoms are severe.
6. Advise the patient about drug misuse or refer for psychiatric consult.

OPIOID POISONING

Opioid are the steroidal anti-inflammatory analgesic drugs such as morphine, codeine, heroin, and methadone.

Sign and symptoms of opioid poisoning-

Excessive ingestion of opioids drug causes poisoning which include following symptoms-

1. Rashes
2. Fever
3. Cough
4. Headache
5. Abdominal pain
6. Runny nose
7. Nausea
8. Vomiting
9. Blurred vision

10. Bradycardia

Management of poisoning

1. Do not delay establishing a clear airway, adequate ventilation and oxygenation if consciousness is impaired.
2. Give naloxone intravenously (IV) (0.4-2 mg for an adult and 0.01 mg/kg body weight for children) if coma or respiratory depression is present.
3. Give intramuscularly (IM) if no vein is available. Repeat the dose if there is no response within two minutes. Naloxone is a competitive antagonist and large doses (4 mg) may be required in a severely poisoned patient.
4. Failure of a definite opiate overdose to respond to large doses of naloxone suggests that another central nervous system (CNS) depressant, or brain damage, is present.
5. Observe the patient carefully for recurrence of CNS and respiratory depression. The plasma half-life of naloxone is shorter than that of all opioid analgesics. Repeated doses may be required. Naloxone IM should be considered if the patient is threatening to self-discharge, as it may help reduce the risk of respiratory arrest when the IV naloxone wears off.
6. If someone takes an overdose of IV heroin it is important to administer naloxone as soon as possible. Often this is done by paramedics but some people have advocated that users should have a supply in case one of their number overdoses and treatment can be started without delay. They are often reluctant to call for help.
7. IV infusions of naloxone may be useful where repeated doses are required. Naloxone 400 micrograms/ml is diluted with sodium chloride 0.9 % or glucose 5%. Five ampoules of naloxone 400 micrograms/ml (2 mg) per 500 ml give 4 µg/ml. Two-thirds of the bolus dose needed to reverse intoxication given hourly as a continuous infusion often maintains respiratory effort without promoting opiate withdrawal. Infusions are not a substitute for frequent review of the patient's clinical state.
8. Give oral activated charcoal, provided the airway can be protected, if a substantial amount has been ingested within two hours.
9. Naltrexone is recommended by the National Institute for Health and Care Excellence (NICE) as a treatment option for people who have been opioid-dependent but who have stopped using opioids and who are highly motivated to

stay free from the drugs in an abstinence programme. It is a competitive opiate antagonist that will block the effect of heroin. It should only be given to people who have been told about the problems associated with treatment and with proper supervision. Treatment with naltrexone should be given as part of a support programme to help the person manage their opioid dependence.

10. There is no consensus about the management of patients if body packing of opioids is confirmed. Options include watchful waiting, with or without the use of laxatives, whole bowel irrigation, endoscopic removal or surgery. A risk-benefit analysis should be performed, taking into consideration whether the patient is symptomatic or asymptomatic and whether the treatment is likely to increase or decrease the risk of package rupture. Most patients can be managed by watchful waiting and discharged from hospital as soon as the package has been evacuated with a normal bowel movement. Surgery should only be performed in body packers with signs of intoxication or ileus.

ATROPINE POISONING

Atropine is a medication used to treat certain types of nerve agent and pesticide poisonings, some types of slow heart rate, and to decrease saliva production during surgery. It is typically given intravenously or by injection into a muscle. Eye drops are also available which are used to treat uveitis and early amblyopia. The intravenous solution usually begins working within a minute and lasts half an hour to an hour. Large doses may be required to treat poisonings.

Common side effects include a dry mouth, large pupils, urinary retention, constipation, and a fast heart rate. It should generally not be used in people with angle closure glaucoma. While there is no evidence that its use during pregnancy causes birth defects, it has not been well studied. It is likely safe during breastfeeding. It is an antimuscarinic (also known as an anticholinergic) that works by inhibiting the parasympathetic nervous system.

Atropine is not an actual antidote for organophosphate poisoning. However, by blocking the action of acetylcholine at muscarinic receptors, atropine also serves as a treatment for poisoning by organophosphate insecticides and nerve gases, such as tabun (GA), sarin (GB), soman (GD) and VX. Troops who are likely to be attacked with chemical weapons often carry autoinjectors with atropine and obidoxime, for rapid injection into the

muscles of the thigh. In a developed case of nerve-gas poisoning, maximum atropinization is desirable. Atropine is often used in conjunction with pralidoxime chloride.

Atropine is given as a treatment for SLUDGE syndrome (salivation, lacrimation, urination, diaphoresis, gastrointestinal motility, emesis) symptoms caused by organophosphate poisoning. Another mnemonic is DUMBBELSS, which stands for diarrhea, urination, miosis, bradycardia, bronchoconstriction, excitation (as of muscle in the form of fasciculations and CNS), lacrimation, salivation, and sweating (only sympathetic innervation using muscarinic receptors).

Some of the nerve agents attack and destroy acetylcholinesterase by phosphorylation, so the action of acetylcholine becomes excessive and prolonged. Pralidoxime (2-PAM) can be effective against organophosphate poisoning because it can re-cleave this phosphorylation. Atropine can be used to reduce the effect of the poisoning by blocking muscarinic acetylcholine receptors, which would otherwise be overstimulated, by excessive acetylcholine accumulation.

Side-effects

Adverse reactions to atropine include ventricular fibrillation, supraventricular or ventricular tachycardia, dizziness, nausea, blurred vision, loss of balance, dilated pupils, photophobia, dry mouth and potentially extreme confusion, dissociative hallucinations and excitation especially amongst the elderly.

In overdoses, atropine is poisonous. Atropine is sometimes added to potentially addictive drugs, particularly anti-diarrhea opioid drugs such as diphenoxylate or difenoxin, wherein the secretion-reducing effects of the atropine can also aid the anti-diarrhea effects.

Although atropine treats bradycardia (slow heart rate) in emergency settings, it can cause paradoxical heart rate slowing when given at very low doses (i.e. <0.5 mg), presumably as a result of central action in the CNS. One proposed mechanism for atropine's paradoxical bradycardia effect at low doses involves blockade of inhibitory presynaptic muscarinic autoreceptors, thereby blocking a system that inhibits the parasympathetic response.

Atropine is incapacitating at doses of 10 to 20 mg per person. Its LD_{50} is estimated to be 453 mg per person (by mouth). The antidote to atropine is physostigmine or pilocarpine.

A common mnemonic used to describe the physiologic manifestations of atropine overdose is: "hot as a hare, blind as a bat, dry as a bone, red as a beet, and mad as a hatter".These associations reflect the specific changes of warm, dry skin from decreased sweating, blurry vision, decreased sweating/lacrimation, vasodilation, and central nervous system effects on muscarinic receptors, type 4 and 5. This set of symptoms is known as anticholinergic toxidrome, and may also be caused by other drugs with anticholinergic effects, such as scopolamine, diphenhydramine, phenothiazine antipsychotics and benztropine.

Contraindications

Atropine is contraindicated in patients pre-disposed to narrow angle glaucoma.

Mechanism of action

In general, atropine counters the "rest and digest" activity of glands regulated by the parasympathetic nervous system. This occurs because atropine is a competitive, reversible antagonist of the muscarinic acetylcholine receptors (acetylcholine being the main neurotransmitter used by the parasympathetic nervous system).

Atropine is a competitive inverse agonist for the muscarinic acetylcholine receptor types M1, M2, M3, M4 and M5. It is classified as an anticholinergic drug (parasympatholytic).

In cardiac uses, it works as a nonselective muscarinic acetylcholinergic antagonist, increasing firing of the sinoatrial node (SA) and conduction through the atrioventricular node (AV) of the heart, opposes the actions of the vagus nerve, blocks acetylcholine receptor sites, and decreases bronchial secretions.

In the eye, atropine induces mydriasis by blocking contraction of the circular pupillary sphincter muscle, which is normally stimulated by acetylcholine release, thereby allowing the radial pupillary dilator muscle to contract and dilate the pupil. Atropine induces cycloplegia by paralyzing the ciliary muscles, whose action inhibits accommodation to allow accurate refraction in children, helps to relieve pain associated with iridocyclitis, and treats ciliary block (malignant) glaucoma.

Physostigmine, given as an **atropine** antidote by slow intravenous injection of 1 to 4 mg (0.5 to 1.0 mg in children), rapidly abolishes delirium and coma caused by large doses of **atropine**.

ORGANOPHOSPHOROUS POISONING

Organophosphate poisoning results from exposure to organophosphates (OPs), which cause the inhibition of acetylcholinesterase (AChE), leading to the accumulation of acetylcholine (ACh) in the body. Organophosphate poisoning most commonly results from exposure to insecticides or nerve agents. OPs are one of the most common causes of poisoning worldwide, are usually associated suicides in agrarian areas. There are around 1 million OP poisonings per year with several hundred thousand resulting in fatalities annually.

Organophosphates inhibit AChE, causing OP poisoning by phosphorylating the serine hydroxyl residue on AChE, which inactivates AChE. AChE is critical for nerve function, so the irreversible blockage of this enzyme, which causes acetylcholine accumulation, results in muscle overstimulation. This causes disturbances across the cholinergic synapses and can only be reactivated very slowly, if at all. Paraoxonase (PON1) is a key enzyme involved in OP pesticides and has been found to be critical in determining an organism's sensitivity to OP exposure.

Examples

- Insecticides including malathion, parathion, diazinon, fenthion, dichlorvos, chlorpyrifos, ethion, trichlorfon
- Nerve gases including soman, sarin, tabun, VX
- Herbicides including tribufos [DEF], merphos are tricresyl phosphate–containing industrial chemicals.

Exposure to any one of the above-listed organophosphates occurs on a daily basis through inhalation, absorption, and ingestion, most commonly of food that has been treated with an organophosphate herbicide or insecticide. Exposure to these chemicals can occur at public buildings, schools, residential areas, and in agricultural areas. The chemicals chlorpyrifos and malathion have been linked to reproductive effects, neurotoxicity, kidney/liver damage, and

birth defects. Dichlorvos has also been linked to reproductive effects, neurotoxicity, and kidney/liver damage, as well as being a possible carcinogen.

Signs and symptoms

The health effects associated with organophosphate poisoning are a result of excess acetylcholine (ACh) present at different nerves and receptors in the body because acetylcholinesterase is blocked.

Accumulation of ACh at motor nerves causes overstimulation of nicotinic expression at the neuromuscular junction. When this occurs symptoms such as muscle weakness, fatigue, muscle cramps, fasciculation, and paralysis can be seen. When there is an accumulation of ACh at autonomic ganglia this causes overstimulation of nicotinic expression in the sympathetic system.

Symptoms associated with this are hypertension, and hypoglycemia. Overstimulation of nicotinic acetylcholine receptors in the central nervous system, due to accumulation of ACh, results in anxiety, headache, convulsions, ataxia, depression of respiration and circulation, tremor, general weakness, and potentially coma.

When there is expression of muscarinic overstimulation due to excess acetylcholine at muscarinic acetylcholine receptors symptoms of visual disturbances, tightness in chest, wheezing due to bronchoconstriction, increased bronchial secretions, increased salivation, lacrimation, sweating, peristalsis, and urination can occur.

The effects of organophosphate poisoning on muscarinic receptors are recalled using the mnemonic SLUDGEM (Salivation, Lacrimation, Urination, Defecation, gastrointestinal motility, Emesis, miosis). An additional mnemonic is MUDDLES: miosis, urination, diarrhea, diaphoresis, lacrimation, excitation, and salivation.

The onset and severity of symptoms, whether acute or chronic, depends upon the specific chemical, the route of exposure, the dose, and the individuals ability to degrade the compound, which the PON1 enzyme level will affect.

Reproductive effects

Certain reproductive effects in fertility, growth, and development for males and females have been linked specifically to OP pesticide exposure. Most of the research on reproductive effects has been conducted on farmers working with pesticides and insecticdes in rural areas. For those males exposed to OP pesticides, poor semen and sperm quality have been seen, including reduced seminal volume and percentage motility, as well as a decrease in sperm count per ejacuate. In females menstrual cycle disturbances, longer pregnancies, spontaneous abortions, stillbirths, and some developmental effects in offspring have been linked to OP pesticide exposure.

Neurotoxic effects

Neurotoxic effects have also been linked to poisoning with OP pesticides causing four neurotoxic effects in humans: cholinergic syndrome, intermediate syndrome, organophosphate-induced delayed polyneuropathy (OPIDP), and chronic organophosphate-induced neuropsychiatric disorder (COPIND). These syndromes result after acute and chronic exposure to OP pesticides.

Cholinergic syndrome occurs in acute poisonings with OP pesticides and is directly related to levels of AChE activity. Symptoms include miosis, sweating, lacrimation, gastrointestinal symptoms, respiratory difficulties, shortness of breath, slowed heart rate, cyanosis, vomiting, diarrhea, as well as other symptoms.

Effects on developing animals

Evidence of exposure to OP pesticides during gestation and early postnatal period have been linked to neurodevelopmental effects in animals, specifically rats.

Cause

OP pesticide exposure occurs through inhalation, ingestion and dermal contact. Because OP pesticides disintegrate quickly in air and light, they have been considered relatively safe to consumers. However, OP residues linger on fruits and vegetables. Certain OP pesticides have been banned for use on some crops, for example methyl parathion is banned from use on some crops while permitted on others.

Pathophysiology

Paraoxonase (PON1) is a key enzyme in the metabolism of organophosphates. PON1 can inactivate some OPs through hydrolysis. PON1 hydrolyzes the active metabolites in several OP insecticides such as chlorpyrifos oxon, and diazoxon, as well as, nerve agents such as soman, sarin, and VX. PON1 hydrolyzes the metabolites, not the parent compounds of insectides.

The presence of PON1 polymorphisms causes there to be different enzyme levels and catalytic efficiency of this esterase, which in turn suggests that different individuals may be more susceptible to the toxic effect of OP exposure. The level of PON1 plasma hydrolytic activity provides more protection against OP pesticides. Rats injected with purified PON1 from rabbit serum were more resistant to acute cholinergic activity than the control rats. PON1 knockouts in mice are found to be more sensitive to the toxicity of pesticides, like chlorpyrifos. Animal experiments indicate that while PON1 plays a significant role in regulating the toxicity of OPs its degree of protection given depends on the compound (i.e. Chlorpyrifos oxon or diazoxon). The catalytic efficiency with which PON1 can degrade toxic OPs determines the degree of protection that PON1 can provide for organism. The higher the concentration of PON1 the better the protection provided. PON1 activity is much lower in neonates, so neonates are more sensitive to OP exposure

Diagnosis

A number of measurements exist to assess exposure and early biological effects for organophosphate poisoning. Measurements of OP metabolites in both the blood and urine can be used to determine if a person has been exposed to organophosphates. Specifically in the blood, metabolites of cholinesterases, such as butyrylcholinesterase (BuChE) activity in plasma, neuropathy target esterase (NTE) in lymphocytes, and of acetylcholinesterase (AChE) activity in red blood cells. Due to both AChE and BuChE being the main targets of organophosphates, their measurement is widely used as an indication of an exposure to an OP. The main restriction on this type of diagnosis is that depending on the OP the degree to which either AChE or BuChE are inhibited differs; therefore, measure of metabolites in blood and urine do not specify for a certain OP.

Treatment

Current antidotes for OP poisoning consist of a pretreatment with carbamates to protect AChE from inhibition by OP compounds and post-exposure treatments with anti-cholinergic drugs. Anti-cholinergic drugs work to counteract the effects of excess acetylcholine and reactivate AChE. Atropine can be used as an antidote in conjunction with pralidoxime or other pyridinium oximes (such as trimedoxime or obidoxime), though the use of "-oximes" has been found to be of no benefit, or possibly harmful, in at least two meta-analyses.

Atropine is a muscarinic antagonist, and thus blocks the action of acetylcholine peripherally. These antidotes are effective at preventing lethality from OP poisoning, but current treatment lack the ability to prevent post-exposure incapacitation, performance deficits, or permanent brain damage. While the efficacy of atropine has been well-established, clinical experience with pralidoxime has led to widespread doubt about its efficacy in treatment of OP poisoning.

Enzyme bioscavengers are being developed as a pretreatment to sequester highly toxic OPs before they can reach their physiological targets and prevent the toxic effects from occurring. Significant advances with cholinesterases (ChEs), specifically human serum BChE (HuBChE) have been made. HuBChe can offer a broad range of protection for nerve agents including soman, sarin, tabun, and VX. HuBChE also possess a very long retention time in the human circulation system and because it is from a human source it will not produce any antagonistic immunological responses.

HEAVY METAL POISONING

Metal toxicity or **metal poisoning** is the toxic effect of certain metals in certain forms and doses on life. Some metals are toxic when they form poisonous soluble compounds. Certain metals have no biological role, i.e. are not essential minerals, or are toxic when in a certain form. In the case of lead, any measurable amount may have negative health effects. Often heavy metals are thought as synonymous, but lighter metals may also be toxic in certain circumstances, such as beryllium and lithium. Not all heavy metals are particularly toxic, and some are essential, such as iron. The definition may also include trace elements when considered in abnormally high, toxic doses. An option for treatment of metal poisoning

may be chelation therapy, which is a technique which involves the administration of chelation agents to remove metals from the body.

Toxic metals sometimes imitate the action of an essential element in the body, interfering with the metabolic process to cause illness. Many metals, particularly heavy metals are toxic, but some heavy metals are essential, and some, such as bismuth, have a low toxicity. Most often the definition of toxic metals includes at least cadmium, manganese, lead, mercury and the radioactive metals. Metalloids (arsenic, polonium) may be included in the definition. Radioactive metals have both radiological toxicity and chemical toxicity. Metals in an oxidation state abnormal to the body may also become toxic: chromium(III) is an essential trace element, but chromium(VI) is a carcinogen.

Toxicity is a function of solubility. Insoluble compounds as well as the metallic forms often exhibit negligible toxicity. The toxicity of any metal depends on its ligands. In some cases, organometallic forms, such as methylmercury and tetraethyl lead, can be extremely toxic. In other cases, organometallic derivatives are less toxic such as the cobaltocenium cation.

Decontamination for toxic metals is different from organic toxins: because toxic metals are elements, they cannot be destroyed. Toxic metals may be made insoluble or collected, possibly by the aid of chelating agents. Alternatively, they can be diluted into a sufficiently large reservoir, such as the sea, because immediate toxicity is a function of concentration rather than amount. However, bioaccumulation has the potential to reverse this.

Toxic metals can bioaccumulate in the body and in the food chain. Therefore, a common characteristic of toxic metals is the chronic nature of their toxicity. This is particularly notable with radioactive heavy metals such as radium, which imitates calcium to the point of being incorporated into human bone, although similar health implications are found in lead or mercury poisoning. The exceptions to this are barium and aluminium, which can be removed efficiently by the kidneys.

Testing for poisoning

People are continually exposed to metals in the environment. Medical tests can detect metals often, but this is to be expected and alone is not evidence that a person is poisoned.

Metal screening tests should not be used unless there is reason to believe that a person has had excessive exposure to metals. People should seek medical testing for poisoning only if they are concerned for a particular reason, and physicians should consider a patient's history and physical examination before conducting tests to detect metals.

Treatment for poisoning

Chelation therapy is a medical procedure that involves the administration of chelating agents to remove heavy metals from the body. Chelating agents are molecules that have multiple electron-donating groups, which can form stable coordination complexes with metal ions. Complexation prevents the metal ions from reacting with molecules in the body, and enable them to be dissolved in blood and eliminated in urine. It should only be used in people who have a diagnosis of metal intoxication. That diagnosis should be validated with tests done in appropriate biological samples.

Chelation therapy is administered under very careful medical supervision due to various inherent risks. When the therapy is administered properly, the chelation drugs have significant side effects. Chelation administered inappropriately can cause neurodevelopmental toxicity, increase risk of developing cancer, and cause death; chelation also removes essential metal elements and requires measures to prevent their loss.

Arsenic poisoning

Arsenic poisoning is a medical condition caused by elevated levels of arsenic in the body. The dominant basis of arsenic poisoning is from ground water that naturally contains high concentrations of arsenic. A 2007 study found that over 137 million people in more than 70 countries are probably affected by arsenic poisoning from drinking water.

British anti lewisite(BAL) and ethyl diamine tetra acetic acid(EDTA) are also used as effective antidote by i.v. routes.

Cadmium poisoning

Cadmium is an extremely toxic metal commonly found in industrial workplaces. Due to its low permissible exposure limit, overexposures may occur even in situations where trace quantities of cadmium are found. Cadmium is used extensively in electroplating, although the

nature of the operation does not generally lead to overexposures. Cadmium is also found in some industrial paints and may represent a hazard when sprayed. Operations involving removal of cadmium paints by scraping or blasting may pose a significant hazard. Cadmium is also present in the manufacturing of some types of batteries. Exposures to cadmium are addressed in specific standards for the general industry, shipyard employment, construction industry, and the agricultural industry.

Copper toxicity

Copper toxicity, also called **copperiedus**, refers to the consequences of an excess of copper in the body. Copperiedus can occur from eating acid foods cooked in uncoated copper cookware, or from exposure to excess copper in drinking water, as a side-effect of estrogen birth control pills, or other environmental sources. It can also result from the genetic condition Wilson's disease.

Iron poisoning

Iron poisoning is an iron overload caused by a large excess of iron intake and usually refers to an acute overload rather than a gradual one. The term has been primarily associated with young children who consumed large quantities of iron supplement pills, which resemble sweets and are widely used, including by pregnant women—see overnutrition (approximately 3 grams is lethal for a 2 year old).

Treatment- chelation with deferoxamine

Lead poisoning

Lead poisoning is a medical condition in humans and other vertebrates caused by increased levels of the heavy metal lead in the body. Lead interferes with a variety of body processes and is toxic to many organs and tissues including the heart, bones, intestines, kidneys, and reproductive and nervous systems. It interferes with the development of the nervous system and is therefore particularly toxic to children, causing potentially permanent learning and behavior disorders. Symptoms include abdominal pain, confusion, headache, anemia, irritability, and in severe cases seizures, coma, and death.

Lithium poisoning

Lithium is used in some medications, specifically to treat bi-polar disorder. The level of "sufficient" medication is thought by many physicians to be close to toxic tolerance for kidney function. Therefore, the patient is often monitored for this purpose.

Manganese poisoning, or manganism

Manganism or manganese poisoning is a toxic condition resulting from chronic exposure to manganese.

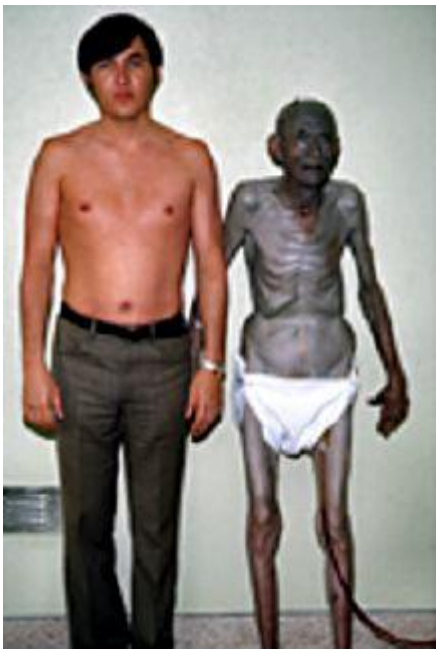
Mercury poisoning

Mercury poisoning is a disease caused by exposure to mercury or its compounds. Mercury (chemical symbol Hg) is a heavy metal occurring in several forms, all of which can produce toxic effects in high enough doses. Its zero oxidation state Hg^0 exists as vapor or as liquid metal, its mercurous state Hg_2^{2+} exists as inorganic salts, and its mercuric state Hg^{2+} may form either inorganic salts or organomercury compounds; the three groups vary in effects. Toxic effects include damage to the brain, kidney, and lungs. Mercury poisoning can result in several diseases, including acrodynia (pink disease), Hunter-Russell syndrome, and Minamata disease.

Symptoms typically include sensory impairment (vision, hearing, speech), disturbed sensation and a lack of coordination. The type and degree of symptoms exhibited depend upon the individual toxin, the dose, and the method and duration of exposure.

Specific antidote- BAL, Sodium thiosulphate and calcium disodium edentate.

Silver poisoning, or Argyria



A 92-year-old Caucasian man (right) with pigmentary changes had used nose drops containing silver for many years. His skin biopsy showed silver deposits in the dermis, confirming the diagnosis of generalized argyria.

Argyria or argyrosis is a condition caused by inappropriate exposure to chemical compounds of the element silver, or to silver dust. The most dramatic symptom of argyria is that the skin turns blue or bluish-grey. It may take the form of *generalized argyria* or *local argyria*. Generalized argyria affects large areas over much of the visible surface of the body. Local argyria shows in limited regions of the body, such as patches of skin, parts of the mucous membrane or the conjunctiva.

Thallium poisoning

Thallium and its compounds are often highly toxic. Contact with skin is dangerous, and adequate ventilation should be provided when melting this metal. Many thallium(I) compounds are highly soluble in water and are readily absorbed through the skin. Exposure to them should not exceed 0.1 mg per m^2 of skin in an 8-hour time-weighted average (40-hour work week). Thallium is a suspected human carcinogen.

Tin poisoning

Tin poisoning refers to the toxic effects of tin and its compounds. Cases of poisoning from tin metal, its oxides, and its salts are "almost unknown"; on the other hand certain organotin compounds are almost as toxic as cyanide.

Zinc toxicity

Even though zinc is an essential requirement for a healthy body, excess zinc can be harmful, and cause **zinc toxicity**. Such toxicity levels have been seen to occur at ingestion of greater than 225 mg of Zinc. Excessive absorption of zinc can suppress copper and iron absorption. The free zinc ion in solution is highly toxic to bacteria, plants, invertebrates, and even vertebrate fish.

Society and culture

It is difficult to differentiate the effects of low level metal poisoning from the environment with other kinds of environmental harms, including nonmetal pollution. Generally, increased exposure to heavy metals in the environment increases risk of developing cancer.

Without a diagnosis of metal toxicity and outside of evidence-based medicine, but perhaps because of worry about metal toxicity, some people seek chelation therapy to treat autism, cardiovascular disease, Alzheimer's disease, or any sort of neurodegeneration. Chelation therapy does not improve outcomes for those diseases.

CHELATION THERAPY-

S.NO.	CHELATING AGENT	TOXIN	ROUTE	DRUG
1.	Dimercaprol	Ar, Pb, Hg	i.m.	Dimercaprol inj
2.	DMSA	Ar, Pb, Hg	p.o.	-
3.	DMPS	Ar	p.o., i.m.	Bulk form
4.	D-Penicillamine	Ar, Pb, Hg	p.o.	Penicillamine, cuprimine
5.	EDTA	Pb	i.v.	Chelamide versanate