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# Neurotoxicity: A Devastation to CNS

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***Abstract:***
***The word "neuro" is originated from the classical Greek word "neuron" which means nerves and nervous system which plays a very essential role in functioning of different body parts of humans and animals.[1] Neurotoxins are those kinds of toxic substances which are when encountered with living body by what's so ever way i.e. Cutaneous, Sub-cutaneous, Ocular, Muscular or Intravenous, causes maladaptive and detrimental behaviour of CNS (Central nervous system) which leads to evolve various diseases and ultimately death. Neurotoxicity is the direct or indirect ramifications of nerve cells and nervous systems which especially effects to the cellular metabolic processes on which CNS mutually depends.[2] Neurotoxicity is usually self-sustaining and rarely progressive when discontinued in exposure with body but there can be delay in between the contact time and the neurotoxic effects.[3]***

***Keywords: Neurotoxicity, Neurotoxins, Neurons, CNS***

## 1. INTRODUCTION:

Neurotoxins were absorbed in body through inhalation, ingestion, skin exposure, or by injection and might have midway or long-lasting effects by administering neurons to disfunction or by agitate interneuron communication. unintelligible words or poor organization thanks to deadly effects on neurons from the consumption of alcohol, for instance, are provisional, whereas psychological feature injury caused by the exposure of neurotoxins is inevitable. [4] The extent to that a toxin affects nerve function depends on the toxicity of the material and on the persons age and health (especially hepatic and nephritic health) at the time of contact with neurotoxins. It additionally depends on the extent and recurrence of exposure with a chemical; An equivalent material will have each therapeutic and deadly effects at totally distinct concentration levels [5].

The nervous system includes the brain, the neural structure, and a complicated network of nerve processes that manages major body functions such as movement, thought, hearing, speech, vision, respiration, heart operate, and diverse alternative physiological mechanisms are controlled by this cluster of nerves, hormones, receptors, transmitters, and channels. Even main systems of body are adversely laid low with deadly substances, the nervous system is especially susceptible to them. Several deadly substances will alter the traditional activity of the nervous system. [6] Some turn out effects occur before long lasting for an amount of many hours. The results of alternative toxin substances could seem solely once continual exposures over weeks or maybe years. Some substances will for good injury the nervous system once one exposure: bound organophosphorus pesticides and metal compounds.

Alternative substances, together with abused medicine like diacetylmorphine and cocaine, could result in addiction, a semi-permanent adverse alteration of nervous system operate. Several toxin substances will cause death once absorbed, inhaled, or eaten in adequately massive amount. It is outlined that any substance is taken into account to possess toxin potential if it negatively affects any of the structural or practical parts of the nervous system. At molecular level, a substance would possibly inhibit with macromolecule synthesis in bound nerve cells, resulting in decreased manufacture of a neurochemical and brain pathology.[7] Substances that adversely have an effect on sensory or motor nervous system, disturbs learning and memory processes, or creates prejudices activity effects are toxin, albeit the underlying cellular and molecular effects on the nervous system haven't been known. Neurotoxic substances embrace present parts like lead and mercury, biological compounds like neurolysin (manufactured by bound bacteria) and artificial compounds, together with several pesticides and industrial solvents. Some commonly encountered materials are toxin however might not be identified intrinsically. For instance, bound associatetibiotics and bactericide (once oft used as a medication agent in soaps) are toxin once adequately massive quantities are eaten or absorbed by the skin; but, contact to massive quantities are rare. [8] Several therapeutic medicine and abused materials even have toxin potential. Toxin materials will cause a spread of negative health effects, starting from impairment of muscular movement to disruption of hearing and vision, to cognitive state and hallucinations. Some materials cause disfunction and death. Often, toxin effects are unstable, that is, the results decrease with time once exposure ceases and no negative effects on the nervous system are remained to stay. At times, the results are inevitable and result in long-lasting changes within the nervous system. [9]

Due to the low detectable property of neurotoxin it is commonly used as an ideal killing poison because its symptoms appear naturally and once after exposure to many neurotoxins such as barbiturates, opium, cocaine, cannabis, datura. Provides natural effects. Psychodelic drugs (lysergic acid diethylamide) alcohol, arsenic, mercury, lead, organophosphorus and carbamates are fairly common neurotoxins. [10]

*Various Neurotoxins:*

*1. Barbiturates:*

Barbiturates are CNS depressants. They act by reducing the activity of nerves inflicting muscle relaxation. Another feature of barbiturates is that they reduce heart rate, breathing, and blood pressure. All barbiturates have an effect on gamma-aminobutyric acid (GABA), a neuro-transmitter agent (chemical) used in communication between nerves.[11]

**Chemical Name:** 2, 4, 6(1H, 3H, 5H) Pyrimidinetrione

**Formula:** C4H3N2O3

**Active Principle**: Pentobarbital, Secobarbital, Butabarbital, Methylphenobarbital, Methohexital.

**Mode of Action:** Barbiturates are usually depressants to all cell of the human body generally acting as a cellular histotoxic agent, however, the cells of the central nervous system are additionally more sensitive to barbiturate drug action once taken with alcoholic beverages having an immediate action by depressing the central nervous system thus by resulting in death.[12]

**Fatal Dose:** 2-6 gms.

**Fatal Period:** 12-24 hours.

**Signs & Symptoms:**

**Acute effect:** Awake, competent, sleepy, comatose, cardio respiratory failure.

**Chronic effect:** Impaired mental ability, Tremors, Ataxia, loss of memory and irritability.
**Medicolegal & Post mortem findings:**
It is quite commonly used as a suicidal poison for painless death particularly for medical personals and is also used majorly as a homicidal poisoning. Commonly these drugs are often mixed with alcoholic beverages. In brain petechial haemorrhages is also found, Internal organs like (lungs, liver, kidney, spleen) were found to be conjested.[14]

*2. Opium:*

Opium is extracted from Papaver somniferum plant, additionally referred to as poppies. These particular plant species is generally belongs to the family of Papaveraceae, and it's characterized by capsulate fruits and solitary. Therefore, the narcotic obtained from such plants are sticky brown paste achieved by aggregation and drying the latex that exudes from the pods of flower.[15] The opium paste or extract contains mainly two groups of alkaloids; the psychoactive component that are within the class of phenanthrenes and alkaloids that haven't any effect on the central nervous systemand are thus categorized within the isoquinolines class. Morphine is the most prevailing and principal organic compound in narcotic, and it's liable for most of the adverse effects of opium. [16]

**Scientific Name:** Papaver somniferum.
**Active Principle:** Opium contains about 25 alkaloids and are divided into two groups

1. Phenanthrene: morphine, codeine, thebaine and their derivative heroine.[17]
2. Benzyl Isoquinoline: papaverine & narcotine.[18]

**Mode of Action:** Once opium is taken in, its effects are shown by activating specific G protein-coupled receptors within the brain, spinal nervous system, and peripheral system nervous. [20] Opium can generate agonist activity which is able to later on open the K channels and prevents the opening of voltage-gated Ca channels. This activity causes decrease in neuron cell excitability and thus obstructs the production of neurotransmitters responsible for the production or feeling any pain. [19]

**Fatal Dose:** 300mg.
**Fatal Period:** 8-12 hours.
**Signs & Symptoms:**
**Acute effect:** Euphoria, hallucinations, flushed face, vomiting, nausea, lethargy.
**Chronic effect:** Deep coma, muscles reflexes are lost, pale yellow face, respiratory depression.
*Medicolegal & Post mortem findings:*
It is quite commonly used as a means of suicidal poison for painless death. It's a rare case if opium is used as means of homicidal poison due to the fact that opium has a characteristic bitter taste and a foul pungent smell. The brain and its membranes are congested, Face and finger nails may turn blue due to cyanosis, trachea is found congested and rosy colored, lungs are full and oedematous. The heart may be filled with blood on the right side and the left is empty.[21]

*3. Cocaine:*

It is additionally referred to as snow and coke, it is a stimulant which is mostly used as a competitive narcotic. it's normally inhaled, snorted, smoked, or dissolved and injected into a vein of the body. Mental changes might include signs such as loss of interaction with reality, feeling of happiness, or agitation.[22]

**Scientific Name:** Erythroxylon coca.
**Formula:** $C_{17}H_{21}NO_4$
**Active Principle:** Cocaine hydrochloride.

**Mode of Action:** The neurotransmitters which are mainly found in the brain that the cocaine disturbs are norepinephrine, serotonin, and dopamine. [24] Once the cocaine is snorted or sniffed it immediately enters the blood stream and thus creates an intense rush or high spirits that lasts for twenty minutes. This rush drains the neurotransmitters, that causes the inhalant to "crash," or destroyed. Because of cocaine's extraordinarily addictive quality, humans might suffer from mental disorders, heart attacks, and others metabolism failure throughout the dosage effect. once the body uses cocaine, the brain gets additionally aggressive and skilled for higher shock levels as compare to normal situation because of the neurotransmitter's absence. The results don't solely rely on the amounts consumed, however, will also be based on the efficiency of the drug and also on the temperament and assumptions of the individual who consumes the drug. [23]

**Fatal Dose:** Oral: 1.25 gm, Injection: 40 mg.
**Fatal Period:** Few minutes to few hours.
**Signs & Symptoms:**
**Acute:** Firstly, it stimulates and then depresses CNS, Euphoria, convulsions and coma.
**Chronic:** Insomnia, pale face, tremors, hallucinations, feeling of insects creeping on the skin – cocaine bugs.
**Medicolegal & Post mortem findings:** Accidental poisoning occurs by internal usage of shots consumed by either means and from urethral, vesicle and rectal injections, suicidal or homicidal poisoning by coke are a seldom occurrence. Brain show congestion, nasal erosion or ulceration. [25]

*4. Cannabis:*

Cannabis, is also called as marijuana as its alternative names, is a mind-altering drug obtained from the Cannabis plant used for recreational or medicinal purposes. The first psychedelic compounds of cannabis plant are THC (Tetrahydrocannabinol), one amongst the 483 illustrious elements within the plant, as well as a minimum of 65 alternative cannabinoids. [26]
**Scientific Name:** Cannabis sativa.
**Formula:** $C_{21}H_{30}O_2$
**Active Principle:** Tetrahydrocannabinol.
**Mode of Action:** It works as a neurotransmitter because it uses to send chemical messages between nerve cells (neurons) within the complete system. They have an effect on brain areas where it influences pleasure, concentration, movement, coordination, memory, thinking, and sensory and time perception. as a result, THC (Tetrahydrocannabinol) is attached to molecules which are called as cannabinoid receptors on nerve cells in these brain areas and activate them, disturbing numerous physical and mental functions.[27]
**Fatal Dose:** 1000-2000 mg.
**Fatal Period:** 12 hours.
**Signs & Symptoms:**
**Acute:** Euphoria, hallucinations, ataxia, brain imbalance.
**Chronic:** Hallucinations and delusions of a painful nature.
**Medicolegal & Post mortem findings:**
Accidental poisoning is extremely common by bhang among collegiates. Homicidal and suicidal poisoning are an extremely rare occurrence. Post mortem appearance is insignificant. [28]

*5. Datura:*

Datura is grown in temperate and tropical region of the world and is an herbaceous plant, Each and every species of genus Datura are toxic in behavior and are aphrodisiac also. The

flowers and seeds are more toxic in nature. Datura is used for fevered state and also for death. [29]

**Scientific Name:** Datura fastuosa.

**Active Principle:** Hyosine (Scopolamine), Hyoscyamine and Atropine.

**Mode of Action:** When dhatura is ingested by a person, they act as competing antagonists to peripheral and central muscarinic neurotransmitter receptors resulting in a general disfunction of the parasympathetic innervated organs. Acute mental psychosis or delirium will occur thanks to its effect on the central system as tertiary amines will inhibit central nervous system receptors. [30]

**Fatal Dose:** 5.5-7.5 gm (50-100 seeds)

**Fatal Period:** 24 hours.

*Signs & Symptoms:*

**Acute:** Skin dryness, sinus tachycardia, blurred vision, flushing, and drowsiness were the most common symptoms and signs.

**Chronic:** Drowsiness leading to coma, deliriant (muttering delirium) and hallucinating, respiratory failure or cardiac arrhythmias.

*Medicolegal & Post mortem findings:*

It is quite common dangerous poison in rural areas and is extremely common homicidal poison and is also employed as an alternative and cheap abortifacient too. Datura seeds and fragments are also found within the abdomen and intestines and other internal organs are also found to be congested. [31]

*6. Alcohol: (Methyl Alcohol):*

Methyl alcohol (CH3OH) is a transparent liquid with a robust odor. it's a toxic substance that may be absorbed through the eyes, skin, lungs, and system.[32] Overexposure will cause death. methyl alcohol seems as a transparent fairly volatile liquid with a sweet pungent odor same as ethyl alcohol and can be completely dissolved in water. The vapors of methyl alcohol are heavier than air and can travel a long way to a supply of ignition and gets returned. Any accumulation of vapors in confined areas, like sewers or buildings, if ignited could explode.[33] Methyl alcohol is also used to create various chemicals, and as a solvent for plastics and paints, And as an ingredient in various chemicals products.

**Chemical Name:** Methyl Alcohol

**Formula:** CH3OH

**Active Principle:** methyl alcohol (methanol)

**Mode of Action:** It works as a nervous systemdepressant; methanol is probably nephrotoxic in amounts as little as one mouthful. once metabolized by hepatic alcohol and organic compound dehydrogenase, methanol forms methanol and acid, each of that are nephrotoxic. The eyes, CNS, and epithelial duct are affected. [34]

**Fatal Dose:** 60-240 ml.

**Fatal Period:** 24-36 hours.

*Signs & Symptoms:*

**Acute:** Dizziness, hypothermia, headache, nausea, vomiting and abdominal pain.

**Chronic:** Fixed dilated pupils, blurred vision, partial or total blindness and cyanosis.

*Medicolegal & Post mortem findings:*

Accidental poisoning is extremely frequent as a result of the adulteration of common alcoholic drinks with denatured alcohol, dangerous and cutthroat poisoning is extremely rare, haemorrhages is seen in brain, hyperaemic abdomen and small intestine mucous secretion membrane, excretory organ shows hollow degeneration, membrane and point show chronic changes. [35]

*7. Arsenic:*

Arsenic and arsenic compounds were created and were used commercially for hundreds of years. The modern and ancient uses of arsenic might include wood preservatives, prescription drugs, agricultural chemicals, and applications within the mining industry, scientific usage, metallurgy, glass-making, and semiconductor industries.[36]

**Chemical Name:** Arsenic trioxide.

**Formula:** $As_2O_3$

**Active Principle:** Arsenic Trioxide,

**Mode of Action:** The arsenic exposure for the overall population is via inhalation of air and consumption of contaminated food or water that inhibits sulphahydryl enzyme that are necessary for cellular metabolism and damages capillaries [37]

**Fatal Dose:** Arsenic trioxide: 180 mg.

**Fatal Period:** 12 to 48 hours for acute poisoning and several weeks for subacute poisoning.

**Signs & Symptoms:**

**Acute & subacute:** Depression, burning pain, projectile vomiting, purging, marked neuritis (sensory motor nerve disturbance), convulsions coma and death.

**Chronic:** Anorexia, lower eyelids, nails are brittle showing linear pigmentation.

*Medicolegal & Post mortem findings:*

It is unremarkably used as homicidal poison as well as a suicidal poison due to the property of arsenic having no characteristic smell or colour. Only a small quantity of arsenic is enough for fatal result and are often mixed with food. accidental poisoning is extremely rare and depends upon the amount of exposure. Sunken eye balls, secretion membrane is engorged with blood spots, acute phrenitis with the trauma spots in brain are seen.[38][39]

*8. Lead:*

A build-up of lead within the body, sometimes over months or years. Lead-based paint and its mud, sometimes found in older buildings, are a common source of exposure. Young kids are particularly in danger. Occupational hazard exposure, like welding, could be a lot of common cause for adults. [40] [41]

**Chemical Name:** Lead oxide, lead acetate, lead chloride, lead iodide etc.

**Formula:** Pbo, Pb(C2H3O2)2, PbCl2, PbI2

**Active Principle:** Lead acetate, lead carbonate.

*Mode of Action:*

Once ingested it acts as a cellular poison by inhibiting its metabolism and performance and additionally inhibits hemoglobin synthesis. Arsenic are leather when exposed to over a wide period of time. [42]

**Fatal Dose:** Lead acetate: 20 gm. lead carbonate: 45gm

**Fatal Period:** 2-3 days

**Signs & Symptoms:**

**Acute & subacute:** acute poisoning is very rare usually occurs from lead acetate, insomnia, muscular cramps, convulsions, numbness and paralysis of lower limbs.

**Chronic:** Anorexia, platelets are decreased, lead paralysis.

*Medicolegal & Post mortem findings:*

Homicidal and suicidal poisoning are not rare and are a seldom occurance. However, accidental poisoning is an extremely common occurance, cerebral dropsy, punctate haemorrhages and proliferation meningitis, shrunk and thickened intestines, cannular sphacelus (necrosis) of urinary organ. [43]

*9. Organophosphorus:*

Organophosphorus are the organic compounds contain of phosphorus. They are mostly used in pest management as an alternate to chlorinated hydrocarbons that are present in the atmosphere. Its compounds are derivatives of oxyacid and are widely used as agricultural, industrial and domestic pesticides. [44]

**Chemical Name:** Alkyl phosphates & Aryl phosphates.

**Formula:** $(C_2H_5O)_2P(O)]_2O$ TEPP (Tetra ethyl pyrophosphate), Triphenyl phosphate (TPhP) $OP(OC_6H_5)_3$

**Active Principle:** TEPP (Tetra ethyl pyrophosphate) most toxic, parathion (follidol)

**Mode of Action:** These compounds are potent inhibitors of enzyme acetyl cholinesterase that hydrolyses the neurotransmitter and toxic effects are thanks to the buildup of neurotransmitter at neuromuscular junction and synapses of a neural structure leading to initial stimulation followed by the palsy of neuro transmission at cholinergic neurons that are present in the nervous system. [45]

**Fatal Dose:** TEPP (Tetra ethyl pyrophosphate): 45-50 mg. (Intra muscular) or 25-100 mg orally.

Parathion (follidol) 80 mg. (Intra muscular) or 25-175 mg orally.

**Fatal Period:** 1 ½ hours to 3 hours.

*Signs & Symptoms:*

**Acute:** Its shows muscarinic and nicotinic effect which includes nausea, vomiting, blurring of vision, pulmonary oedema, hypotension, cyanosis, flaccid paralysis, fasciculations, hypertension, tremors, ataxia, convulsions.

*Medicolegal & Post mortem findings:*

It is unremarkably used as suicidal and homicidal poisoning and additionally accidental poisoning is extremely common in farmers whereas spraying in agricultural fields, petechial haemorrhage is also seen, acute pneumonic oedema.[46]

*10. Carbamates:*

Carbamates belongs to the category of pesticides structurally and mechanically the same as insecticide (OP) pesticides. These are N-methyl carbamates which are derived from a carbamic acid and causes carbamylation of acetylcholinesterase at neural synapses, fasciculus junctions and neuro-muscular junction. [47]

**Chemical Name:** Carbamic acid

**Formula:** (NH2COOH).

**Active Principle:** Carbaryl (1-naphthyl N-methylcarbamate)

**Mode of Action:** Carbamates starts working by inhibiting AChE which can be founded by carbamylation of a serine hydroxyl residue at the site of the enzyme present, a method that includes cleavage of the carbamate molecule, that in effect is treated by the enzymes as if it were ACh[48]

**Fatal Dose:** 120 mg.

**Fatal Period:**1 ½ hours to 3 hours.

*Signs & Symptoms:*

**Acute:** Its shows muscarinic and nicotinic effect which includes nausea, vomiting, blurring of vision, pulmonary oedema, hypotension, cyanosis, flaccid paralysis, fasciculations, hypertension, tremors, ataxia, convulsions.

*Medicolegal & Post mortem findings:*

It is unremarkably used as suicidal as well as homicidal poisoning and additionally accidental poisoning is extremely common in farmers whereas spraying in agricultural fields, petechial harm is also seen, acute pneumonic oedema.[49][50]

## 2. CONCLUSIONS:

Exposure to neuro toxin chemicals might have injurious influences on the functions and structure of the nervous system. It's been estimated that one out of six kids include a developmental incapacity, and in most cases these disabilities have an effect on the nervous systems. Whether or not developmental exposure to neuro toxics might accelerate nervous system disturbances related to aging still remains being investigated; at identical time initial experimental evidences points dead set problematic issues concerning the silent neurotoxicity, subclinical alterations that, once superimposed to the traditional aging method or to further insults, would lead to frank neurotoxicity, like neurodegenerative diseases.

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