Pharm.D –4th Year_4.6- Clinical Toxicology_7_Clinical symptoms and management of acute poisoning with the following agents

7. Clinical symptoms and management of acute poisoning with the following agents-

a) Pesticide poisoning: Organophosphorous compounds, carbamates, organochlorines and pyrethroids

Organophosphorous compounds

Pesticides are compounds that are used to kill pests which may be insects, rodents, fungi, nematodes, mites, ticks, molluscs, and unwanted weeds or herbs. Accidental exposure or overexposure to pesticides can have serious implications. The potential for pesticide accidents is real. While most of these pesticides can be used with relatively little risk (as long as label directions are followed), some are extremely toxic and require special precautions. Various types of pesticides that cause poisoning are: Insecticides, Rodenticides, Fungicides, Nematicides, Acaricides, Molluscicides and Herbicides.

Organophosphates (OPs) are lipophilic compounds formulated in petroleum distillates as emulsifiable concentrates or suspensions. Wettable powders, dusts and granules are also available. Some products are formulated as impregnated resins, fogging formulations or smokes. They are used extensively as insecticides, miticides and amphicides in agriculture and horticulture contributing maximum to the incidence and mortality due to acute poisonings. Certain rapid acting OPs have been developed as "nerve gases" for chemical warfare. Various petroleum distillates in which they are formulated may also cause toxic or irritant effects.

Clinical features

- ✓ Muscarinic effects in moderate to severe poisoning include miosis. salivation, lacrimation, urination, defecation, gastrointestinal distress, emesis, bronchorrhea, bronchoconstriction, diaphoresis, bradycardia and hypotension.
- ✓ Bronchorrhea and bronchoconstriction may lead to compromised pulmonary functions including non-cardiogenic pulmonary edema along with chemical pneumonitis due to aspiration of hydrocarbon vehicle.
- ✓ Nicotinic effects include muscle fasciculations, cramps, hypertension, tachycardia, pupillary dilatation, weakness that can progress to areflexia and paralysis.

- ✓ Central nervous system effects in mild to moderate poisoning are headache, giddiness, anxiety, restlessness / drowsiness, confusion, tremors, slurred speech and generalized weakness.
- ✓ Delirium, psychosis, seizures, coma and cardiorespiratory depression are noted in severe cases.
- ✓ Delayed or permanent peripheral neuropathy may be developed, after 6-21 days of exposure, by some agents.
- ✓ Intermediate syndrome characterized by the development of proximal weakness and paralysis within 12 hrs. to 7 days of exposure has been observed.
- ✓ Signs of paralysis include inability to lift neck or sit up, slow eye movement, facial and limb weakness, difficulty in swallowing, areflexia and respiratory paralysis which may cause death.
- ✓ Mild inhalation exposure to vapors rapidly produces mucous membrane and upper airway irritation and bronchospasm followed by systemic symptoms if exposed to significant concentrations.
- ✓ Dermal exposure causes burning sensation, hives and angioedema.

Diagnosis

It involves history of exposure, characteristic muscarinic, nicotinic and CNS manifestations, breath odor of petroleum distillate and garlic. Qualitative test of lavage sample and determination of plasma and red blood cell cholinesterase activity also aid in the diagnosis.

Laboratory / Monitoring

- ✓ Depression of 25% or more in the red blood cell acetyl cholinesterase (AChE) activity from baseline indicates exposure. Plasma pseudocholinesterase, though a sensitive indicator, is not as reliable as AChE activity.
- ✓ Monitor electrolytes, glucose, BUN, creatinine, liver transaminases, arterial blood gases, serum pancreatic isoamylase, chest X-ray and ECG.
- ✓ Urine assay for alkyl phosphate and phenolic organophosphate metabolites may be a sensitive indicator of exposure.

Management

Pre-hospital

- ✓ Remove the patient from the source of exposure to fresh air.
- ✓ Remove contaminated clothing and discard leather items if any.
- ✓ Give artificial respiration if the patient is unable to breath, avoiding mouth to mouth breathing.
- ✓ Do not induces vomiting and lay patient on side to prevent aspiration of vomitus.
- ✓ In case of seizures, put a spoon in patients mouth to prevent injury to tongue.
- ✓ Wash affected skin includıng hair and nails with copious amounts soap and water and irrigate eyes with tepid water.

- ✓ Avoid contact with contaminated clothing and vomitus and wear pay gloves while washing patient's skin or hair.
- ✓ Shift the patient to hospital and carry the container alongwith to aid diagnosis.

Hospital

- ✓ Ensure a clear airway by nasopharyngeal suction of vomitus and secretions.
- ✓ Provide oxygenation and ventilatory support as required.
- ✓ Perform gastric lavage cautiously protecting the airway in alert patients and using cuffed endotracheal tube in unconscious patients.
- ✓ Replace fluid loss by IV fluids.
- ✓ Administer activated charcoal as a slurry.
- ✓ Give cathartics for gut decontamination. Do not administer oil based cathartics like castor oil and liquid paraffin.
- ✓ Control seizures with anticonvulsants.
- ✓ Treat recurrent seizures with phenobarbital.
- ✓ Avoid using drugs like morphine, theophylline, succinylcholine and phenothiazines.
- ✓ Atropine and pralidoxime are the specific antidotes.

Organochlorines

Organochlorine compounds are widely used as pesticides in agriculture and as environmental pesticide control products. Commercial preparations are commonly dissolved in petroleum distillates which form emulsions when added to water. The γ- isomer of benzene hexachloride called lindane is used clinically as an ectoparasiticide. Organochlorines are of toxicological concern and some like dichloro diphenyl trichloroethane (DDT) and chlordane have been banned for commercial use as they persist in environment and accumulate in biological systems. Based on their chemical structure they are categorized into DDT and analogs. γ – benzene hexachloride and cyclodienes.

Clinical features

- ✓ DDT and analogs cause nausea, vomiting, headache, dizziness, hyperesthesia, paresthesia (face and extremities), muscle incoordination, tremors, confusion, agitation, and ataxia.
- ✓ In severe poisoning, myoclonic jerking movements, opsoclonus, generalized tonic-clonic convulsions followed by coma, respiratory depression and death have been observed.
- ✓ Benzene hexachloride causes nausea, vomiting, diarrhea, seizures, headache, dizziness, numbness of hands and arms, ataxia, CNS depression and coma.
- ✓ Cyclodienes cause sudden onset of convulsions.
- ✓ Delayed and recurrent seizures are common with chlordane and aldrin.
- ✓ Aspiration of formulations containing petroleum distillates may result in pneumonitis.
- ✓ Fever secondary to central mechanisms, increased muscle activity and or aspiration pneumonitis is common with all the classes of organochlorines.
- ✓ Signs of hepatic or renal injury may develop.
- ✓ Inhalation of hexachlorobenzene may cause irritation of respiratory membranes.

- ✓ Extensive dermal contact causes irritation.

Diagnosis

It is mainly based on the history of exposure and clinical presentation.

Laboratory / Monitoring

- ✓ Monitor electrolytes, glucose, BUN, creatinine, liver transaminases, prothrombin time and ECG.
- ✓ Measurement of organic halogen compounds in urine is suggested to be an indicator of exposure.

Management

Pre-hospital

- ✓ Remove contaminated clothing and discard leather items.
- ✓ Wash affected skin, including hair and nails with copious amounts of water and soap.
- ✓ Irrigate eyes with copious amounts of tepid water or saline in case of eye exposure.
- ✓ In case of seizures put a spoon in the patient's mouth to prevent injury to tongue.
- ✓ Lay patient on side to prevent aspiration of vomitus.
- ✓ Do not induce vomiting.
- ✓ Do not give oil, milk or cream orally.
- ✓ Rescuers should avoid contact with contaminated clothing and vomitus.

Hospital

- ✓ Maintain the airway and assist ventilation if required. Administer supplemental oxygen.
- ✓ Perform gastric lavage and administer activated charcoal as a slurry in water or cathartic.
- ✓ Repeat dose activated charcoal may be beneficial.
- ✓ Give cathartics for gut decontamination.
- ✓ Do not give oil based cathartics
- ✓ Control seizures with anticonvulsants.
- ✓ Treat recurrent seizures with phenobarbital.
- ✓ Give dopamine for resistant hypotension. *
- ✓ Avoid epinephrine or atropine as they may lead to cardiac arrhythmias.
- ✓ Administer cholestyramine, a non-absorbable bile acid binding: anion exchange resin to all symptomatic patients.
- ✓ There is no specific antidote.

Carbamates

Carbamates are widely used as miticides, aphicides and insecticides in agriculture and veterinary practice. Many household sprays contain their formulation in petroleum distillates

and are applied as spray droplet emulsions. Granular formulations are also available for agricultural use.

Clinical features

- ✓ Characterstic signs of exposure are salivation, lacrimation, urination defecation, gastrointestinal distress and emesis (SLUDGE syndrome).
- ✓ Other signs and symptoms include miosis, headache, altered sensorium dyspnea, rales, respiratory depression, chest tightness, bronchospasm. diaphoresis, bradycardia, hypotension, muscle twitching, tremors, paresthesias, cramping, weakness, tachycardia and pupillary dilatation.
- ✓ In severe poisoning respiratory depression, mental confusion, unconsciousness and convulsions may occur. Children are more susceptible to seizures than adults.
- ✓ Aspiration pneumonitis may be precipitated after ingestion of formulations in hydrocarbon vehicles.
- ✓ Inhalation of dusting powders causes laryngeal irritation, violent cough, diaphoresis and tachypnea.
- ✓ Death is rare and may be due to respiratory failure.

Diagnosis

Diagnosis is based on history of exposure and characteristic muscarinic, nicotinic and CNS signs and symptoms.

Laboratory / Monitoring

- ✓ Red blood cell cholinesterase and plasma cholinesterase are not reliable indicators of carbamate poisoning because of the rapid and spontaneous recovery of enzyme activity within several minutes or hours. However. depression of 25% or more from an individual's baseline value indicates exposure.
- ✓ Immediate analysis of sample is essential as *in vitro* hydrolysis of carbamates can occur.

Management

Pre-hospital

• Prehospital treatment remains the same as in the case of organophosphates.

Hospital

- ✓ Maintain the airway and assist ventilation if required.
- ✓ Perform gastric lavage and administer activated charcoal as a slurry in water or cathartic.
- ✓ Administer IV fluids.
- ✓ Give cathartics for gut decontamination.
- ✓ Control seizures with anticonvulsants.
- ✓ Treat recurrent seizures with phenobarbital.

- ✓ Avoid theophylline, succinylcholine and phenothiazines.
- ✓ Atropine is the specific antidote.
- ✓ Role of pralidoxime is controversial. However, it is indicated if there is

  (a) severe muscle weakness, fasciculations, paralysis or decreased respiratory effort

  (b) continued excessive requirement of atropine or

  (c) concomitant organophosphate and carbamate exposure.

Pyrethrins and Pyrethroids

Pyrethrins are active insecticidal ingredients present in oleoresin extract of dried chrysanthemum flowers. They are esters of pyrethric and chrysanthemic acids formed by the keto-alcoholspyrethrolone, cinerolone and jasmlolone. Pyrethrin I and pyrethrin II are the two most potent pyrethric and chrysanthemic ester insecticides. The synthetically derived compounds used as "insect knockdowns" are called pyrethroids which are subtly modified to resist photolysis and to improve stability in the natural environment. Piperonyl butoxide is added to these compounds to increase their effectiveness and prolong the activity. Many pyrethrin-pyrethroid insecticides are formulated in petroleum distillates for spray applications and some are marketed in cans pressurized by propellants.

Clinical features

- ✓ Ingestion causes salivation, nausea, vomiting, abdominal cramps, tenesmus and gastritis.
- ✓ Neurological symptoms include paresthesias, headache, dizziness, choreoathetosis, fatigue and weakness. Massive exposure may result in hyperexcitability, seizures and coma.
- ✓ Large doses of concentrated formulations may cause coma (within 20 mins.), fasciculations and seizures.
- ✓ Dermal exposure causes burning, tingling, itching and numbness.
- ✓ Irritant contact dermatitis is not common. Common lesion is erythematous dermatitis with vesicles, papules in most areas and intense pruritis. A bulbous dermatitis may develop.
- ✓ Inhalation commonly causes congestion, running nose and irritation in the throat.
- ✓ Hypersensitivity reactions and asthma like symptoms characterized by pneumonitis, cough, dyspnea, wheezing, chest pain and bronchospasm are observed.
- ✓ Rare cases of respiratory paralysis and cardiopulmonary arrest are reported.

Diagnosis

It is based on history of exposure. There are no specific laboratory tests or characteristic clinical symptoms which may help in their identification.

Laboratory / Monitoring

- ✓ Monitor electrolytes, glucose and arterial blood gases.
- ✓ Detection of parent compound is usually not useful because it is rapidly metabolized in the body.

Management

Pre-hospital

- ✓ Move the patient to fresh air from the source of exposure in case of inhalation and observe for any signs and symptoms of systemic toxicity.
- ✓ Wash affected skin with copious amounts of soap and water. Irrigate eyes with lots of tepid water.
- ✓ Do not induce vomiting.
- ✓ Consider prehospital administration of activated charcoal as an aqueous slurry in patients who are awake and able to protect their airway.

Hospital

- ✓ Treatment is supportive and symptomatic.
- ✓ Protect the airway. Give 100% humidified supplemental oxygen with assisted ventilation as required in case of inhalation.
- ✓ Administer activated charcoal and cathartics.
- ✓ Perform gastric lavage only after a potentially life threatening ingestion.
- ✓ Control seizures with anticonvulsants.
- ✓ Treat mild cases of anaphylaxis with antihistamines with or without epinephrine.
- ✓ Treat severe anaphylaxis with oxygen supplementation, aggressive airway management, epinephrine and IV fluids and monitor ECG.
- ✓ Apply Vitamin E oil topically to relief paresthesias.
- ✓ There is no specific antidote.

b) opiates overdose

Opioid overdose is an acute condition due to excessive opioids. Examples of opioids are morphine, heroin, tramadol, oxycodone, and methadone. It differs from opioid dependency. Although opioid overdose does not constitute a majority of the overdoses seen in the emergency department it is important to rule out in people given its potential for mortality and the ease of reversal. Dependence on prescription opioids can stem from treatment of chronic pain and in recent years is the cause of the increased number of opioid overdoses.

Risk factors

- ✓ Prescription drug abuse
- ✓ Changes in metabolism can affect the way that a medication is absorbed. Those with a metabolic disorder must be closely monitored while taking prescription pain medications.
- ✓ Elderly patients may forget that they already took their medication and accidentally take another dose.

Clinical Symptoms

- ✓ Central nervous system - CNS depression is the major clinical manifestation. Increasing doses lead to increasing degrees of sedation with initial analgesia and sedation, followed by loss of response to verbal stimuli, loss of response to tactile stimuli, loss of control over normal respiration and failure of temperature and blood pressure regulation.
- ✓ Cardiac - Dextropropoxyphene may lead to cardiac effects and ECG changes. The ECG seen in Propoxyphene overdose are similar to those seen in tricyclic antidepressant poisoning with QRS and QT prolongation, varying degrees of heart block and tachyarrhythmias.
- ✓ Pulmonary- Aspiration and non- cardiogenic pulmonary oedema are acute common complications.
- ✓ Intravenous Abuse - Complications of intravenous use of opioids include systemic fungal infection, abscess formation, cellulitis, osteomyelitis, acute transverse myelitis, tetanus, thrombophlebitis, hepatitis and HIV infection.

Investigations/Diagnosis

- ✓ **Imaging -** A chest X-ray should be obtained in severe opioid overdose as aspiration and non-cardiogenic pulmonary oedema are common complications.
- ✓ An ECG should be done in overdoses involving propoxyphene and methadone.
- ✓ Blood concentrations - Drug concentrations are not helpful in the management of overdose.
- ✓ **Urine drug screen -** Patients with recreational overdoses should have a urine drug screen for drugs of abuse to identify other substances that may have been taken or abused but is not helpful in the management of an acute overdose.
- ✓ **Other investigations -** Patients with suicidal ingestions who present with an opioid syndrome should have paracetamol, salicylate and electrolytes done to detect coingestion of paracetamol and/or aspirin, as combination tablets are a frequent source of codeine or propoxyphene. ln patients abusing ibuprofen/codeine combinations renal tubular acidosis and or gastropothy may be seen.
- ✓ **Differential diagnosis-** The differential diagnosis for a patient presenting with a typical opioid syndrome is any other sedating drug.The presence of miosis is not limited to opioid drug overdose but occurs in benzodiazepine, chloral hydrate, barbiturates, phenothiazine alcohol, clonidine and organophosphate overdose.

Management

- ✓ Supportive Management of opioid toxicity is centered on the maintenance of respiration and cardiopulmonary function,as well as appropriate use of an opioid antagonist. Patients should be closely observed for the development of respiratory depression. If necessary, naloxone can be given to counteract the sedating effect of opioids. Intubation and ventilation will occasionally be required for patients who have developed respiratory complications of their overdose.
- ✓ Gastric decontamination is effective, particularly in those ingesting sustained released forms. After eliminating the existence of potential contraindications such as ileus,

activated charcoal can be administered up to 4 hours post-ingestion of a standard release formulation or up to 12 hours after a sustained release formulation.

- ✓ Antidotes - Naloxone given 0.1-0.4 mg IV or IM repeated every 2-3 minutes up to a total dose of 2 mg.

c) Antidepressants

Antidepressants refer to the drugs used to treat depression of varied clinical etiology. They can be classified into different groups as tricyclic antidepressants (TCAS), monoamine oxidase (MAO) inhibitors, selective serotonin reuptake inhibitors (SSRIs) and miscellaneous agents.

Presently TCAs and SSRIS are considered to be the first line drugs for the treatment of mild to moderate depression. SSRIs are however, the treatment of choice owing to their superior safety profile. They are not indicated in severe depression where electroconvulsive therapy is used. All antidepressants have almost equal efficacy and latency after which their therapeutic effects become evident. Apart from major and minor depressive disorders they are indicated in a variety of medical and psychiatric conditions. Some indications are however, not approved by the US FDA and are considered to be the "off label" indications. The indications of antidepressants include major depression, recurrent depression, depressive phase of bipolar disorders, prophylaxis of mania-depressive disorders, obsessive compulsive disorders (clomipramine), panic disorders, post traumatic stress disorders, bulimia nervosa (fluoxetine), premenstrual tension (fluoxetine recently approved by FDA), prophylaxis of generalized anxiety disorders, chronic pain, fibromyalgias, nocturnal enuresis, sleep apnea syndrome, chronic urticaria, attention deficit hyperkinetic disorders etc.

Toxic dose

Fatal – serum drug level of more than 1000ng/ml (10 to 20 mg/kg p.o.) is usually fatal. 10 times the therapeutically daily dose of a cyclic antidepressant is potentially fatal.

Clinical features

- ✓ Toxic effects of TCAs are usually manifested within 6 hrs. of acute overdose ingestion.
- ✓ Characteristic symptoms include QRS widening, cardiac conduction defects, arrhythmias, hypotension, psychological complications, hyperthermia, seizures and coma.
- ✓ Rhabdomyolysis, acute renal failure, adult respiratory distress syndrome (ARDS), acid base imbalance (acidosis) may complicate severe overdose.
- ✓ Seizures, respiratory arrest, cardiac arhythmias and circulatory collapse have been noted in severe intoxication with desipramine.
- ✓ Nortriptyline overdose produces relatively less hypotension than imipramine.
- ✓ Cardiac failure and pulmonary edema are reported in amoxepine overdose.

Diagnosis

Diagnosis should be suspected in patients having a history of depression and those showing characteristic cardiac and CNS toxicity features.

Laboratory / Monitoring

- ✓ Levels of TCAs are not useful in the initial assessment as they do not predict the clinical symptoms.
- ✓ Monitor ECG (QRS interval prolongation), electrolytes, bicarbonates, pH, renal and liver function tests, CPK, arterial blood gases, urinalysis, chest X-ray in patients suspected of significant toxicity and patients presenting with pulmonary symptoms.
- ✓ Perform qualitative tests.
- ✓ Serum / plasma levels of TCAs can be detected by immunoassays.
- ✓ HPLC and GC-MS have been employed to detect TCAs in hairs.
- ✓ Monitor serum paracetamol and aspirin levels to detect occult ingestion.

Management

Pre-hospital

- ✓ Do not induce emesis with syrup of ipecac because of risk of abrupt development of coma or seizures.
- ✓ Prevent aspiration in case of spontaneous emesis.
- ✓ Administer activated charcoal preferably within 1 hr. of ingestion.
- ✓ Protect airway in patients who are at risk of sudden onset of seizures or have undergone mental status deterioration.

Hospital

- ✓ Treatment is supportive and symptomatic.
- ✓ Perform early gastric lavage (within 1-1.5 hrs. Post ingestion). However, late gastric lavage and charcoal may also be useful.
- ✓ Treat arrhythmias (QRS widening) with IV sodium bicarbonate. If arrhythmias do not respond to sodium bicarbonate, lidocaine may be given. Continuous sodium bicarbonate infusion is not recommended.
- ✓ Treat seizures with anticonvulsants, control recurrent seizures with phenytoin / phenobarbital or other class I_A, antiarrhythmics.
- ✓ Correct hypotension with IV fluids and vasopressors if required.
- ✓ Maintain respiration.
- ✓ Dialysis and diuresis are not effective.
- ✓ Do not administer flumazenil, procainamide, quinidine and disopyramide.
- ✓ There is no specific antidote.

d) Barbiturates and benzodiazepines

Barbiturates

Barbiturates, the derivatives of thiobarbituric acid were widely used sedative-hypnotics till 1960s. However, they have been largely replaced by BDZs now-a-days. The popularity of barbiturates has decreased because of their adverse effects, high incidence of drug dependence, withdrawal symptoms on sudden stoppage and their abuse potential.

Major groups of barbiturates are:

Long acting (6-12 hrs.)- Phenobarbital, Mephobarbitone Barbitone and Primidone.

Short acting (2-3 hrs.)- Secobarbitone, Pentobarbitone and Hexobarbitone.

Intermediate acting (4 -6 hrs.)- Amylobarbitone, Butobarbitone and Aprobarbital.

Ultrashort acting (15-30 mins.)- Thiopentone and Thiamylal Methohexital.

As far as the toxicity of barbiturates is concerned, above classification does not hold true as duration of CNS depression after an acute overdose is comparable for all, except phenobarbital and primidone, which exert toxicity features for prolonged duration because of their long elimination $t_{1/2}$.

Clinical features

Long acting

- ✓ Manifestations of toxicity start at 1-2 hrs. of exposure.
- ✓ In mild / moderate doses nystagmus, dysarthria, ataxia, drowsiness, bullae and crystaluria are noted.
- ✓ In massive overdose features like coma, respiratory depression, aspiration, hypotension, hypothermia and acute renal failure are seen.
- ✓ Toxicity is enhanced with concomitant use of other CNS depressants.

Short acting

- ✓ CNS and respiratory depression, bullous skin lesions and aspiration pneumonia may be noted.
- ✓ Hypothermia is seen in mild to moderate poisoning.
- ✓ Renal failure, muscle necrosis, hypotension, hypoglycemia occur in severe poisoning.
- ✓ Toxicity is enhanced with concomitant use of other CNS depressants.

Diagnosis

Diagnosis is based on history of exposure and presenting clinical features. Barbiturate poisoning should be suspected in epileptic patients presenting with stupor or coma. Skin bullae

nay be seen in barbiturate poisoning. However, it is not the characteristice feature of poisoning. Rule out other causes of bullae and coma. A few drugs (tricyclics and benzodiazepines) and chemicals may produce bullae. Coma may be seen with general CNS depressants, sympatholytic agents, in cellular hypoxia and by certain other toxins.

Laboratory / Monitoring

- ✓ Blood levels of barbiturates are unreliable in predicting the duration and severity of overdose and are closely related to the concentrations in the brain rather than plasma.
- ✓ Plasma levels of 3.5 mg / dl and 10mg / L for short and long acting barbiturates respectively, indicate severe toxicity. However, the quantitative assays just measure barbiturate moiety and do not differentiate between various barbiturates.
- ✓ Monitor electrolytes, glucose, BUN, creatinine, arterial blood gases or pulse oximetry and chest X-ray.

Management

Pre-hospital

- ✓ Induce emesis with syrup of ipecac immediately within few minutes of ingestion.
- ✓ Administer activated charcoal.

Hospital

- ✓ Secure the airway and provide ventilatory support if required.
- ✓ Correct hypotension with IV fluids and vasopressors.
- ✓ Perform gastric lavage preferably within I hr. of ingestion.
- ✓ Treat withdrawal symptoms with IV benzodiazepine/barbiturate as needed.
- ✓ Multiple dose activated charcoal may enhance elimination.
- ✓ Perform forced alkaline diuresis with IV furosemide.
- ✓ Forced alkalıne diuresis is of little value in short acting barbiturate poisoning.
- ✓ Charcoal hemoperfusion/hemodialysis is recommended in severe hypotension and is highly effective, however it is less efficacious in poisoning by short acting barbiturates.
- ✓ Analeptics like metrazol and bemegride are contraindicated because of their narrow margin of safety and precipitation of convulsions even in comatose patients. Chances of mortality may increase. Doxapram may be used initially before providing respiratory support.

Benzodiazepines

Benzodiazepines (BDZS) are the frequently prescribed antianxiety drugs. They are available as tablets, capsules, suspension and as injectables and are indicated for the symptomatic relief of anxiety, seizures and sleep disorders, alcohol / hypnotic withdrawal. They are also used as pre-anaesthetic medications and as muscle relaxants. Benzodiazepines have replaced barbiturates in the treatment of anxiety and insomnia as they are more safe, effective and produces less tolerance and physical dependence when used chronically. They have minimal cytochrome P-450 induction ability.

Clinical features

- ✓ Acute BDZ overdose is manifested by varying degree of CNS depression (drowsiness to coma).
- ✓ Mild symptoms are drowsiness, ataxia, lethargy, confusion and slurred speech.
- ✓ Drowsiness, agitation and ataxia are more common in children.
- ✓ Most obtunded patients become arousable within 12-36 hours.following overdose.
- ✓ Specifie features of diazepam overdose are somnolence, confusion, dysarthria, diplopia, diminished reflexes and coma. Bullous skin eruption is a rare toxicity.
- ✓ Grade I coma with absent deep tendon reflexes are reported in oxazepam toxicity.
- ✓ Respiratory arrest is more likely with triazolam, alprazolam and midazolam as compared with other BDZs.
- ✓ Hostility and hallucinations are reported with IV overdose of midazolam. Emergence of delirium is reported in children.

Diagnosis

Diagnosis is based on history of exposure. Rule out the toxic ingestion of sedative hypnotics, antidepressants, psychopharmacological agents, narcotics, etc.

Laboratory / Monitoring

- ✓ Plasma / serum levels of BDZs may be available but are not usually clinically useful in emergency management.
- ✓ Monitor glucose, ABG, creatinine, electrolytes and creatinine phosphokinase (CPK), urinalysis, BUN and ECG.
- ✓ Perform CT (head), lumbar puncture and chest X-ray if necessary.
- ✓ Monitor PCM, aspirin and ethanol to detect occult ingestion.
- ✓ Immunoassays and HPLC may be useful in detection of certain benzodiazepines.

Management

Pre-hospital

- ✓ Induce emesis with syrup of ipecac within few minutes of exposure. Avoid emesis in patients who have ingested ultrashort acting BDZs such as triazolam.
- ✓ Administer activated charcoal.

Hospital

- ✓ Treatment is supportive and symptomatic.
- ✓ Perform gastric lavage in massive overdose preferably within one hour of ingestion.
- ✓ Administer activated charcoal.
- ✓ Regularly monitor vital signs especially respiration and provide assisted ventilation if required.
- ✓ Correct hypotension by infusing IV fluids and vasopressors.

- ✓ Role of forced dieresis is not well established, however, it has been found to improve symptoms in diazepam poisoning.
- ✓ Hemodialysis is not effective.
- ✓ Manage initial withdrawal symptoms with Phenobarbital/diazepam, then reduce the dose by about 10% per day of intial dose required to control symptoms.
- ✓ Flumazenil is the specific antidote. However, it should be administered only to severely poisoned patients.

e) Alcohol: Methanol and ethanol

Methanol

Methanol (methyl alcohol) is a colorless liquid used in paints, varnish removers, perfumes, household cleaners and as an industrial solvent. Other applications are as an antifreeze, ethanol denaturant, and as a fuel. It is also used in the manufacture of formaldehyde, acetic acid etc.

Toxic dose

Methanol itself is harmless, but its metabolites are toxic. 0.25 ml/kg of 100% methanol produces severe toxic effects. 1-2 ml/kg is considered to be lethal. Serum methanol levels of more than 20 mg /dl are toxic and above 40 mg /dl produces severe toxicity.

Clinical features

- ✓ Main toxic effect is on nervous system, particularly optic nerves. The condition can progress to permanent blindness.
- ✓ Breathlessness, an early sign, is related to unmetabolized methanol.
- ✓ In the first few hours inebriation and gastritis are noticed.
- ✓ Onset of effects may be delayed for 12-24 hrs.
- ✓ Hyperapnea usually develops to compensate for metabolic acidosis.
- ✓ Blurred or double vision, constricted visual fields, sharply reduced visual acuity, optic atrophy, blindness, nystagmus, and whiteness in the visual field may be observed.
- ✓ Fixed dilated pupils suggest severe poisoning
- ✓ In fatal poisoning marked bradycardia may develop.
- ✓ Cardiac failure and severe hypotension may also occur.
- ✓ In severe cases tachypnea from metabolic acidosis and in terminal stages sudden respiratory and circulatory failure may occur.
- ✓ Seizures, coma and symptoms similar to ethanol intoxication may occur.
- ✓ GI effects include abdominal pain, anorexia, nausea and vomiting.
- ✓ Hepatic failure is reported in fatal cases.
- ✓ Acute renal failure and hematuria are also reported.
- ✓ Hypokalemia, hypomagnesemia, and elevated anion gap metabolic acidosis may occur.

- ✓ Leukocytosis, coagulation disorders and hyperglycemia are reported following severe methanol intoxication.
- ✓ Permanent effects may include basal ganglia infarcts, parkinsonism, toxic encephalopathy and polyneuropathy.

Diagnosis

History of exposure, signs and symptoms, and laboratory findings form the basis of diagnosis. In methanol poisoning increased anion gap is not accounted for by elevated lactate levels.

Laboratory / Monitoring

- ✓ Monitor electrolytes, CBC, urinalysis, glucose, BUN, creatinine, serum osmolality and osmolar gap, arterial blood gases, and lactate levels.
- ✓ Measure serum pH and anion gap.
- ✓ Measure serum ethanol levels on an hourly basis to guide ethanol therapy.
- ✓ Estimate serum methanol levels (more than 20 mg / dl are toxic and above 40 mg / dl result in severe intoxication).
- ✓ Measure serum formate concentrations (better measure of toxicity).

Management

Pre-hospital

- ✓ Induce emesis with syrup of ipecac within an hour of ingestion.
- ✓ Lay the patient on a side to prevent aspiration of vomitus.

Hospital

- ✓ Provide symptomatic and supportive care as required.
- ✓ Ensure clear airway.
- ✓ Provide ventilatory support as required.
- ✓ Perform gastric lavage if presented within 4 hrs. after ingestion.
- ✓ Treat acidosis with sodium bicarbonate with close monitoring of arterial blood gases.
- ✓ Ethanol is the specific antidote (orally or as IV infusion). Ethanol therapy is indicated in patients with a history of significant amount of methanol ingestion, metabolic acidosis and an osmolar gap greater than 5-10 mosm / L or if concentration of methanol in blood is greater than 20 mg / dl.
- ✓ Hemodialysis is indicated when serum methanol concentration is more than 40 mg / dl, there is significant metabolic acidosis and fluid and electrolyte disturbances despite therapy, visual effects or in case of renal compromise.
- ✓ Folic acid may enhance the conversion of formate to carbon dioxide and water.
- ✓ 4- methyl pyrazole, an experimental drug may be tried.

Ethanol

Ethanol (ethyl alcohol) is a clear and colorless liquid. It is used in alcoholic beverages, toiletries, perfumes, antiseptics, pharmaceuticals and as a solvent. It is one of the most commonly abused substances and a common coingestant with other agents in suicide attempts.

Toxic dose

Blood levels of 150-300 mg/dl produces toxic effects. Fatal dose is 5-6 g/kg in non-tolerant adults and 3 g/kg in children. Clinical effects in the intolerant ethanol drinker with respect to blood levels are as follows: Blood levels of 30 mg/dl produces mild euphoria and disinhibition. Levels of 50 mg / dl are associated with mild incoordination. Ataxia is observed at blood ethanol levels of 100 mg / dl and drowsiness and confusion at 200 mg/dl. The levels of 300 mg/dl result in stupor, coma while ethanol levels above 400 mg/dl may produce hypoglycemia, hypothermia, respiratory failure, coma and death.

Clinical features

- ✓ CNS effects include altered mental status, euphoric feelings, slurred speech, altered perception, impaired judgment, ataxia, incoordination, nystagmus and CNS depression.
- ✓ GI effects are nausea, vomiting and abdominal pain.

Diagnosis

History of exposure, characteristic odor of fresh alcohol, odor of acetaldehyde or other metabolites, the clinical effects associated with intoxication and laboratory screens form the basis of diagnosis.

Laboratory / Monitoring

- ✓ Measure serum ethanol levels
- ✓ Monitor glucose and electrolytes.
- ✓ Obtain chest X-ray, if aspiration is suspected.
- ✓ Liver and renal function tests and arterial blood gases monitor.

Management

Pre-hospital

- ✓ Lay the patient on side to prevent aspiration of vomitus.
- ✓ Induce emesis at the scene if it can be done within a few minutes of exposure.

Hospital

- ✓ Provide symptomatic and supportive care.
- ✓ Intubate and ventilate if required.
- ✓ Perform gastric lavage immediately, in case of a potentially life threatening exposure (within 30 min. of ingestion).

- ✓ Airway protection and seizure control are mandatory prior to gastric decontamination.
- ✓ Administer IV fluids as required (avoid excessive use).
- ✓ Administer glucose (if bedside glucose level is less than 60 mg /dl) preceded by 100 mg thiamine if chronic alcoholism or malnutrition is suspected.
- ✓ Administer naloxone to patients with an abnormal mental status.

f) Paracetamol and salicylates

Paracetamol

Paracetamol (PCM) is a nonsteroidal anti-inflammatory drug (p-amino phenol derivative). It is available alone as tablets, syrups, suspensions, injectable drops and in combination (tablets, capsules, suspensions) usually with one or more of the drugs like ibuprofen, diclofenac, phenylbutazone, chlormezanone, oxyphenbutazone, dextropropoxyphene, pentazocine, metoclopramide, dicyclomine, etc. It is mainly used as an analgesic and antipyretic agent. It has weak anti-inflammatory property at therapeutic doses which makes it unsuitable for use in inflammatory conditions.

Toxic dose

Liver toxicity is likely to occur with the oral ingestion of 140 mg / kg of PCM in adults. A single acute overdose of 10-15 g of the drug is potentially fatal. The risk of toxicity increases in chronic alcoholics and in patients chronically taking INH, rifampicin or both presumably because of induction of liver microsomal enzymes and impairment of glutathione synthesis and consequently increased formation of toxic metabolites of PCM. Children are less susceptible to acute overdose effects as compared with adults. Gilbert's disease is also one of the risk factors for paracetamol poisoning.

Clinical features

Clinical manifestations occur in the following stages:

- ✓ **Stage I** (0.5-24 hrs.) is an early stage characterized by Gl symptoms (nausea, vomiting, anorexia, diarrhea), pallor, diaphoresis and malaise.
- ✓ **Stage II** (24- 48 hrs.) is characterized by right upper quadrant abdominal pain, pain in flanks, hematuria and metabolic acidosis. Sometimes acute renal failure occurs with or without liver damage. Acute pancreatitis is also seen. Prolongation of prothrombin time, bilirubin and elevation in transaminase levels indicate hepatic necrosis.
- ✓ **Stage III** (48-96 hrs.) Shows massive liver damage leading to hepatic failure, encephalopathy, renal insufficiency and myocardial damage.
- ✓ **Stage IV** is the recovery stage occurring one week post ingestion.
- ✓ Death occurs due to hepatic and renal failure.

Diagnosis

It is based on history of exposure and quantitative estimation of plasma paracetamol levels.

Laboratory / Monitoring

- ✓ Monitor 4 hrs, post ingestion plasma paracetamol levels and predict the severity of toxicity with the help of paracetamol nomogram (time in hrs. after paracetamol ingestion vs. plasma / serum paracetamol concentration (ug / ml)].
- ✓ Perform liver function tests (SGOT, SGPT, total bilirubin and INR or PT) in patients suspected to have toxic paracetamol levels immediately on admission in the hospital and daily for 3 days or until levels begin to return to normal. If significant abnormality in LFT is seen, then monitor creatinine, BUN, electrolytes, glucose, hemoglobin, hematocrit, amylase and ECG.

Management

Pre-hospital

- ✓ Induce emesis with syrup of ipecac within 30 min. of exposure.
- ✓ Lay patient on left side to prevent aspiration.
- ✓ Administer activated charcoal.

Hospital

- ✓ Provide oxygenation and ventilatory support if required.
- ✓ Control spontaneous vomiting by metoclopramide.
- ✓ Perform gastric lavage preferably within 4 hrs. post ingestion, however it has been found to be effective upto 6 hrs. post ingestion.
- ✓ Administer activated charcoal, IV fluids and manage metabolic acidosis with sodium bicarbonate.
- ✓ Hemoperfusion, though effective, is generally not indicated.
- ✓ Massive hepatic failure may necessitate liver transplantation.
- ✓ N-acetylcysteine (NAC) is the specific antidote.

Salicylates

Salicylate poisoning is a potentially life threatening condition which is characterised by extreme acid-base disturbances, electrolyte disturbances and decreasing level of consciousness. There is a wide variation in the clinical spectrum of toxicity. There are differences between acute and chronic toxicity and a varying clinical picture which is dependent on the age of the patient and renal function.

Uses

Sodium salicylate and acetyl salicylic acid used as a Antipyretic, analgesic, treatment of rheumatoid arthritis, low dose aspirin is used in the prophylaxis of cerebrovascular ischaemic

events, angina pectoris, and is also recommended by some authorities for the prevention of colon cancer, and migraine. Sodium aminosalicylate is used to treat tuberculosis. Bismuth subsalicylate is used to treat diarrhea and Prophylaxis for travellers diarrhea. Mesalamine: Suppository or rectal suspension enema for its local effects in the treatment of inflammatory bowel disease, ulcerative colitis. Locally acting salicylates: Methyl salicylate used as a flavoring agent for candy and homomenthyl salicylate is used as a sunscreen agent.

Toxic dose

The severity of toxicity depends on the amount of drugs taken

Severity	**Mild (150 mg/kg)**	**Moderate (150–300 mg/kg)**	**Severe (300–500 mg/kg)**
Toxicity	No toxicity expected	Mild to moderate toxicity expected	Life-threatening toxicity expected

Clinical symptoms

- ✓ In children hyperventilation, dehydration and neurological dysfunction are greater in chronic overdoses compared with single acute ingestions. Symptoms can occur with declining salicylate concentrations because CNS trapping of ionized salicylate.
- ✓ Acid-base disturbance - Respiratory alkalosis is the earliest acid-base disturbance in salicylate poisoning.
- ✓ Electrolyte imbalance- patients are often significantly dehydrated (chronic> acute). Electrolyte abnormalities are common which include hyponatraemia, hypernatraemia, hypokalaemia and hypocalcaemia.
- ✓ Mild pyrexia is common and is due to increased metabolic activity.
- ✓ Nausea and vomiting are common. Less common are epigastric pain and haematemesis. Vomiting contributes significantly to electrolyte imbalance and dehydration.
- ✓ Rises in transaminases occur not uncommonly, are usually not clinically significant, and resolve over several days.
- ✓ Non-cardiogenic pulmonary oedema and renal failure occur occasionally and always in association with other signs of significant poisoning.

Investigation/Diagnosis

The following investigations should be done in all patients

- ✓ FBC, coagulation profile, Electrolytes, calcium, creatinine. Glucose, arterial blood gases, urinalysis and urine P^H, plasma salicylate concentration.

- ✓ **Biochemistry -** Patients with moderate or severe poisoning (by any measure) will need 2nd hourly measurement of electrolytes and glucose. CSF glucose concentrations may be low despite normal plasma concentrations.
- ✓ **Blood concentrations-** Plasma salicylate should be estimated urgently in any patient who has a potentially serious poisoning, electrolyte or acid-base disturbance.
- ✓ **Differential diagnosis-** Poisonings can present with metabolic acidosis and impaired concentration or consciousness.

Management

- ✓ In patients with severe poisoning, examine the urine for calcium oxalate crystals. Also, monitor calcium and renal function (BUN, creatinine).
- ✓ Local treatment with cold milk or ice cream as a demulcent is sufficient in most cases. Cold water or sucking on crushed ice will also relieve oral pain. Remove all visible evidence of plant debris from the oropharynx.
- ✓ In severe cases, parenteral opioids, corticosteroids, IV fluids, and endotracheal intubation may be required. Tetany should be treated with intravenous calcium gluconate.
- ✓ Ocular exposure to sap resulting in chemical conjunctivitis and corneal abrasions must be treated with copious irrgation, systemic analgesics, and expert ophthalmologic consultation exposure.

g) Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the frequently sold over the-counter drugs. Their popularity is widespread all over the world on account of their excellent anti-inflammatory, analgesic and antipyretic properties. Despite their varied chemical nature, they are very similar in their clinical efficacy and are available as tablets and capsules, sustained release tablets and capsules, suspensions and ophthalmic solutions. They are also available in combination usually with paracetamol. NSAIDs are indicated for the treatment of ankylosing spondylitis, fever, corneal ulcers, seasonal allergic conjunctivitis, headache, prophylaxis of myocardial infarction, degenerative joint diseases (osteoarthritis, rheumatoid arthritis etc.), acute musculoskeletal disorders, tendonitis and unstable angina etc.

Toxic dose

Significant toxicity occurs after acute ingestion of 5-10 times the usual therapeutic dose of NSAIDs. Ibuprofen is relatively safe compared with other members of its group. Symptoms usually do not occur at the dose of 100 mg/kg body weight. Life threatening symptoms occur at the dose of 400 mg/kg. The mild toxic dose in children is 200-400 mg/kg. Severe toxicity occurs in children if the dose exceeds 400 mg/kg. The adult toxic dose of piroxicam is 300-600 mg. Severe multisystem organ toxicity has been observed with 100 mg of piroxicam in a 2 year old child. Severe toxicity occurs with the ingestion of 300-500 mg/kg of sodium salicylate. Death has been reported with the ingestion of 10-30 g. Ingestion of 1.5 g of

diclofenac produces toxic symptoms. Death is reported within 2 days after acute ingestion of 5 g of diclofenac in a young male. The toxicity of indomethacin is less as compared with oxyphenbutazone and phenylbutazone. Renal failure is reported in a preterm infant with symptomatic patent ductus arteriosus who received 100 fold overdose of indomethacin. The toxic doses of naproxen and sulindac are 10g to 12g. respectively, in adults. Mefenamic acid and meclofenamate are relatively more toxic than other NSAIDs, Severe symptoms have been observed in an adult female with acute ingestion of 22.5g of mefenamic acid. Oxyphenbutazone and phenylbutazone are more toxic in overdose. More than 4g of phenylbutazone is associated with severe toxicity. Acute toxic dose of oxaprozin, nimesulide, meloxicam, celecoxib, rofecoxib and tolmetin is not known as yet.

Clinical features

- ✓ Acute overdose mostly causes lethargy, GI upset (nausea, vomiting. Abdominal pain, diarrhea), metabolic acidosis, respiratory alkalosis, electrolyte disturbance, hematuria, sodium and water retention, pulmonary edema, etc.
- ✓ Severe overdose may cause hypotension, coma, respiratory depression, GI bleeding or acute renal insufficiency rarely.
- ✓ Risk of kidney damage is similar with both selective (COX-2) and non-selective cyclooxygenase (COX-1 and COX-2) inhibitors.
- ✓ Hepatic necrosis is also reported. Seizures are reported most commonly after mefenamic acid overdose but may rarely occur after severe overdose of other NSAIDs also.
- ✓ Nimesulide, meloxicam, celecoxib, rofecoxib have lesser potential for upper GI toxicity compared with conventional NSAIDs.
- ✓ Severe toxicity of piroxicam overdose produces hyponatremia, hypocalcemia, thrombocytopenia, hematuria, prolongation of prothrombin time and rarely pulmonary edema.
- ✓ In addition to general toxic features of NSAIDs, severe toxicity of sodium salicylate overdose also produces, hyperglycemia/ hypoglycemia, fever, oliguria, dehydration, renal failure, iritability, disorientation and confusion progressing to coma and death. Death occurs due to respiratory insufficiency and cardiovascular collapse.
- ✓ Life threatening symptoms of diclofenac overdose are loss of consciousness, increased intracranial pressure and aspiration pneumonitis.
- ✓ Unsteadiness, blurred vision, diarrhea, GI upset and bleeding, headache, agitation, incoherence, confusion, drowsiness and coma are reported in flurbiprofen overdose.
- ✓ Tinnitus, confusion, disorientation, restlessness and agitation are also reported with indomethacin.
- ✓ Hepatitis has been reported with sulindac in children.

Diagnosis

Diagnosis is based on history of exposure. NSAIDs usually produces mild and nonspecific symptoms.

Laboratory / Monitoring

- ✓ Monitor complete blood count (CBC), electrolytes, calcium, magnesium, glucose, BUN, creatinine, liver transaminases and prothrombin time (PT). and Carry out urinalysis.

Management

Pre-hospital

- ✓ Induce emesis with syrup of ipecac as early as possible (preferably within few minutes of ingestion). Do not induce emesis in mefenamic acid intoxication or ibuprofen ingestion of more than 400 mg / kg.
- ✓ Administer activated charcoal within 1 hr. of ingestion.

Hospital

- ✓ Treatment is supportive and symptomatic.
- ✓ Maintain the airway and assist ventilation if necessary. Administer supplemental oxygen.
- ✓ Treat seizures with anticonvulsants. Control recurrent seizures with phenobarbital.
- ✓ Perform gastric lavage within one hour after massive overdose. Gastric lavage is not necessary if charcoal can be given immediately. Multiple dose activated charcoal is useful in enhancing elimination.
- ✓ Treat coma and hypotension.
- ✓ Give antacids or sucralfate for GI iritation. Replace fluid losses with IV fluids.
- ✓ Vitamin K1 for elevated prothrombin time (due to hypoprothrombinemia)
- ✓ Hemodialysis is unlikely to enhance elimination, however, it may be useful if oliguric renal failure occurs.
- ✓ Peritoneal dialysis and forced diuresis are not effective. However, forced diuresis has been found effective in diclofenac overdose.
- ✓ There is no specific antidote for NSAIDs poisoning.

h) Hydrocarbons: Petroleum products and PEG

Petroleum products

A hydrocarbon is an organic compound consisting entirely of hydrogen and carbon, and thus are group 14 hydrides. These include a wide array of chemical substances found in thousands of commercial products.

Classification

- ✓ **Aliphatic Hydrocarbons (Paraffins)-** These comprise compounds with saturated molecules (containing no carbon-carbon double or triple bonds) which have straight or branched-chain arrangements. Common examples include butane, ethane, methane, and propane (gaseous); gasoline or petrol, diesel oil, kerosene, mineral seal oil,

lubricating oil or mineral oil, and turpentine (liquids); paraffin wax, petroleum jelly or vaseline, grease (semi-liquids or solids).

- ✓ **Aromatic Hydrocarbons-** They contain at least one benzene ring and are unsaturated compounds. Common examples include benzene, toluene, xylene, styrene and naphthalene.
- ✓ **Halogenated Hydrocarbons-** Most of these are clear, colorless liquids which have a chloroform-like odor. Common examples include carbon tetrachloride, ethylene dibromide.
- ✓ **Cycloparaffins (Naphthenes) –** They are saturated hydrogen compounds which are arranged in closed rings. Common examples include cyclohexane and methylcyclopentane.
- ✓ **Alkenes (Olefins) -** These compounds contain one carbon-carbon double bond in the molecule. They are mostly used in the manufacture of other hydrocarbon products such as halogenated hydrocarbons.

Uses

Butane, propane, diesel oil, gasoline (petrol), kerosene are used as fuel, benzine is used as solvent, mineral seal oil is used as furniture polish and turpentine is used as paint thinner, paint remover.

Clinical Symptoms

- ✓ After ingestion of even a very small amount of liquid hydrocarbon, patients initially cough, choke, and may vomit. Young children may have cyanosis, hold their breath, and cough persistently. Older children and adults may report burning in the stomach.
- ✓ Aspiration pneumonitis causes hypoxia and respiratory distress. Symptoms and signs of pneumonitis may develop a few hours before infiltrates are visible on x-ray. Substantial systemic absorption, particularly of halogenated hydrocarbon, may cause lethargy, coma and seizures. Nonfatal pneumonitis usually resolves in about 1 week; mineral or lamp oil ingestion usually resolves in 5 to 6 weeks.
- ✓ Arrhythmias usually occur before presentation and are unlikely to recur after presentation unless patients have excessive agitation.
- ✓ Acute exposure can cause dermatitis, and if this is prolonged it may result in full thickness burns. Chronic exposure to kerosene can cause severe acne. Contact with liquefied a petroleum gases (e.g. propane, butane, propylene, isobutane, butenes, n-butane), ethane, etc. can result in frostbite or effects resembling frostbite.
- ✓ Disseminated intravascular coagulation, haemolytic anaemia and pancytopenia have occasionally been reported following vapour inhalation, aspiration, or ingestion of hydrocarbons.
- ✓ Chronic exposure to some hydrocarbons can result in aplastic anaemia, hepatic necrosis, and jaundice.
- ✓ Hydrocarbons exposure have been associated laryngeal and intestinal carcinoma.

Investigations / Diagnosis

- ✓ Chest x-ray and oximetry done about 6 h after ingestion • if patients are too obtunded to provide a history, hydrocarbon exposure may be suspected if their breath or clothing has an odor or if a container is found near them. Paint residue on the hands or around the mouth may suggest recent paint sniffing.
- ✓ Obtain baseline CBC, electrolytes, glucose-6-phosphate dehydrogenase level, liver enzymes and renal function tests, urinalysis and urine dipstick test for haemoglobinuria.
- ✓ Measurement of urinary metabolites may help to confirm the diagnosis.
- ✓ Diagnosis of aspiration pneumonitis is by symptoms and signs as well as by chest x-ray and oximetry, which affects done about 6 h after ingestion or sooner if symptoms are severe. If respiratory failure is suspected, ABGs are measured.
- ✓ CNS toxicity is diagnosed by neurological examination and MRI.

Management

- ✓ Consider pre-hospital administration of patients with a potentially toxic ingestion who are awake and able to protect their airway.
- ✓ No specific antidotes are available for hydrocarbon poisoning. Treatment with corticosteroids and prophylactic antibiotics is not beneficial. In some cases, steroids may be harmful.
- ✓ Consider gastric lavage with a large-bore orogastric tube after a potentially life-threatening ingestion if it can be performed soon after ingestion (generally within 60 minutes).
- ✓ Remove contaminated clothing and wash exposed area extremely thoroughly with soap and water.
- ✓ Treat renal failure with dialysis and hepatic failure with fresh frozen plasma, vitamin K, low-protein diet, neomycin and lactulose.

PEG: Polyethylene glycol

Polyethylene glycol (PEG) colorless, odorless, sweet-tasting chemical. It is poisonous if swallowed. PEG may be swallowed accidentally, or it may be taken deliberately in a suicide attempt. PEG has been widely applied in various medical fields due to its outstanding properties such as satisfactory safety, biocompatibility, hydrophilicity etc. Although PEG is normally considered as almost non-toxic, some unsafe problems of PEG with low molecular weights have been noticed by researchers.

Toxicity Levels

- ✓ Acute toxicity increases with decreasing molecular weight of polyethylene glycol (PEG). Liquid forms of PEG have a lower molecular weight and are used as vehicles for intravenous or topical medications.

- ✓ Toxicity has resulted in patients receiving prolonged, high dose infusions of lorazepam containing PEG 400 and in burn patients receiving repeat dermal application of PEG 200 to 400.
- ✓ An intentional oral ingestion of 2 liters of PEG 400 by an adult resulted in serious toxicity. Solid forms of PEG have a higher molecular weight (MW greater than 3000) and are not readily absorbed with oral ingestion; therefore, these formulations rarely produce toxicity.

Clinical Symptoms

- ✓ Nausea, vomiting, abdominal fullness, delayed gastric emptying, diarrhea, and taste disorders may develop after ingestion.
- ✓ Contact dermatitis and immediate urticarial reactions may develop after dermal exposures.
- ✓ Metabolic acidosis, increased serum osmolality, acute renal failure, increased total serum calcium with normal or decreased ionized calcium, and ventricular dysrhythmias (PVCs, ventricular tachycardia) may develop.
- ✓ Aspiration causes severe pulmonary edema that is usually reversible. Acute pancreatitis and angioedema have been reported rarely.

Investigations / Diagnosis

- ✓ Monitor acid-base balance, osmolal gap, serum electrolytes, renal function and pulmonary function in symptomatic patients.
- ✓ Blood levels are not generally available or clinically useful. A tandem quadrupole mass spectrometry technique can identify PEG and its metabolites.
- ✓ Monitor pulmonary function and chest X-ray in cases of suspected PEG aspiration or systemic fluid overload. Assess adequacy of oxygenation with pulse oximetry or arterial blood gases.

Management

- ✓ Treatment is symptomatic and supportive.
- ✓ Patients will generally recover with supportive care. Administer IV fluids to maintain adequate urine output. Acute anaphylactic reactions associated with PEG administration are managed as anaphylaxis from other causes.
- ✓ Aspiration may required supplemental oxygen mechanical ventilation with PEEP, bronchoalveolar lavage may be used for treatment. For patients with dermal exposure, irrigate the site of exposure and provide supportive care.
- ✓ Decontamination: Gastrointestinal decontamination and activated charcoal is not required. Gastric aspiration soon after an acute ingestion of a large amount of low molecular weight PEG solution may be beneficial.
- ✓ There is no specific antidote. Competitive antidiuretic hormone inhibitor therapy (eg: fomepizole, ethanol) may inhibit PEG metabolism. However, efficacy on clinical outcomes after PEG intoxication is unknown and they are not generally recommended.

- ✓ Extracorporeal techniques may be helpful in managing patients with PEG toxicity, particularly with hepatic or renal dysfunction. Dialysis can correct acid base and electrolyte abnormalities, and reduces the osmolal gap. It is rarely necessary as most patients do well with supportive care.

i) Caustics: inorganic acids and alkali

Acids

Any chemical causing tissue injury to the gastrointestinal tract and mucus membranes when ingested is treated as' caustic. Caustics may be divided into alkalies and acids. Acids produces coagulation necrosis of the gut mucosa and unless the agent is unusually strong or the contact prolonged, the formation of eschar limits the damage to superficial layers, while alkalies cause liquefactive necrosis of esophagus with saponification and continued penetration into underlying tissues causing extensive damage.

Acids are used in a variety of household products like toilet bowl cleaners, metal cleaners, antirust compounds, battery fluid and pool sanitizers. Industrial uses of concentrated acids include electroplating, photography, leather tanning bleaching, printing and rayon manufacturing. Acidic caustic substances include phosphoric acid, sulfuric acid, oxalic acid, nitric acid and chromic acid. Acetic acid is used as a disinfectant and hairwave neutralizer. Concentrations of 5-10% are weak and irritant and more than 50%, corrosive. Vinegar is <5% acetic acid. Chromic acid is used in photography, electroplating and tanning. Oxalic acid is used for removing writing from the paper. It is a common household remedy for removing ink and rust stains from linen. Hydrochloric acid less than 5% is a weak irritant, 5% to 10% is strong irritant and more than 10% is corrosive. Sulfuric acid is used as drain and metal cleaner. Concentrations of greater than 10% are corrosive. Phosphoric acid is used in metal cleaning and disinfectants. Concentrations of 15% to 35% are weak irritants, 35% to 60% are strong irritants and more than 60%, corrosive. Nitric acid 5% is used in engraving and in some gun barrel cleaners. Concentrations of more than 5% are corrosive.

Toxic dose

The toxic dose varies tremendously with the type and concentration of the acid. Phosphoric acid as little as 8 ml may be fatal if ingested. Ingestion of 15 ml of hydrochloric acid may be fatal. Acute ingestion of 5 g of oxalic acid has caused death. The mean lethal dose for an adult is probably about 15 to 30 g. Death may occur within a few hours.

Ingestion of 3-5 ml of glacial acetic acid may cause death but 200 ml of vinegar may not be harmful. A few drops of concentrated sulfuric acid and 5 ml of nitric acid may cause death from suffocation.

Clinical features

- ✓ Ingestion of corrosive acids causes oral pain, dysphagia, drooling and pain in the throat, chest or abdomen. Esophageal perforation may occur.
- ✓ Cardiovascular collapse may develop soon after severe poisoning.
- ✓ Metabolic acidosis, shock, Gl hemorrhage and renal failure are rare.
- ✓ Concentrated acetic or sulfuric acid exposure may cause hemolysis.
- ✓ Disseminated intravascular coagulation may be a rare complication in severe cases. .
- ✓ Inhalation of corrosive fumes may cause upper respiratory tract injury. with stridor, hoarseness, wheezing and noncardiogenic pulmonary edema. In severe cases, adult respiratory distress syndrome may develop.
- ✓ Ocular exposure effects range from corneal burns to opacification, blindness. Conjunctivitis and lacrimation are common.
- ✓ Dermal toxicity ranges from irritation to full thickness burns.

Diagnosis

Diagnosis is based on history of exposure to a corrosive agent and characteristic findings. The victim complains of pain in throat due to oral burns.

Laboratory / Monitoring

- ✓ Obtain baseline CBC and electrolytes in patients with significant burns
- ✓ Monitor renal functions and coagulation profile in patients with severe burns.
- ✓ Obtain an upright chest X-ray in patients with pulmonary symptoms or suspected perforation.

Management

Pre-hospital

- ✓ Do not induce emesis.
- ✓ Do not attempt neutralization with a basic solution and avoid carbonated beverages.
- ✓ Dilute with milk or water (120-240 ml) avoiding excessive amounts.
- ✓ Irrigate mouth with water.
- ✓ Wash affected skin with water and irrigate exposed eyes with copious amounts of water.
- ✓ Move patients of inhalation exposure to fresh air.

Hospital

- ✓ Administer oxygen to all patients with pulmonary symptoms.
- ✓ Do not perform gastric lavage because of the potential for perforation.
- ✓ Attempt suction through a soft nasogastric tube in substantial ingestion.
- ✓ Administer IV fluids and vasopressors if required.
- ✓ Perform endoscopy within first 24 hrs to predict early hemonhage or perforation and late risk of stricture.

- ✓ Obtain chest X ray for mediastinitis or GI perforation.
- ✓ Perform laparotomy, in case endoscopy reveals Grade III burns with thickness necrosis of esophagus or stomach or when signs and symptoms of GI perforation are evident at the time of initial presentation.
- ✓ Give antibiotics only for suspected infection or perforation.
- ✓ Role of corticosteroids is controversial.
- ✓ In case of hydrofluoric acid (HF) poisoning, monitor ECG, Ca^{2+} and K^{+}. Go there is evidence of hypocalcemia or severe hyperkalemia, give calcium gluconate. For topical exposure apply gel containing calcium gluconate.
- ✓ In case of picric acid ingestion, administer large amounts of IV dextrose as it aids in redaction of picric acid to less poisonous picramic acid.
- ✓ In case of formic acid ingestion, correct metabolic acidosis with sodium bicarbonate.
- ✓ Hemodialysis is effective in formic acid ingestion.
- ✓ There is no specific antidote for most of the agents.

Alkalies

Caustic alkaline substances include ammonia, calcium carbide, calcium hydroxide, calcium oxide, caustic potash, caustic soda (sodium hydroxide), clinitest tablets, potassium carbonate, sodium carbonate, trisodium phosphate etc. Ammonia is a highly volatile and water soluble alkali. Anhydrous ammonia is a colorless, irritating, noxious, water soluble gas used in the manufacture of fertilizers, plastics, explosives, nylon and as a commercial refrigerant gas. Household ammonia solutions are 5-10% aqueous solutions. Solutions greater than 10% are corrosive. Ingestion of industrial strength, 30% or greater, can produces strictures. Aqueous ammonia and chlorine bleach produces chloramine gas which causes pulmonary injury. Calcium oxide (lime) when mixed with water forms calcium hydroxide. Dry calcium hydroxide is corrosive and a strong irritant (pH 11-13) used in making Portland cement. Potassium hydroxide (KOH) or caustic potash less than 1% is a weak irritant, and solutions of greater than 1% are corrosive. Potassium permanganate ($KMnO_4$) is an oxidizer with corrosive properties.

Alkaline corrosives are used as drain openers, oven cleaners, dairy and industrial pipeline cleaners, bathroom and household cleaners, hair relaxers (pH 11-14), cleaners of non-disposable glass containers, electric dishwasher soaps and low phosphate detergents. Clinitest tablets contain sodium hydroxide (50%), sodium carbonate, copper sulphate and citric acid producing corrosive, (4-6% sodium hypochlorite) are capable of producing supertical mocosal burns.

Toxic dose

Just a few milliliters of highly caustic alkali (sodium hydroxide) can cause severe injury. The toxic doses of other alkalies vary widely.

Clinical features

- ✓ Ingestion may produce burns in the oropharynx, upper airway, esophagus and occasionally stomach. Absence of visible oral burns does not reliably exclude the presence of esophageal burns. Presence of stridor, vomiting and drooling are associated with serious esophageal injury in most cases.
- ✓ Metabolic acidosis may develop in patients with severe GI bleeding or massive tissue necrosis after ingestion of corrosive agents.
- ✓ Renal failure is a rare complication of severe burns, accompanied by shock and GI bleeding.
- ✓ Inhalation of alkaline vapours may cause upper airway edema, respiratory failure, wheezing, pulmonary edema, and pneumonitis.
- ✓ Ocular exposure may produces severe conjunctival irritation and chemosis, corneal epithelial defects, limbal ischemia, permanent visual loss and perforation in severe cases.
- ✓ Dermal contact with alkaline corrosives may produce pain, redness, irritation or full thickness burns of skin.

Diagnosis

Diagnosis is based on history of exposure and pH of the substance.

Laboratory / Monitoring

- ✓ Obtain CBC in patients symptomatic of alkaline corrosive ingestion.
- ✓ Obtain renal function tests, PT or INR, PTT, type and cross match for blood in severe burns, perforation or bleeding.
- ✓ Obtain chest X-ray.

Pre-hospital

- ✓ Do not induce emesis.
- ✓ Dilute immediately with milk or water, avoiding excessive amounts
- ✓ Do not administer activated charcoal unless a coingestant is suspected,
- ✓ Irrigate exposed eyes with sterile water or saline for at least 20 min. and continue until the pH returns to normal.

Hospital

- ✓ Provide supportive and symptomatic care.
- ✓ Ensure clear airway and provide ventilatory support if required.
- ✓ Administer IV fluids and vasopressors if required.
- ✓ Avoid prophylactic use of antibiotics.
- ✓ Steroids may be tried in patients with Grade II burns.
- ✓ Surgical evaluation must be considered for any patient with Grade III esophageal injury.
- ✓ There is no specific antidote for alkaline corrosive poisoning.

j) Radiation poisoning

Radiation is defined as the energy given off by atoms in form of particles or electromagnetic rays. Most radiocontrast agents in use are iodinated contrast material which may be ionic or non-ionic compounds.

1**. Ionizing radiation:** radiation that has enough energy to remove electrons from atoms which convert to ions in form of particles or rays (particles, g-rays, x-rays).

2. **Non-ionizing radiation**: radiation that gives off enough energy to make atoms vibrate, however not enough energy to remove electrons (ex: radio waves, visible light, microwaves).

Uses

- ✓ **Urography:** The agents used for urography comprise mainly small molecule, water soluble, low protein binding, high plasma concentration compounds which are given IV. eg: diatrizoates, iothalamates and metrizoates.
- ✓ **Angiography:** These agents are water soluble, with low viscocity and radiodensity. eg: Non-ionic monomers: iohexol.
- ✓ **Contrast radiography of GI tract:** These are nonabsorbable agents which form a homogenous coat on the GI mucosa and do not interact with GI secretions. eg: Barium sulfate.
- ✓ **Computerized tomography of GI tract:** These are nonabsorbable iodinated water-soluble agents with high osmolality. eg: Diatrizoate
- ✓ **Myelography:** Agents for this are non-ionic, water soluble. and miscible with CSF. eg: Metrizamide and iotralan.
- ✓ **Lymphography, lymphangiography:** These agents are water insoluble with high radiodensity. eg: lodised oil, iotasol.
- ✓ **Magnetic resonance imaging -** Gadolinium, manganese, and iron.
- ✓ **Cholecystography, cholangiography:** These agents are preferentially excreted in the bile after absorption from GI tract. eg: Ipodates, iocetamic acid.

Clinical Symptoms

- ✓ Development of radiation burns (look like thermal burns); erythema, desquamation, blistering, appear over a period of days. Extent of localized injury is dependent on extent of penetration of radiation.
- ✓ Inadvertent administration of ionic contrast agents such as diatrizoate or iodamine, instead of iopanidol, by the intrathecal route, has resulted in fatalities.
- ✓ Gastrointestinal syndrome (death of intestinal mucosal cells).
- ✓ Maximal leukopenia and thrombocytopenia occurs several weeks after exposure-hemorrhage and infection can be major problems at this time.
- ✓ Long term sequelae of radiation exposure relates to the chance event of chromosomal injury.

- ✓ Cardiovascular collapse and central nervous system damage with symptoms of lethargy, tremor, seizure, ataxia and death in 24-72 hours.
- ✓ Death usually follows due to radiation pneumonitis, denudation of the alimentary tract, hepatic and renal dysfunction.

Investigations / Diagnosis

- ✓ When a person has experienced known or probable exposure to a high dose of radiation from an accident or attack, medical personnel take a number of steps to determine the absorbed radiation dose. This information is essential for determining how severe the illness is likely to be, which treatments to use and whether a person is likely to survive.
- ✓ **Vomiting and other symptoms:** The time between radiation exposure and the onset of vomiting is a fairly accurate screening tool to estimate absorbed radiation dose.
- ✓ **Blood tests:** Frequent blood tests over several days enable medical personnel to look for drops in disease-fighting white blood cells and abnormal changes in the DNA of blood cells. These factors indicate the degree of bone marrow damage, which is determined by the level of an absorbed dose.
- ✓ **Dosimeter:** A device called a dosimeter can measure the absorbed dose of radiation but only if it was exposed to the same radiation event as the affected person.
- ✓ Survey meter: A device such as a Geiger counter can be used to survey people to determine the body location of radioactive particles.

Management

- ✓ Prophylactic drugs against radiation exposure: Amifostine and Androstenediol. Patients with a history of radiocontrast medium-related oedema should be given prophylactic corticosteroids.
- ✓ Decontamination is accomplished by removing clothing and using soap and water - be careful not to abrade skin.
- ✓ A wound that is contaminated should be copiously irrigated with saline.
- ✓ Any person who reports nausea, vomiting, diarrhea should be taken to the hospital for evaluation of whole body exposure.
- ✓ Chelators can be used for appropriate metals; Ca-DTPA (diethylenediaminepentaacetic acid) has been used for the actidine series (transuranics plutonium, neptunium, americium).
- ✓ Prussian blue should be considered for cesium, thallium, and rubidium exposures.

Pharm.D 4thYear_4.6_ClinicalToxicology_Substance Abuse

Substance abuse:

Signs and symptoms of substance abuse and treatment of dependence:

a) CNS stimulants: Amphetamine

Amphetamine makes up a class of medications known as CNS stimulants. There are many other closely related medications. Amphetamine belongs to the phenylethylamine family with a methyl group substitution in the alpha carbon position. Numerous substitutions of the phenylethylamine structure are possible, resulting in several amphetamine-like compounds. These compounds have now collectively come to be known as “amphetamines”, and include amphetamine phosphate, amphetamine sulfate, benzphetamine.

Abuse potential of amphetamine

The brain is made up of neurons (nerve cells) that communicate with each other through the release of chemicals called neurotransmitters. Amphetamines exert their influence on a family of key brain neurotransmitters (norepinephrine and dopamine) that are related to attention, alertness, blood flow, reward, motor control, and motivation. Amphetamines boost the effects of these chemicals in the brain and body. The associated increase in activity of these neurotransmitters can induce a feeling of euphoria, as well as a rewarding feeling that motivates continued use.

People who use amphetamines regularly can develop a tolerance to them, which means they need to regularly boost their dosage to achieve the same effect. Amphetamine users may find themselves taking increasingly larger doses in order to experience the drug's expected "high" effect. This process will continue for as long as a person keeps taking the drug. The resulting cycle of amplified tolerance and increasingly compulsive drug use fosters addiction and accounts for amphetamines' high addictive potential.

A person trying to quit amphetamine use may experience very pronounced physical and psychological cravings for the drug. As addicts use amphetamines, their bodies chemically adjust to the persistent presence of the drug, and may feel or perform subjectively worse or sub-optimally when the drug is removed. This state of physiological dependence can result in powerful cravings for the drug when the individual is not using a major contributor to relapse. Cravings can last for several weeks, while accompanying effects of withdrawal such as depression can last for months and even years after discontinuing use.

Clinical symptoms

- ✓ **CNS -** Euphoria, Agitation, Headache, Paranoia, Anorexia. Hyperthermia, hypothalamic dysfunction, metabolic and muscle hyperactivity, or prolonged seizures. Hyperreflexia, Choreoathetoid movements and Convulsions are associated with a high mortality rate.
- ✓ **Intracerebral haemorrhage-** Abuse of amphetamine and related drugs can increase the risk for cerebrovascular incidents in young adults.
- ✓ **Coma-** If it occurs, is associated with a high mortality rate.
- ✓ **CVS-** Tachycardia, hypertension, arrhythmias, vasospasm, myocardial ischaemia and cardiomyopathy.
- ✓ **Sympathetic Effects-** Mydriasis, sweating, tremor, tachypnoea, nausea.
- ✓ **Other Effects-** muscle rigidity, pulmonary edema, ischaemic colitis, Rhabdomyolysis and Metabolic acidosis.
- ✓ **Complications-** Psychosis with visual and tactile, hallucinations, Cerebral infarction, Myocardial infarction, Ventricular fibrillation and Acute renal failure.
- ✓ Deterioration of social (family problems), physical (slovenly, unkempt appearance), bankruptcy) status, Paranoid psychosis, unpredictable violence, Vomiting and diarhoea are common. Heightened sexual activity initially, followed by impotence and sexual dysfunction.
- ✓ **Adverse psychological reactions-** anxiety reactions, amphetamine psychosis, exhaustion syndrome, depression and hallucinosis.
- ✓ Death due to amphetamine toxicity most commonly results from arrhythmias, hyperthermia, or intracerebral haemorrhage. In cases of survival, symptoms gradually resolve as the drug is excreted over a period of 24 to 48 hours.

Investigations / Diagnosis

- ✓ Urine is the specimen of choice. Levels above 2mg/100ml indicate acute toxicity. Methods of analysis include TLC, RIA, HPLC, and GC-MS.
- ✓ A new method (electron-impact mass fragmentography) enables detection even quantitation of methamphetamine in hair, nails, sweat and saliva.
- ✓ Hair analysis may provide documentation of methamphetamine or other drug exposure for several months or longer

Management

- ✓ Stabilization - IV line, Oxygen should be provided. Shock is a poor prognostic sign and needs to be managed effectively Consider the need for rightsided heart catheterisation to measure right-sided filling pressure and cardiac output.
- ✓ Supportive Measures- Airway management, ventilatory support, Rapid rehydration, Mannitol diuresis and Gastric decontamination.

- ✓ Symptomatic treatment - Anxiety, agitation, and hyperactivity can usually be controlled with benzodiazepines. Diazepam is the drug of choice, and is administered in a dose of 10 mg IV at intervals. Hyperthermia should be tackled aggressively with hypothermic blankets, ice baths, and dantrolene infusions. Other complications should be treated symptomatically accordingly as follows:
    - Lignocaine and amiodarone are generally first line agents for stable monomorphic ventricular tachycardia.
    - For rhabdomyolysis: Early aggressive fluid replacement is the mainstay of therapy, and may help prevent renal insufficiency.
    - Diazepam and chlorpromazine have been effective in treating amphetamine-induced chorea.
- ✓ Most casual users of amphetamines do not need treatment. Those with moderately severe dependency can be treated on an outpatient basis without using drugs.
- ✓ A wide variety of pharmacological agents have been tried as adjuncts to (or major elements in) the treatment of amphetamine dependence. These include drugs such as imipramine and fluoxetine, but results have been disappointing.

b) Opioids

Opioids present with a syndrome which includes miosis, coma, respiratory depression and vomiting. A rapid response to naloxone is usual if hypoxic brain damage or other events have not been superimposed. The treatment is primarily supportive, although naloxone may also be used in certain circumstances. In recreational overdoses (i.e. dependent patients), a withdrawal reaction to non-titrated doses naloxone is common.

Clinical symptoms

Often, the facts about the effects of opiate use are misleading because they may only focus on the short-term impact. For example, opiates often cause vomiting and diarrhea, sedation and delayed reactions in the short term.

- ✓ Physical symptoms: Noticeable elation / euphoria, Marked sedation / drowsiness, confusion, Constricted pupils, Slowed breathing, Intermittent nodding off, or loss of consciousness and Constipation.
- ✓ Other signs of opiate abuse include: Doctor shopping (getting multiple prescriptions from different doctors) and Shifting or dramatically changing moods. Extra pill bottles turning up in the trash. Social withdrawal / isolation and Sudden financial problems.
- ✓ Long-term symptoms include: Weakened immune system functioning, Gastric problems ranging from the troublesome to severe, A plethora of medical issues secondary to intravenous administration (eg: localized abscesses, embolic events, systemic infection, contraction of bloodborne illnesses) and Significant respiratory depression; cumulative hypoxic end- organ injury.

Opiate Abuse Treatment abuse

Opiate recovery typically starts with questions related to the nature of the addiction, such as:

- How long have you taken the drug?
- When was the last time you took the drug?
- How do you usually get your supply?

Three major options for opiate treatment include detoxification (or, simply, detox programs), inpatient rehabilitation, and outpatient therapy.

- ✓ Detox involves withdrawing from the drug, often slowly with the use of stabilizing and maintenance medication under the supervision of a medical treatment team. If detoxing from powerful opiates, it might be prescribed methadone or buprenorphine to make the transition more manageable. Detoxification is completed on an inpatient basis to maintain safety.
- ✓ Following the transition from detox, most will be referred for continued treatment via residential rehab or outpatient might be therapy depending on a number of factors. Influencing the decision for treatment type is the individual's level of opiate use, the presence of any home or family supports, as well as taking into account any previous attempts at recovery. Rehab typically lasts anywhere from 30 to 90 days with much of the time being devoted to individual therapy, group therapy and other activities that help promote recovery from opiates.
- ✓ During therapy, you will attend sessions with a therapist or counselor. This will help vou to uncover the triggers of your addiction. It helps to impart effective coping skills to resist the temptation of drugs while seeking out helpful supports. It can also help you reconnect with your family and friends.
- ✓ In conjuction with outpatient treatment, some in recovery may require more support. For someone in recovery from opiate addiction, this might take the form of a halfway house or sober living facility, which gives former users the chance to get sober and rebuild their live in a safe and supportive environment. Others may simply need a peer support group such as narcotics anonymous.

c) CNS depressants

Central nervous system (CNS) depressants, a category that includes tranquilizers, sedatives, and hypnotics, are substances that can slow brain activity. This property makes them useful for treating anxiety and sleep disorders. The following are among the medications commonly prescribed for these purposes.

Benzodiazepines, such as diazepam, clonazepam, and alprazolam, are sometimes prescribed to treat anxiety, acute stress reactions, and panic attacks. Clonazepam may also be prescribed to treat seizure disorders. The more sedating benzodiazepines, such as triazolam and estazolam are prescribed for short-term treatment of sleep disorders. Usually, benzodiazepines are not prescribed for long-term use because of the high risk for developing tolerance, dependence, or addiction.

Non-benzodiazepine sleep medications, such zolpidem, eszopiclone, and zaleplon, known as z-drugs, have a different chemical structure but act on the same GABA type A receptors in the brain as benzodiazepines. They are thought to have fewer side effects and less risk of dependence than benzodiazepines.

Barbiturates, such as mephobarbital, phenobarbital, and pentobarbital sodium are used less frequently to reduce anxiety or to help with sleep problems because of their higher risk of overdose compared to benzodiazepines. However, they are still used in surgical procedures and to treat seizure disorders.

Clinical Symptoms

Although withdrawal from benzodiazepines can be problematic, it is rarely life threatening, whereas withdrawal from prolonged use of barbiturates can have life-threatening complications. Therefore, someone who is thinking about discontinuing a sedative or who is suffering withdrawal from CNS depressants should speak with a physician or seek immediate medical treatment.

- ✓ Delirium, seizures, mental confusion, hallucinations, changes in pulse, respiratory rate, or blood pressure, insomnia, nausea and vomiting, agitation, digestive problems, tremors, body spasms, body aches and pains.
- ✓ Heart palpitations, blackouts, periods of depression, mood swings and inability to keep up with their family and social commitments.
- ✓ Secretive behavior, loss of interest in activities they previously enjoyed and even though these drugs are causing obvious harm the individual continues to use them.

Investigations

- ✓ Barbiturates: Urine Test: (remains positive for 24 hours to 7 days after last dose)
- ✓ Benzodiazepines: Urine Test (remains positive for 3+ days after last dose)

Management

The most effective treatment for depressant addiction is complete abstinence. How this is achieved will depend on the type of drug. With barbiturates and benzodiazepines a common approach is to taper the individual off the drug. The drug is not stopped immediately but instead it is given at a reducing rate over time until abstinence is reached.

Cognitive Behavioral Therapy (CBT) is extremely beneficial not only in treating CNS Depressant dependency but any type of addiction. Addiction not only affects a person physically but mentally and psychologically as well. Trained Therapists and counselors are there to help you not only with confidence but help you find better ways to deal with stress and everyday challenges that may come your way while working toward recovery and sobriety.

Detoxing can be not only complicated but very uncomfortable. Depending on the extent of abuse and dependency and if there are multiple drugs that are being abused detoxing can be complicated.

d) Hallucinogens: LSD

Hallucinogens are substances that induce changes in thought, perception, and mood, without causing major disturbances in the autonomic nervous system. Perceptual alterations can take the form of illusions, synaesthesias, or hallucinations. An illusion is the result of misinterpretation of an actual experience, while synaesthesias are sensory misperceptions (e.g. hearing colour or seeing sounds). Both require external stimuli for their institution.

Lysergic acid diethylamide (LSD) is the synthetic diethylamide derivative of ergot alkaloids, and was originally synthesized exclusively from these alkaloids produced by the fungus *Claviceps purpurea*, which is a contaminant of rye and certain other grains. Today, most LSD is synthesised entirely in the laboratory, and typically sold to addicts as liquid-impregnated blotting paper, or sugar cubes, tiny tablets (“microdots”), gelatin squares (“window panes”), liquid, or powder. LSD is said to be the most powerful of all hallucinogens, and is active in doses of 50 to 100 mg. It occurs as a water-soluble, colorless, tasteless and odourless powder.

Drugs related to LSD (lysergamides) occur naturally in plants such as "Morning glory" (*Rivea corymbosa*) and "Hawaiian baby woodrose" (*Ipomoea violacea*). Seeds of morning glory contain lysergic acid hydroxyethylamide, which is 1/10th as powerful as LSD. At least 200 to 300 seeds have to be pulverized - intact seed coat resists digestion and ingested, for inducing hallucinogenic effects.

Clinical Symptoms

- ✓ Physical signs - Dilated pupils, Salivation or dry mouth, Tingling fingers or toes, Weakness, Negative effects including emotional distress, anxiety, depression, disorientation or paranoia dizziness, nausea, rapid heart rate and convulsions, Sweating or chills, Blurred vision, Inability to perform complex tasks like driving or operating machinery.
- ✓ Distortions of time, depth, space, size and shape, Hallucinations of things that are not there or that stationary items are moving - in most cases, the person is aware of the unreality of these effects but in those situations where this is not true, injury or death can occur.

- ✓ Altered perceptions of speed, blended sensory experience, in other words, "hearing" colors or "seeing" music
- ✓ Intensified senses of sound, touch or sight - visual hallucinations may range from color intensification or flashes of light to moving geometric or other patterns that can be seen with eyes open or shut.
- ✓ The sensation that a person has left his or her body or that their body has changed shape.
- ✓ Feeling of inner tension, often relieved by laughing or crying and religiosity and a feeling of "oneness with the universe".

Investigations / Diagnosis

Of all the hallucinogens, LSD is the most potent known to man. Taken orally, it takes as little as 25 micrograms or 0.000025 grams of LSD to produce rich and vivid hallucinations in the user. While it is possible to test one's urine for LSD, the very tiny amounts involved makes detection very difficult. There is also the fact that it is rapidly removed from the body, usually within 24-48 hours.

- ✓ **Abuscreen -** This is a series of RadiolmmunoAssay (RIA) tests developed by Roche Diagnostic Systems. One of these tests is used to screen whole blood, serum (blood), urine and stomach contents for LSD and its metabolites.
- ✓ **EMIT -** Standing for Enzyme Multiplied Immunoassay Technique, EMIT is also a series of tests that can be done to detect LSD and its metabolites in serum and urine.
- ✓ **HPLC** (high pressure / performance liquid chromatography) of serum and urine,
- ✓ **GC-MS** (gas chromatography - mass spectrometry) can confirm positive LSD urine levels to a lower limit of 5 pg / ml.

Management

- ✓ Treat acute panic attacks with quiet environment, reassurance, supportive care and administration of diazepam (5-10 mg IV) or haloperidol (in severe cases).
- ✓ Treat acute psychotic reactions with cautious administration of neuroleptics such as haloperidol. Avoid phenothiazines which can cause hypotension, sedation, extrapyramidal reactions, lowered seizure threshold, and potentiation of anticholinergic effects.
- ✓ Treat flashbacks with psychotherapy, anti-anxiety agents, and neuroleptics.
- ✓ Treat post-hallucinogen perception disorder with longlasting benzodiazepines such as clonazepam, and to a lesser extent anticonvulsants such as valproic acid pue carbamazepine.
- ✓ This approach must be combined with behavioral therapy. The patient must be instructed not to consume alcohol, cannabis, caffeine, and other drugs which can intensify the disorder.

e) Cannabis group

Cannabis preparations (vide infra) are derived from Indian hemp plant (Cannabis sativa), which is a hardy, aromatic annual herb that grows wild under most climatic conditions. The plant grows to a height of 5 to 15 feet, and is characterised by an odd number of leaflets on each leaf (varying from 5 to 9), all having serrated or saw-tooth edges, and small, green flowers. The male and female flowers are borne on separate plants. After pollination, the male plants die back.

Active principles

The main active principle is d9 (delta-9) tetrahydrocannabinol (THC) which is a cannabinoid found in both the male and female plants.

THC is a lipid-soluble, water-insoluble compound which can be synthesized in the laboratory. The synthetic form, however, is very expensive to produce, and so frequently, other illicit drugs such as phencyclidine, mescaline, or LSD are sold in the guise of THC. A product called "super weed" or "super grass" is dusted with phencyclidine. Apart from THC, Cannabis sativa contains a number of other cannabinoids, including cannabidiol, cannabinol, cannabidolic acid, cannabicyclol and cannabigerol.

Sources

1. Marijuana: The term "marijuana" refers to any part of the plant or its extract that is used to induce psychotomimetic or therapeutic effects. Synonyms incude Mary Jane, MJ, maconha, pot, weed, grass, puff, and dagga.

2. Ganja: Although some texts refer to ganja as being synonymous with marijuana, while others consider it to be a resinous mass composed of leaves and bracts, in India (where the term actually originated), it is used to refer to crushed leaves and inflorescences of female plants. It is usually smoked in a pipe (chillum) or in the form of cigarettes ("reefer" or "joint or" number). Ganja is said to contain 1 to 2% THC.

3. Bhang: Bhang consists of dried mature leaves and flower stems that are ground with water and mixed with milk or fruit juice. It is consumed by Hindus in India during festivals such as Holi and Shiv Ratri.

4. Hashish (Charas): This preparation is made out of dried resin collected from flower tops, and contains varying concentrations of THC up to 10%. It is popular in the Middle East and North Africa. Hashish oil or liquid hashish "is an alcohol or petrol extract which

occurs as a dark green viscous liquid with the consistency of tar. It is the most potent of all cannabis preparations and contains 20 to 30% (or more) THC.

5. Sinsemilla: It is the most popular form of cannabis in the USA, and refers to seedless (unpollinated female) plant which averages 5% of THC.

6. Marijuana "Blunts": This is nothing but cheap cigars sliced open, packed with cannabis and resealed. The harsh stench of the cigar masks the characteristic sweet smell of cannabis. Blunts are very popular among the youth in some parts of the USA.

Clinical symptoms

- ✓ Euphoria with increased garrulity and hilarity, especially when smoked in a social group setting.
- ✓ Temporal and spatial disorientation with intensification of sensation, at high doses, the user experiences ataxia, dizziness, sedation, hallucinations and sometimes dysphoria characterized by unpleasant sensations, fear, and panic.
- ✓ Tachycardia, palpitations, hypertension (high doses). Large doses can also cause postural hypotension
- ✓ Bloodshot eyes due to conjunctival congestion, reduced bowel motility and urinary retention have occasionally been observed.
- ✓ Pupils are usually not affected. Occasionally, mydriasis and nystagmus may occur.
- ✓ Amotivational Syndrome: Chronic indulgence is said to induce an amotivational syndrome characterized by apathy, poor concentration, social withdrawal, and lack of motivation to study or work.
- ✓ Heavy cannabis users demonstrate an increased tendency to develop manic, schizophreniform, and confusional psychoses over a period of time.
- ✓ Medical complications: Chronic lung disease and carcinogenesis, Cancers of mouth and larynx, Aspergillosis, Non-specific ST wave, Gynaecomastia and mild abstinence syndrome.

Investigations

- ✓ Identification of suspected specimen: Suspend leaf or stem fragments in several drops of chloral hydrate (10%) on a microscope slide and examine under low power for characteristic "cystolith hairs". Add a drop of 20% HCI and note the gentle effervescent release of carbon dioxide gas in tiny bubbles.
- ✓ Urine levels of cannabinoids: THC is hydrophobic and accumulates in adipose tissue. Screening tests may be positive for up to 70 or more days, depending on the cut-off levels used and the individual's lipid stores of THC. False positive results may occur with therapeutic use of ibuprofen, fenoprofen, and naproxen.
- ✓ Screening tests usually employ EMIT or RIA, while confirmation is done by using GC-MS.

Management

- ✓ Decontamination measures in cases of ingestion. Activated charcoal is beneficial.
- ✓ Acute psychotic reactions respond to benzodiazepines. 5 to 10 milligrams of diazepam orally is usually sufficient.
- ✓ Psychosocial therapy consisting of attempts to promote realistic and rewarding altenatives to the drug and associated life styles, along with a commitment to abstinence from self-administered unprescribed psychotropic drugs.
- ✓ Drug-focussed group therapy comprising strategies such as social pressure reinforce abstinence, teaching socialization and problem solving skills, reducing stress and the sense of isolation common with drug abuse, relapse prevention exercises and varying degrees of confrontation.
- ✓ Short-term use of antipsychotic medication may be required if there are persistent delusional ideas or frightening flash backs.

f) Tobacco

Tobacco is one of the most widely abused substances in the world. It is highly addictive. The Centers for Disease Control and Prevention estimates that tobacco causes 6 million deaths per year. This makes tobacco the leading cause of preventable death. Nicotine is the main addictive chemical in tobacco. It causes a rush of adrenaline when absorbed in the bloodstream or inhaled via cigarette smoke. Nicotine also triggers an increase in dopamine. This is sometimes referred to as the brain's "happy" chemical.

Sources: Nicotiana attenuata (Wild tobacco), Nicotiana glauca (Tree tobacco), Nicotiana longiflora (Cultivated ornamental), Nicotiana rustica, Nicotiana tabacum (Commercial tobacco) and Nicotiana trigonophylla (Desert tobacco).

Active Principles: Nicotiana tabacum and Nicotiana rustic contain the following alkaloids: Nicotine , Nornicotine, Anabasine and Anabatine.

Mode of Intake

By far the commonest source of nicotine poisoning (acute or chronic) results from smoking tobacco in the form of cigarettes. When a cigarette is lit and inhaled, the smoker is exposed to both gaseous and particulate matter. Nicotine and tar are part of the particulate phase of cigarette smoke. When a cigarette is smoked, more than half the nicotine escapes in the sidestream smoke, while a large fraction remains in the butt and filter, and it is only 0.5 to 2 mg (average 1 mg) of nicotine that finally is delivered to the smoker.

In India, "bidis are very popular, especially among the poorer sections of society, since they are much cheaper than cigarettes. Bidis are small, brown, hand-rolled cigarettes consisting of tobacco wrapped in a tendu or temburni leaf (Diospyros

melanoxylon). After cigarettes, the next common source of nicotine toxicity results from smokeless tobacco which is of two kinds - snuff and chewing tobacco. Because smoking is not involved, people generally believe that snuff is more socially acceptable and less harmful. This is however not true. Snuff is usually available as finely cut tobacco powder which is packaged dry or moist. It contains approximately 14 mg of nicotine per gram of tobacco.

Clinical Symptoms

- ✓ Early Effects (15min to 1 hour)
  - GIT: Nausea, salivation, vomiting, abdominal pain.
  - CVS: Tachycardia, hypertension.
  - RS: Tachypnoea, bronchorrhoea.
  - CNS: Agitation, anxiety, sweating, headache, blurred vision, confusion, vertigo, tremor, ataxia, muscle fasciculations, convulsions. Pupils are at first constricted, but may dilate later. A primary position upbeat nystagmus is seen following cigarette smoking. Chewing of nicotine gum, and ingestion of nicotiana glauca leaves, and is the direct result of nicotine.
- ✓ Delayed Effects (after1 hour)
  - GIT: Diarrhoea.
  - CVS: Bradycardia, arrhythmias, hypotension, shock.
  - RS: Hypoventilation, apnoea.
  - CNS: lethargy, weakness, hyporeflexia, hypotonia, paralysis, coma.

Death may occur, especially in the case of ingestion of cigarettes (inadvertently) by children, or exposure to insecticidal nicotine.

Nicotine dependence is the most widely prevalent and deadly of all substance dependencies. DSM-IV defines two nicotine-related disorders: nicotine dependence and nicotine withdrawal.

Health consequences of tobacco uses

- ✓ Lung cancer.
- ✓ Non-pulmonary cancers: Mouth, larynx, oesophagus, stomach, liver, pancreas, bladder, uterine cervix, breast, brain.
- ✓ Respiratory diseases: Emphysema, bronchitis, asthma, pneumonia.
- ✓ Cardiovascular diseases: Coronary heart disease, hypertension, arterial thrombosis, stroke.
- ✓ Obstetric and neonatal conditions: Abortion, abruptio placenta, placenta praevia, preterm labour, pre-eclampsia, growth retardation, congenital malformations, sudden infant death syndrome, foetal or neonatal death,
- ✓ Other conditions: Peptic ulcer, osteoporosis and Alzheimer's disease.

Nicotine withdrawal

Manifestations of nicotine withdrawal can occur within 4 to 8 hours of the last cigarette, In fact most chronic smokers experience some withdrawal symptoms on waking up each morning. Manifestations include changes in mood, insomnia, difficulty concentrating, restlessness, decreased heart rate (average decline is 8 beats per minute), and weight gain (average is 2 to 3 kg).

Investigations

- ✓ Acute poisoning can be confirmed by estimating plasma nicotine level; but the short half-life of nicotine necessitates early withdrawal of blood. High pressure liquid chromatography is generally utilised to assay nicotine levels. Plasma level greater than 40 to 50 ng / ml indicates serious toxicity.
- ✓ Polymorphonuclear leucocytosis and glycosuria are often encountered in nicotine overdose.
- ✓ Passive tobacco smoke exposure is usually determined by estimating cotinine levels in plasma, urine, or saliva.

Management

- ✓ Decontamination by stomach wash. Emesis is contraindicated. Activated charcoal is effective and must be administered in the usual manner. Since nicotine is weakly alkaline, excretion can be enhanced by acidification of urine.
- ✓ Symptomatic and supportive measures - Benzodiazepines for convulsions, Atropine for bradycardia, IV fluids and vasopressors (dopamine or noradrenaline) for hypotension, Respiratory compromise is managed by oxygen, intubation, and positive pressure ventilation.
- ✓ Nicotine replacement therapy
- ✓ Nicotine gum (Polacrilex)
- ✓ Nicotine transdermal patch
- ✓ Nicotine spray
- ✓ Other therapies - Clonidine, Antidepressants- doxepin and sertraline, Nicotine agonists and antagonists eg: Lobeline.