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Lec1: Introduction

- Definition of Toxicology

- Toxicology is:
  - **"The science of poisons."**
  - **"The study of adverse effects of chemicals or physical agents on living organisms."**
- According to Paracelsus:
  "The dose determines whether something is a poison."

- Toxic Response

- A **poison** is any substance that can cause harmful effects in the body.
- **Almost all chemicals can be toxic** if the dose is high enough.
- Most toxic effects are **dose-dependent**.

❗ Exceptions (Not dose-related):

- **Allergic reactions**
- **Idiosyncratic reactions**

-Allergic Reactions

- Immune-mediated response after prior exposure (sensitization).
- Can occur even at **very low doses**.
- Often involves formation of a **hapten–protein complex** → triggers antibodies.
- Severity ranges from mild rash → **anaphylactic shock**.

- Idiosyncratic Reactions

- **Genetically determined abnormal response**.
- Can cause:
  - Extreme sensitivity to low doses
  - Or no response to high doses
- Examples:
  - G6PD deficiency
  - Succinylcholine (Scoline) apnea
  - Disulfiram reactions

Classification of Toxic Agents

1. **Physical state** → gas, liquid, solid
2. **Chemical properties** → flammable, explosive
3. **Chemical structure** → aromatic amines, hydrocarbons
4. **Toxicity level** → highly toxic, slightly toxic
5. **Mechanism of action** → enzyme inhibitors, etc.

-Chemical Interactions: When chemicals are combined, their effects may change.

Types of Interactions:

1.Additive Effect

- Total effect = **sum of individual effects**
- Example: alcohol + sedative → increased CNS depression

2.Synergism

- Combined effect is **greater than the sum**
- Examples:
  - Smoking + asbestos → ↑ lung cancer risk
  - Ethanol + carbon tetrachloride → ↑ liver toxicity

3.Potentiation

- One chemical (non-toxic alone) **increases toxicity of another**
- Examples:
  - Isopropanol ↑ toxicity of carbon tetrachloride
  - Drug displacement (e.g., warfarin from albumin)

4.Antagonism

- One chemical **reduces or blocks the effect** of another

Types of Antagonism:

- **Functional** → opposite physiological effects
- **Chemical** → direct chemical interaction
  - Example: protamine for heparin
- **Dispositional** → affects absorption, metabolism, excretion
- **Receptor** → compete for same receptor
  - Examples:
    - Naloxone vs opioids
    - Flumazenil vs benzodiazepines
    - Atropine vs acetylcholine

Lec2: Principles of Management of Acute Poisoning

-Incidence & Severity of Poisoning

- Poisoning can vary in severity:
  - **Simple**
  - **Serious**
  - **Fatal**

-Sources of Poison

1. **Household products**
   - Medications, cosmetics, cleaning agents
2. **Food poisoning**
3. **Environmental**
   - Toxic gases, pesticides
4. **Occupational exposure**
5. **Substance abuse**
6. **Plants & chemicals**

-Routes of Poisoning

- **Oral (most common)**
- **Inhalation**
- **Parenteral (injection)**
- **Dermal (skin absorption)**

- Circumstances of Poisoning

- **Accidental**
- **Suicidal**
- **Homicidal**

#General Approach to Management

1.Patient Stabilization (ABC + D)

Focus on vital functions:

- **A** → Airway
- **B** → Breathing
- **C** → Circulation
- **D** → CNS depression (Drugs)

#Common emergency treatments:

- Oxygen
- Glucose
- Thiamine
- Naloxone
- Atropine (in some cases)

2.Complete Patient Assessment

- **History**
- **Physical examination**
- **Lab tests** (LFT, KFT, CBC, glucose)
- **Toxicology screening**

Goals:

- **Ide**ntify poison
- Decide if antidote is needed
- Understand mechanism
- Guide treatment
- Monitor organ function

3.Poison Decontamination

Remove unabsorbed poison to reduce toxicity

Sites:

- GI tract
- Skin
- Mucous membranes

Gastrointestinal Decontamination Methods

-Dilution

- Used in **corrosive ingestion**
- Use: milk, egg white
- Avoid neutralizing agents

-Emesis (Vomiting)

- Removes poison early
- Limited use today (not always recommended)

Methods:

- Ipecac syrup (safe, effective)
- Apomorphine (fast but risky)
- Detergents
- Gag reflex (low efficiency)
- Hypertonic saline (**avoid**)

-Gastric Lavage

- Done in hospital
- Requires airway protection
- Uses warm fluids

Complications:

- Aspiration pneumonia
- Perforation
- Electrolyte imbalance

Contraindications:

- Hydrocarbon ingestion
- Unprotected airway

-Adsorbents

Activated charcoal

- Binds many toxins
- Dose:
    - Adults: 50–100 g
    - Children: 15–20 g

Not effective for:

- Metals
- Alcohols (ethanol, methanol)
- Acids/alkalis
- Hydrocarbons

-Cathartics

- Increase elimination via intestines
- ⚠ Avoid in:
  - Renal failure
  - Heart failure
  - Intestinal obstruction

4.Enhancement of Elimination

Methods:

1. **Renal excretion**
   - Forced diuresis
   - Urine pH manipulation
2. **GI elimination**
   - Repeated charcoal
   - Interrupt enterohepatic circulation
3. **Dialysis**
4. **Plasma exchange**
5. **Exchange transfusion**

Urine pH Manipulation

- **Alkaline urine ($NaHCO_3$)** → ↑ excretion of acidic drugs
  - e.g., salicylates
- **Acidic urine (NH_4Cl)** → ↑ excretion of basic drugs
  - e.g., amphetamines

⚠ Risks:

- Electrolyte imbalance
- Pulmonary/cerebral edema

Dialysis

- Works for toxins that are:
  - Small
  - Water-soluble
  - Low protein binding
- **Hemodialysis > Peritoneal dialysis**

5.Antidotes

- Naloxone → opioids
- Flumazenil → benzodiazepines
- N-acetylcysteine → paracetamol
- Ethanol / fomepizole → methanol poisoning
- Chelators → heavy metals

6.Supportive Care

Manage complications:

- Hypothermia / Hyperthermia
- Seizures
- Coma

Lec3: Alcohol

1.Ethanol Intoxication

- Occurs when intake exceeds individual tolerance
- Causes **behavioral + physical impairment**
- Very common in emergency and forensic settings
- Major cause of death (especially ages 15–45)

Sources of Ethanol

- Alcoholic drinks:
  - Spirits: **40–50%**
  - Wine: **10–20%**
  - Beer: **2–6%**
- Other sources:
  - Mouthwash (up to 75%)
  - Colognes (40–60%)
  - Medications

Mechanism of Action

- **CNS depressant**
- Acts on **GABA receptors**
- Affects brain areas in order:
  1. Frontal lobe → behavior
  2. Occipital lobe → vision
  3. Cerebellum → coordination

Metabolic Effects

- ↓ NAD^+/NADH ratio → metabolic disturbance
- Pyruvate → lactate → **lactic acidosis**
- ↑ uric acid
- Fat accumulation in liver → **fatty liver**

Pharmacokinetics

- Rapid absorption:
  - Stomach (20%)
  - Small intestine (80%)
- Peak: **30–60 min**
- Vd:
  - Total body water (Vd ≈ 0.6–0.7 L/kg)
- Metabolism:
  - Liver (90%) via:
    - Alcohol dehydrogenase (ADH)
    - MEOS (high doses)
- Elimination rate:
  - 15–20 mg/dL/hour (higher in alcoholics)

⚠ Clinical Features

- CNS depression (drowsiness → coma)
- Slurred speech, ataxia
- Hypoglycemia (especially children)
- Hypothermia
- Respiratory depression
- Cardiac effects (arrhythmias)

Complications

- Liver disease
- Stroke risk
- Fetal alcohol syndrome
- Vitamin deficiencies (B1, B6, B12)

Special Reaction

- Disulfiram-like reaction (e.g., with metronidazole):
  - Flushing
  - Vomiting
  - Tachycardia

Diagnosis

- Blood ethanol level
- Glucose (hypoglycemia)
- Electrolytes (anion gap)

Management

- ABC support
- Correct hypoglycemia & electrolytes
- **Thiamine before glucose** (prevent Wernicke syndrome)
- Decontamination (rapid absorption)

2.Methanol Poisoning

📌 Sources

- Antifreeze
- Windshield fluid
- Paints, solvents

Toxic Mechanism

Methanol → Formaldehyde → **Formic acid (toxic)**

Causes:

- Metabolic acidosis
- Optic nerve damage

Clinical Features

- Latent period: 12–24 h
- Visual symptoms:
  - Blurred vision
  - Blindness
- CNS depression
- Severe acidosis → coma

Severity

- 20 mg/dL → symptoms
- 100 mg/dL → eye toxicity
- 150–200 mg/dL → death

Management

- **Antidotes:**
  - Ethanol
  - Fomepizole
- Folate → enhances metabolism
- **Hemodialysis (very important)**

3. Ethylene Glycol Poisoning

📌 Sources

- Antifreeze (sweet taste → common in children)

Mechanism

Ethylene glycol → glycolic acid → **oxalic acid**

Leads to:

- Calcium oxalate crystals
- Kidney damage

Clinical Stages

1.Early (CNS phase)

- Like ethanol intoxication
- Vomiting, ataxia, coma

2.Cardiopulmonary (12–24 h)

- Tachycardia
- Pulmonary edema
- Heart failure

3.Renal phase (24–72 h)

- Kidney failure
- Flank pain
- Oliguria

Investigations

- ABG → metabolic acidosis
- Urine → crystals
- Kidney function

Management

- Correct acidosis
- Calcium for hypocalcemia
- **Antidotes:**
  - Ethanol
  - Fomepizole
- Hemodialysis
- Vitamins:
  - Thiamine
  - Pyridoxine

Summary:

Feature	Ethanol	Methanol	Ethylene Glyco
🧪 Source	Alcoholic drinks, meds	Antifreeze, solvents	Antifreeze (sweet taste)
⚙️ Toxic Metabolite	❌ None (parent compound)	**Formic acid**	**Oxalic acid**
🎯 Target Organs	CNS	Eyes (optic nerve)	Kidneys
🧠 Main Effect	CNS depression	Blindness + acidosis	Renal failure + acidosis
⏳ Onset	Rapid (30–60 min)	Delayed (12–24 h)	مراحل (CNS → قلب → كلى)
🔬 Key Symptoms	Slurred speech, coma	Blurred vision, coma	Flank pain, oliguria
⚠️ Special Feature	Hypoglycemia	Visual loss	Calcium oxalate crystals
🧾 Lab Findings	Normal AG غالبًا	↑ Anion gap acidosis	↑ AG + ↓ Ca^{2+}
💊 Antidote	❌ Supportive	Ethanol / Fomepizole	Ethanol / Fomepizole
🏥 Dialysis	Rare	Important	Important

Lec4: Doping in Sports

📌 Definition of Doping

- Use of **prohibited substances or methods** to enhance performance
- Includes **attempts to conceal use**
- Regulated by World Anti-Doping Agency

Why Doping is Dangerous

- Damages:
  - Integrity and fairness of sport
  - Athlete health
- Many substances were **not designed for performance use**

History

- Ancient Greeks used plants for performance
- In 1976, International Olympic Committee started drug testing
- Despite testing → doping still increasing

Why Athletes Dope

- Improve performance
- Increase alertness
- Improve appearance
- Other reasons:
  - Injury recovery
  - Weight control
  - Peer pressure

Types of Doping Methods

Non-Pharmacological

- Blood transfusion
- Hypoxia training
- Gene doping

1.Anabolic Steroids (AAS)

- Related to testosterone
- Increase:
  - Muscle mass
  - Protein synthesis

Effects:

- Muscle growth
- Fat reduction

Side Effects:

- Hypertension
- Heart disease
- Liver damage
- Infertility
- Psychiatric effects

⚠ **Special:**

- Gynecomastia (males)
- Virilization (females)

Patterns of Abuse

- **Cycling** → periods of use
- **Stacking** → multiple drugs
- **Pyramiding** → gradual increase then decrease

2.Growth Hormone (GH)

- Produced by pituitary gland
- Increases:
  - Body mass
  - Linear growth

Side Effects:

- Acromegaly
- Diabetes
- Heart enlargement

3.Erythropoietin (EPO)

- Increases RBCs → ↑ oxygen delivery
- Used in endurance sports

Risks:

- Stroke
- Hypertension
- Thick blood (viscosity)

4.Stimulants (e.g., amphetamines)

- Increase:
  - Alertness
  - Endurance
  - Reaction time

Side Effects:

- Anxiety, insomnia
- Tachycardia
- Stroke, heart attack
- Addiction

5.Narcotics

- Pain relief
- May reduce performance (sedation)

Risks:

- Dependence
- Respiratory depression

6.Beta Blockers

- Decrease:
  - Heart rate
  - Tremor

Useful in:

- Shooting
- Archery

Side Effects:

- Hypotension
- Bronchospasm

7.Diuretics

- Increase urine output
- Used for:
  - Weight loss
  - Masking drugs

Side Effects:

- Dehydration
- Arrhythmias
- Kidney problems

Detection of Doping

- Based on:
  - Testosterone / epitestosterone ratio
- Normal: **4:1**
- Positive: **≥ 6:1**

Organizations Involved

- World Anti-Doping Agency
- International Olympic Committee
- FIFA
- National Basketball Association
- National Football League

⚠ Therapeutic Use Exemption (TUE)

- Allows athletes to use banned drugs **for medical reasons**

🎯 Key Exam Points

- Doping = **performance enhancement + prohibited substances**
- AAS → muscle + many side effects
- EPO → ↑ oxygen → risk of stroke
- Methanol? ❌ (not doping, toxicology topic)
- Beta-blockers → used in precision sports
- Diuretics → **masking agents**

Lec5: Carbon Monoxide (CO)

Properties

- Colorless, odorless, tasteless, non-irritant gas
- Produced by **incomplete combustion**
- Common sources:
  - Car exhaust
  - Charcoal/fire smoke
  - Gas heaters
  - Tobacco smoke
  - Methylene chloride

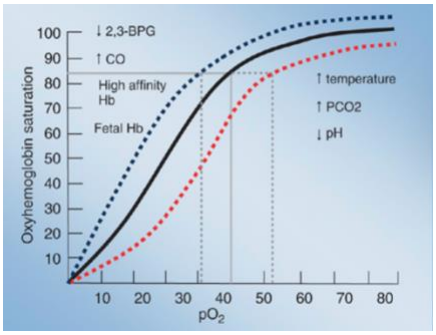
Epidemiology

- Very common cause of poisoning worldwide
- Peak:
  - Time: **6–10 PM**
  - Months: **December–January**
- **~89% occur at home**

Mechanism of Toxicity

- CO binds hemoglobin **200–300× stronger than O_2**
- Forms **carboxyhemoglobin (COHb)**

Effects:



- ↓ Oxygen delivery (**functional anemia**)
- Left shift of Hb–O_2 curve → ↓ oxygen release
- Binds:
  - Myoglobin
  - Cytochromes

Most affected organs:

- **Brain (CNS)**
- **Heart (CV system)**

Half-Life of CO

- Room air: **4–6 hours**
- 100% O_2: **~80 minutes**
- Hyperbaric O_2: **~20 minutes**

Carboxyhemoglobin (COHb) Levels & Symptoms

Mild (5–20%)

- Headache
- Dizziness
- Nausea
- Shortness of breath
- May be asymptomatic

Moderate (21–40%)

- Severe headache
- Confusion
- Syncope
- Chest pain
- Tachycardia

Severe (41–60%)

- Arrhythmias
- Hypotension
- Seizures
- Coma
- Cardiac arrest

⚠ High-Risk Groups

- Infants
- Pregnant women (fetus at high risk)
- Elderly
- Patients with:
    - Heart disease
    - COPD
    - Anemia

Complications

Cardiovascular

- Myocardial ischemia
- Increased risk of death

Neurological

- Delayed neuropsychiatric syndrome (10–30%)
  - Memory loss
  - Cognitive impairment
  - Dementia

Management

1. Remove patient from exposure
2. Ensure **ABC (airway, breathing, circulation)**
3. Give **100% oxygen immediately**
4. Consider **hyperbaric oxygen** (severe cases)
5. CPR if needed

Prevention

- Proper ventilation
- Avoid running engines in closed spaces
- No charcoal indoors
- Install **CO detectors**

Lec 6: Cyanide Poisoning

📌 Sources of Cyanide

- **Hydrocyanic acid (prussic acid)**
- Drugs:
  - Sodium nitroprusside
- Fire exposure (🔥 very important exam point)
- Industrial exposure:
  - Electroplating
  - Gold/silver extraction
  - Plastics, fumigants

Natural sources:

- Amygdalin-containing seeds:
  - Apple, peach, apricot, cherry, bitter almond

Endogenous:

- Small amounts from **vitamin B12 metabolism**

Mechanism of Toxicity

Main concept: Histotoxic hypoxia

- Cyanide binds to **cytochrome oxidase (Fe^{3+})** in mitochondria
- Blocks **electron transport chain**

Results:

- Cells **cannot use oxygen**
- Oxygen remains in blood (venous blood stays oxygenated)
- Shift to **anaerobic metabolism**
- ↓ ATP production → **cell death**

Metabolism

- Main pathway:
  - Via **rhodanese enzyme** → thiocyanate → renal excretion
- Also:
  - Binds with vitamin B12 → cyanocobalamin
- Minor excretion:
  - Breath & sweat

⚠ Clinical Features

Target organs:

- CNS
- Cardiovascular system

Early symptoms:

- Headache
- Dizziness
- Weakness
- Nausea & vomiting
- Tachycardia
- Flushing

Severe:

- Rapid collapse
- Seizures
- Cardiac arrest

Management

1.Immediate Actions

- ABC (Airway, Breathing, Circulation)
- Remove from exposure
- Decontamination

2.Antidote Therapy

Cyanide Antidote Kit:

Step 1:

- **Amyl nitrite (inhalation)**

Step 2:

- **Sodium nitrite (IV)**
  👉 Converts Hb (Fe^{2+} → Fe^{3+}) → forms **methemoglobin**

Step 3:

- **Sodium thiosulfate (IV)**
  👉 Converts cyanide → **thiocyanate (non-toxic)**

Mechanism of Antidotes

1. Nitrites:
   - Hb (Fe^{2+}) → MetHb (Fe^{3+})
   - MetHb binds cyanide → pulls it away from cytochrome
2. Thiosulfate:
   - Enhances detox via rhodanese → thiocyanate

Lec7: Substance Abuse

Substance abuse is defined as the use of a substance for its pharmacological effects without medical indication or cultural acceptance.

Problems of Substance Abuse

Repeated substance abuse is associated with:

- Toxic effects under the influence of the substance
- Physical and psychological dependence
- Tolerance
- Withdrawal

Problems Related to Methods of Abuse

- **Injection:** infections, HIV, hepatitis
- **Sniffing:** suffocation risk
- **Snorting:** mucosal irritation, nasal septum perforation
- **Smoking:** lung diseases, cancer

Substance Additives Effects

- Allergic reactions
- Altered drug effects (synergistic or additive effects)

Social and Financial Effects

- Financial loss
- Criminal behavior
- Social deterioration

Categories of Substances of Abuse

- CNS depressants
- Stimulants
- Hallucinogens
- Volatile substances

CNS Depressants

Narcotics (Opioids)

Examples:

- Morphine, codeine, pethidine, buprenorphine, heroin

Effects:

- Pain relief (analgesia)
- Euphoria and relaxation
- Respiratory depression
- Pinpoint pupils
- Constipation
- Physical dependence

Mechanism of Action

- Act on opioid receptors (mu, kappa, delta)
- Regulate pain, mood, respiration, and GI function

Routes of Abuse

- Injection (most common, especially heroin)
- Smoking
- Oral (e.g., methadone)

Management

- Supportive care
- Antidote: **Naloxone**
- Withdrawal treatment: methadone or benzodiazepines
- Psychosocial support

Opioids (Heroin)

Heroin

- Rapid CNS penetration (15–20 seconds)
- Metabolized to morphine and 6-MAM

Clinical Features

- Respiratory depression
- Pinpoint pupils
- Sedation

- Hypotension
- Decreased consciousness

Withdrawal

- Starts 6–12 hours after last dose
- Peaks in 1–3 days
- Symptoms:
  - Yawning, lacrimation
  - Muscle cramps
  - Sweating, chills
  - Irritability, anxiety

Management of Opioid Intoxication

- Airway and breathing support
- IV fluids
- Monitoring
- **Naloxone (opioid antagonist)**

Maintenance Therapy

- Methadone (long-acting opioid agonist)
- Buprenorphine (partial agonist)

Lec 8: Stimulants

📌 Definition

- Stimulants are substances that increase CNS activity:
  - ↑ alertness and vigilance
  - ↑ energy and euphoria
  - ↓ fatigue and sleep

Examples

- **Amphetamines**
  - Methamphetamine (Crystal meth)
  - Methylphenidate (Ritalin)
  - MDMA (Ecstasy)
- **Cocaine**
- **Caffeine**
- **Nicotine**

Clinical Effects (General)

- Euphoria
- Increased alertness & energy
- Insomnia
- Anorexia (weight loss)
- Anxiety, irritability

⚠ Toxic effects:

- Chest pain
- Tachycardia, hypertension
- Headache
- Abdominal pain
- Arrhythmias
- Stroke / MI

Physical Exam Findings

- ↑ Blood pressure & heart rate
- Dilated pupils (mydriasis)
- Hyperthermia
- Arrhythmias
- Seizures
- Stroke
- Rhabdomyolysis → renal failure

Mental Status Effects

- Agitation, anxiety, restlessness
- Euphoric or aggressive mood
- Paranoia
- Hallucinations (visual, auditory, tactile)
- Delirium, confusion
- Impaired judgment

Withdrawal

- Fatigue, sedation
- Depression, irritability
- Drug craving
- Possible suicidal ideation
- Poor concentration & memory

Routes of Abuse

- Oral
- Snorting
- Smoking (crystal meth, crack cocaine)
- Injection

COCAINE

📌 Source

- From coca plant (*Erythroxylum coca*)

Mechanism

- Blocks reuptake of:
  - Dopamine
  - Norepinephrine
  - Serotonin
    - 👉 ↑ CNS stimulation & reward system activation
- Also blocks Na^+ channels → local anesthetic effect

Forms

- **Crack (base)** → smoked
- **Cocaine salt** → snorted or injected

Effects by system

Cardiovascular

- Vasoconstriction
- Hypertension
- Tachycardia
- Chest pain (most common)
- MI, arrhythmias

CNS

- Agitation
- Seizures
- Stroke / intracranial hemorrhage

Respiratory

- Bronchospasm
- Pneumothorax
- Pulmonary complications

GI

- Ischemia
- Ulceration, perforation

Management (Cocaine)

- **Supportive care (ABC)**
- Treat:
  - Agitation
  - Hypertension
  - Arrhythmias
  - Hyperthermia
- No specific antidote

AMPHETAMINES

Mechanism

- ↑ release of dopamine, norepinephrine, serotonin
- Blocks reuptake

  👉 Sympathomimetic toxicity

Effects

- CNS stimulation → euphoria, agitation, seizures
- CVS → tachycardia, hypertension, arrhythmias
- Other → GI upset, sweating, tremor

⚠ Pregnancy risk

- Miscarriage
- Teratogenic effects

METHAMPHETAMINE (Crystal Meth)

📌 Features

- Strong CNS stimulant
- Highly addictive
- Most abused after cannabis

Mechanism

- Releases dopamine, norepinephrine, serotonin
- Blocks reuptake transporters
  👉 Massive synaptic stimulation

Clinical Effects

- Increased energy & alertness
- Insomnia
- Weight loss
- Bruxism (teeth grinding)
- Anxiety, aggression
- Hallucinations
- "Meth mouth" (tooth decay)

Management

- Supportive care only
- Control agitation & hyperthermia
- Treat cardiac complications
- No antidote

Lec 7: Hallucinogens

Hallucinogens are substances that alter perception, mood, and cognition and may cause hallucinations.

Examples

- Cannabis (THC)
- LSD (Lysergic acid diethylamide)
- Psilocybin (mushrooms)
- Mescaline
- Phencyclidine (PCP)

Cannabis

Source

Derived from the dried leaves and flowers of *Cannabis sativa*.

Forms

- Marijuana
- Hashish
- Hash oil / resin

-Absorption

Inhalation (most common):

- Onset: a few minutes
- Duration: 2–3 hours

Ingestion:

- Onset: ~30 minutes
- Duration: 5–8 hours

Pharmacokinetics:

- Plasma half-life: 18 hours – 4 days
- Highly lipid-soluble → stored in fat for up to 30 days

Pathophysiology

- Cannabinoids act on **CB1 and CB2 receptors**
- Δ9-THC is the main psychoactive compound
- Acts mainly on **CB1 receptors in the brain**

Brain areas affected:

- Cerebral cortex (especially frontal lobe)
- Basal ganglia
- Cerebellum
- Hippocampus
- Anterior cingulate cortex
- Minimal effect on brainstem

Effect:

- Increased dopamine release → euphoria and altered perception

Clinical Manifestations

Low dose (~2 mg THC)

- Relaxation
- Euphoria ("high")
- Increased sensory perception

Moderate dose (5–7 mg)

- Disturbed thinking
- Ataxia
- Short-term memory impairment

High dose (>15 mg)

- Paranoia
- Depersonalization
- Disorientation
- Tachycardia
- Sensory disturbances
- ↓ Libido
- No loss of consciousness (NO LOC)

Dependence & Withdrawal

- Physical dependence is controversial
- Heavy chronic use may cause withdrawal within ~1 week

Withdrawal symptoms:

- Irritability, anger, anxiety
- Insomnia, disturbing dreams
- Loss of appetite, weight loss
- Restlessness, depressed mood
- Physical symptoms: sweating, chills, tremors, headache, abdominal pain

Acute Toxicity (rare)

Usually after IV abuse:

- Nausea, vomiting, diarrhea
- Abdominal pain
- Fever
- Hypotension
- Pulmonary edema
- Acute renal failure
- DIC
- Possible death

Investigations

- **Urine test:** cannabinoids detectable up to 21 days in chronic users
- **Blood test:** THC levels help distinguish recent use from residual elimination

Lec 10: Pesticides

General Overview

- Pesticides are chemicals used to kill or control pests to improve agriculture and environmental hygiene.
- Ideally, they should be selective (kill pests only), but most are not fully selective.
- Benefits must always be weighed against risks.
- Major risks include environmental contamination, entry into food chains, water pollution, and bioaccumulation.

Benefits

- Control of vector-borne diseases
- Increased agricultural productivity
- Control of urban pests

Types of Pesticides

- **Insecticides** → kill insects (organophosphates, carbamates, organochlorines, pyrethroids)
- **Rodenticides** → kill rodents (anticoagulants, thallium, etc.)
- **Herbicides** → kill weeds (paraquat, 2,4-D)
- **Fungicides** → kill fungi (dithiocarbamates, captan)
- **Fumigants** → toxic gases for sterilization (methyl bromide, ethylene dibromide)

INSECTICIDES

1.Organophosphates (OPs)

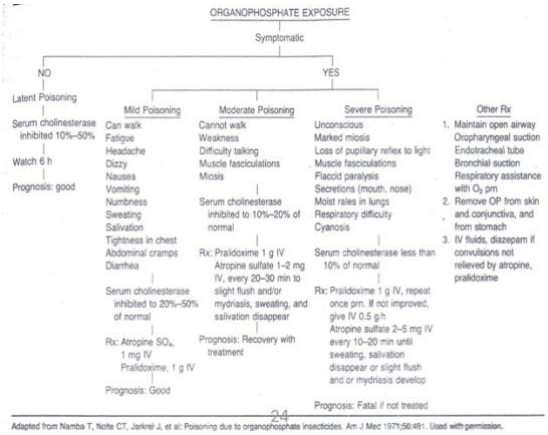
Mechanism of Toxicity

- Inhibit acetylcholinesterase → enzyme phosphorylation
- Causes accumulation of acetylcholine
- Leads to overstimulation then failure of cholinergic synapses
- Inhibition is usually irreversible

Clinical Effects

Muscarinic effects

- Bronchoconstriction, bronchial secretions
- Miosis (pupil constriction)
- Bradycardia
- Increased gland secretions



Adapted from Namba T, Nolte CT, Jarkrel J, et al: Poisoning due to organophosphate insecticides. Am J Med 1971;50:491. Used with permission.

Nicotinic effects

- Muscle fasciculations
- Weakness → paralysis

CNS effects

- Anxiety, restlessness
- Ataxia, headache
- Convulsions → coma
- Respiratory depression

Delayed Neurotoxicity

- Caused by Wallerian degeneration ("dying back" of axons)
- Due to inhibition of neurotoxic esterase
- Mainly affects large myelinated fibers

Clinical Presentation

- Symptoms appear within minutes to hours
- Garlic-like odor may be present
- Pulmonary edema may occur
- Skin irritation
- Neuropsychiatric effects (anxiety, confusion, depression)

Chronic Effects

- Peripheral neuropathy (weakness, cramps, paresthesia)
- Long-term neurobehavioral changes (fatigue, irritability, depression)

Diagnosis

Requires:

- History of exposure
- Typical symptoms
- ↓ Plasma or RBC cholinesterase activity (<50% of normal)

Laboratory

- RBC cholinesterase = most accurate indicator of exposure

Management

1. Stabilization

- Airway protection and ventilation
- Treat respiratory failure and hypoxia
- ICU monitoring

2. Decontamination

- Remove contaminated clothing
- Wash skin with soap and water
- Avoid aspiration risk (many solvents present)

3.Antidotes

Atropine

- Blocks muscarinic and CNS effects
- Does NOT reverse muscle weakness
- Dose: repeated IV doses until atropinization achieved

Pralidoxime (2-PAM)

- Reactivates acetylcholinesterase (if given early)
- Improves muscle weakness and CNS symptoms
- Must be combined with atropine

Important Precautions

Avoid:

- Physostigmine
- Succinylcholine
- Phenothiazines
- Antihistamines
- CNS depressants (opiates)

2.CARBAMATES

Key Differences from OPs

- Reversible enzyme inhibition (shorter duration)
- Less CNS penetration
- Symptoms are usually milder and shorter

Treatment

- Same as OPs
- Atropine is used
- Pralidoxime usually NOT needed

3.ORGANOCHLORINES

Examples

- DDT (banned in many countries)
- Lindane
- Methoxychlor

Toxicokinetics

- Highly lipid-soluble → stored in fat
- Slow metabolism and excretion
- Absorbed via skin, lungs, and GI tract

Toxic Effects

CNS stimulation

- Anxiety, tremor
- Headache, dizziness
- Convulsions → coma

Cardiovascular

- Cardiac arrhythmias

Severe toxicity

- Seizures → hypoxia
- Metabolic acidosis
- Death

Management

Stabilization

- Treat seizures immediately
- Correct hypoxia and acidosis

Anticonvulsant

- **Diazepam (drug of choice)**

Decontamination

- Remove clothes
- Wash skin thoroughly with soap and water
- Prevent dermal absorption

Lec11: Acetaminophen Toxicity

Mechanism

- Normal: glucuronidation + sulfation → non-toxic
- Small amount → **CYP450 → NAPQI (toxic)**
- NAPQI detoxified by **glutathione**

Overdose:

- Pathways saturated → ↑ NAPQI
- ↓ Glutathione (<30%)
- → **Hepatocellular injury & necrosis**

Toxic Dose ("Rule of 150s")

- **>150 mg/kg** (children)
- **>7.5 g** (adults)
- **>150 mcg/mL at 4 hours**

Clinical Phases

Phase I (0–24 h)

- Often asymptomatic ("silent")
- Nausea, vomiting, abdominal pain

Phase II (24–72 h)

- Temporary improvement
- RUQ pain
- ↑ AST/ALT, bilirubin, PT

Phase III (3–4 days) ⚠

- Peak liver injury
- AST/ALT ↑↑ (up to 10,000)
- Liver failure, encephalopathy, acidosis
- Death possible

Phase IV (>4 days)

- Recovery (if survives)

Diagnosis

Acute ingestion:

- Measure level at **4 hours**
- Use **Rumack-Matthew Nomogram**

Treat if:

- ≥150 mcg/mL at 4 hours
- ≥150 mg/kg ingestion
- ≥7.5 g ingestion
- Unreliable history

Unknown time:

- Treat if:
  - Any liver injury (↑ AST/ALT)
  - Detectable APAP + symptoms

Chronic ingestion:

- Nomogram NOT used
- Treat if:
  - AST elevated
  - APAP ≥25 mcg/mL
  - Symptomatic

Treatment — N-acetylcysteine (NAC)

Mechanism:

- Replenishes **glutathione**
- Detoxifies NAPQI
- Antioxidant effect

Timing:

- **Best within 8 hours**
- Prevents liver failure if early
- Still beneficial even late (never too late)

Dosing:

Oral:

- 140 mg/kg loading
- 70 mg/kg every 4 hrs × 17 doses

IV:

- Bolus + infusion
- Preferred in severe cases

Labs

- AST, ALT
- PT/INR
- Electrolytes
- BUN/Cr
- Glucose

Special Points

- Chronic alcohol → ↑ CYP450 → ↑ toxicity risk
- Children tolerate slightly higher doses
- Renal failure may occur in severe cases