# DRUG POISONING &OVERDOSE


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# How to approach to poisoned patient

## (DIAGNOSIS)

01

### Detailed history

-Does the patient know what toxin he ingested?
-Dose the patient know what time is it ingested?

02

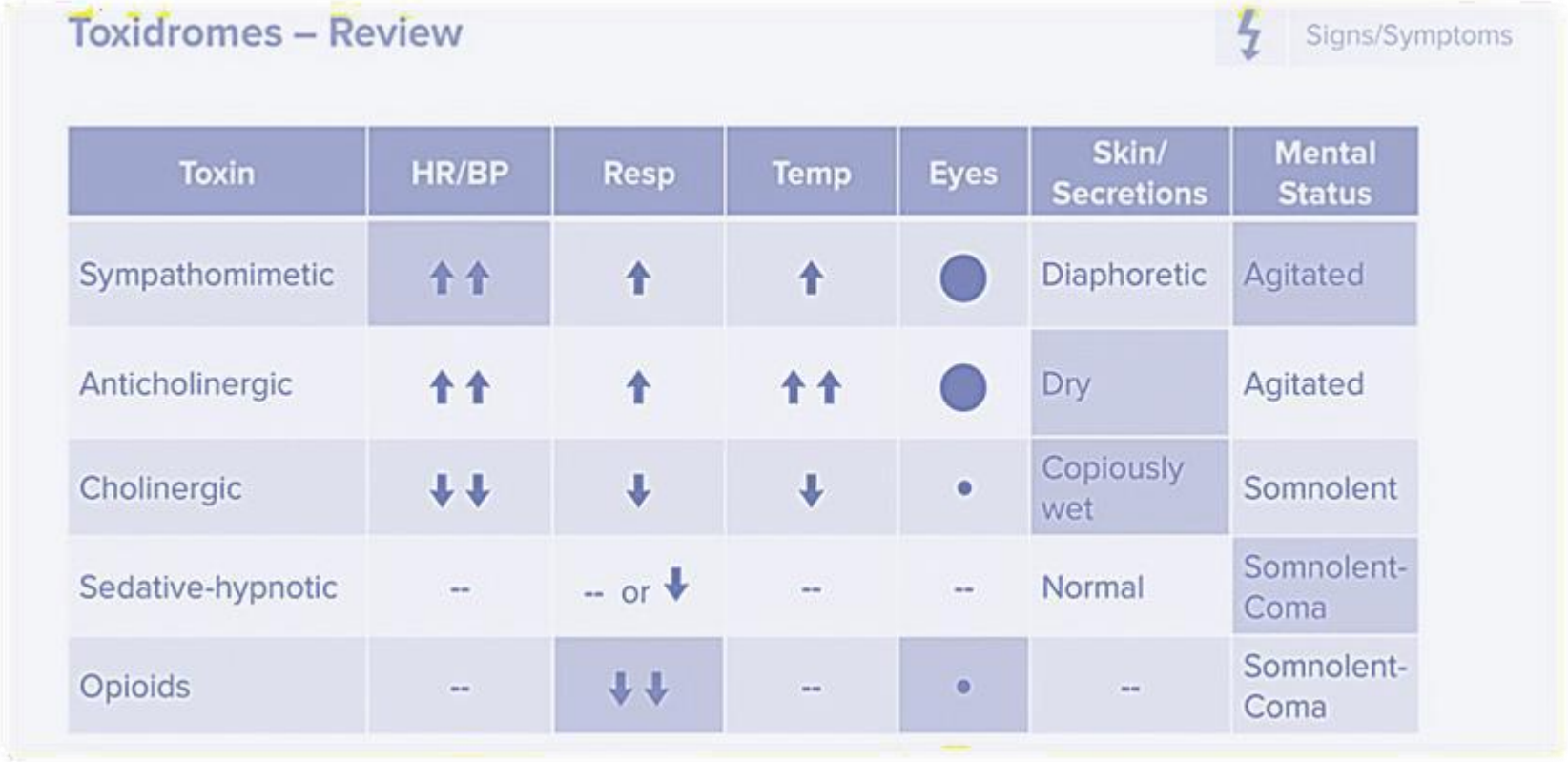
### Physical examination

-check the vital signs
-Glascow coma scale
-check the pupils reactivity

03

### Diagnostic work-up

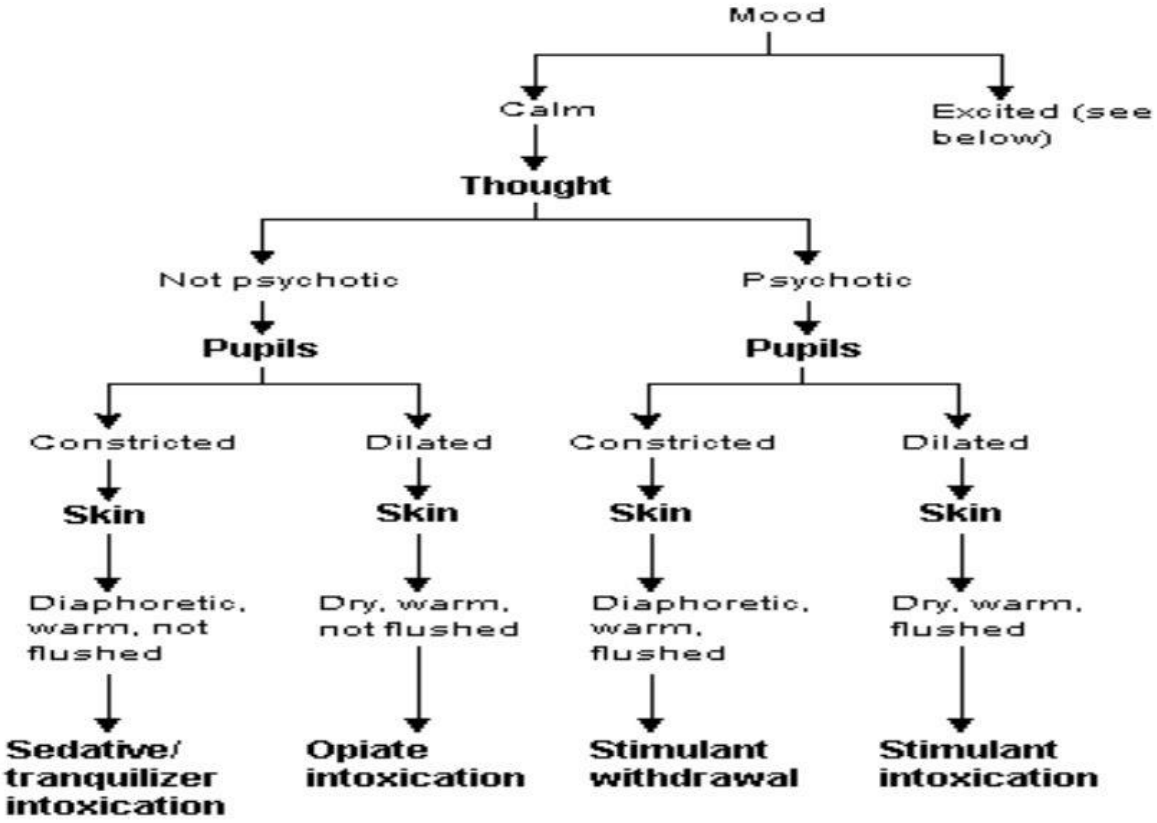
# Vitals with different Toxins

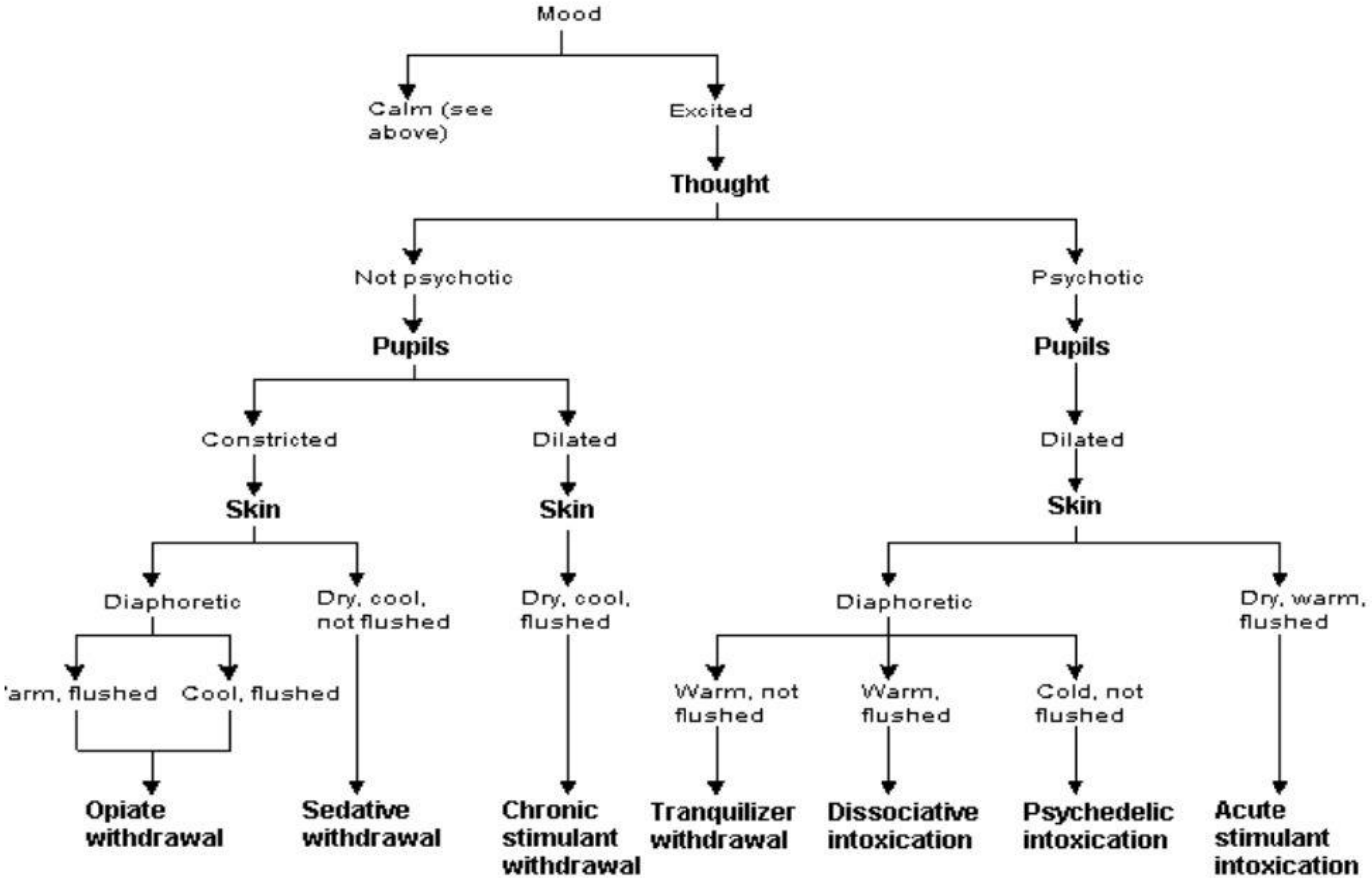


## Toxidromes – Review

Signs/Symptoms

| Toxin | HR/BP | Resp | Temp | Eyes | Skin/ Secretions | Mental Status |
|---|---|---|---|---|---|---|
| Sympathomimetic | ↑↑ | ↑ | ↑ | ● | Diaphoretic | Agitated |
| Anticholinergic | ↑↑ | ↑ | ↑↑ | ● | Dry | Agitated |
| Cholinergic | ↓↓ | ↓ | ↓ | • | Copiously wet | Somnolent |
| Sedative-hypnotic | -- | -- or ↓ | -- | -- | Normal | Somnolent-Coma |
| Opioids | -- | ↓↓ | -- | • | -- | Somnolent-Coma |


Mood
Calm
Excited (see below)
Thought
Not psychotic
Psychotic
Pupils
Pupils
Constricted
Dilated
Constricted
Dilated
Skin
Skin
Skin
Skin
Diaphoretic, warm, not flushed
Dry, warm, not flushed
Diaphoretic, warm, flushed
Dry, warm, flushed
Sedative/ tranquilizer intoxication
Opiate intoxication
Stimulant withdrawal
Stimulant intoxication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Dry, cool, flushed
Diaphoretic
Dry, warm, flushed
'arm, flushed
Cool, flushed
Warm, not flushed
Warm, flushed
Cold, not flushed
Opiate withdrawal
Sedative withdrawal
Chronic stimulant withdrawal
Tranquilizer withdrawal
Dissociative intoxication
Psychedelic intoxication
Acute stimulant intoxication

**Common sympathomymetics: adrenaline & isoproterenol(Used for the treatment of bradycardia,heart block. It is a non-selective beta adrenoceptoragonist**

**Common anticholinergicd: Atropine (Used to treat certain types of nerve agent and pesticide poisoning.**

**Common cholinegrics: organophosphate**

**Common sedative : Benzodiazepines**

**Common opioids: Morphine & Codiene**

# Diagnostic work-up

**-Blood gases**

(O2CT) / (O2Sat) / (PaO2) / (PaCO2) / (PH) / (HCO3)

**-Anion gap**

(Na+ - (HCO3- +Cl-)) “normal 10 ± 2”

**-Specific toxins level**

# How to approach to poisoned patient

## (TREATMENT)

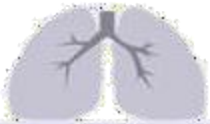
## 01 Check ABCs

Initial Stabilization

Examination

**Airway**

- Patients are often obtunded and may be unable to protect airway
- Consider intubation for GCS < 8, pooling secretions, vomiting, hypoxia



**Breathing**

- Monitor O2 sat and ETCO2
- Supplemental oxygen and respiratory support as needed

**Circulation**

- Cardiac monitor and frequent BP checks, vascular access
- IV fluid/pressor support for shock, manage dysrhythmias

**Disability/Dextrose**

- Perform neurologic primary survey (GCS, pupils, four-extremity movement)
- **Always check glucose**

# How to approach to poisoned patient

## (TREATMENT)

02 Check glucose & give Dextrose if hypoglycemic

03 Decontamination: skin irrigation & Removal of the substance from the system “Dialysis, Gastric lavage or whole bowel irrigation

04 Check glucose & give Dextrose if hypoglycemic

Administer antidote

# Common poisoning and their antidotes

| | | |
|---|---|---|
| Atropine | - | neostigmine/physiostigmine |
| benzodiazepine | - | flumazenil |
| carbonmonoxide | - | 100% o2 |
| cupper | - | penicillamine |
| cynaide | - | sodium thiosulphate |
| heparin | - | protamine sulphate |
| iron | - | disferroxamine |
| isoniazid | - | pyridoxine |
| lead | - | Ca Na2 EDTA |
| mercury | - | dimercapol |
| methanol | - | ethanol |
| mushroom | - | atropine |
| opoid analgesic | - | naloxone |
| oral anticogulant | - | vitamin k |
| organophosphorus | - | atropine/pralidoxime |
| paracetamol | - | N-acetyl cysteine |
| universal antidote | - | activated charcold |

# THE APPROACH TO THE POISONED PATIENT


DIAGNOSIS

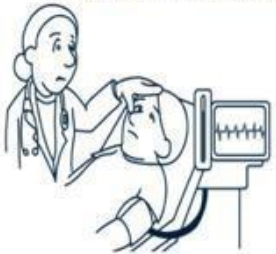
## STEP 1: HISTORY


WHAT WAS THE TOXIN?

WHAT TIME INGESTED?

DIAGNOSIS

## STEP 2: PHYSICAL EXAMINATION



- TEMPERATURE
- HEART RATE
- RESPIRATORY RATE
- BLOOD PRESSURE
- SIZE OF PUPILS
- SKIN
- LEVEL OF CONSCIOUSNESS

DIAGNOSIS

## STEP 3: DIAGNOSTIC TESTS

- BLOOD GAS
- ANION GAP
- SPECIFIC DRUG LEVELS

## STEP 1: ABC STABILIZATION

## STEP 2: BLOOD SUGAR AND OPIOID REVERSAL

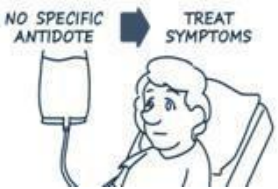


## STEP 3: DECONTAMINATION



## STEP 4: ANTIDOTE


## STEP 5: SUPPORTIVE TREATMENT



# Carbon monoxide poisoning

-In Jordan the most common way is inhalation of CO produced by kerosene heaters

-For hemoglobin, CO has 250 times greater affinity then that for oxygen, it binds to hemoglobin, myoglobin, mitochondrial cytochrome oxidase & decreased oxygen delivery to the tissue

# Diagnosis:

-increased COHB measured by cooximetry of a venous blood gas sample

-CXR: ground-glass appearance

-CT: cerebral edema

# Symptoms

| CO amount in blood (%) | Symptoms |
|---|---|
| <10 | Non |
| 10-20 | Mild headache |
| 20-30 | Headache, drowsiness & tachypnea |
| 30-40 | Blurred vision, impaired judgment, SOB & headache |
| 40-50 | The above Sx become very severe |
| >50 | Coma & eventually death |

# Management

-Prompt removal from the source of CO

-In a patient with suspected or confirmed CO poisoning,initial treatment with high-flow mask,regardless of pulse oximetry or arterial PO2 , until HbCO levels have normalized

Hyperbaric O2 should be used if :

- COHB level >25 percent
- COHB level >15 percent in a pregnant patient
- Loss of consciousness
- Sever metabolicacidosis(pH <7.25)

-Admit the patient if there are any cardiac abnormalities

# Pesticides

# Pesticides

- 2 main types
  - Organophosphate Compounds (OPCs)
  - Carbamates

  - Structurally different but have similar clinical manifestations and generally require the same management.

- Sources
  - Agriculture
  - Chemical warfare and terrorist attacks (sarin)

# Pathophysiology

- Inhibition of Acetylcholinesterase (AChE) → **excess Ach** in synapses → Muscarinic & Nicotinic signs and symptoms

# History and Physical Exam

- History of exposure
- Symptoms of **severe cholinergic activity**
  - Death is by Respiratory Failure *(However, death is rare (0.04-1% of cases))*

- **S** – Salivation
- **L**- Lacrimation
- **U** – Urinary incontinence
- **D** – Diarrhoea + diaphoresis
- **G** – GI upset
- **E** –Emesis

**D** – Diaphoresis & diarrhoea
**U** - Urination
**M** - Miosis
**B** – Bradycardia, bronchospasm
**E** – Excess
**L** – Lacrimation &
**S** - Salivation

# Diagnostics & Treatment

- Serum AChE and RBCs AChE activities can guide management
  - May not be readily available

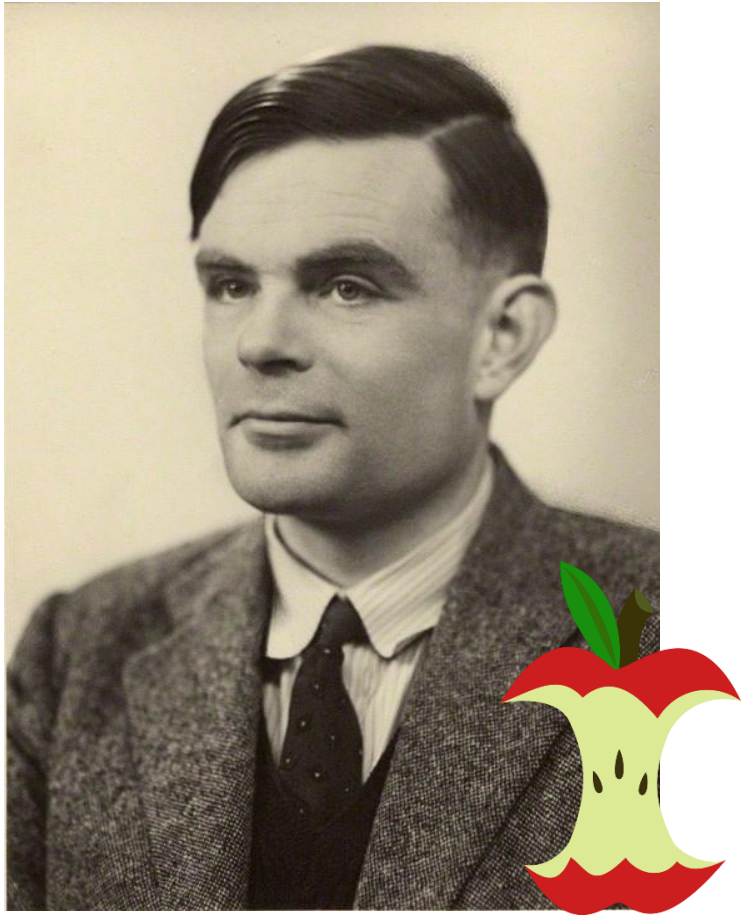
- Treatment
  - ABCs
  - Decontamination
  - **Atropine** → *2-5 mg (can repeat every 5-10min)*
  - Oximes (e.g. pralidoxime (2-PAM)) → *1-2g IV infusion (can repeat every 1h)*

# Cyanide Poisoning

# Cyanide

- Generally **rare**
- Possible sources
  - **Smoke** inhalation
  - Long term consumption of **cyanide-containing drugs/foods**
  - **Suicide**
  - Chemical **warfare**
- Routes of exposure
  - Digestion
  - Inhalation
  - Skin/eye contact

- **Lethal doses**
  - Inhalation → death in 6-8 min
  - Oral ingestion → HCN (50mg), Cyanide salts (100-200 mg)
  - Skin absorption → 100 mg/kg




"BENEDICT CUMBERBATCH IS OUTSTANDING"
★★★★
"A SUPERB THRILLER"
★★★★
"THE BEST BRITISH FILM OF THE YEAR"
★★★★★
"AN INSTANT CLASSIC"
★★★★★
THE TRUE ENIGMA WAS THE MAN WHO CRACKED THE CODE
BENEDICT CUMBERBATCH
KEIRA KNIGHTLEY
THE IMITATION GAME
IN CINEMAS NOVEMBER 14

# Epidemiology & Pathophysiology

- 5000 – 10000deaths per year reported in the US from cyanide inhalation
- Hundreds on suicide cases

- **Principal toxicity:** inactivating cytochrome oxidase → uncoupling mitochondrial oxidative phosphorylation → **inhibiting cellular respiration**

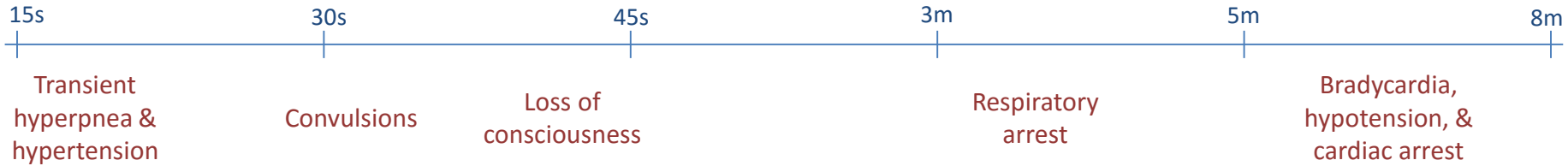
- Aerobic to anaerobic metabolism → increase **lactic acid** concentrations → profound damage to the brain and heart

# History & Physical Exam

- Onset of symptoms
  - Inhalational → few seconds
  - Oral → 15-60 minutes

- If there was smoke, inquire about smoke color and odor
- Presents with
  - Breath smell of **bitter almonds**
  - Neuro → confusion, agitation, headache, seizures, coma
  - GI → nausea and vomiting
  - CVS → chest pain, arrythmias
  - RS → SOB, respiratory failure
  - Postmortem → cherry red livor mortis

- **$O_2$Sat CAN BE NORMAL** (why?)




Timeline of symptoms after **high concentration cyanide inhalational** accident

# Diagnostics & Treatment

- Labs
  - ABGs → high anion-gap metabolic acidosis
  - Increase in lactic acid concentration
  - CO oximetry (why?)

- Decontamination
- **100% oxygen**
  - $O_2$Sat levels do not matter
  - Has proven effects on survivability
  - Can help with concomitant CO poisoning
- Antidote
  - **Hydroxocobalamin**
  - **Sodium nitrate**/Amyl nitrate

  - DO NOT WAIT FOR LABS, give antidote when cyanide poisoning is suspected!

# Ethylene Glycol

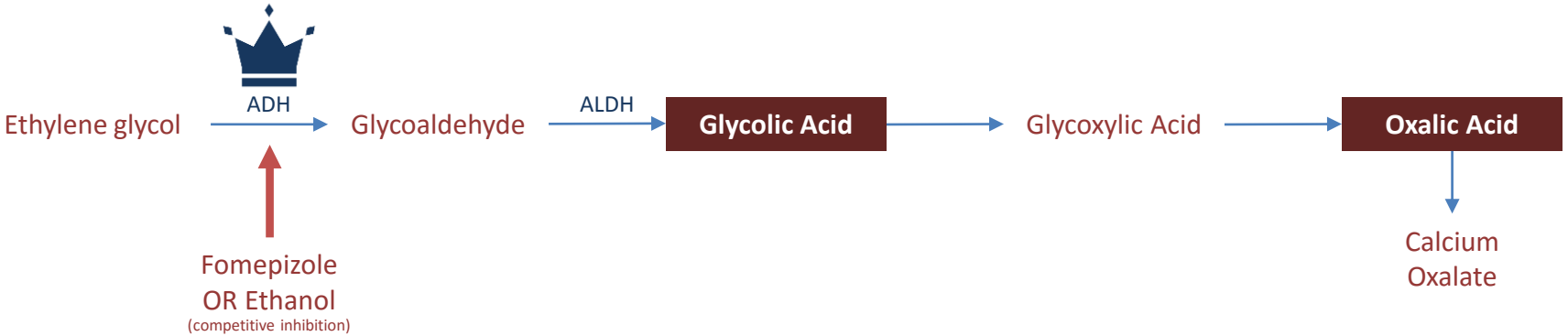
(a.k.a antifreeze)

# Ethylene Glycol

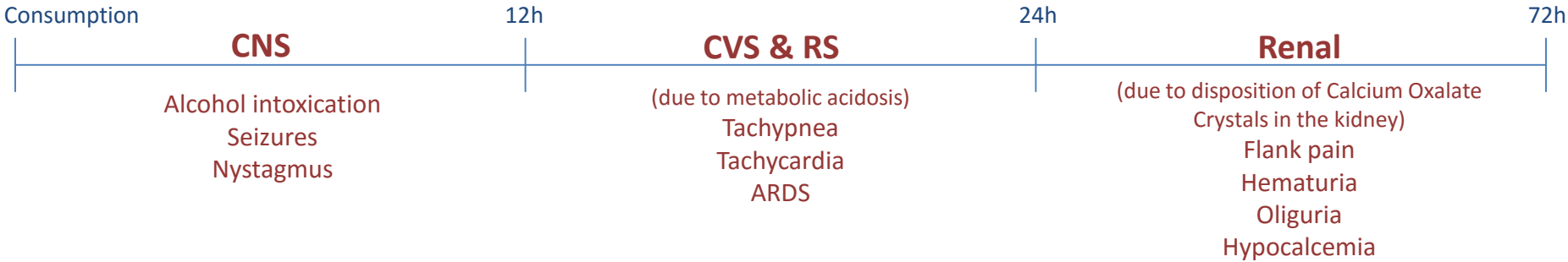
- Sweet tasting alcohol
- Main ingredient in antifreeze

- Commonly seen in
  - Suicide attempts
  - Children
  - Workspace accidents
  - Cats and dogs

# Pathophysiology



# History & Physical Exam



# Diagnostics & Treatment

- Ethylene Glycol toxicity is often a **clinical diagnosis**

- Antidote → **Fomepizole**
- Vitamin replacement
  - Thiamine
  - Pyridoxine

- Hemodialysis

# Iron Toxicity

# Iron

It commonly occurs in children of pregnant women taking pre-natal vitamins because children often
confuse brightly colored iron pills for candy.

When ingested in large amounts, elemental iron is corrosive to the gastrointestinal mucosa, causing abdominal pain, nausea, vomiting, diarrhea, and hematemesis within 30 minutes to 6 hours of ingestion.

- Patients are at risk of gastric scarring and pyloric stenosis within weeks of ingestion.

The mechanism of iron poisoning is free radical production and lipid peroxidation, which impairs various cell processes, leading to systemic manifestations.

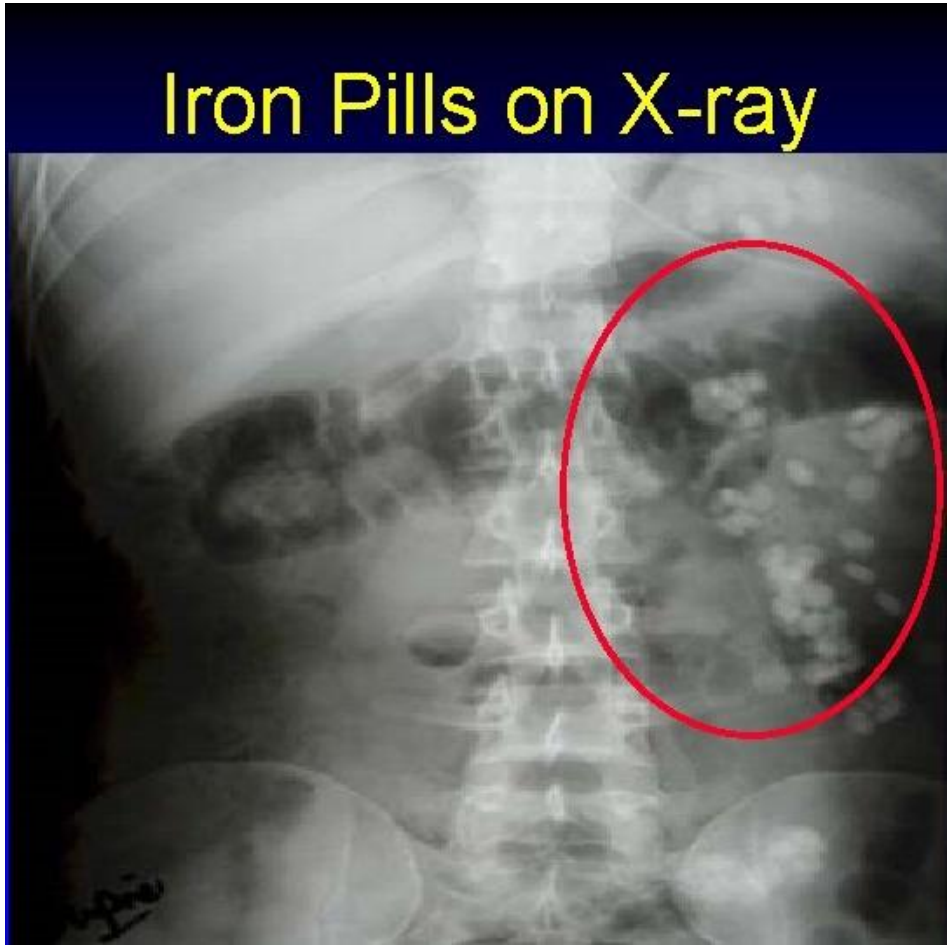
Severely affected patients develop hypotensive shock and anion-gap metabolic acidosis from poor perfusion and accumulation of lactic acid. These patients may become tachypneic and develop respiratory alkalosis to compensate for the acidosis.

Other dangerous complications include liver necrosis, coagulopathy, seizures, and death.

The diagnosis is confirmed by measuring serum iron levels. Iron is radiopaque, and visualization of gastric tablets on abdominal x-ray further supports the diagnosis.

Treatment depends on the severity of the poisoning. Whole-bowel irrigation is sometimes instituted, but other methods of decontamination (activated charcoal, syrup of ipecac, gastric lavage) are not routinely recommended. Chelation therapy with intravenous deferoxamine which binds ferric iron, allowing urinary excretion

# Iron Pills on X-ray



# Lithium Toxicity

# Lithium

- Lithium toxicity is usually the result of  therapeutic overdose.
- Narrow therapeutic index
- Renal excretion .RF for toxicity : renal insufficiency , volume depletion
- **Management : Hemodyalysis**

# Digoxin toxicity

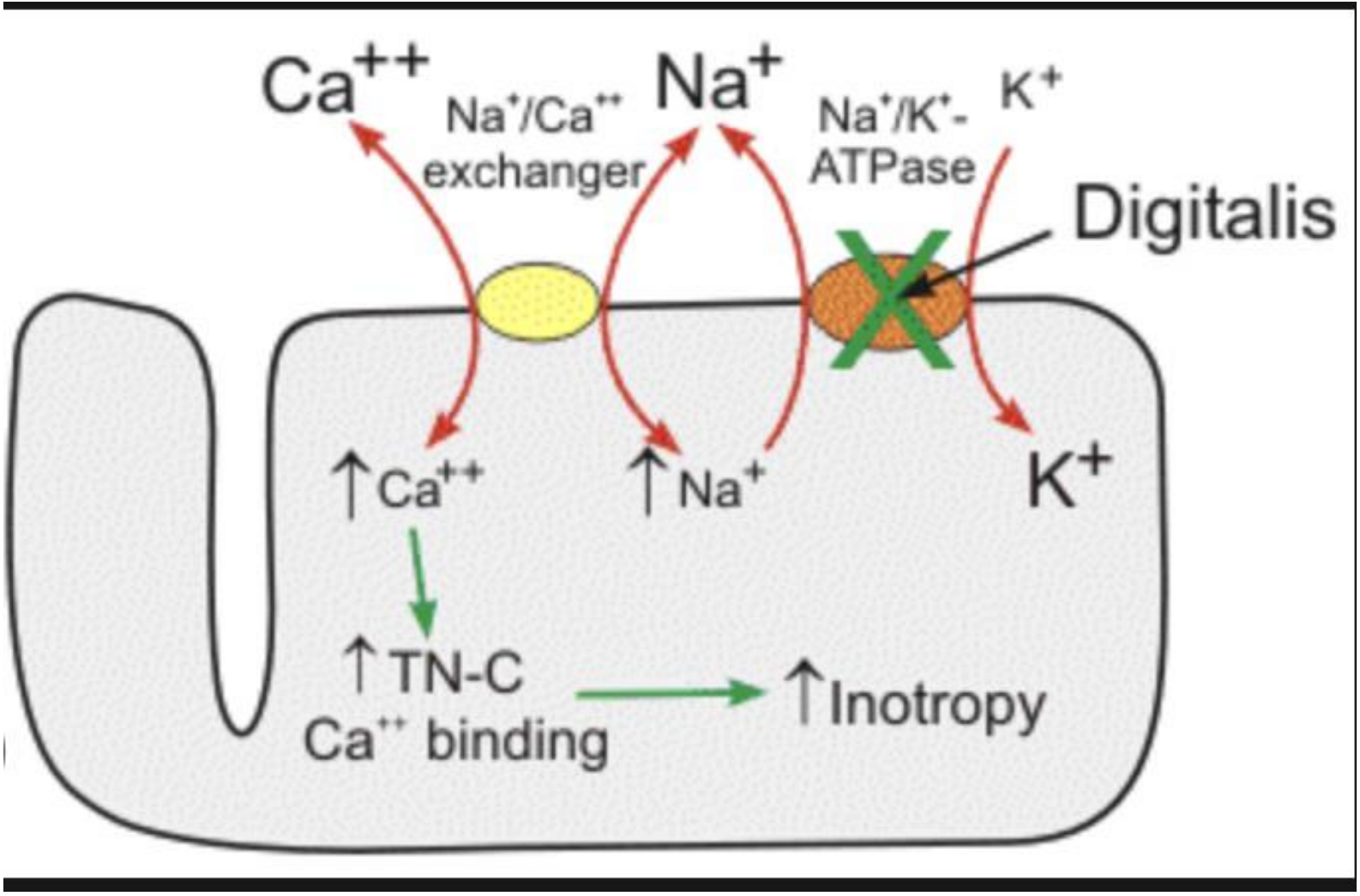
Poisoning with digoxin is usually accidental, arising from the prescription of an excessive dose, impairment of renal function or drug interactions.

**The mechanism of action**

The positive inotropic effect of digitalis has the following components:

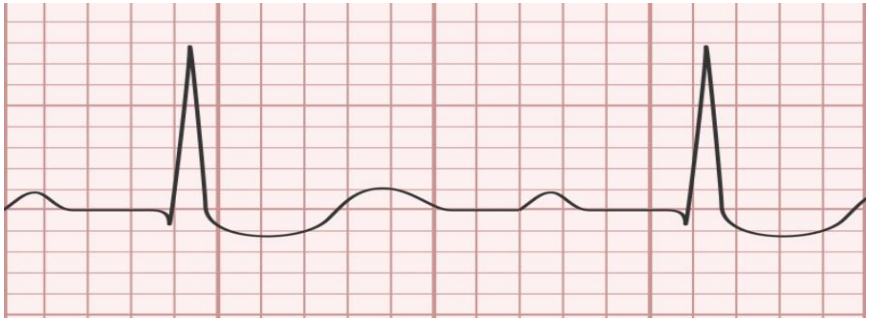
Direct inhibition of membrane-bound Na*/K* -ATPase, which normally pumps 3 Na* outside the cell in exchange with 2 K+ inside the cell is responsible for the maintenance of resting membrane potential (RMP) in most excitable cells.

Digoxin also stimulates the parasympathetic system via the vagus nerve so will lead to a decreasing heart rate.


Ca++
Na+/Ca++
exchanger
Na+
Na+/K+-
ATPase
K+
Digitalis
↑Ca++
↑Na+
K+
↑TN-C
Ca++ binding
↑Inotropy

**Clinical features of toxicity**

tachyarrhythmias (either atrial or ventricular) and bradycardia, with or without atrioventricular block.
Hyperkalemia (due to inhibition of the Na+-K+-ATPase)
GI symptoms (abdominal pain, nausea, vomiting, diarrhea) **IS THE MOST COMMON**
Anorexia, fatigue
Visual changes (diplopia, blindness, photophobia) **YELLOW HALOS AROUND OBJECT**
CNS symptoms (confusion, weakness, hallucinations )
ECG changes indicating conduction and repolarisation delay (prolonged QRS and QT intervals)



**Investigation**

ECG

Premature ventricular beats (most common) and reentry or enhanced automaticity: Vtach or Vib, atrial tachycardia with AV block, Afib or atrial flutter

Depressed conduction (vagal effect): sinoatrial arrest, sinoatrial block, AV block

Digitalis effect: waveform changes that occur in the presence of digoxin but do not necessarily indicate digoxin toxicity

T-wave inversion or flattening

prolonged QRS

Decrease QT interval

Increase PR interval

Laboratory studies

Serum digoxin concentration: Measure 6 hours after ingestion to avoid overtreatment unless the patient is severely symptomatic.

0.7-1.1 ng/mL: therapeutic range

1.1-3 ng/mL: indeterminate range; arrhythmias possible

≥ 2.5 ng/mL: incidence of arrhythmia > 50%

Serum electrolytes

Potassium: hyperkalemia (associated with poor prognosis)

Creatinine and blood urea nitrogen to evaluate renal function

## Management

Correct hypoxia, electrolytes, and acidosis to reduce arrhythmia risk. **Magnesium** can help with ventricular arrhythmias.

Bradycardias may be treated with **atropine** 1.2–2.4 mg IV or temporary pacing.

Use **digoxin-specific antibody fragments** for severe ventricular arrhythmias or unresponsive bradycardias in digoxin.

Dialysis also may be indicated in patients with acute renal failure or refractory hyperkalemia; however, it is not useful as a treatment for digoxin toxicity itself.

# Cocaine

**Mechanism of action**

A strong CNS stimulant. Cocaine hinders the reabsorption of biogenic amines. It causes psychomotor agitation by blocking dopamine reuptake. Inhibiting noradrenaline reuptake leads to tachycardia, and inhibiting serotonin reuptake triggers hallucinations. Cocaine heightens CNS alertness by strengthening the impact of excitatory amino acids. Additionally, cocaine acts as a potent local anesthetic and vasoconstrictor.

Three stages of acute cocaine toxicity have been described and include the following:

**Stage 1**

CNS: Headache, nausea, mydriasis, vertigo, twitching, pseudohallucinations (**Hallucination tactile( bugs crawling on my skin ),** , and preconvulsive movements

•Vascular: Increased BP, ectopic beats

•Pulmonary: Tachypnea

•Skin: Hyperthermia

•Psychiatric: Paranoia, euphoria, confusion, aggression, agitation, emotional lability, restlessness

**Stage 2**

•CNS: Encephalopathy, seizures, increased deep tendon reflexes, incontinence

•Cardiac: Hypertension, arrhythmias, peripheral cyanosis

•Pulmonary: Tachypnea, gasping, apnea, irregular breathing

•Skin: Hyperthermia

**Stage 3**

•CNS, Areflexia, coma, fixed and dilated pupils, loss of vital functions

•Cardiac: Hypotension, ventricular fibrillation, cardiac arrest

•Pulmonary: Apnea, respiratory failure, cyanosis, agonal breathing

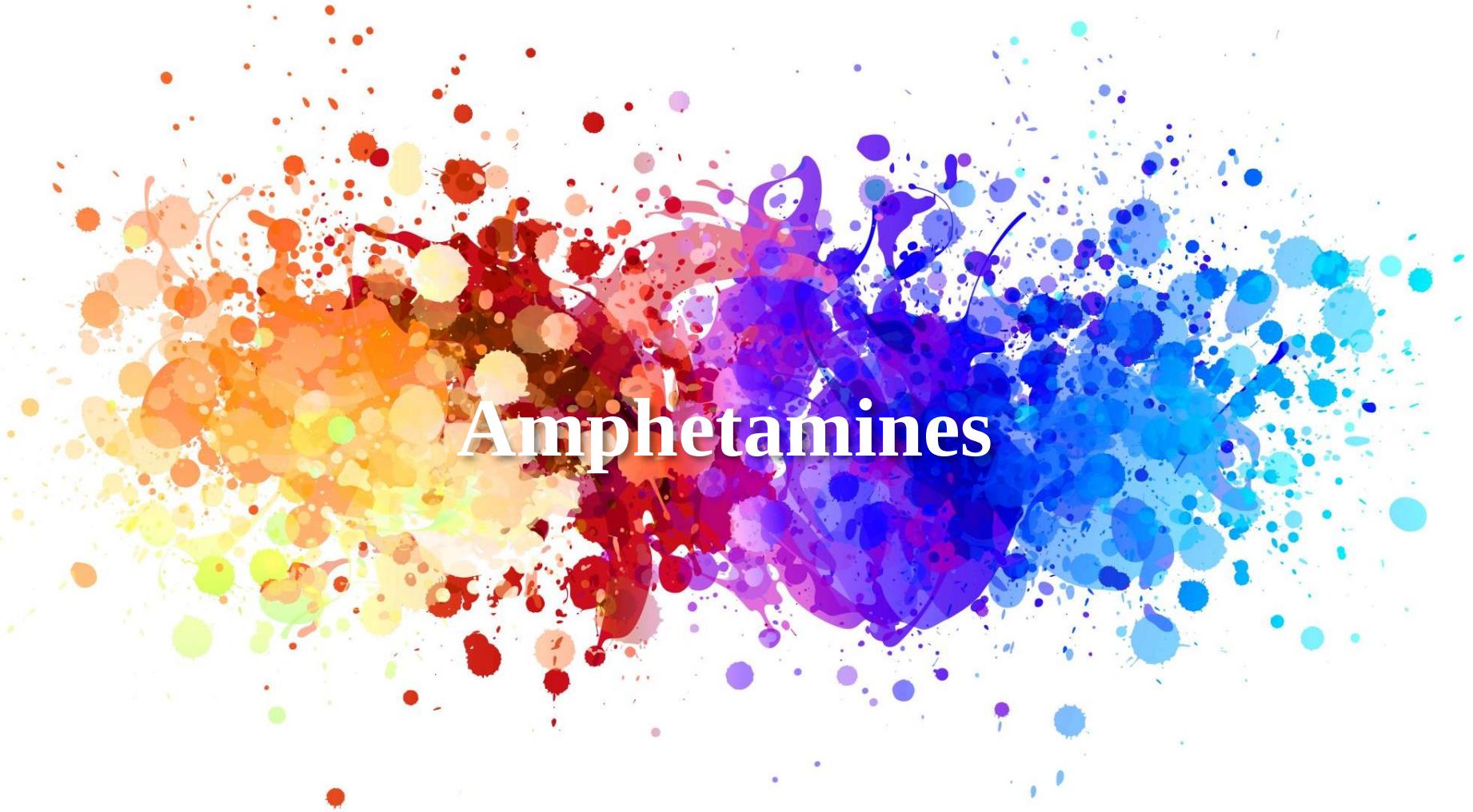
**If a young person presents with a stroke or myocardial infarction, cocaine poisoning, because of its vasoconstrictor effect, is a possible diagnosis**.

## Investigations

Essential tests include complete blood count, comprehensive chemistry panel, troponin, B-type natriuretic peptide, creatine kinase, urinalysis, urine toxicology screen, and electrocardiogram. Imaging may involve chest and abdominal X-rays, along with a head CT for altered mental status.

## Management

For agitation and seizures, administer IV diazepam (10-20 mg).
Actively cool hyperthermia.
Sedation and cooling typically alleviate hypertension and tachycardia.
If hypertension persists, use IV nitrates like glyceryl trinitrate (starting at 1-2 mg/h, max 12 mg/h).
Alternatively, consider **calcium channel blockers** (nifedipine, verapamil, or diltiazem). Beta-blockers' use is debatable.
**Benzodiazepines** early on can ease non-cardiac chest pain from cocaine use.
Administer Aspirin and Nitrates for suspected cardiac chest pain. Treat myocardial ischemia/infarction in a standard manner.
Several patients with accelerated or malignant hypertension have been described in whom the habitual use of cocaine appears to have accelerated the development of renal failure, often requiring dialysis


Amphetamines

**Mechanism of action**

Stimulating the release and inhibiting the reuptake of certain neurotransmitters in the brain, particularly dopamine, norepinephrine (noradrenaline), and to a lesser extent, serotonin.

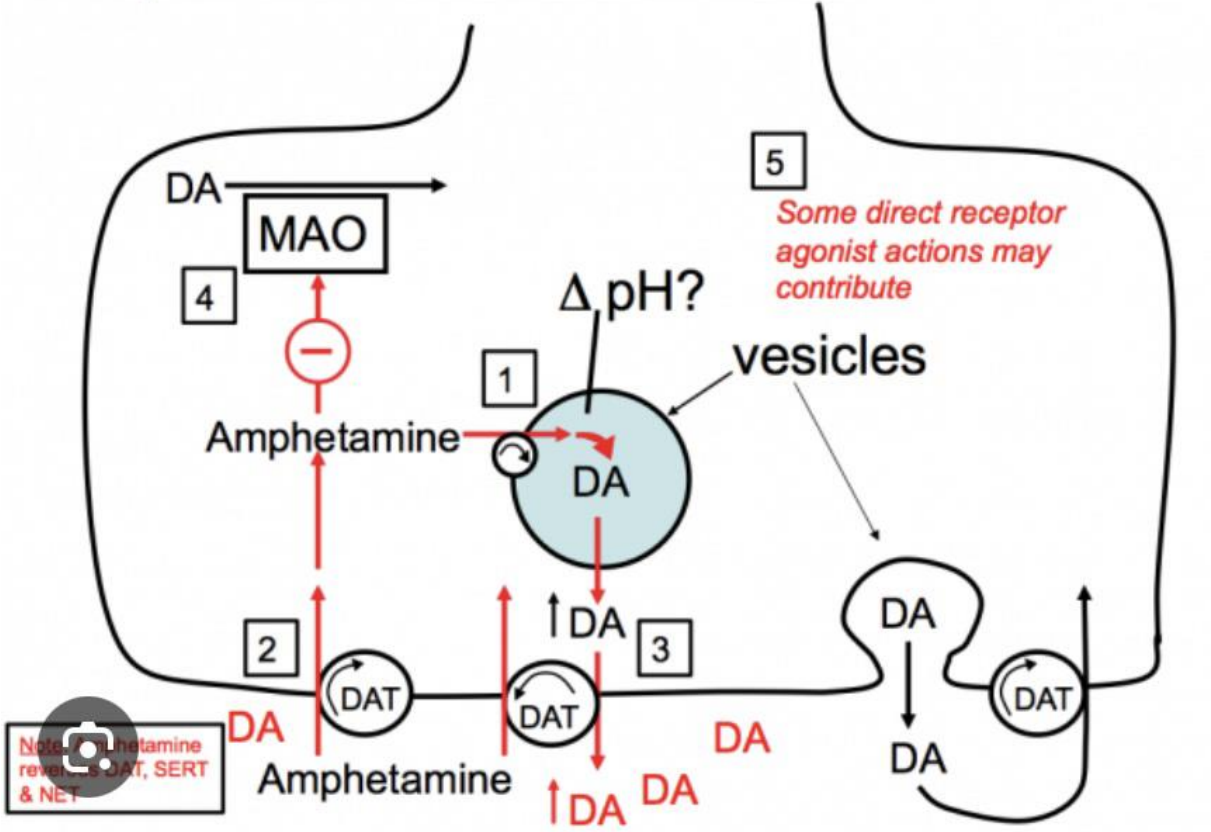
**Release of Neurotransmitters** of dopamine and norepinephrine from presynaptic neurons into the synaptic cleft.
**Inhibition of Reuptake** of dopamine and norepinephrine by blocking the dopamine transporter (DAT) and norepinephrine transporter (NET), respectively.

**Reverse Transport (Efflux) of Neurotransmitters** increases the concentration of these neurotransmitters in the synaptic cleft.

**Release of Vesicular Stores** dopamine and other neurotransmitters stored in vesicles within the presynaptic neuron.

**Stimulation of Postsynaptic Receptors by** The increased concentration of dopamine and norepinephrine in the synaptic cleft

# Amphetamine Mechanism



Tolerance is prevalent among regular users, prompting them to seek increasingly higher doses.

**Clinical Features:**

| ORGAN SYSTEM | SIDE EFFECTS |
|---|---|
| 1.CNS | Euphoria, agitation, headache, paranoia, anorexia, hyperthermia, convulsions, hyperreflexia, intracerebral haemorrhage and coma |
| 2.CVS | Tachycardia, hypertension(pulmonary hypertension), arrythmias, vasospasm, myocardial ischemia and cardiomyopathy |
| 3.SYMPATHETIC EFFECTS | Mydriasis, sweating, tremor, tachypnoea and nausea |
| 4.OTHER EFFECTS | Muscle rigidity, pulmonary oedema, ischemic colitis, rhabdomyolysis and metabolic acidosis |
| 5.COMPLICATIONS | Psychosis, cerebral and myocardial infarction, aortic dissection, ventricular fibrillation and acute renal failure |

**Investigations**

Blood count (CBC), comprehensive metabolic panel, serum creatine kinase levels, and urinalysis. A CXR and ECG may be required if patients complain of chest pain or palpitations. A CT scan for altered mental status or patients with seizures to rule out any intracranial hemorrhages or stroke.

**Management**

Anxiety, agitation, and hyperactivity can usually be controlled with IV benzodiazepines. Diazepam is the drug of choice

Hyperthermia should be tackled aggressively with hypothermic blankets, ice baths, and dantrolene infusions. Large IV doses of benzodiazepines can help.

Tachycardia can be managed with beta-blockers (atenolol). maybe preferable if tachycardia is associated with hypertension.

A short-acting, such as sodium nitroprusside should be considered if hypertension is unresponsive to benzodiazepines.

For ventricular arrhythmias: Lignocaine and amiodarone are generally first-line agents for stable monomorphic ventricular tachycardia.

For rhabdomyolysis: Early aggressive fluid replacement is the mainstay of therapy a. Diuretics such as mannitol or furosemide may be needed to maintain urine output.

• Although peritoneal dialysis and hemodialysis have been demonstrated to enhance the elimination of amphetamines.

# Benzodiazepine toxicity

Benzodiazepines may be prescribed or used illicitly. They are of low toxicity when taken alone in overdose but can enhance CNS depression when taken with other sedative agents, including alcohol. They may also cause significant toxicity in the elderly and those with chronic lung or neuromuscular disease.

**Mechanism of action**

They act by facilitating the binding of the inhibitory neurotransmitter GABA at various GABA receptors throughout the CNS which will cause depression

**Clinical features**

Reduced respiratory rate and ventilation
Hypotension
Confusion, hallucinations, slurred speech
Sedation, coma
Ataxia, reduced muscle tone Hypothermia
Diplopia, strabismus, nystagmus Normal pupil size
Respiratory depression and hypotension may occur with severe poisoning in susceptible groups, especially after intravenous administration of short-acting agents.

**Investigations**

As the approach of the poisoned patient

**Management**

Activated charcoal may be useful after ingestion in susceptible patients or after mixed overdose if given within 1 hour.

Conscious level, respiratory rate, and oxygen saturation should be monitored for at least 6 hours after a substantial overdose.

The specific benzodiazepine antagonist **flumazenil** increases consciousness level in patients with overdose **but** carries a risk of seizures, and is contraindicated in patients co-ingesting proconvulsant agents such as TCAs and in those with a history of seizures.

Hemodialysis, or whole bowel irrigation plays **no** role in managing benzodiazepine toxicity due to their large volume of distribution and lipid solubility

# Salicylates poisoning.

- The principal pathophysiologic effect of toxic doses of salicylates is characterized by :
  1) stimulation of the respiratory center of the brain ➔ hyperpnea and respiratory alkalosis
  2) inhibition of Krebs cycle enzymes ➔ decreases glucose availability and increases organic acid ( metabolic acidosis )
  3) alterations in lipid metabolism and amino acid metabolism ➔ enhancing metabolic acidosis
  4) increased fluid and electrolyte losses ➔ leading to dehydration, sodium depletion, potassium depletion, and loss of buffer capacity
  5) Increases pulmonary capillary permeability ➔ ARDS with pulmonary edema

- toxic manifestations of respiratory alkalosis and metabolic acidosis, altered glucose availability and depletion, fluid and electrolyte losses, and hypermetabolism result in serious morbidity and are potentially fatal. Therapy of salicylate intoxication should be aimed principally at the replacement of fluid electrolytes, correction of acidemia, administration of glucose, and prevention of further salicylate absorption and enhancement of salicylate elimination.

# Clinical symptoms :

Early symptoms: tinnitus, nausea, vomiting, tachypnea hyperpnea

Late symptoms: hyperthermia, agitation, delirium, seizures, noncardiogenic pulmonary edema

| Severity of salicylate poisoning [3] | | |
|---|---|---|
| | Serum salicylate level | Clinical features |
| Mild poisoning | • Adults: 30–60 mg/dL<br>• Children/older adults: 20–45 mg/dL | • Tinnitus<br>• Nausea/vomiting<br>• Lethargy |
| Moderate poisoning | • Adults: 60–80 mg/dL<br>• Children/older adults: 45–70 mg/dL | • Tachypnea<br>• Diaphoresis |
| Severe poisoning | • Adults: > 80 mg/dL<br>• Children/older adults: > 70 mg/dL | • Coma<br>• Seizures<br>• Pulmonary edema<br>• Renal failure<br>• Hypercarbia |

# Diagnostic tests :

ABG: mixed respiratory alkalosis and increased anion gap metabolic acidosis

Serum salicylate level > 40mg/dL

BMP: hypokalemia, increased BUN, and creatinine

Note: Because salicylate levels may be falsely low **within 4 hours of ingestion** and do not necessarily correlate with clinical presentation, a high index of suspicion should be maintained when caring for a patient with symptoms of salicylate poisoning. Rapid treatment is essential.

## Management :

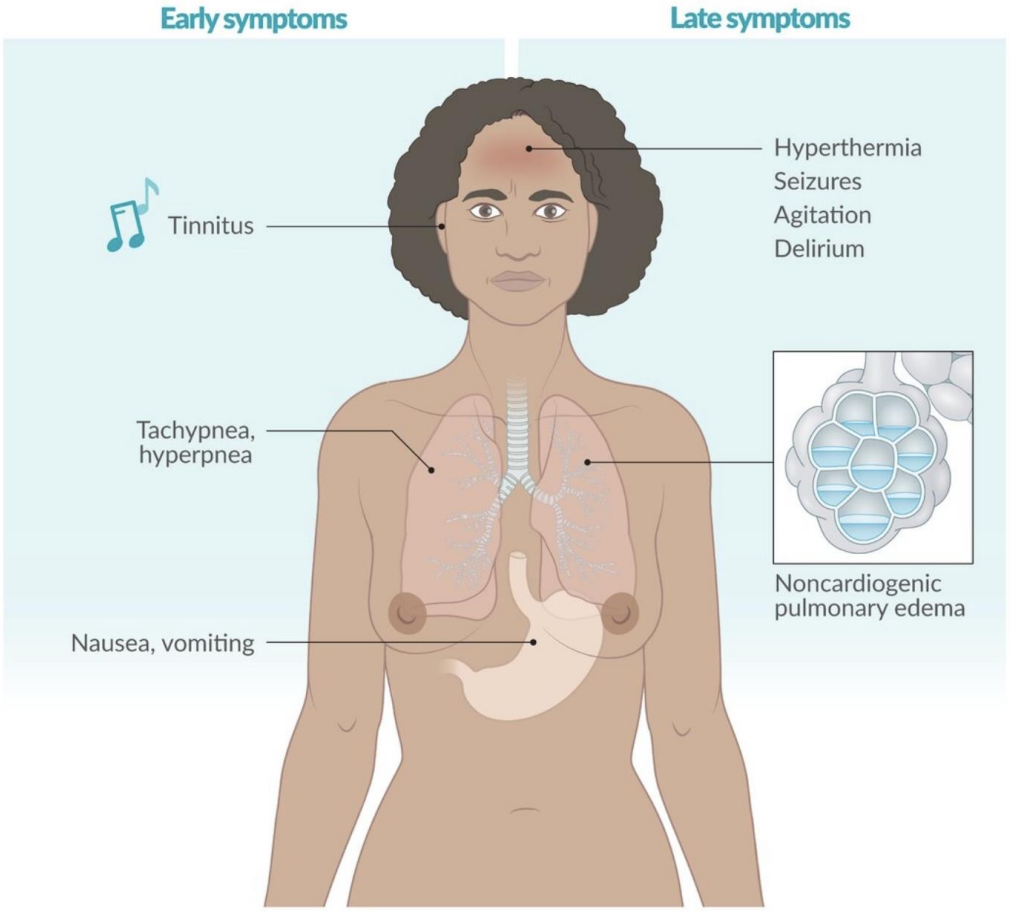
1) Activated charcoal: should be administered if the patient presents within 1 hour. Multiple doses of activated charcoal may enhance salicylate elimination but currently are not routinely recommended.
2) The plasma salicylate concentration should be measured at least 2 (in symptomatic patients) or 4 hours (asymptomatic patients) after overdose and repeated in suspected serious poisoning, since concentrations may continue to rise some hours after overdose.
3) Dehydration should be corrected carefully, as there is a risk of pulmonary edema.
4) Once plasma potassium has been corrected, metabolic acidosis should be identified and treated with intravenous sodium bicarbonate (8.4%).
5) Urinary alkalinization is indicated for adults with salicylate concentrations above 50 mg/dL.
6) **Haemodialysis** should be considered when :

- Serum concentrations above 70mg/dl
- Renal faliure
- Pulmonary oedema
- Convulsions
- Refractory acidosis

## Salicylate poisoning

**Diagnostics**
- ABG: mixed respiratory alkalosis and increased anion gap metabolic acidosis
- Serum salicylate level: > 40 mg/dL
  BMP: hypokalemia, ↑ BUN, ↑ creatinine
- Serial serum salicylate level (every 2 hours) until downtrending
- Salicylate level may be falsely low within 4 hours of ingestion

**Treatment**
- Stabilization of vital signs
- Gastric decontamination: consider indications for oral activated charcoal or gastric lavage
- Fluid and acid-base management: fluid resuscitation, alkalinization with IV sodium bicarbonate
- Hemodialysis in severe cases



# Acetaminophen toxicity

90% of acetaminophen is metabolized in the liver.
Toxicity results from the formation of an intermediate reactive metabolite that binds covalently to cellular proteins, causing cell death. This results in hepatic and occasionally renal failure.
Hepatotoxicity due to acetaminophen overdose (drug-induced hepatitis)
The minimum toxic dose in adults is 7.5g/day
**Pathophysiology**:

1)Exhaustion of hepatic metabolic pathways causes increased formation of a toxic metabolite of Acetaminophen, N-acetyl-p-benzoquinoneimine (NAPQI).

2) Glutathione initially inactivates NAPQI, but its reserves are eventually depleted, leading to NAPQI build-up.

3) NAPQI → irreversible oxidative hepatocyte injury → liver cell necrosis.

## Clinical features :

The clinical course of acetaminophen toxicity is divided into four stages :

1) During the first stage (30 min to 24 hours), the patient may be asymptomatic or may have emesis.
2) In the second stage (24 hours to 72 hours), there may be emesis plus right upper quadrant pain and hypotension.
3) In the third stage (72 hours to 96 hours), liver dysfunction is significant with renal failure, coagulopathies, metabolic acidosis, and encephalopathy. Gastrointestinal (GI) symptoms reappear, and death is most common at this stage.
4) The fourth stage (4 days to 3 weeks) is marked by recovery.

- **managment**

## 1) Activated charcoal :

used in patients presenting within 1 hour.

## 2) N-acetylcysteine :

Antidotes for paracetamol act by replenishing hepatic glutathione

should be administered to all patients with paracetamol concentrations above the ‘treatment line’

highly efficacious if administered within 8 hours of the overdose. However, since efficacy declines thereafter, administration should not be delayed in patients presenting after 8 hours to await a paracetamol blood concentration result.

most important adverse effect of acetylcysteine is related to dose-related histamine release, the ‘anaphylactoid’ reaction, which causes itching and urticaria, and in occasional severe cases, bronchospasm and hypotension.

managed by temporary discontinuation of acetylcysteine and administration of an antihistamine.

alternative antidote is methionine 2.5 g orally (adult dose)

dialysis: high dialyzability of both acetaminophen and acetylcysteine. Hemodialysis appears to be a beneficial therapeutic option in cases of massive acetaminophen ingestion with coma and lactic acidosis. infusion rate of acetylcysteine must be more than double during hemodialysis to compensate for its ongoing removal and provide similar plasma concentrations to the usual acetylcysteine regimen.

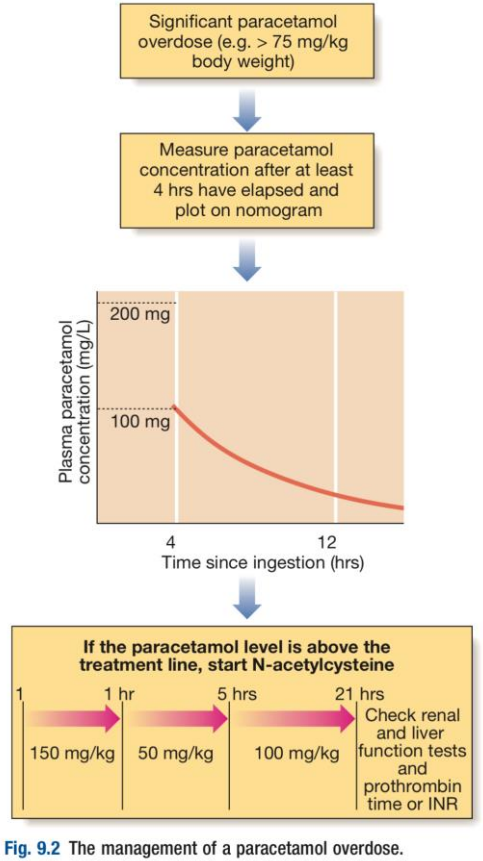



Fig. 9.2 The management of a paracetamol overdose.

# Opioid

Opioid overdose is the most common cause of drug overdose death.

Risk factors for opioid overdose :

**Opioid specific factor :**

- High dose
- High potency ( fentanyl )
- Long half life ( methadone )

**Patients with risk factors for opioid-related harm :**

- Concurrent use of sedative-hypnotics
- Mental health conditions ( depression, SUD )
- Prescriptions from multiple providers
- Release from incarceration in the last few weeks
- Recent cessation of medications for opioid use disorder

# Clinical features :

The classic triad consists of opioid toxicity :

1. Altered mental status (e.g., CNS depression, euphoria)
2. Bilateral miosis (pinpoint pupils)
3. Opioid-induced respiratory depression

Note: the absence of miosis does not rule out opioid intoxication.

opioid-induced respiratory depression (OIRD), the most common cause of death from opioid overdose :

1. decrease respiratory rate and apnea
2. Decrease tidal volume
3. Disordered control of breathing
4. Signs of respiratory distress
5. Signs of hypercapnic respiratory failure
6. Can progress to respiratory arrest

Other clinical features :

1) Respiratory:
   noncardiogenic pulmonary edema
2) Neurological:
   Myoclonic jerks, seizures
   Diminished or absent gag reflex
3) Gastrointestinal:
   Constipation and decreased bowel sounds
   Nausea, vomiting
4) Cardiovascular:
   Bradycardia
   Hypotension
5) Other:
   hypothermia
   Pruritus, flushing

# Diagnosis :

•Opioid overdose is a clinical diagnosis based on suggestive clinical features (e.g., opioid toxidrome) and a compatible history of substance exposure.

•Begin empiric management of opioid overdose as soon as it is clinically suspected; do not wait for confirmatory diagnostic tests.

# Acute management

1) ABCDE
2) Start SpO2 monitoring and establish IV access
3) Initiate oxygen therapy and airway management as needed.
4) Administer naloxone for opioid overdose in patients with opioid-induced respiratory depression.
5) Consider diagnostic tests to support the diagnosis, identify complications, and evaluate for comorbidities.
6) Determine if the overdose was intentional, e.g., a suicide attempt.
7) Assess for comorbid conditions.

# Naloxone for opioid overdose

- **Goal**: restore respiratory drive while avoiding precipitated withdrawal
- **Indication**: opioid-induced respiratory depression (OIRD)
  - There is no validated definition for the severity of opioid-induced respiratory depression.
  - Use clinical judgment in patients with stupor and a spontaneous respiratory rate≤ 12 breaths/minute.

- **Pharmacology**
  - Mechanism of action: competitive μ-opioid receptor antagonist neutralizing opioid agonist effects
  - Onset (IV): < 2 minutes
  - Duration: 20–90 minutes (shorter than most opioids)

•**Dosage**:

There is no consensus on the optimal regimen for in-hospital settings; follow local protocols when available.

- Choose the lowest possible starting dose to avoid precipitated withdrawal then titrate as needed to reverse OIRD.

- Consider empiric dosage adjustment for:

  - The type and amount of opioids taken
  - Presence of opioid dependence
  - Patient weight
  - The risk of respiratory arrest

- There is no direct correlation between OIRD severity and the naloxone dose required to reverse it.

# Antidepressant:

Tricyclic antidepressants (TCAs) are used frequently in overdose and carry a high morbidity and mortality relating to their:

1) sodium channel-blocking.
2) anticholinergic.
3) α-adrenoceptor-blocking effects.

Clinical symptoms:

The three Cs of tricyclic poisoning :

1) Convulsion
2) Coma
3) Cardiac conduction abnormalities ( prolonged QT interval )

## Diagnostics:

Tricyclic antidepressant (TCA) overdose is a clinical diagnosis, but studies may be performed to support the diagnosis and determine severity.

ECG findings of TCA poisoning

Toxicology studies ( serum TCA level )

BMP

VBG

## Management:

•Perform an ABCDE approach in poisoning and initiate resuscitation.

•Manage agitation and toxic seizures with benzodiazepines.

•Provide supportive care for poisoned patients, e.g., fluid resuscitation, treatment of hypoglycemia, and electrolyte repletion.

GI decontamination:

Activated charcoal is recommended for the majority of recent ingestions in patients who are alert and/or have a protected airway.

Gastric lavage may be appropriate for recent TCA or MAOI poisoning because of the associated increased morbidity.

Hemodialysis and hemofiltration would both expect to correct acidosis much quicker than bicarbonate infusion and could therefore contribute to clinical improvement despite a lack of meaningful TCA removal