

Al-Mustaqbal University
College of Pharmacy
5th stage
Clinical Toxicology
Lecture: 6



Abused Substances Toxicity (opioids)

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Opioids Toxicity

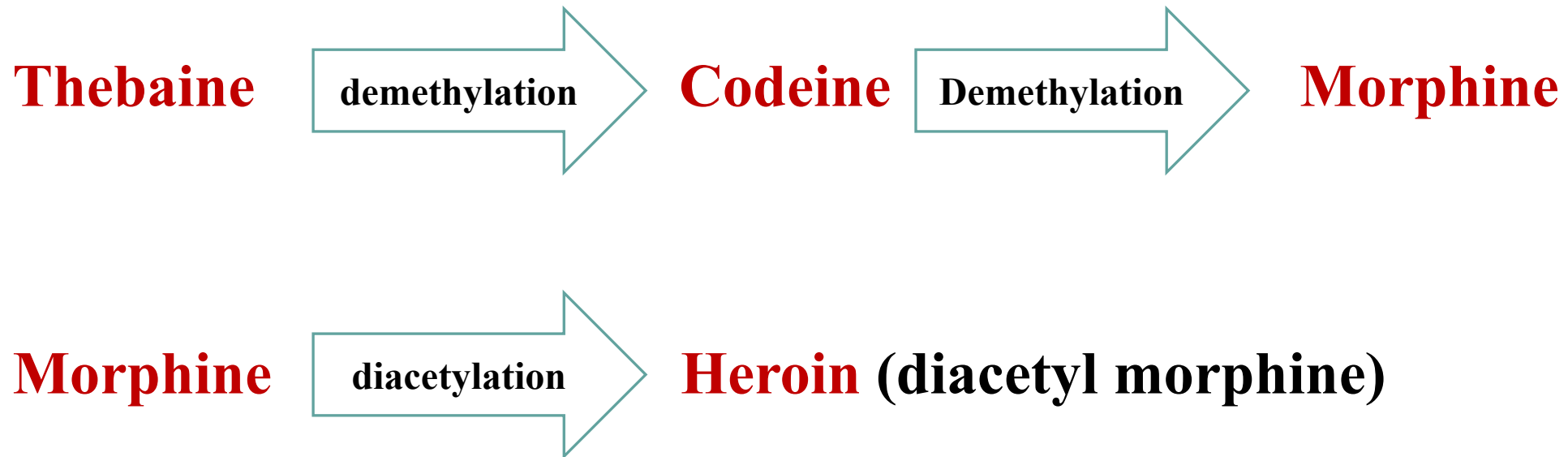
Opium (Opiates):

- ✓ Is the air **dried milky exudates** obtained by incising the **unripe** capsules of ***Papaver somniferum***.
- ✓ More than **30** different alkaloids have been obtained from opium and its extracts.
- ✓ The most important of these are **thebaine, codeine and morphine**.



Opioids Toxicity

Opium (Opiates):



Opioids Toxicity

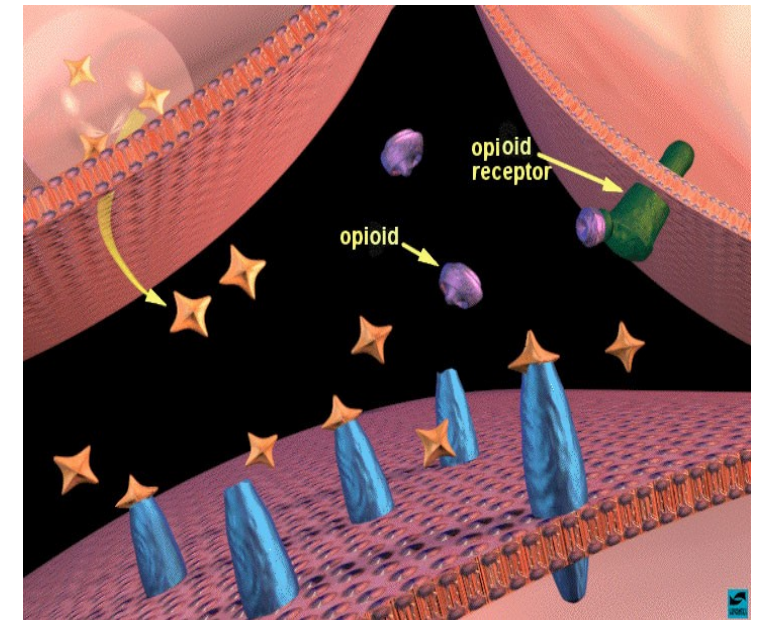
Opioids :

- ✓ Refer to **synthetic** morphine like compounds.
- ✓ Many of opioids offer the same **narcotic and pain** relieving properties as morphine but **not** as habit – forming.
- ✓ Other posses the **cough relieving activity** of codeine but are **not addictive**.
- ✓ Opioids include **oxycodone, hydrocodone, and fentanyl**.



Pathophysiology of Opioids Toxicity

- ✓ **Activation** of opioid receptors results in **inhibition** of synaptic neurotransmission in the central nervous system (**CNS**) and peripheral nervous system (**PNS**).
- ✓ The **physiological** effects of opioids are mediated principally through (**mu**) and (**kappa**) receptors in the CNS and periphery.



Pathophysiology of Opioids Toxicity

(Mu) receptor effects include:

✓ **Analgesia, Euphoria, Respiratory Depression, and Miosis.**

(Kappa) receptor effects include:

✓ **Analgesia, Miosis, Respiratory Depression, and Sedation.**

Pathophysiology of Opioids Toxicity

- ✓ **Two** other opioids receptors that mediate the effects of certain opiates include (**sigma**) and (**delta**) sites.
- ✓ **Sigma** receptors mediate **dysphoria, hallucinations, and psychosis.**
- ✓ **Delta** receptor agonism results in **euphoria, analgesia, and seizures.**
- ✓ The opioid antagonists (eg, **naloxone, nalmefene, naltrexone**) antagonize the effects at all **4 opioid receptors.**

Pathophysiology of Opioids Toxicity

- ✓ Common classifications divide the opioids into:
 1. **Agonist** agents
 2. **Partial agonist** agents
 3. **Agonist-antagonist** agents
- ✓ Also, opioids can be classified as **natural**, **semisynthetic**, or **synthetic**.
- ✓ Opioids **decrease** the sensitivity to pain, rather than **eliminate** or reduce the painful stimulus.
- ✓ Additionally, it can induce **slight euphoria**.

Pathophysiology of Opioids Toxicity

- ✓ The **GI tract** and the **respiratory mucosa** provide easy **absorption** for most opioids.
- ✓ **Peak** effects generally are reached in
- ✓ **10** minutes with the **intravenous** route,
- ✓ **15** minutes after **nasal inhalation**,
- ✓ **30** minutes with the **intramuscular** route,
- ✓ **90** minutes with the **oral route**, and **2-4** hours after **dermal** application.

Pathophysiology of Opioids Toxicity

- ✓ Following **therapeutic** doses, most absorption occurs in the **small intestine**.
- ✓ **Toxic doses** may have **delayed absorption** because of delayed gastric **emptying** and slowed gut **motility**.
- ✓ Most opioids are metabolized by **hepatic conjugation** to **inactive** compounds that are excreted readily in the **urine**.
- ✓ Certain opioids are more **lipid soluble** and can be stored in the **fatty tissues** of the body.

Pathophysiology of Opioids Toxicity

- ✓ **Methadone**, a **long-acting** narcotic often used to attenuate **withdrawal** symptoms and used in narcotics recovery programs,
- ✓ Also it has extensive potential for **abuse**.
- ✓ It can be ingested **orally** or pills can be **crushed** and used **intravenously** or **intranasally**.



Signs & Symptoms of Opioids Toxicity

- ✓ Opioid toxicity **characteristically** presents with a **depressed** level of **consciousness**.
- ✓ Opiate toxicity should be **suspected** when **CNS** depression, **respiratory** depression, and **pupillary** miosis are present.
- ✓ It is important for the clinician to be aware that opioid exposure does **not always** result in miosis (pupillary constriction) and that **respiratory depression** is the most **specific** sign.
- ✓ **Drowsiness** and **euphoria** are seen frequently.

Signs & Symptoms of Opioids Toxicity

- ✓ **Needle tracks** are observed occasionally, depending on the **route of abuse**.
- ✓ **Street users** commonly use **heroin** and **morphine** by **subcutaneous** and **intravenous** injection.
- ✓ **Raw opium** usually is eaten or smoked, and sometimes the powder is **sniffed**.



Signs & Symptoms of Opioids Toxicity

- ✓ Other important presenting signs are **ventricular arrhythmias, acute mental status changes, and seizures.**
- ✓ Reliance on pupillary miosis to diagnose opioid intoxication can be **misleading.**
- ✓ If sufficiently severe, hypertension and pupillary dilation may present because of **CNS hypoxia.**
- ✓ **Morphine, meperidine, pentazocine, diphenoxylate, and propoxyphene** sometimes are associated with **mydriasis or midpoint pupils.**
- ✓ Both **bradypnea** and **hypopnea** are observed, rates as slow as **4-6** often are observed with **moderate-to-severe** intoxication.

Signs & Symptoms of Opioids Toxicity

- ✓ Mild peripheral **vasodilation** may occur and result in **orthostatic** hypotension.
- ✓ Opioids **prolong** GI transit times, possibly causing **delayed** and **prolonged** absorption.
- ✓ Initial tendencies for nausea and emesis are **transient**.
- ✓ **Pink** frothy sputum, muscular rigidity, dyspnea, hypoxia and bronchospasm strongly suggest **acute lung injury**.

Signs & Symptoms of Opioids Toxicity

- ✓ Nightmares, anxiety, agitation, euphoria, dysphoria, depression, paranoia, and hallucinations are encountered **infrequently**, mainly with **high doses**.
- ✓ Pruritus, flushed skin, and urticaria may arise because of **histamine release**.
- ✓ **Generalized seizures** are infrequent; they occur most commonly in infants and **children** because of initial CNS **excitation**.
- ✓ In contrast, seizure activity in **adults** is suggestive of **meperidine** or **propoxyphene** ingestions.
- ✓ **Hearing** loss has been associated with **heroin** and alcohol but is generally considered **recoverable**.

Management of Opioids Toxicity

- ✓ **Death** following opioid overdose is **preventable** if the person receives **basic life support** and the timely administration of the drug **naloxone**.
- ✓ Naloxone is an **antidote** to opioids that will **reverse** the effects of an opioid overdose if administered in time.
- ✓ Naloxone has virtually **no effect** in people who have **not taken opioids**.

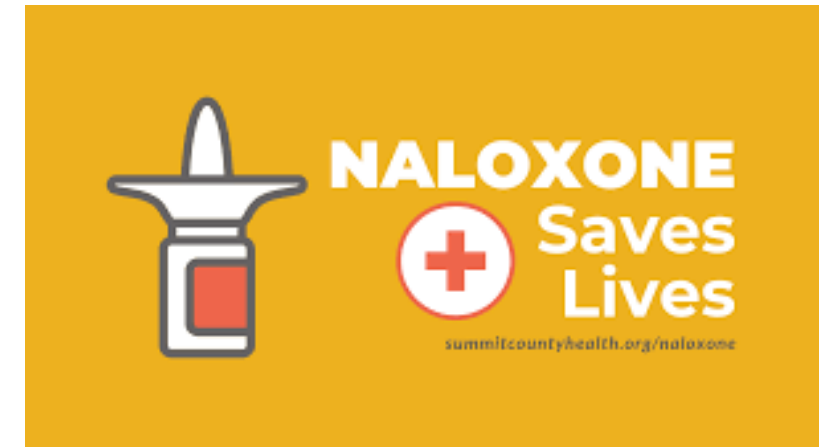


Management of Opioids Toxicity

- ✓ In **many countries** there is still **limited availability** of naloxone even in medical settings, including in **ambulances**.
- ✓ On the other hand, **some countries** have already made naloxone **available in pharmacies** without prescription.
- ✓ **Several countries** (Australia, Canada, Italy, the United Kingdom of Great Britain and Northern Ireland and Ukraine) have introduced **naloxone as over-the-counter medication** and have also started **proactive dissemination** in communities.

Management of Opioids Toxicity

- ✓ **Naloxone** is a **competitive antagonist** of opioid receptors and lacks **any agonist** activity.
- ✓ Adverse effects are **rare** at therapeutic doses.
- ✓ Naloxone can be given **IV, IM or intranasal.**



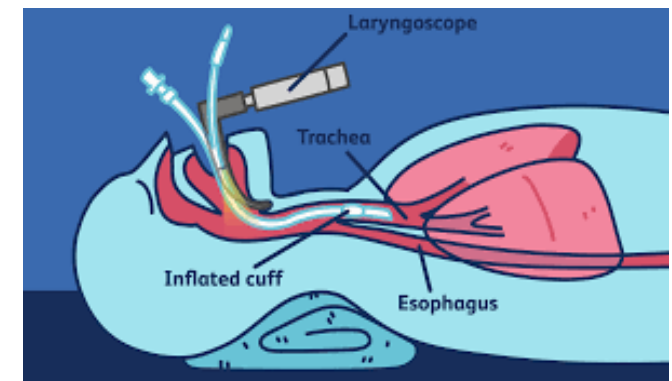
Management of Opioids Toxicity

- ✓ **Nalmefene** and **naltrexone** are other opioid antagonists that have **longer** half-lives than naloxone.
- ✓ The **routine use** of a long-acting antagonist in the patient who is unconscious for **unknown** reasons is **not recommended**.
- ✓ In addition, the fear of **precipitating** prolonged opioid **withdrawal** likely prevents the widespread use of these antagonists for **emergency** reversal of **opiate** intoxication.



Management of Opioids Toxicity

- ✓ In patients **lacking** spontaneous respirations, **intubation** is preferred, and **intravenous naloxone** may be given to reduce respiratory depression.
- ✓ **Airway** control and **adequate oxygenation**.
- ✓ As with **all unknown unconscious patients**, determination of serum **glucose level** is required.



Management of Opioids Toxicity

- ✓ Activated **charcoal** is the GI decontamination **method of choice** for patients with opiate intoxication following ingestion.
- ✓ Because of impairment of gastric emptying and GI motility produced by opiate intoxication, activated charcoal still may be effective when patients present **late following ingestion**.
- ✓ Decontamination with activated charcoal should be attempted in **all symptomatic patients** (as long as it is not contraindicated), regardless of the time of ingestion in relation to hospital presentation.
- ✓ **Airway** has to be protected **prior** to administration of charcoal in order to prevent charcoal lung **aspiration**.