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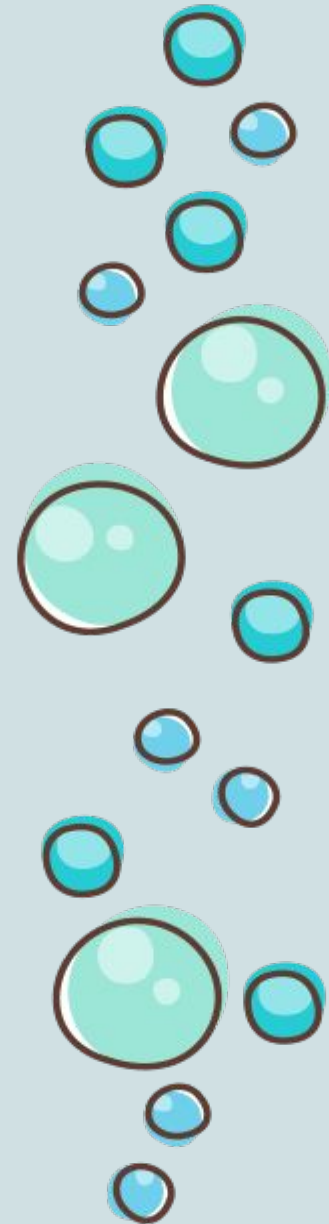
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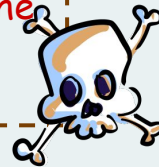
# OPIOIDS AND SEDATIVES



# Objectives

? Not given ):

Don't skip any note in this  
lecture, please (:  
You can [click here](#) to check the  
lecture from the textbook



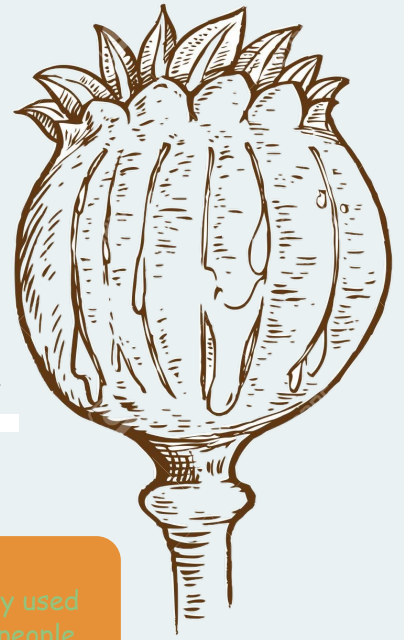
NOTES EXTRA BOOK IMPORTANT GOLDEN NOTES

# Introducing Opioids



## What are opioids:

- Exudate of the opium poppy (*Papaver somniferum*), **Most common in Afghanistan.**
- Addiction to opium became a commonplace e.g. sickle cell patients



## Known to:

Relieve pain

Relieve diarrhea

Produce euphoria

## Examples:

### Morphine

Good for analgesia. But causes nausea and vomiting. (Commonly used analgesic in the hospital)

Fentanyl: Synthetic, doesn't have a histaminic effect.

Heroin **Mostly used by lower class people.**

### Codeine

metabolized into morphine. however, 30% of our population (Arab descents) don't metabolize it, that's why morphine is preferred. Codeine can be given orally.

### Methadone

### Tramadol

Meperidine (pethidine). Synthetic, **More euphoria less analgesia and more side effects.** Should be given in a controlled setting. It is very addictive.

**Morphine (Natural) vs Fentanyl (Synthetic):**  
 -Morphine Causes vasodilation due to release of histamines, not used in hemodynamically unstable patients.  
 -Fentanyl Does NOT cause hypotension.

the most common drugs abused are heroin (abused by low class individuals), and cocaine (abused by the high class individuals).



## Opioid vs Opiate vs Narcotic?

### Opioid:

natural and synthetic

### Opiate:

natural (e.g. morphine)

### Narcotic:

any illegal hypnotic drug/drugs that make you sleep. it's mostly a legal term used by DEA



## Opioid receptors:

MU ( $\mu$ )

Located at supraspinal and spinal sites. (Analgesia and **respiratory depression**, Miosis, **euphoria**, reduced **GI** motility)

KAPPA ( $\kappa$ )

Dorsal horn of spinal cord and brainstem. (Analgesia, miosis, **sedation**)

DELTA ( $\delta$ )

Binding sites for endogenous peptides. (Analgesia, **dysphoria**, **delusions**, **hallucinations**)

Important!!

Opioids do not work on GABA, it has very specific receptors and each one of those receptors has its own specific effect. Some are more analgesic and cause less nausea and vomiting, whereas some cause constipation.

In general the most important features of opioids are:  
 -Effect on the CNS.  
 -Effect of on the respiratory system (in a very specific way).  
 -Effect on the cardiovascular system causing hypotension.  
 -GI (patients taking fentanyl must take laxatives).

# Opioids Toxicity

## Opioids Toxidrome

### Toxidrome and other effects

-(CNS depression, Respiratory depression<sup>1</sup>, Miosis "pinpoint Pupils")

- Sensorineural hearing loss<sup>2</sup>
- Mild hypotension (Histamine release)
- Bradycardia
- Nausea & Vomiting (watch out for ileus)
- Urinary Retention
- Pruritus/ Urticaria and Flushing

1-Respiratory depression AKA Hypoventilation. Minute Ventilation is calculated as:

$$\text{Minute Ventilation} = (\text{Respiratory rate} \times \text{Tidal volume})$$

In Opioids, the **tidal volume** is **normal**. But the **respiratory rate** is **low**

2-Other drugs causing hearing loss:

- Aminoglycosides** (gentamicin)
- Loop diuretics** (furosemide)
- Aspirin** >It also causes tinnitus.

### Management

- ABCDE's**<sup>3</sup> and Supportive therapy (D in toxicology stands for decontamination)
- Antidote** (Naloxone)

3-**ABCDE's**:

- A> Airway
- B> Breathing
- C> Circulation
- D> Decontamination
- E> Exposure, (Part of the exposure in toxicology is looking in the pockets...)

### Routes of administration of Opioids:

Orally

IV

Smoking

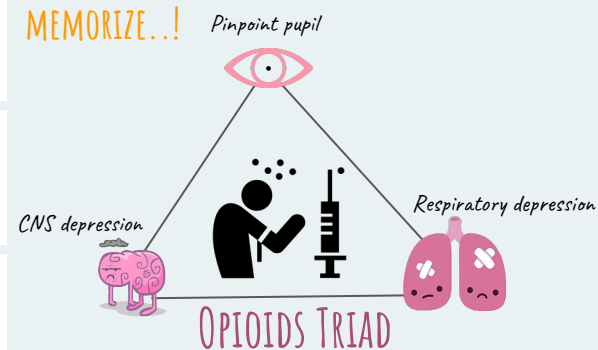
(heating up a spoon and inhaling the smoke "chasing the dragon")

Sniffing

(more for cocaine)



MAKE IT MORE FUN TO MEMORIZE..!



### Naloxone:

-Pure Opioid antagonist (Naloxone)

- Routes: **IV, IM, SC, intra-Nasal**

- **Mechanism**: Competitively binds opioid receptors and reverses all opioid mediated action

- **Dose**. Injectable solution (0.4-1mg/mL), IM/SC auto-injector (0.4mg/0.4mL "2 auto-injectors/package")

- **Half-life** is important. Opioids half-life is **much longer** than Naloxone's half-life.

Half-life



-Naloxone 1/2 life is **1 -2 hours**

-Morphine 1/2 life approx. **2 hours**

"The duration of action of many opioids, especially after overdose, is significantly longer than that of naloxone. Patients responsive to naloxone should be observed for recurrence of opioid toxicity after the effect of naloxone has resolved."



# Withdrawal & Chronic Use



## Opioid Withdrawal:

In withdrawal patients go into hyperadrenergic state. They are NOT life threatening Symptoms: [\(image\)](#)

-Sweating (diaphoresis)  
-Hypertension

-Mydriasis  
-Yawning

-Diarrhea  
-Nausea and vomiting

**Goosebumps**  
classical sign  
(Piloerection)

-Abdominal pain  
-Muscle cramps

-Tachypnea  
-Tachycardia

CNS excitation (Restlessness, agitation, dysphoria and insomnia)

**Management:** Opioid withdrawal patients > Clonidine is the drug of choice

### IN THE ED

#### Supportive and Symptoms based:

- IV fluids
- Electrolytes replacement
- Antiemetic
- Clonidine (Alpha2 agonist) can be used to suppress sympathetic hyperactivity and shorten the duration of withdrawal

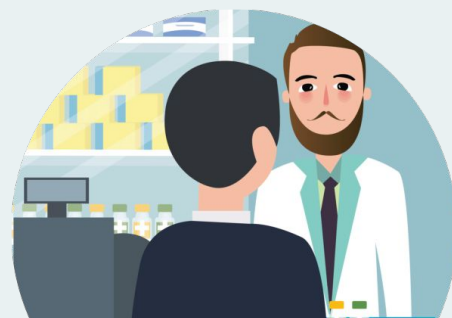
### CHRONIC OPIOID ABUSERS "Long term maintenance therapy, provided by addiction clinics"

- Methadone:** Given to heroin addicts to get them their "fix" and go off of street work. Could be given to pregnant ladies.
- Long half life and requires a dose every 24 hours

### OUTPATIENT TREATMENT

- Buprenorphine and Buprenorphine-Nalaxone combined as single product.
- Doesn't require inpatient treatment unless severe symptoms.

Doctor insisted to know this part from the textbook so please make sure to study this part very well; we wanted to save your time so we added this point from book here (; Good luck!



YES, THE PHARMACIST GIVES METHADONE TO ADDICTORS!

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# Benzodiazepine

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## Benzodiazepines

### Mechanism of action (Not important)

-Benzodiazepines bind to benzodiazepine receptor & potentiates **GABA** effects on the **chloride channel** → **increasing intracellular flux of Cl ions** & hyperpolarizing the cell (lowers the action potential to be more negative, so it will be harder to stimulate the cell)  
 - The net effect is a diminished ability of the nerve cell to initiate an action potential, which leads to inhibiting neural transmission (like alcohol & barbiturates)

### Clinical effects

- **Anticonvulsant** (The strongest indication.)
- Sedative
- Hypnotic
- Anxiolytic

### Examples

Examples (commonly used) you need to know:

- Alprazolam (Xanax)
- Diazepam (Valium)
- Lorazepam (Ativan)
- Midazolam (Versed)

[Click here to see the full list of these drugs \(:\)](#)

5% of the population have used an illicit drug once in their life.  
 The most common benzodiazepine drug abused is **Xanax** (alprazolam).

Barbiturates, Benzodiazepines, and alcohol.  
 All are depressants (Downers)↓  
 Opioids are stimulants (Uppers)↑

## Benzodiazepines Toxicity

### Toxicity

- CNS depression (spectrum)<sup>1</sup>
- Respiratory depression (**non central**)<sup>2</sup>
- Potential complications: aspiration, pressure sore
- Hypotension (uncommon) seen only if given intravenously in large doses

1-It's a spectrum. From slurred speech all the way to coma.  
 2-Respiratory depression is unlike opioids (Opioids have a central effect. Affecting the medulla hence lowering the respiratory rate), Benzodiazepines non-central, affecting the muscles. The patient feels too weak to breathe

### Diagnosis

-Clinical and History.  
 (no labs)

### Differential diagnosis

- Hypoglycemia
- Stroke

### Management

- Supportive
- Antidote (**Flumazenil**)

**High Anion Gap metabolic acidosis (HAGMA): Why?**  
 Benzodiazepines themselves don't cause it, it's usually combined with **propylene glycol as a preservative** which causes the HAGMA.

**Examples causing HAGMA: (MUD PILES)**  
 M-Methanol U-Uremia D-Diabetic ketoacidosis  
 P-Paraldehyde I- Iron, Isoniazid L-Lactic acid  
 E-Ethanol, Ethylene glycol S-Salicylates (Aspirin)

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# Benzodiazepine

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## Flumazenil

### What is Flumazenil?

Nonspecific competitive **antagonist of the benzo receptor.**

Reverse benzodiazepine-induced sedation after:

GA (general anesthesia)

PSA (procedural sedation and analgesia "conscious sedation") e.g. A fib, drainage, dislocated shoulder

confirmed benzodiazepine overdose

Not recommended for the routine reversal of sedative overdose in the ED.



### To give or not to give?

#### Indications

-Isolated benzodiazepine overdose in non habituated user (e.g., accidental pediatric exposure)  
-Reversal of conscious sedation

**Given only in:**

- 1- overdose
- 2- we are sure that the patient only took benzodiazepines (because they usually combine different drugs, if so, we do supportive management only).
- 3- we give it just once.

#### Contraindications

**A-absolute contraindication (Extremely important)**  
-suspected co-ingestant that lowers seizure threshold (because flumazenil causes seizures) (e.g., tricyclic antidepressants, cocaine, lithium, methylxanthines, isoniazid, propoxyphene, monoamine oxidase inhibitors, bupropion, diphenhydramine, carbamazepine, cyclosporine, chloral hydrate)  
-Patient taking benzodiazepine for control of a potentially life-threatening condition (e.g., seizures)  
-Concurrent sedative-hypnotic withdrawal.  
**-Seizure activity or myoclonus**  
-Hypersensitivity to flumazenil or benzodiazepines  
-Patient with neuromuscular blockade

**B-relative contraindication:**  
-Chronic benzodiazepine use, **not taken** for control of life-threatening condition  
-Known seizure disorder **not treated with benzodiazepines**  
-Head injury  
-Panic attacks  
-Chronic Alcoholism

#### Complications

Seizures

Dysrhythmia

Reported mortalities

Precipitate withdrawal

#### Withdrawal

-Anxiety  
-Depression  
-Insomnia  
-Tremor  
-Tachycardia  
-sweating

-Visual hallucinations  
-Delirium  
-Seizures

NONSPECIFIC

SEVERE (RARE)

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# Summary

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## Opioid:

### Known to:

- Relieve pain.
- Relieve diarrhea.
- Produce euphoria.

### Examples:

Morphine, Fentanyl, Heroin, Tramadol, Methadone, Codeine, Meperidine (pethidine).

### Opioid vs Opiate vs Narcotic?

- Opioid: **natural and synthetic.**
- Opiate: **natural (e.g. morphine).**
- Narcotic: **any illegal hypnotic drug/drugs that make you sleep. it's mostly a legal term used by DEA.**

## Opioid receptors:

- **Mu(μ):** Located at supraspinal and spinal sites. (Analgesia and **respiratory depression**, Miosis, **euphoria**, reduced **GI** motility).
- **Kappa (κ):** Dorsal horn of spinal cord and brainstem. (Analgesia, miosis, **sedation**).
- **Delta (δ):** Binding sites for endogenous peptides. (Analgesia, **dysphoria**, **delusions**, **hallucinations**).

## Routes of administration of Opioids:

1. Orally
2. IV
3. Sniffing
4. Smoking

### Opioid Toxicidrome and other effects:

- CNS depression, Respiratory depression, Miosis pinpoint Pupils.
- Sensorineural hearing loss.
- Mild hypotension (Histamine release).
- Bradycardia.
- Nausea & Vomiting (watch out for ileus).
- Urinary Retention.
- Pruritus/ Urticaria and Flushing.

### Management:

- ABCDE's and Supportive therapy (D in toxicology stands for decontamination).
- Antidote (Naloxone).

### Opioids withdrawal:

- Sweating (diaphoresis). -Mydriasis. -Diarrhea. -Goosebumps.
- Abdominal pain. -Muscle cramps.



## Benzodiazepines Toxicity:

### Toxicity

- CNS depression (spectrum).
- Respiratory depression (**non central**).
- Potential complications: aspiration, pressure sore.
- Hypotension (uncommon).

### Diagnosis

- Clinical and History. (no labs)

### Differential diagnosis

- Hypoglycemia.
- Stroke.

### Management

- Supportive.
- Antidote. (**Flumazenil**)
- Flumazenil Complications:** Seizures, Dysrhythmia, Reported mortalities, Precipitate withdrawal.
- Flumazenil Withdrawal:** Nonspecific : Anxiety, Depression, Insomnia, Tremor, Tachycardia, sweating. Severe (rare): Visual hallucinations, Delirium, Seizures.



# How toxic is your knowledge

**1-Which one of the following is an appropriate clinical indication of benzodiazepine ?**

- A. it may be used as an induction agent
- B. it may be used as an analgesic
- C. it may be used as an antipsychotic
- D. it may be used as an antidepressant

**2-Benzodiazepine potentiate inhibitory GABAergic neurotransmission through which one of the following ?**

- A. Increasing intracellular flux of calcium ions.
- B. decreasing intracellular flux of calcium ions.
- C. increasing intracellular flux of chloride ions.
- D. decreasing intracellular flux of chloride ions.

**3-An intravenous heroin user rushed to the ER after he was found unresponsive with shallow breathing and weak pulses, which one of the following is the first in the management ?**

- A. give him an IV bolus of normal saline .
- B. start a cardiac massage .
- C. control his airways and breathing .
- D. administer activated charcoal .

**4-A 23 years old male patient is brought to the emergency department after using some drugs. His initial examination reveals that the patient is drowsy, has bilateral constricted pupils and slow breathing. Which of the following toxidrome is present in this patient?**

- A- Sympathomimetic
- B- Anticholinergic
- C- Cholinergic
- D- Opioid

**5-Which of the following is the drug of choice for opioid withdrawal?**

- A- Clonidine
- B- Methadone
- C- Naloxone
- D- Ethanol

**6-Which one of the following is the antidote for opioid poisoning?**

- A- Flumazenil
- B- Atropine
- C- Naloxone
- D- Pethidine

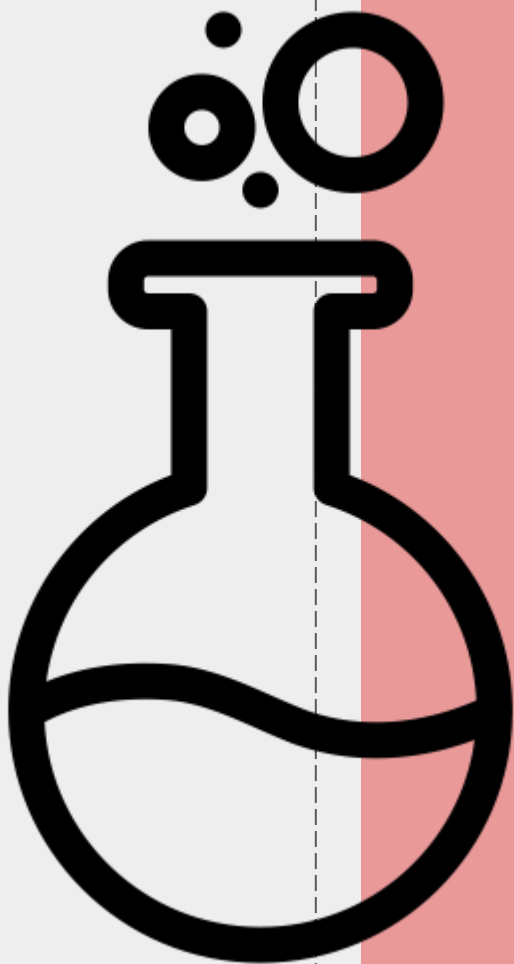
**7-After injecting intravenous heroin a patient developed severe opioid poisoning and is being treated in the emergency department. Which one of the following is the first step in the management?**

- A- Give a CNS stimulant drug
- B- Give a respiratory stimulant drug
- C- Airway control and breathing
- D- Give 2L normal saline



- 1-A
- 2-C
- 3-C
- 4-D
- 5-A
- 6-C
- 7-C

# THANK YOU AND GOOD LUCK!



VERY TOXIC BUT YOU ARE  
GONNA DO IT!

*A+ is yours (:*

• Email us at:

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