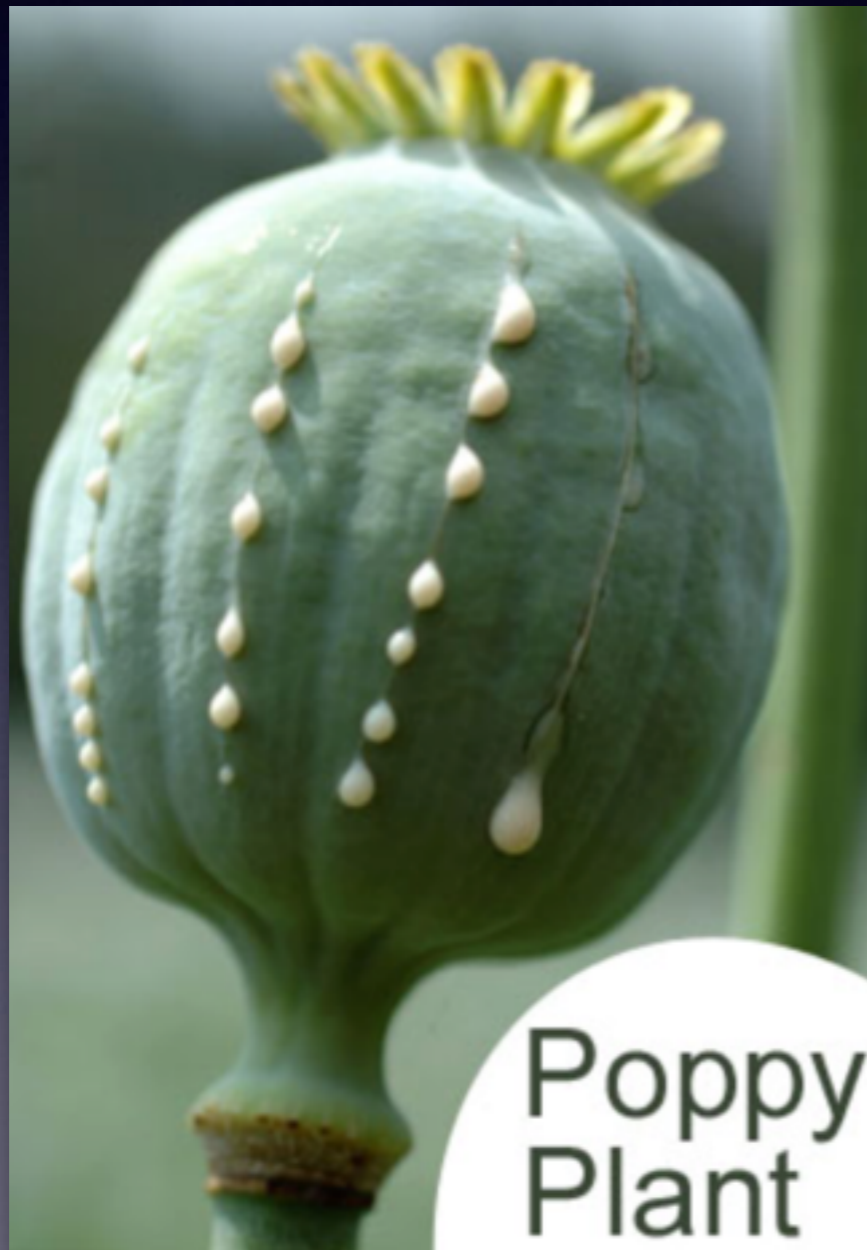


# Opioids & Sedatives Toxicity

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# What Are Opioids?



- Exudate of the opium poppy (*Papaver somniferum*)
- Known to relieve pain, diarrhea, produce euphoria
- Addiction to opium became commonplace

*Opioid vs Opiate vs Narcotic?*

# Examples of Opioids

Morphine

Heroin

Codeine

Fentanyl

Meperidine

Methadone

**On What Receptors do  
Opioids work on?**

- 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 brain stem
  - Analgesia, miosis, sedation
- Delta ( $\delta$ )
  - Binding sites for endogenous peptides
  - Analgesia, dysphoria, delusions, hallucinations

***WHAT IS THE TOXIDROME  
OF OPIOID TOXICITY?***





# The Opioid Toxidrome

CNS depression

Respiratory depression

Miosis

# Other Opioid Effects

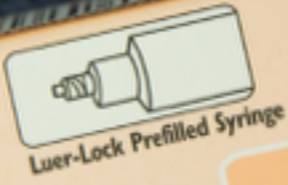
- Sensorineural hearing loss
- Mild hypotension (Histamine release) and Bradycardia
- Nausea & Vomiting (watch out for ileus)
- Urinary Retention
- Pruritus/ Urticaria and Flushing

# Management

- **ABC's and Supportive therapy**
- **Antidote**



▲ open



Luer-Lock Prefilled Syringe

Rx Only

NDC 76329-3369-1 STOCK NO. 3369

**NALOXONE  
HYDROCHLORIDE**  
INJ., USP  
(1 mg/mL)

2 mg  
per  
2 mL

FOR INTRAVENOUS, INTRAMUSCULAR  
OR SUBCUTANEOUS USE  
AS A NARCOTIC ANTAGONIST

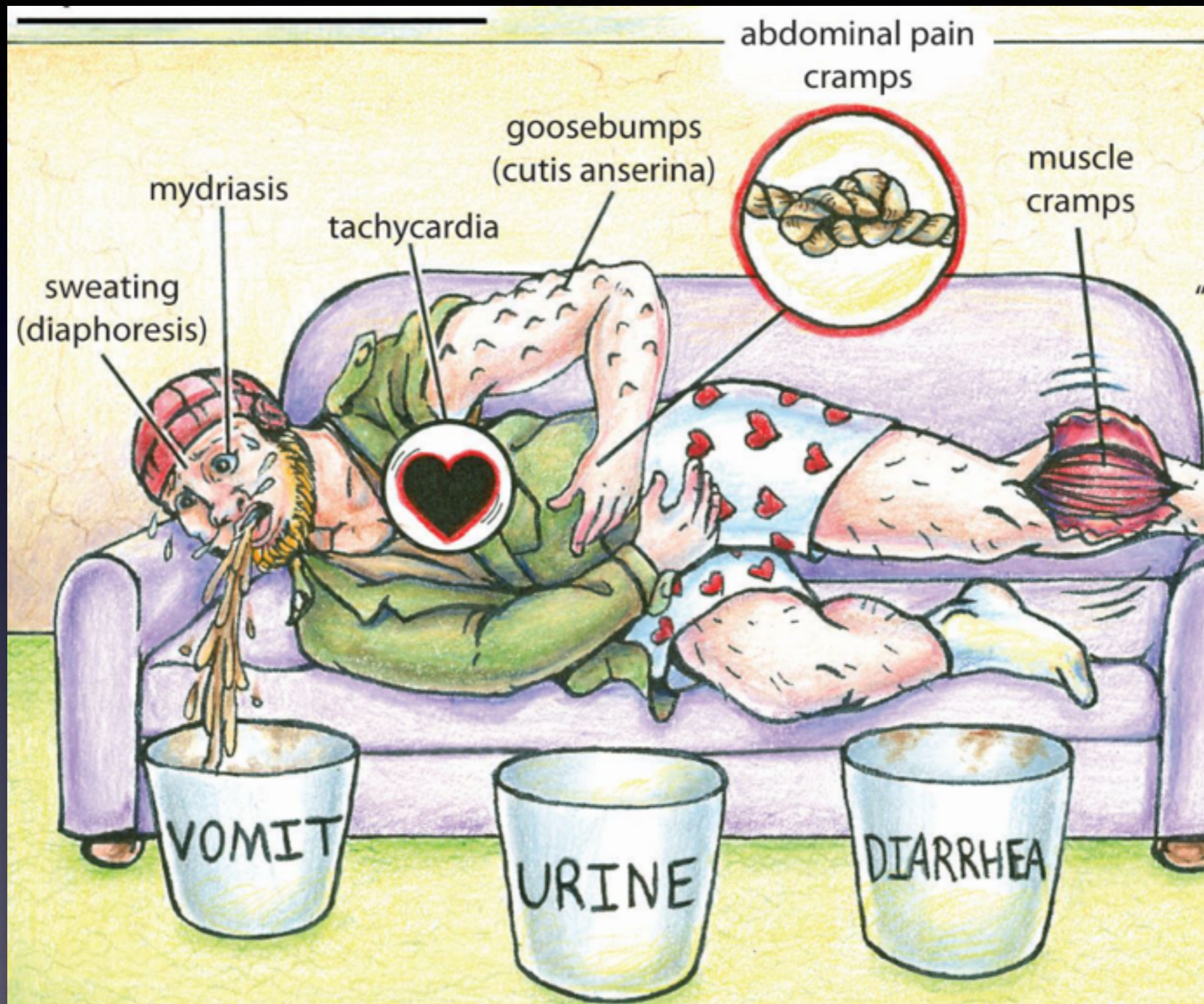
LUER-JET™ LUER-LOCK PREFILLED SYRINGE

- Pure Opioid antagonist
- Routes?
- Competitively bind opioid receptors and reverses all opioid mediated action
- Dose ?
- ***Half Life? Why is it important??***

- 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.*

# Opioid Withdrawal



***NOT LIFE THREATENING!***



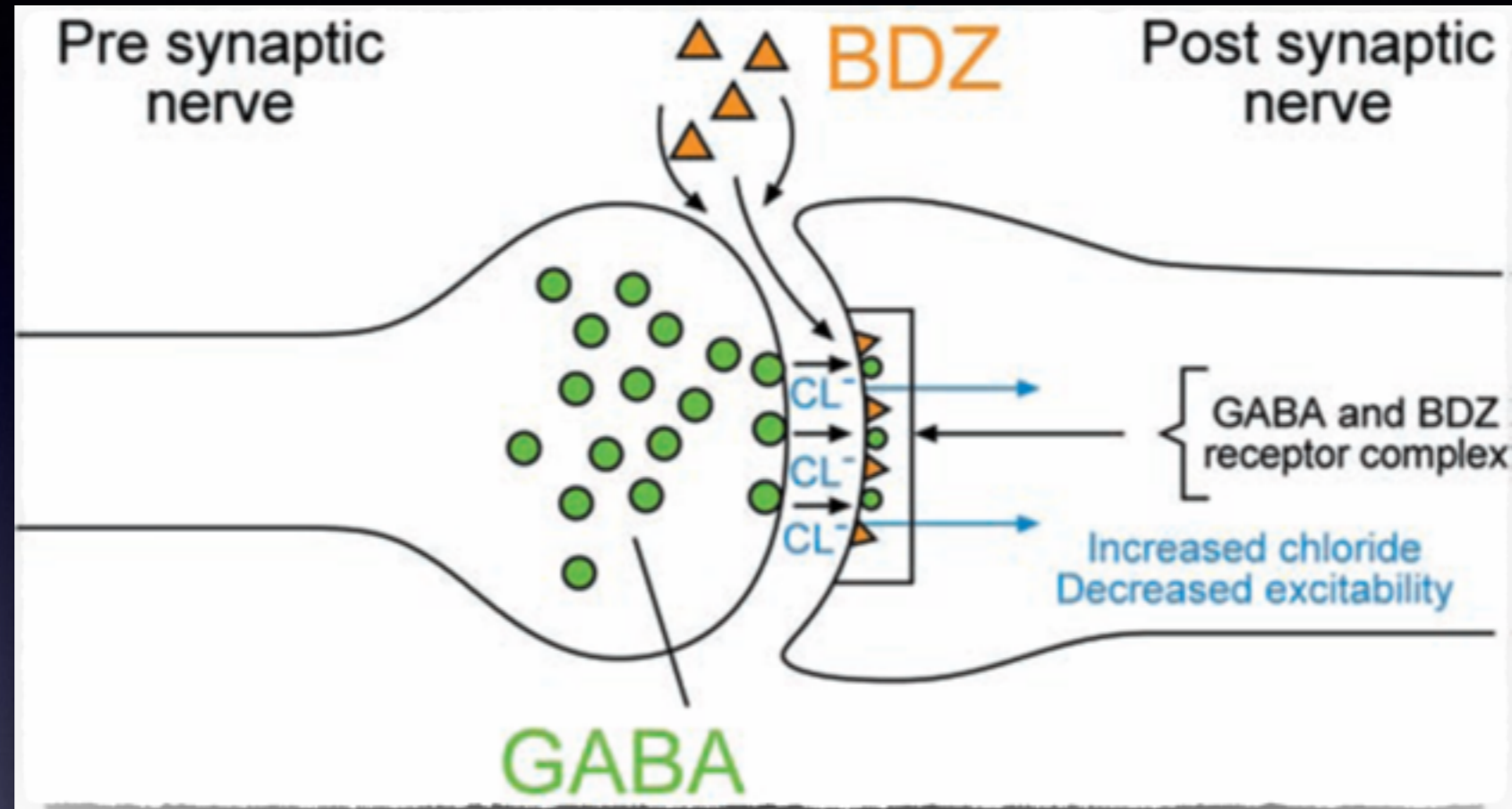


# Methadone

- Long half life
- Requires a dose every 24hrs

# **Benzodiazepine Toxicity**

# Mechanism of Action



Benzodiazepine bind to benzodiazepine receptor & potentiates GABA effects on the chloride channel —> increasing intracellular flux of CL ions & hyperpolarizing the cell

The net effect is a diminished ability of the nerve cell to initiate an action potential, inhibiting neural transmission!

# Clinical Effects

- Sedative
- Hypnotic
- Anxiolytic
- Anticonvulsant

NAME	USUAL DOSE	ORAL PEAK (hr)	HALF-LIFE (hr)	PARENT METABOLITE ACTIVITY
Alprazolam (Xanax)	0.25-0.5 mg	1-2	6-27	Inactive
Chlordiazepoxide(Librium)	5-25 mg	0.5-4	5-30	Active
Clonazepam (Klonopin)	0.25-0.5 mg	1-2	18-50	Inactive
Clorazepate (Tranxene)	7.5-15 mg	1-2	1-3	Active
Diazepam (Valium)	2-10 mg	0.5-1	20-50	Active
Estazolam (ProSom)	1-2 mg	2	8-28	Inactive
Flurazepam (Dalmane)	15-30 mg	0.5-1	2-3	Active
Halazepam (Paxipam)	20-40 mg	1-3	14	Active
Lorazepam (Ativan)	0.5-2 mg	2-4	10-20	Inactive
Midazolam (Versed)	0.025-0.1 mg/kg	1-2	1.5-3	Active
Oxazepam (Serax)	10-30 mg	2-4	5-20	Inactive
Quazepam (Doral)	7.5-15 mg	2	39-41	Active
Temazepam (Restoril)	7.5-30 mg	1-2	3-19	Inactive
Triazolam (Halcion)	0.125-0.25 mg	1-2	1.5-5.5	Inactive

# Clinical Features of Benzo Poisoning

- CNS depression (spectrum)
- Resp. depression (non central)
- Hypotension (uncommon)
- Potential complications:  
Aspiration - Pressure sores

**Why do they get  
HAGMA ACIDOSIS?**



- ***How to Diagnose?***
- ***Differential Diagnosis?***

# Management

- **Supportive**
- **Antidote**



# Flumazenil

Nonspecific competitive antagonist of the benzo receptor

Reverse benzodiazepine-induced sedation after GA, PSA, & confirmed benzodiazepine overdose

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

### **Indications**

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

### **Absolute Contraindications**

Suspected coingestant that lowers seizure threshold (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

### **Relative Contraindications**

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

## **Nonspecific**

Anxiety, depression, insomnia, tremor, tachycardia, sweating

## **Severe (rare)**

Visual hallucinations, delirium, seizures

# QUESTIONS?

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