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

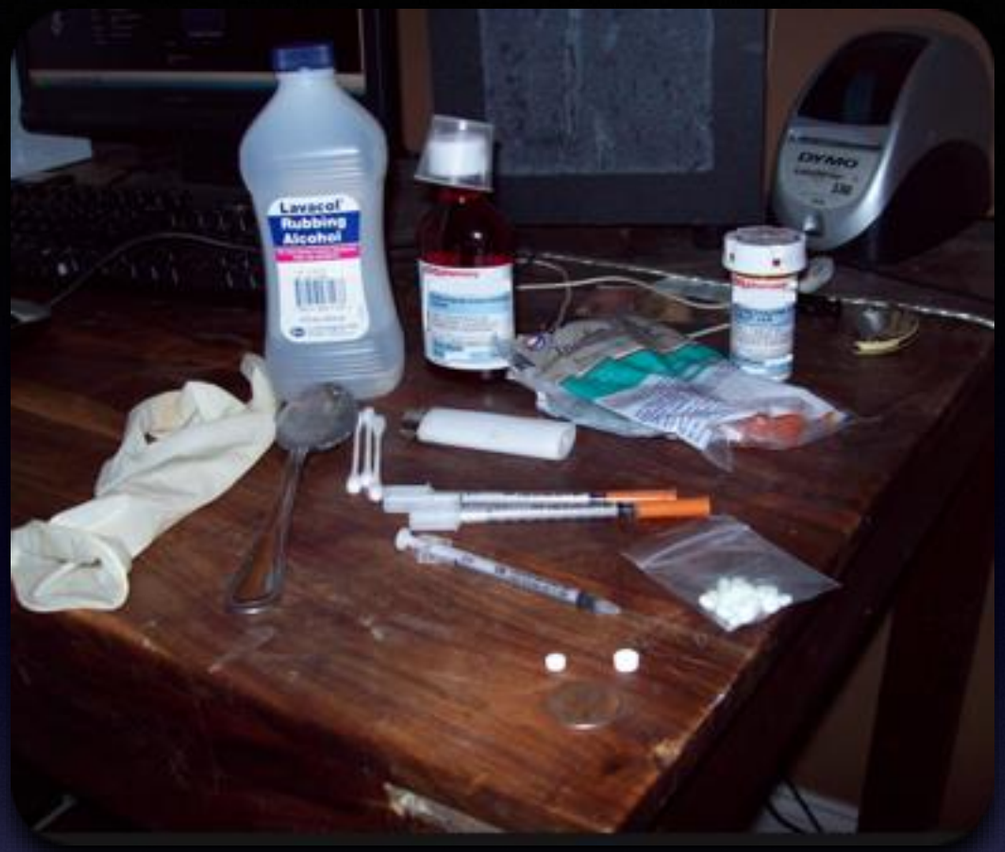
On What Receptors do Opioids work on?

- Mu (ˆ)
  - Located at supraspinal and spinal sites
  - Analgesia and respiratory depression
  - Mioisis, euphoria, reduced GI motility

- Kappa (ˇ)
  - Dorsal horn of spinal cord and brain stem
  - Analgesia, miosis, sedation

- Delta (™)
  - Binding sites for endogenous peptides
  - Analgesia, dysphoria, delusions, hallucinations

WHAT IS THE TOXIDROME OF OPIOID TOXICITY?


Lysol
Rubbing
Alcohol

The Opioid Toxidrome

CNS depression

Respiratory depression

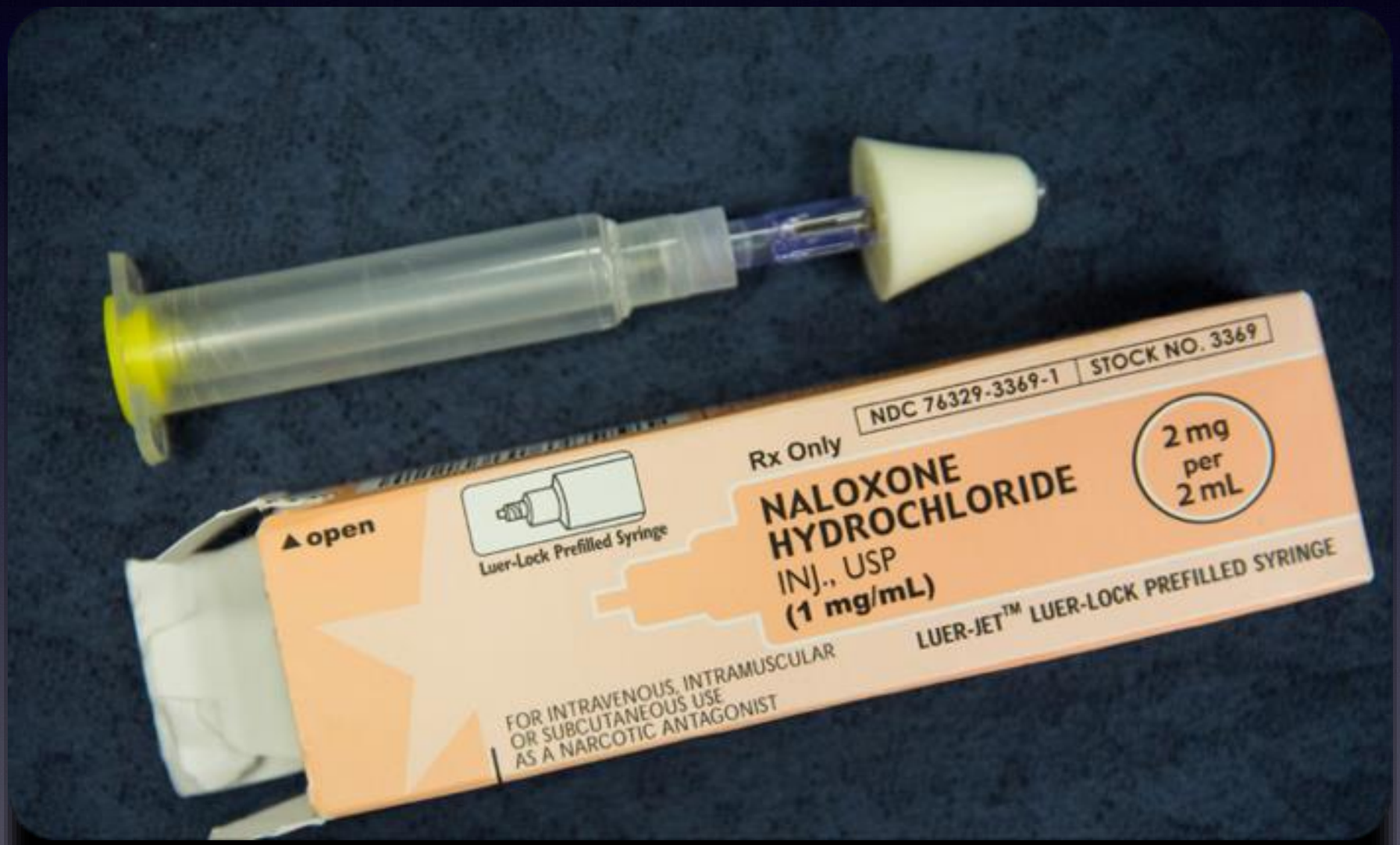
Miosis

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**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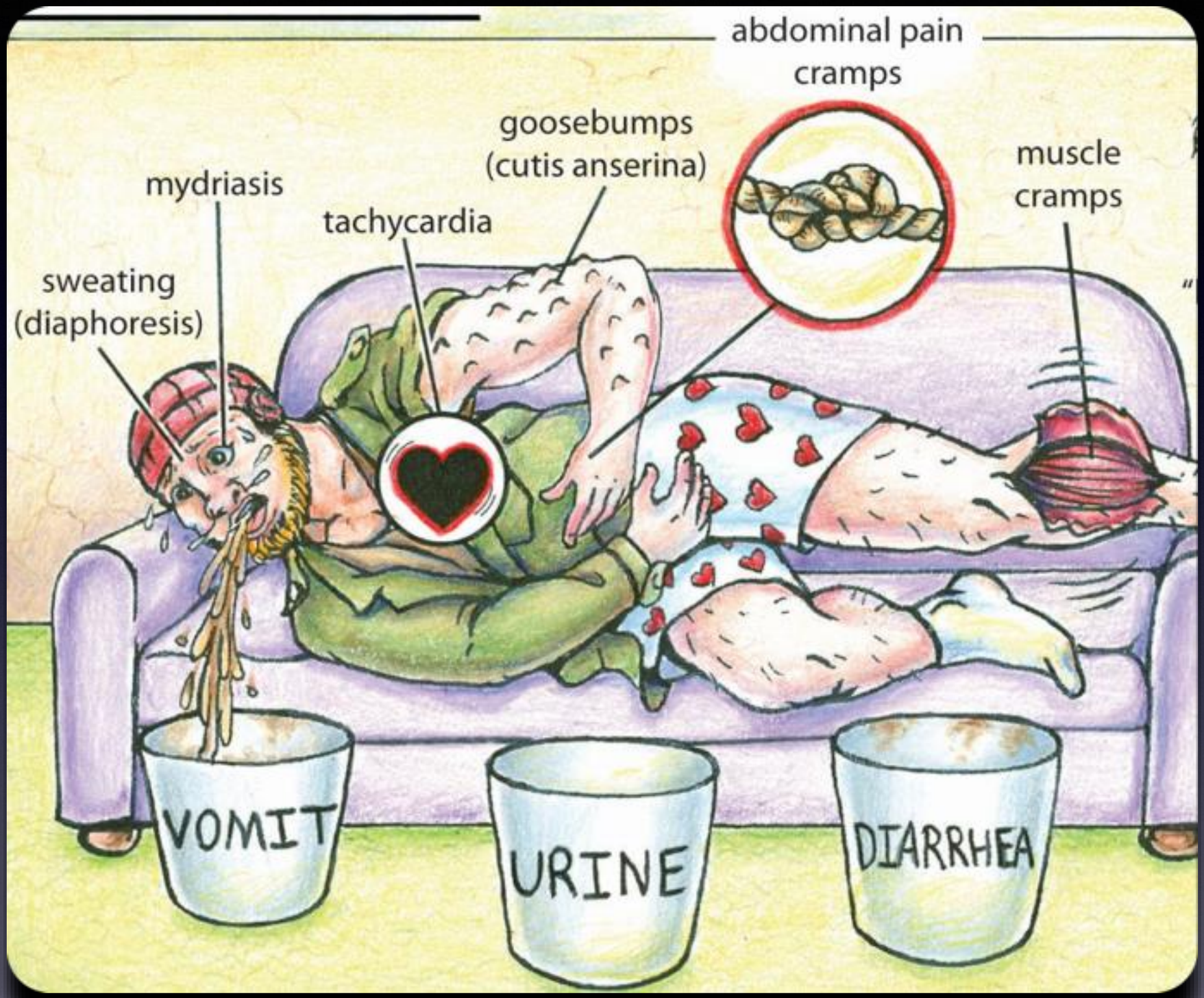
NALOXONE HYDROCHLORIDE
INJ., USP
(1 mg/mL)
2 mg per 2 mL
LUER-JET™ LUER-LOCK PREFILLED SYRINGE
FOR INTRAVENOUS, INTRAMUSCULAR OR SUBCUTANEOUS USE AS A NARCOTIC ANTAGONIST

- 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!


TEST

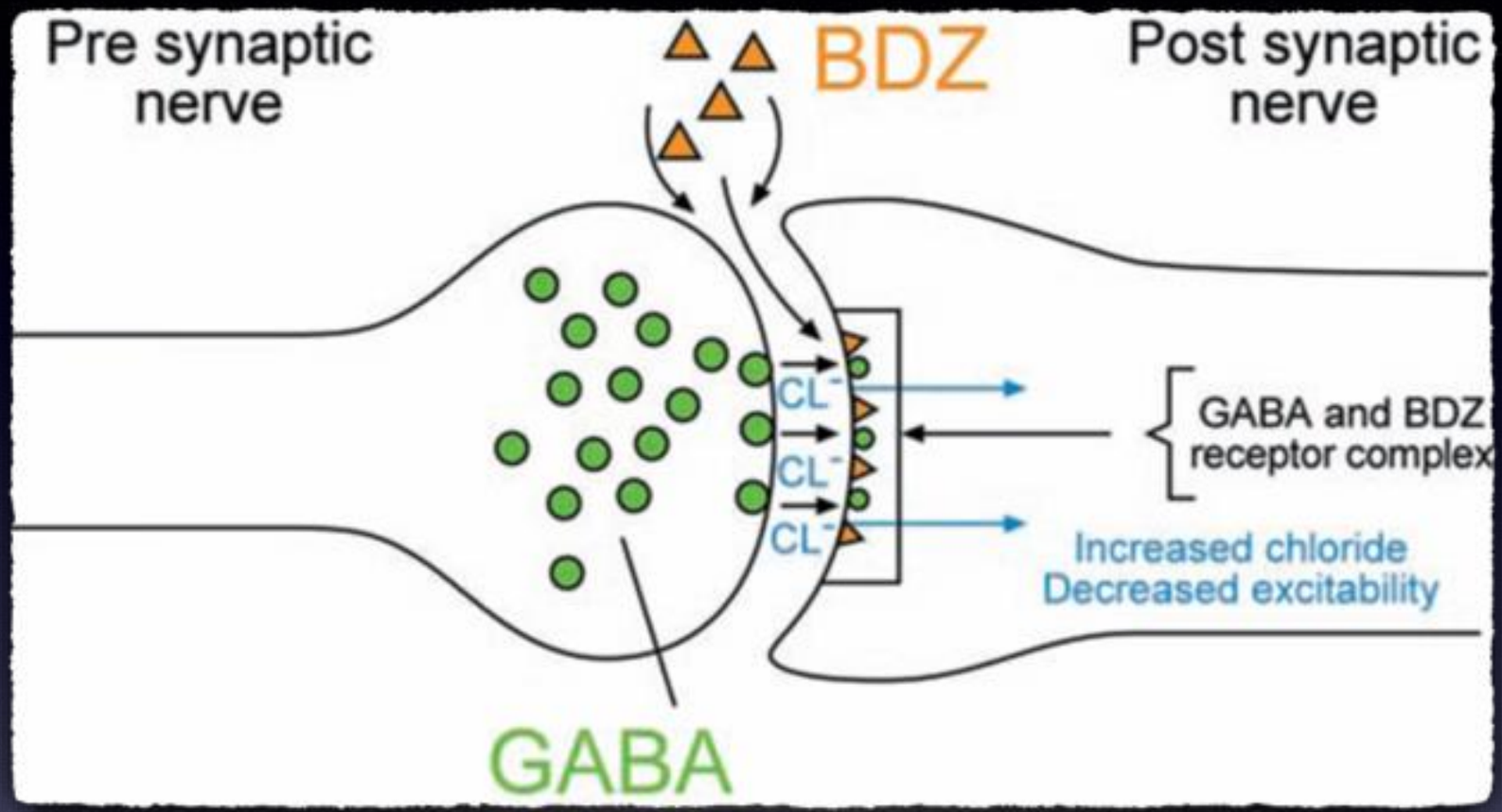

Two
Free

Methadone

- Long half life
- Requires a dose every 24hrs

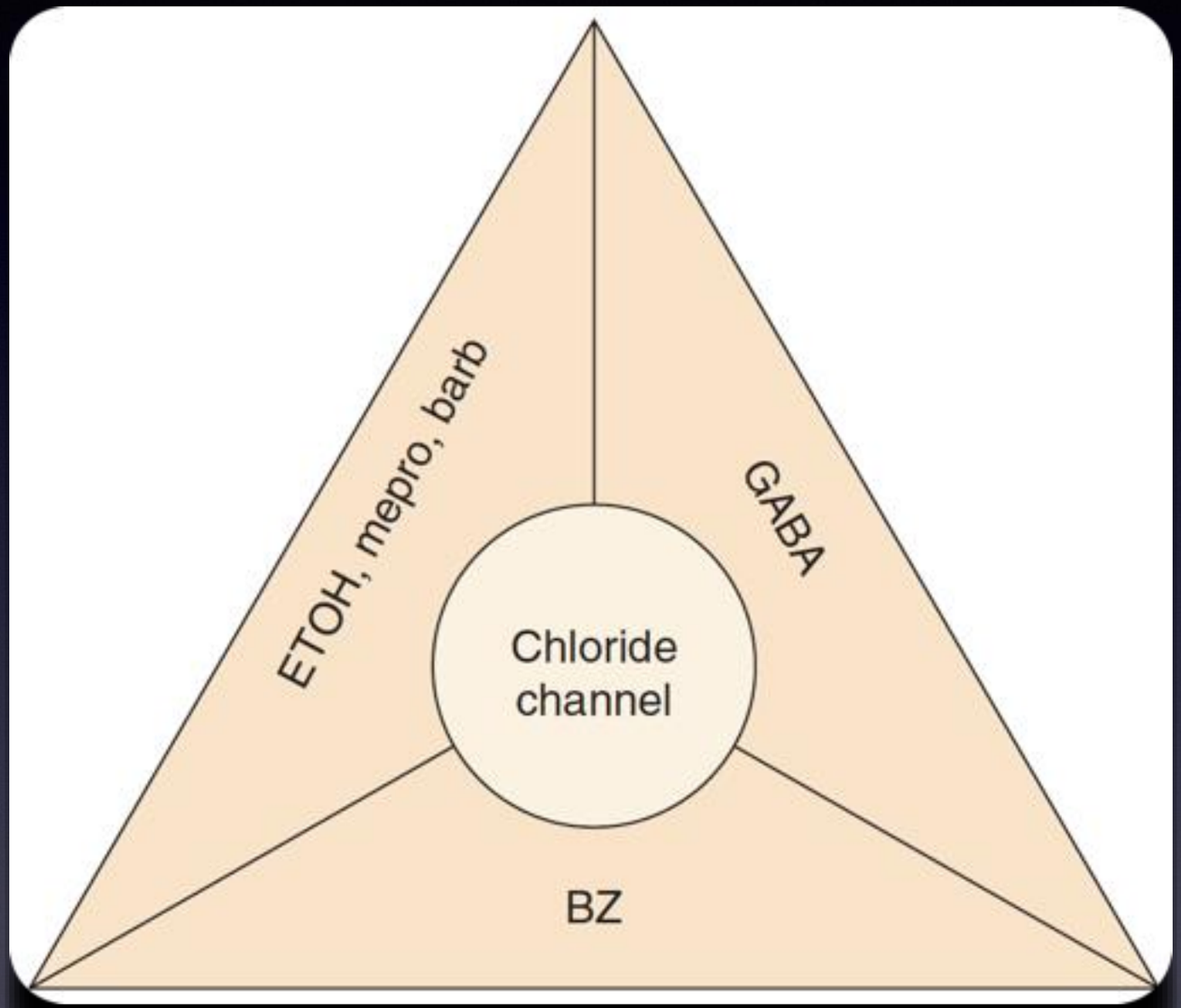
Benzodiazepine Toxicity

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!


ETOH, mepro, barb
GABA
Chloride channel
BZ

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)
- Potentail 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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