CAMPBELL UNIVERSITY | Jerry M. Wallace School of Osteopathic Medicine

# Autonomic Cardiovascular Physiology I and II

## Connecting the Basic Science and Clinical Components

September 25, 2025

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# Case #1

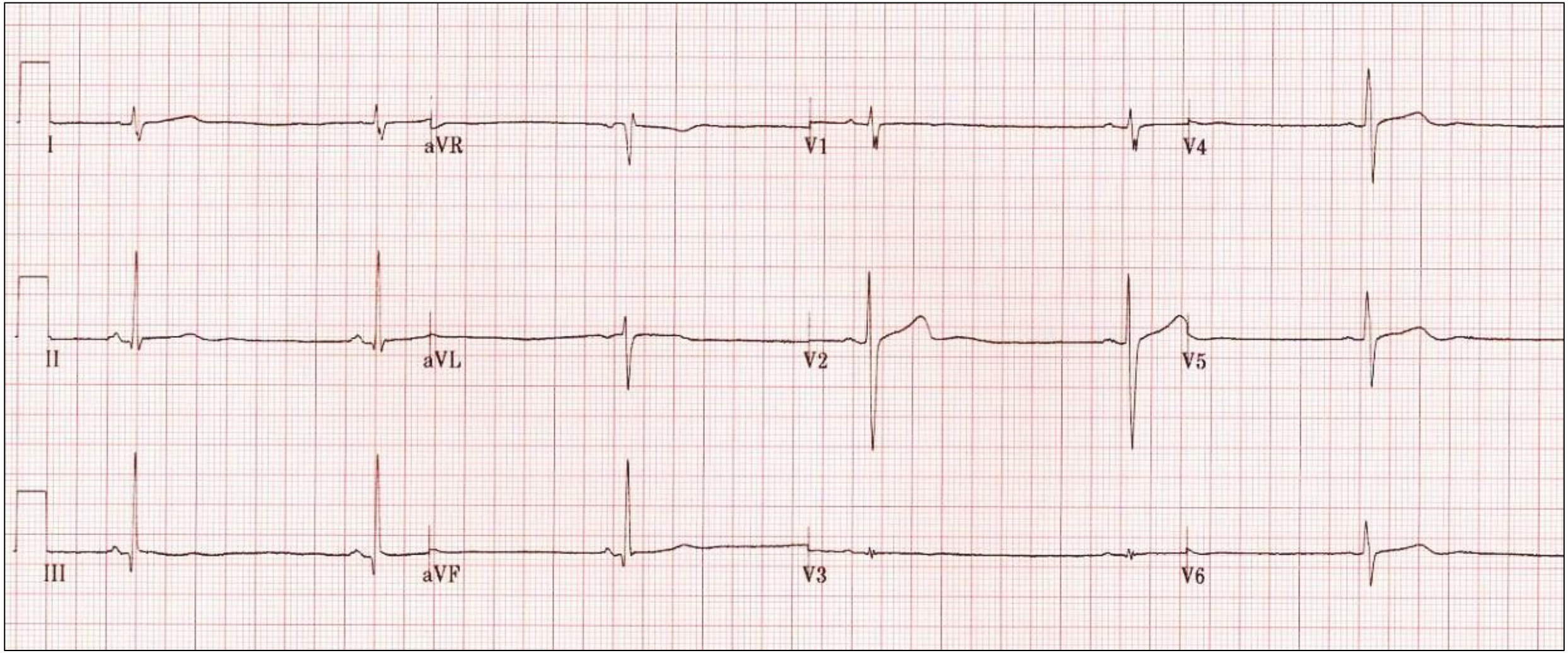
## Case #1

- A 26-year-old male presents to the ED after taking a handful of unknown pills in a suicide attempt.
- On arrival he is lethargic, confused, and unable to provide any medical history.
- He was seen at his PCP's office one week ago and his vital signs at that time were as follows:
  - Pulse: 88
  - Blood pressure: 138/84
  - Respiratory rate: 18

# Physical Exam

| | Findings |
|---|---|
| **General Appearance** | Lethargic, pale |
| **Vital Signs** | Pulse 40; BP 80/46; RR 22; T 98.4; Pox 96%. |
| **HEENT** | Mucosa dry, no thyromegaly; pupils midpoint |
| **Cardiovascular** | Bradycardia; S1 & S2 noted. No murmurs, rubs or gallops |
| **Pulmonary** | Bilateral wheezing |
| **Gastrointestinal** | Abdomen soft and non-tender |
| **Extremities** | Pale and slightly moist; weak peripheral pulses |
| **Neuro** | Lethargic – oriented only to self; cranial nerves intact; moves all 4 extremities with normal strength |

# EKG




Interpret the EKG

# Question 1

What component of the autonomic nervous system is most likely affected?

A. Parasympathetic
B. Sympathetic
C. Enteric
D. Both parasympathetic and sympathetic
E. Both parasympathetic and enteric

# Question 2

What is the most likely agent he ingested?

A. Calcium channel blocker
B. Beta blocker
C. Digoxin
D. Alpha blocker
E. Angiotensin receptor blocker
F. Hydralazine

# Question 3

A medication is administered and results in the following change in his vitals.

**What was the most likely agent administered?**

| | At PCP one week prior | After ingestion | After medication administration |
|---|---|---|---|
| **Pulse** | 88 | **40** | **60** |
| **Blood Pressure** | 138/84 | **80/46** | **90/54** |

A. Phenylephrine
B. Atropine
C. Dobutamine
D. Epinephrine

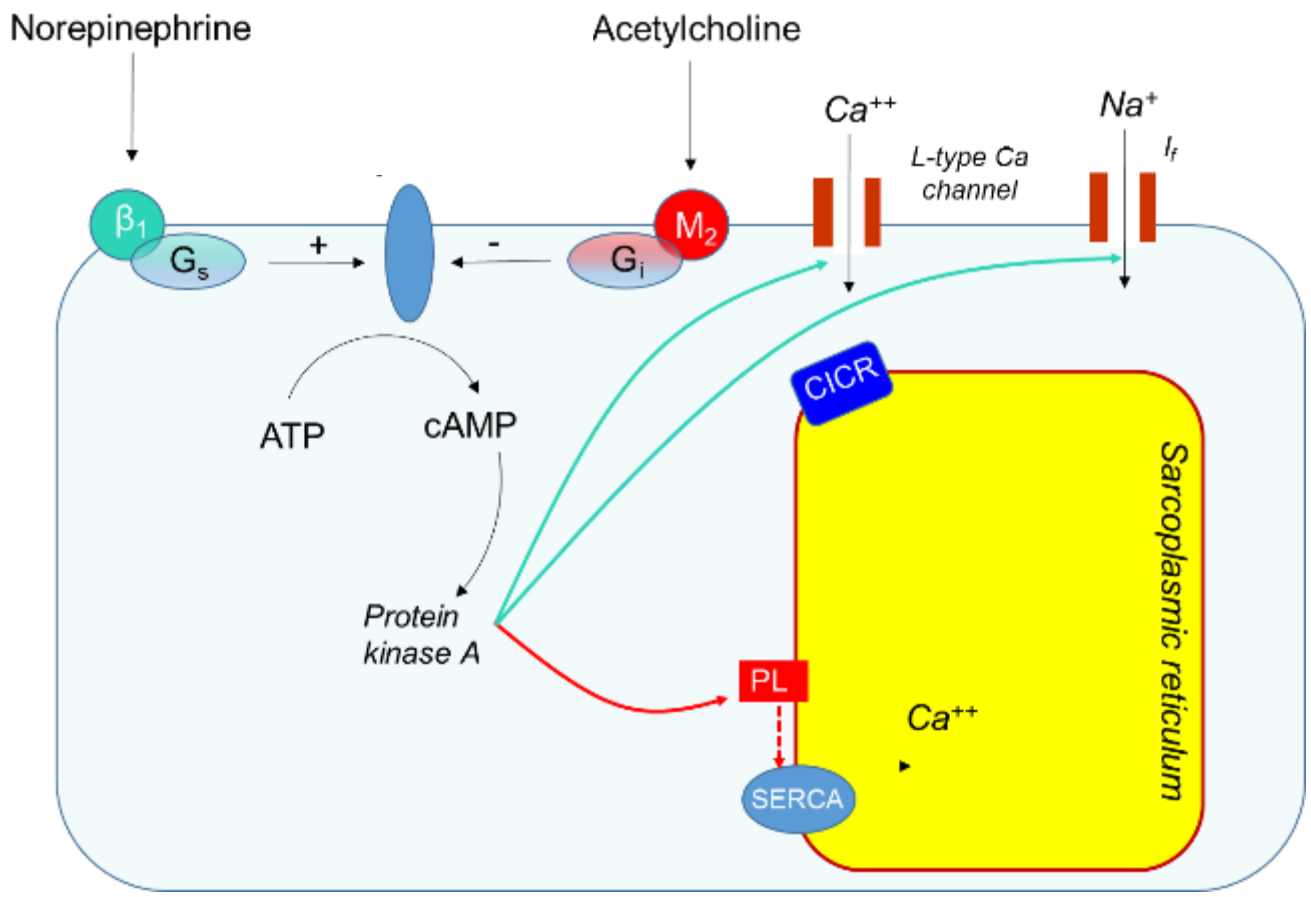
# Beta Blockers

Modulate activity of myocyte & vascular smooth muscle contraction by **↓ $Ca^{++}$ entry into the cell**

**Blockade of which receptors result in the following?**

- Bradycardia, ↓ contractility & hypotension
- Bronchoconstriction
- Vasoconstriction & ↑ vascular resistance

What is the mechanism?

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# Regulation of Smooth Muscle


Ca channel blockers, $MgSO_4$

α-1 antagonists

$PGI_2$

β-2 blockers

Endothelin antagonists

Ca

NE

L-type Ca channel

α-1

$PGI_2$

E

$\beta_2$

NO

PDE inhibitor

$IP_3$

Gq coupled receptor

$G_s$

PDE

$ET_A$

↑Guanylyl cyclase

Endothelin-1

CICR → Ca + CaM

A-Cyclase

GTP → **cGMP** → GMP

ACE inhibitors

↑MLC kinase

cAMP

↑MLC phosphatase

Ang-II

MLC - Ⓟ

MLC Ⓟ→

PKG

ARB

actin→ ←myosin

←actin myosin→

K channel opener

K channel

Ca

- α-1 agonists: NE
- β-2 agonists: E
- α-1 antagonists: prazosin, terazosin, tamsulosin
- Ca channel blockers: nifedipine, amlodipine
- K channel opener: minoxidil
- Endothelin antagonists: bosentan, ambrisentan
- ACE inhibitors: enalapril
- ARB: losartan
- PDE inhibitor: sildenafil (Viagra)

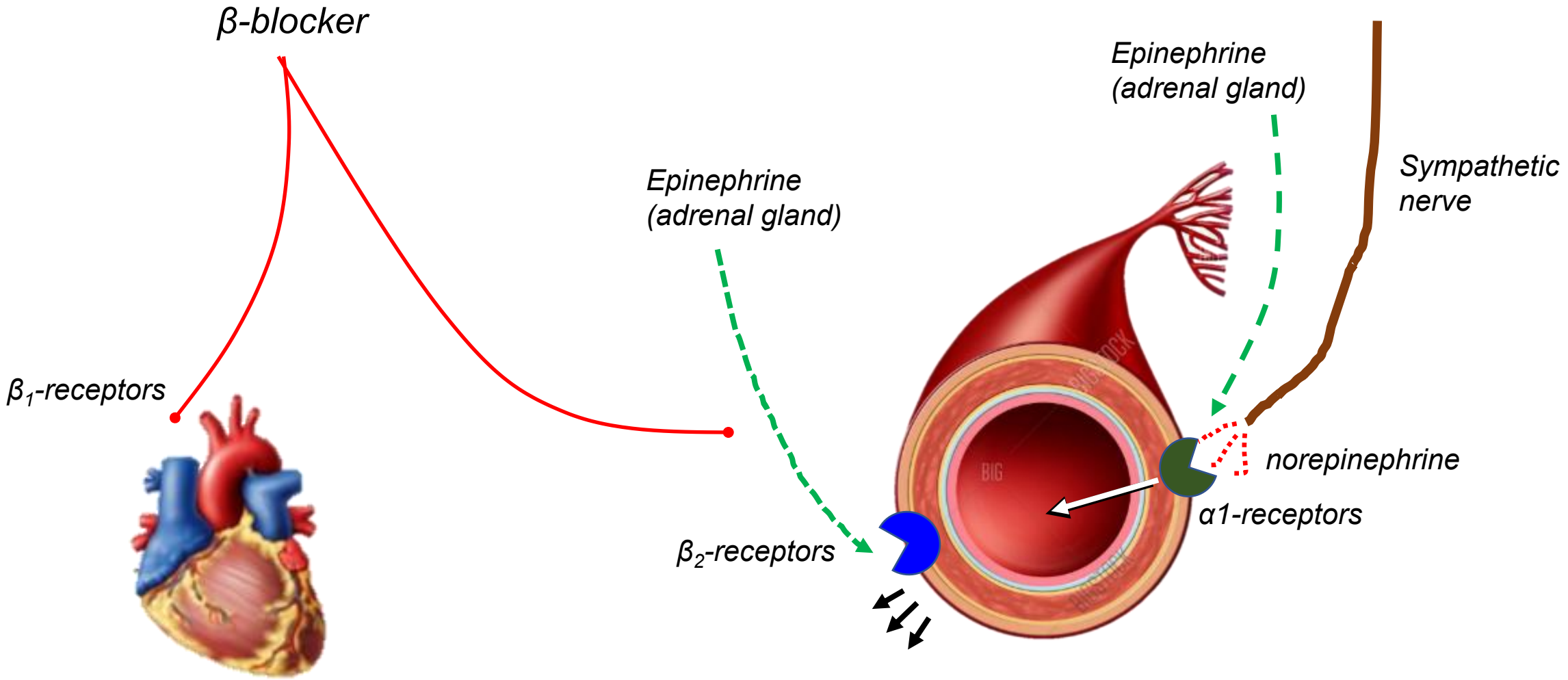
CaM: calmodulin
MLCK: myosin light chain kinase
Ⓟ - phosphate
PDE: phosphodiesterase
PDEi: PDE inhibitor
$PGI_2$: prostacyclin - Treprostinil



Contraction

Relaxation

# Beta blocker effect




- $\beta_2$-receptors: activated by epinephrine
- $\alpha_1$-receptors: require much higher amount of E, mostly under NE

*Hypotensive effect*

*Loss of vasodilation (β2) and presence of vasoconstriction (α1)→ ↑TPR → hypertension*

# Summary of Adrenoreceptors

| Receptor | Second messenger | Primary effect |
|---|---|---|
|  α-1 (peripheral vessel go from relaxed (α) to constricted (I) | ↑ IP3<br>Sensitive more to NE<br>Produce excitation (contraction/constriction) | - *Location:* vascular smooth muscle of the skin, splanchnic region, GI tract, bladder sphincter, iris<br>- *Peripheral vasoconstriction*<br>- Urethral constriction<br>- Pupillary dilation |
| α-2 | ↓cAMP<br>Produce inhibition (dilation/relaxation) | - Relaxation or dilation of smooth muscles GI tract<br>- ↓ insulin release<br>- ↓ intestinal mobility |
|  β-1 organ # 1 HEART | ↑cAMP<br>Very sensitive to NE and E<br>Produce excitation | - Located: SA, AV nodes, heart ventricular muscles<br>- ↑ *Cardiac contractility & HR*<br>- ↑ renin release by JG cells of the kidney |
|  β-2 (two legs, two hands, two lungs) | ↑cAMP<br>Produce relaxation (dilation)<br>More sensitive to E than to NE | - Location: vascular smooth muscle of skeletal muscle, bronchial smooth muscle, walls of GI and bladder<br>- *Peripheral vasodilation*<br>- Bronchodilation<br>- ↑Glucagon release by alpha cells |

# Question 4

## What medication did the patient most likely ingest?

A. Atenolol
B. Esmolol
C. Metoprolol
D. Propranolol

**The patient was initially presenting:**
Pulse 40: Bradycardia
BP 80/46: Hypotension
Lethargy + Wheezing

A Beta-Blockers that would cause both wheezing and lethargy would need to be able to i. cross the blood brain barrier and ii. target and block beta-2 receptors in VSMc in the lungs

| Drug Class | Cardioselective or Nonselective | Cross BBB? | Target β2? | Match this case? |
|---|---|---|---|---|
| **Atenolol** | Cardioselective | **No** | **No** | **No** |
| **Esmolol** | Cardioselective | **No** | **No** | **No** |
| **Metoprolol** | Cardioselective | **No** | **No** | **No** |
| **Propranolol** | Nonselective | **Yes** | **Yes** | **Yes** |

# Question 5

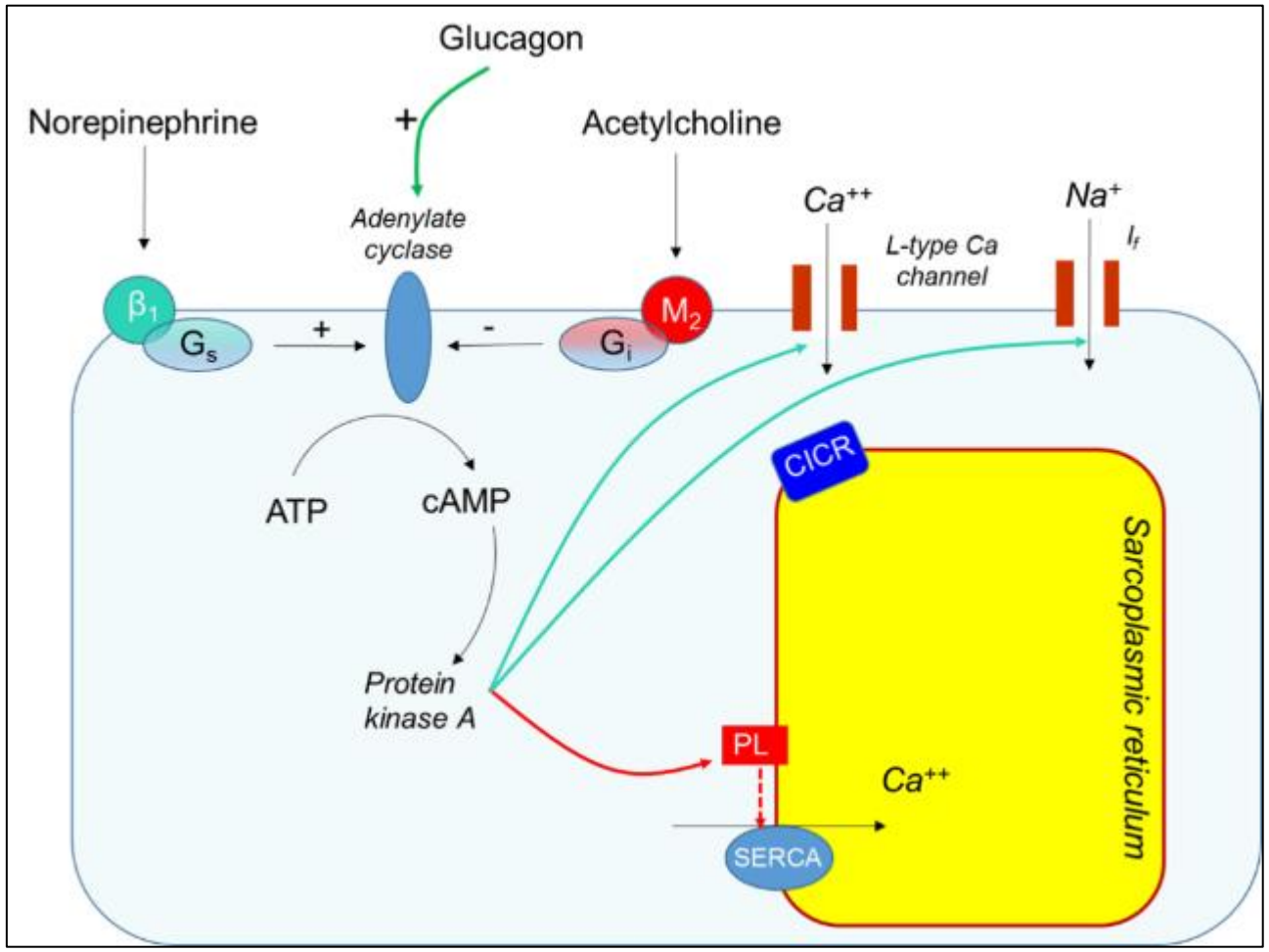
A 2nd medication is given resulting in the following change in his VS.

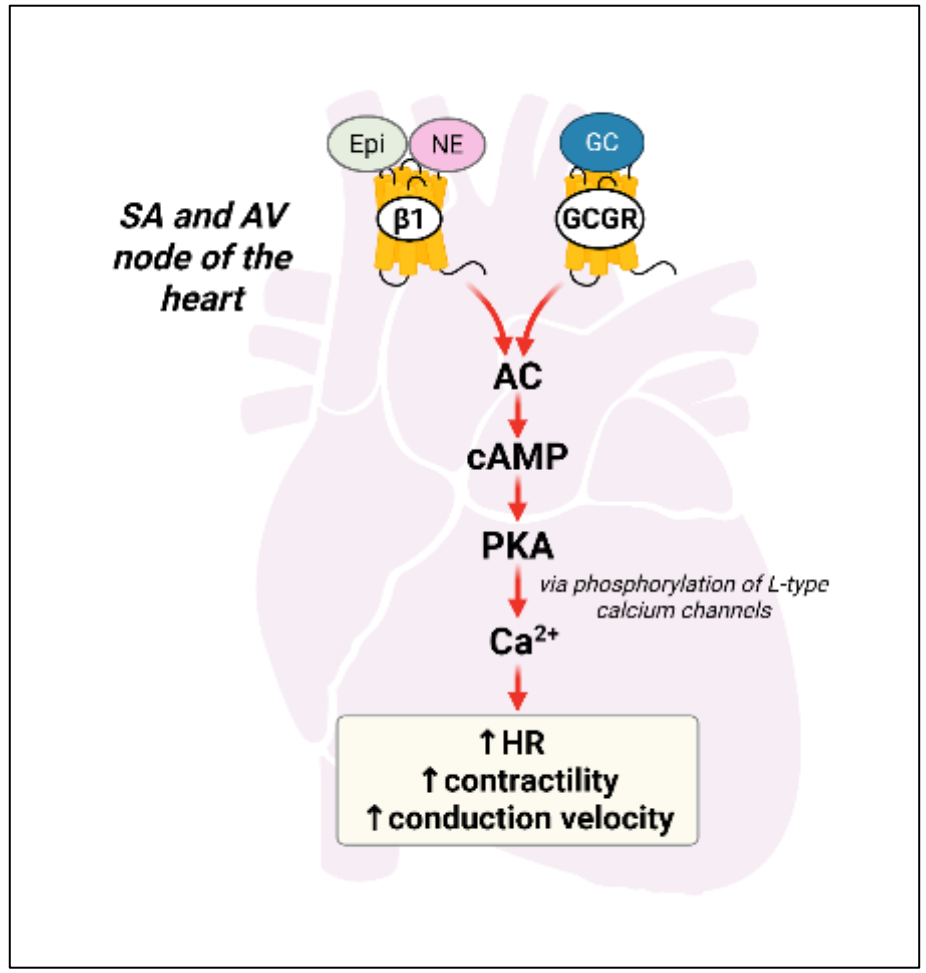
**What physiologic mechanism would best explain these effects?**

| | After ingestion | After medication #1 administration | After medication #2 administration |
|---|---|---|---|
| **Pulse** | 40 | 60 | **86** |
| **Blood Pressure** | 80/46 | 94/54 | **108/65** |

A. Independent activation of cellular adenylate cyclase
B. Increase in cellular cGMP
C. Dopamine D1 receptor stimulation
D. Stimulation of nicotinic receptors
E. Direct inhibition of Na/K ATPase

- Independent activation of myocardial adenylate cyclase **bypasses the impaired β-receptor**
- Activated adenylate cyclase (AC) then **converts ATP** to **cAMP**



# Summary – Beta Blocker Overdose

- A leading cause of poison center calls & a significant cause of severe toxicity & mortality
- β-blockers modulate activity of myocyte & vascular smooth muscle contraction by ↓ calcium entry into the cell
- Excessive β-blockade may lead to profound **pump failure** with bradycardia, ↓ contractility, and hypotension
- Primary organ system affected is the CV system; hallmark of **severe toxicity** is **bradycardia & shock**
- **Nonselective** β-blockers may antagonize the β2-receptor in bronchial smooth muscle causing **bronchospasm**
- Diagnosis of β-blocker toxicity primarily made on clinical grounds, including patient history, physical examination findings, and results of basic diagnostic testing
- **Specific pharmacologic therapies** directed at restoring perfusion to critical organ systems by improving myocardial contractility, increasing heart rate, or both.
  - Includes fluid resuscitation & administration of **adrenergic agonists, glucagon**, high-dose insulin.

All

# Case #2

## Case #2

- A 42-y/o male is transported to the ED by EMS for confusion, vomiting, and shortness of breath.

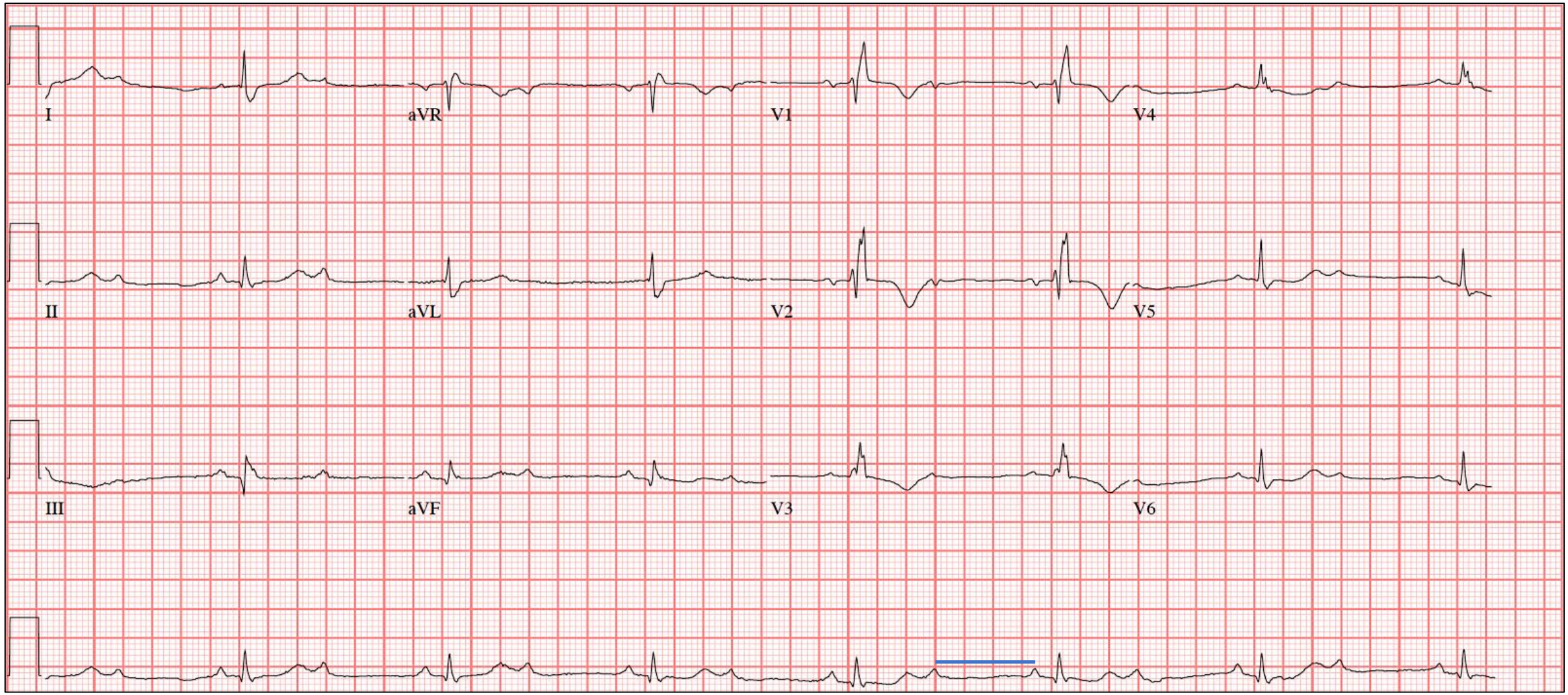
- His has a history of hypertension and depression but can’t recall his medications.

- His only allergies are to bee stings but otherwise has no other medical problems. He admits to working in the yard earlier in the day and going swimming in a local lake but does not recall any bee stings.

# Physical Exam

| | Findings |
|---|---|
| **General Appearance** | Restless; appears to have difficulty breathing. Vomits and has an episode of diarrhea during triage |
| **Vital Signs** | Pulse 42; BP 86/40; RR 24; T 98; Pox 90% |
| **HEENT** | Pupils pinpoint with notable tearing. Oropharynx with copious secretions |
| **Cardiovascular** | Bradycardia; S1 & S2 noted. No murmurs, rubs or gallops |
| **Pulmonary** | Diffuse wheezing with harsh crackles noted at the bases |
| **Gastrointestinal** | Abdomen soft with mild diffuse tenderness. Hyperactive bowel sounds noted |
| **Extremities** | Pale; weak peripheral pulses |
| **Neuro** | CN intact. No focal weakness but fasciculations noted |

# EKG




**Interpret the EKG**

# Question 1

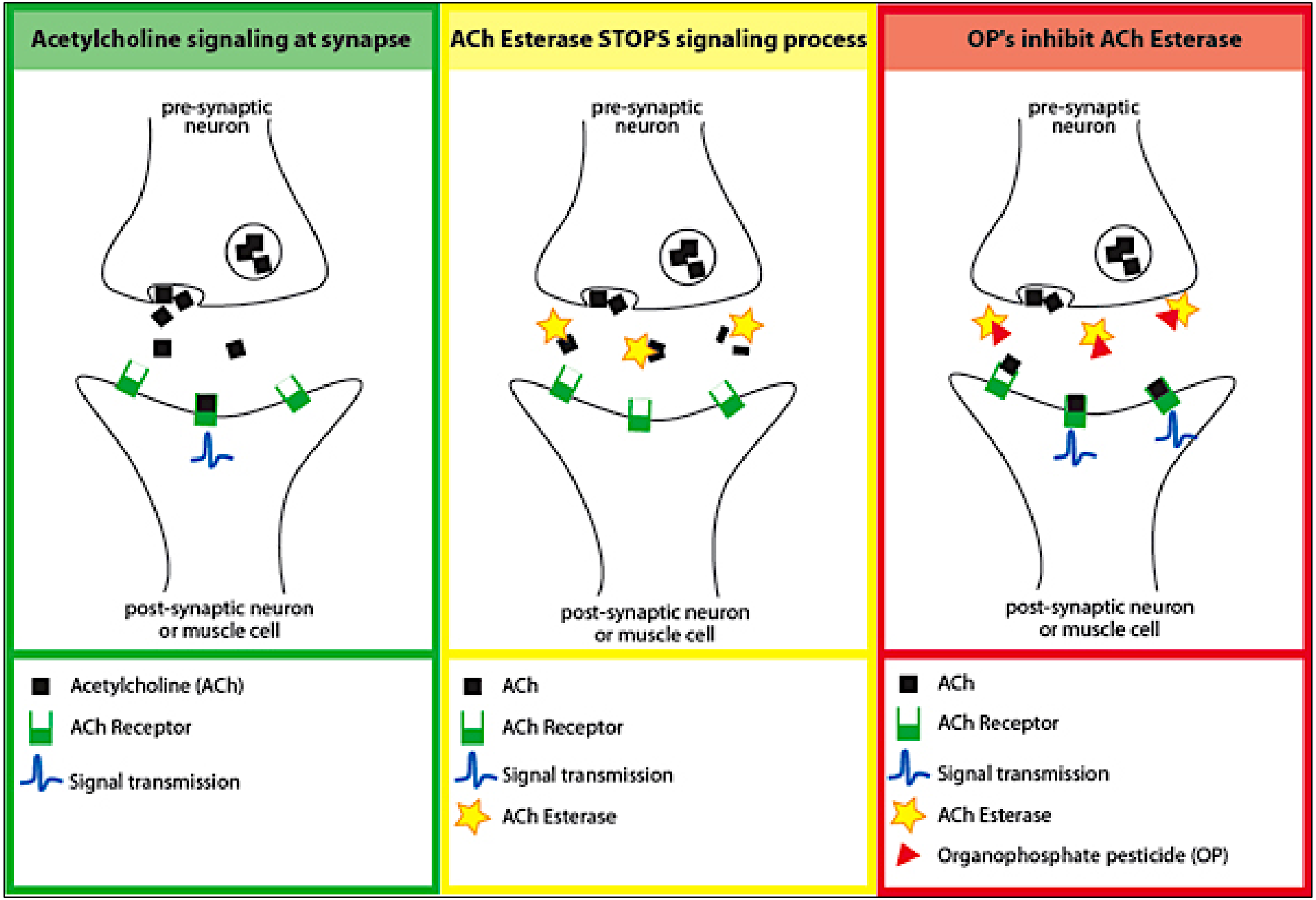
**What component of the autonomic nervous system is most likely affected?**

A. Parasympathetic
B. Sympathetic
C. Enteric
D. Both parasympathetic and sympathetic
E. Both parasympathetic and enteric

# Question 2

## Which of the following agents is most likely to cause his presentation?

A. Alpha-1 receptor blocker
B. Clonidine
C. Cyanide
D. Organophosphate
E. Physostigmine
F. Tricyclic antidepressant


Acetylcholine signaling at synapse
pre-synaptic neuron
post-synaptic neuron or muscle cell
Acetylcholine (ACh)
ACh Receptor
Signal transmission
ACh Esterase STOPS signaling process
pre-synaptic neuron
post-synaptic neuron or muscle cell
ACh
ACh Receptor
Signal transmission
ACh Esterase
OP's inhibit ACh Esterase
pre-synaptic neuron
post-synaptic neuron or muscle cell
ACh
ACh Receptor
Signal transmission
ACh Esterase
Organophosphate pesticide (OP)

# Question 3

An agent is administered IV resulting in the following:
A decrease in oral secretions & pulmonary crackles and VS changes

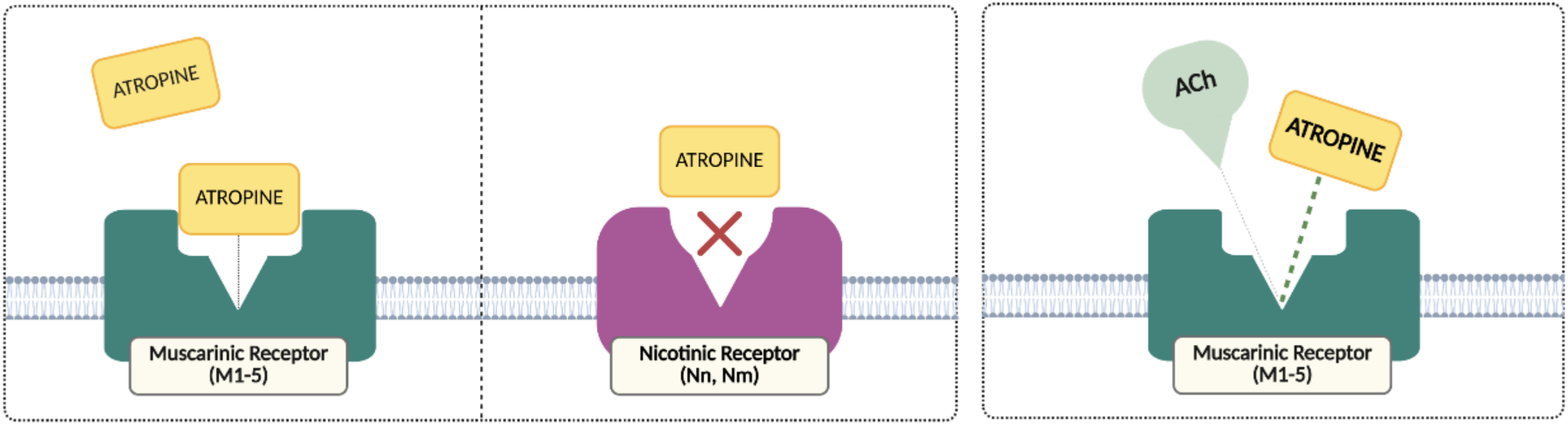
| | Before administration | After medication administration |
|---|---|---|
| Pulse | 42 | 58 |
| Blood Pressure | 86/40 | 94/50 |

**Which agent was most likely administered?**

A. Flumazenil
B. Epinephrine
C. Norepinephrine
D. Atropine
E. Edrophonium

# **Atropine** - key antidote

- Competitive antagonist of acetylcholine at central & peripheral muscarinic receptors
- Reverses effects of excessive cholinergic stimulation



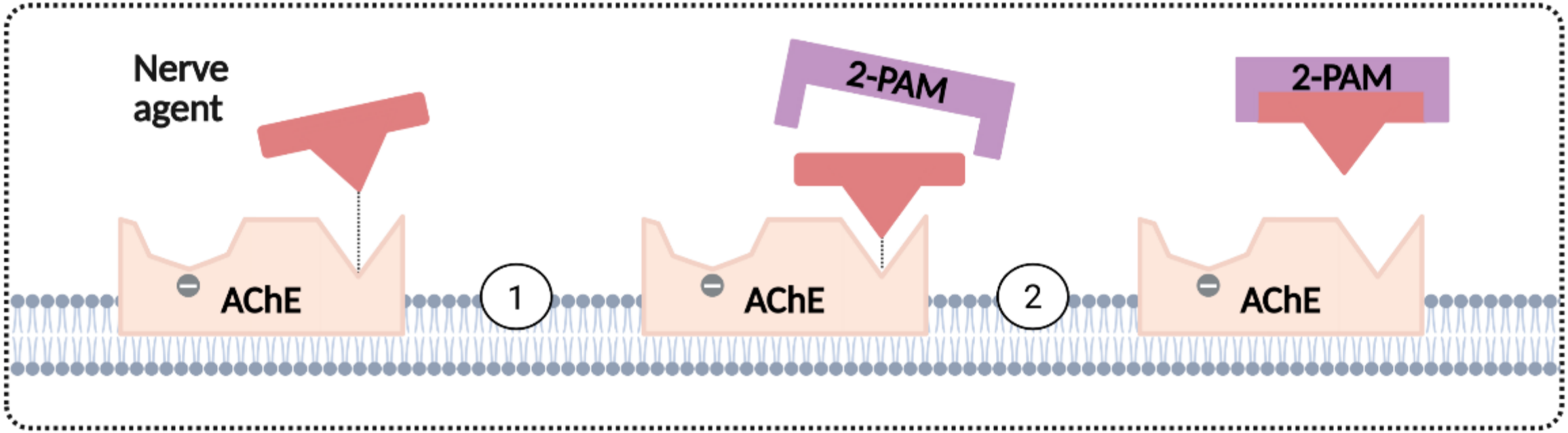
# Question 4

**Based on autonomic pathophysiology, what other agent should be administered?**

A. Pralidoxime
B. Physostigmine
C. Donepezil
D. Methyldopa
E. Diphenhydramine

# Pralidoxime

- Displaces organophosphates from active site of acetylcholinesterase
- Reactivates the enzyme



# Compare & Contrast Our 2 Cases

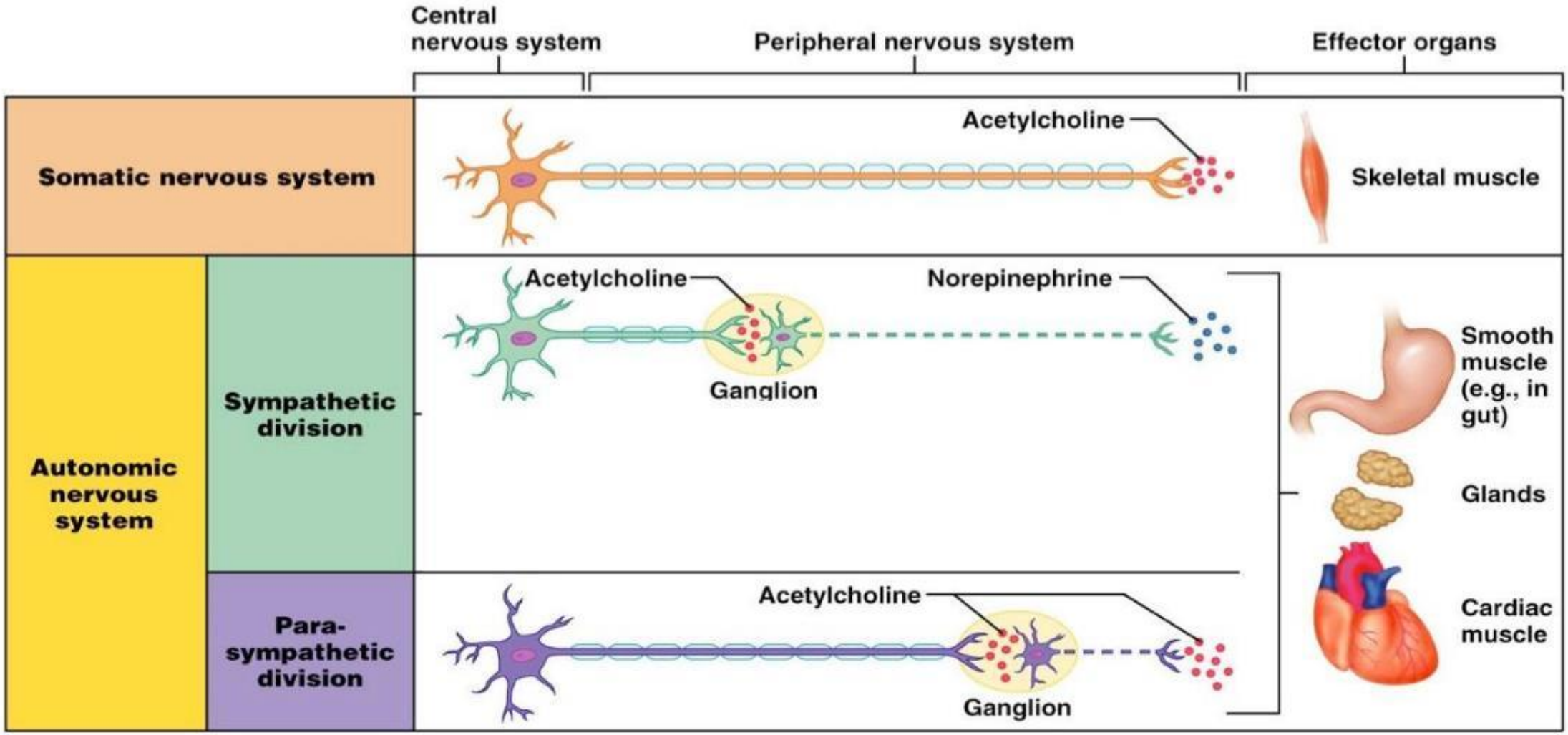
| | Cholinergic Crisis 2º to Organophosphates | Beta Blocker Overdose |
|---|---|---|
| **Pulse** | 42 | 40 |
| **Blood Pressure** | 86/40 | 80/46 |
| **Pupils** | Pinpoint; tearing | Midpoint |
| **Mucosa** | Copious secretions | Dry |
| **Cardiovascular** | Bradycardia | Bradycardia |
| **Respiratory** | Harsh crackles at bases; wheezing | Wheezing |
| **Gastrointestinal** | Mild tenderness; Hyperactive bowel sounds; vomiting; diarrhea | Soft, non-tender |
| **Neuro** | Fasciculations | Lethargic, disoriented |

# Summary - Organophosphates

- Organophosphate compounds are insecticides most commonly associated with systemic illness
- Organophosphates bind to and inhibit the enzyme cholinesterase; can be used **as chemical weapons**
- Inhibition of cholinesterase leads to acetylcholine accumulation at nerve synapses and NMJ, resulting in **overstimulation** of acetylcholine receptors.
- Acute poisoning results in **CNS, muscarinic, nicotinic, and somatic motor** manifestations
- Excess acetylcholine results in a cholinergic crisis that manifests as a central and peripheral clinical toxidrome (**SLUDGE** or **DUMBELLS**)
- **Miosis & muscle fasciculations** are considered reliable signs of organophosphate toxicity
- **Atropine** is the antidote for organophosphate poisonings. Atropine, a competitive antagonist of acetylcholine, will reverse the effects $2^{o}$ to excessive cholinergic stimulation.
- **Pralidoxime** used to displace organophosphates from active site of acetylcholinesterase - reactivates the enzyme.

All

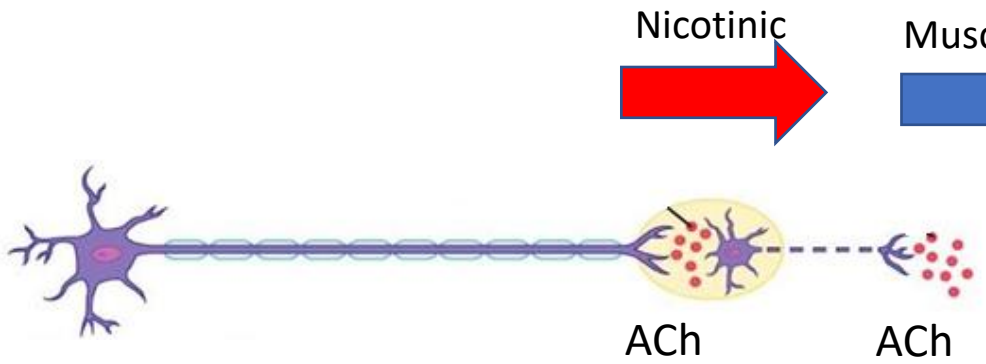
# Sympathetic, Parasympathetic, and Somatic Innervation

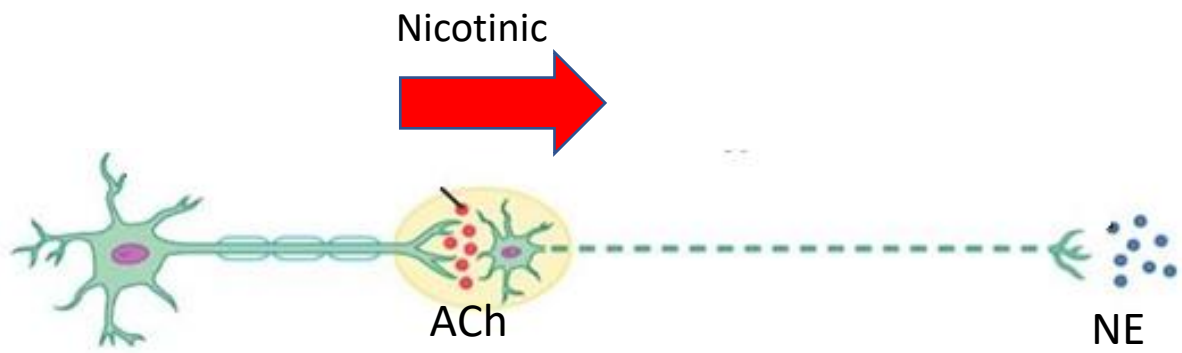


Parasympathetic

Sympathetic

# MUSCARINIC VERSUS NICOTINIC STIMULATION



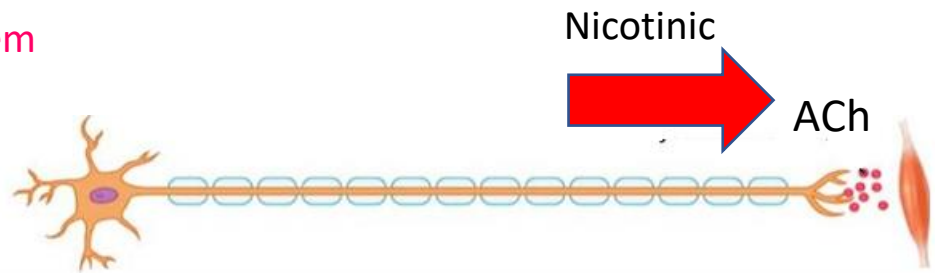

Muscarinic effect signs (activation of parasympathetic system):
Bronchoconstriction
↑ bronchial secretion
Salivation
Lacrimation
Sweating
Nausea
Vomiting
Diarrhea
Miosis (muscarinic sign)
Slow heart rate (?)

**SLUDGE:** effects indicative of massive discharge of the parasympathetic nervous system (salivation, lacrimation, urinary incontinence, defecation, GI distress, emesis (vomiting)

Nicotinic effect signs (activation both sympathetic and parasympathetic):
Activation both sympathetic and parasympathetic. Manifested by the signs which are originally get more sympathetic innervation
Cyanosis, elevated blood pressure (nicotinic sign)

CNS effect (anxiety, restlessness, confusion, headache)

Somatic nervous system effects:
Twitching
Fasciculation
Muscle weakness




Nicotinic effect can be achieved by inhibition of acethycholinesterase → stimulation of all types of cholinergic neurons: sympathetic, parasympathetic, somatic

Thanks so Much!!!!