Organophosphate Poisoning

- Organophosphates are a common class of insecticides. But large doses of organophosphates can also harm people and other animals. Organophosphate poisoning can occur when you're exposed to them for too long or at high levels.
- Organophosphates are typically colorless-to-brown liquids at room temperature. Some may be unscented, while others have a fruit-like smell.

Overview

- say as many as 25 million agricultural workers across the developing world have at least one episode of organophosphate poisoning per year. It's being seen with more frequency in areas where there is limited access to insecticide safety gear, such as suits and breathing apparatuses.
- Terrorist use of organophosphates is rare, but it has occurred. Sarin, an organophosphate poison, has been ntentionally used twice in terrorist attacks in Japan.

Mechanism of Action

- inhibiting acetylcholinesterase, the indirect-acting drugs increase the endogenous acetylcholine concentration in synaptic clefts and neuroeffector junctions. The excess acetylcholine, in turn, stimulates cholinoceptors to evoke increased responses. These drugs act primarily where acetylcholine is physiologically released and are thus amplifiers of endogenous acetylcholine.

Mild organophosphate exposure symptoms

- narrowed, pinpointed pupils
- impaired, blurry vision
- stinging eyes
- runny nose
- watery eyes
- excess saliva
- glassy eyes
- headache
- nausea
- muscle weakness
- muscle twitching
- agitation

Moderate signs of OPs exposure

- very narrowed pupils
- dizziness
- disorientation
- coughing and wheezing
- sneezing
- difficulty breathing
- drooling or excessive phlegm
- muscle twitching and tremors
- muscle weakness
- fatigue
- severe vomiting and diarrhea
- involuntary urination and defecation

Emergency signs of OPs poisoning

- very narrowed pupils
- confusion
- agitation
- convulsions
- excessive body secretions, including sweat, saliva, mucus, and tears
- irregular heartbeat
- collapse
- respiratory depression or arrest
- coma

Anti Dote

- Atropine causes reversible blockade of cholinomimetic actions at muscarinic receptors; that is, blockade by a small dose of atropine can be overcome by a larger concentration of acetylcholine or equivalent muscarinic agonist.

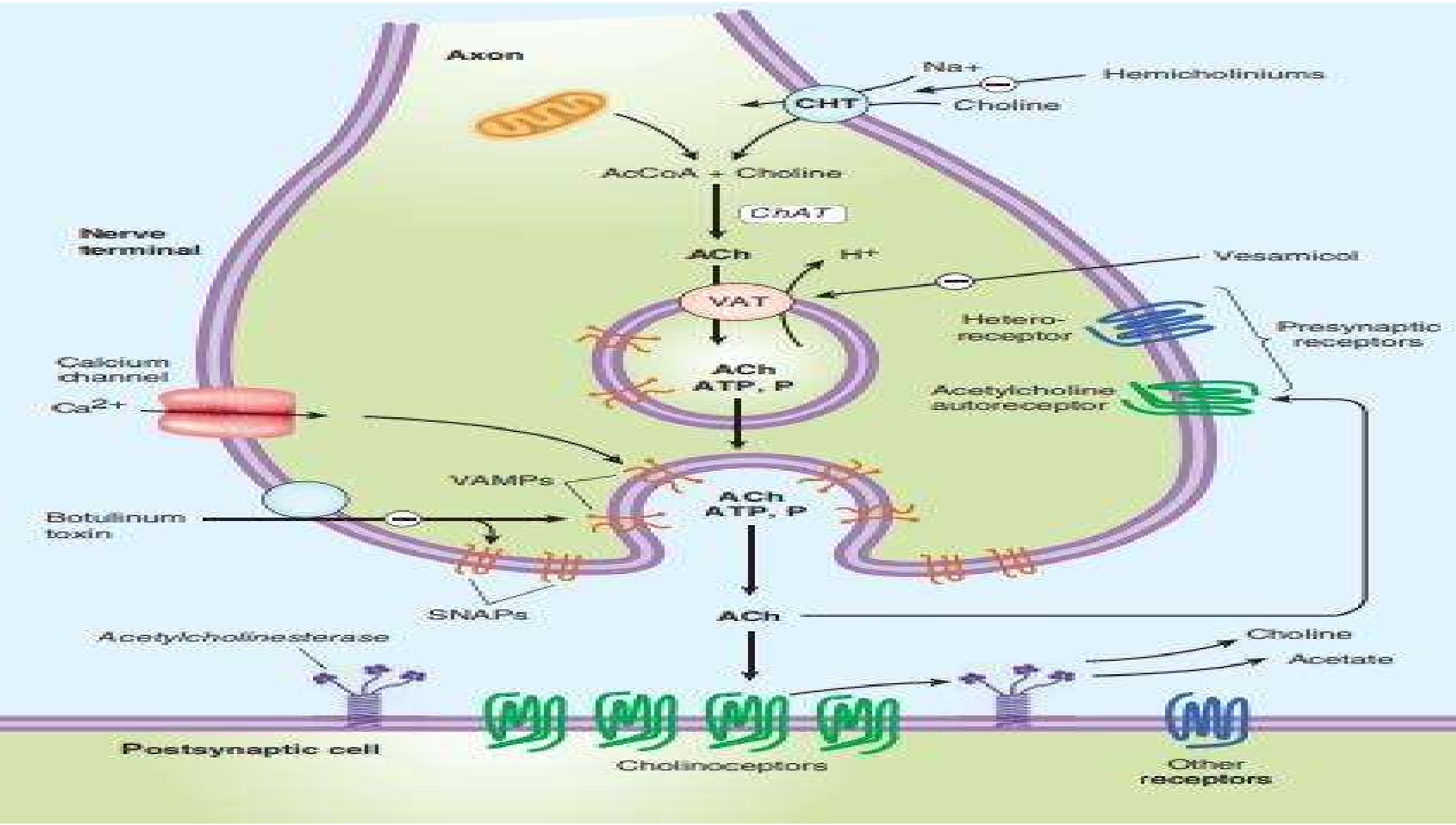
Axon
Na+
Hemicholiniums
CHT
Choline
AcCoA + Choline
ChAT
Nerve terminal
ACh
H+
Vesamicol
VAT
Hetero-receptor
Presynaptic receptors
Calcium channel
Ca2+
ACh ATP, P
Acetylcholine autoreceptor
VAMPs
ACh ATP, P
Botulinum toxin
SNAPs
ACh
Acetylcholinesterase
Choline
Acetate
Postsynaptic cell
Cholinoceptors
Other receptors

TABLE 8–1 Muscarinic receptor subgroups important in peripheral tissues and their antagonists.

Property	Subgroup		
	M_1	M_2	M_3
Primary locations	Nerves	Heart, nerves, smooth muscle	Glands, smooth muscle, endothelium
Dominant effector system	↑ IP_3, ↑ DAG	↓ cAMP, ↑ K^+ channel current	↑ IP_3, ↑ DAG
Antagonists	Pirenzepine, telenzepine, dicyclomine,[1] trihexyphenidyl[2]	Gallamine,[3] methoctramine, AF-DX 116[4]	4-DAMP,[4] darifenacin, solifenacin, oxybutynin, tolterodine
Approximate dissociation constant[5]			
Atropine	1	1	1
Pirenzepine	25	300	500
AF-DX 116	2000	65	4000
Darifenacin	70	55	8

Cholinoceptors		
Muscarinic M_1	CNS neurons, sympathetic postganglionic neurons, some presynaptic sites	Formation of IP_3 and DAG, increased intracellular calcium
Muscarinic M_2	Myocardium, smooth muscle, some presynaptic sites; CNS neurons	Opening of potassium channels, inhibition of adenylyl cyclase
Muscarinic M_3	Exocrine glands, vessels (smooth muscle and endothelium); CNS neurons	Like M_1 receptor-ligand binding
Muscarinic M_4	CNS neurons; possibly vagal nerve endings	Like M_2 receptor-ligand binding
Muscarinic M_5	Vascular endothelium, especially cerebral vessels; CNS neurons	Like M_1 receptor-ligand binding
Nicotinic N_N	Postganglionic neurons, some presynaptic cholinergic terminals; pentameric receptors typically contain α- and β-type subunits only (see Chapter 7)	Opening of Na^+, K^+ channels, depolarization
Nicotinic N_M	Skeletal muscle neuromuscular end plates; receptors typically contain two α_1- and β_1-type subunits in addition to γ and δ subunits	Opening of Na^+, K^+ channels, depolarization