Organophosphate Poisoning

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BY :

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Organo Phosphate Poison

- **Chief complain**:
  - Epigastric Pain
  - Headache
  - Slurred speech
  - Altered behaviour(not oriented with time)

- Presenting the case of 30 year old female patient admitted in new civil hospital in female medicine ward on dated 19/10/2016 at 10:40pm
- The police was informed since when poisoning was detected and it underwent the case of MLC i.e Medico Legal Case
- History of ingestion of Bug Killing Medicine

- **On Examination**
  - Pupil was pin point

Normal Pupil - The normal pupil size in adults is 2-4 mm in diameter in bright light and 4-8 mm in dark

Pin point pupil - When the size of pupil reduces below 2mm in diameter under normal lighting condition

Pin-Point pupil and Normal pupil

Investigation

BIOCHEMICAL TEST [ON 20/10/2016]

Examination	Results	Reference Range
RBS	256	<200 mg/dl

Examination	Reference Range
Fasting Blood Sugar	70-110 mg/dl
Post prandial Blood Sugar	<140 mg/dl
Random Blood Sugar	<200 mg/dl

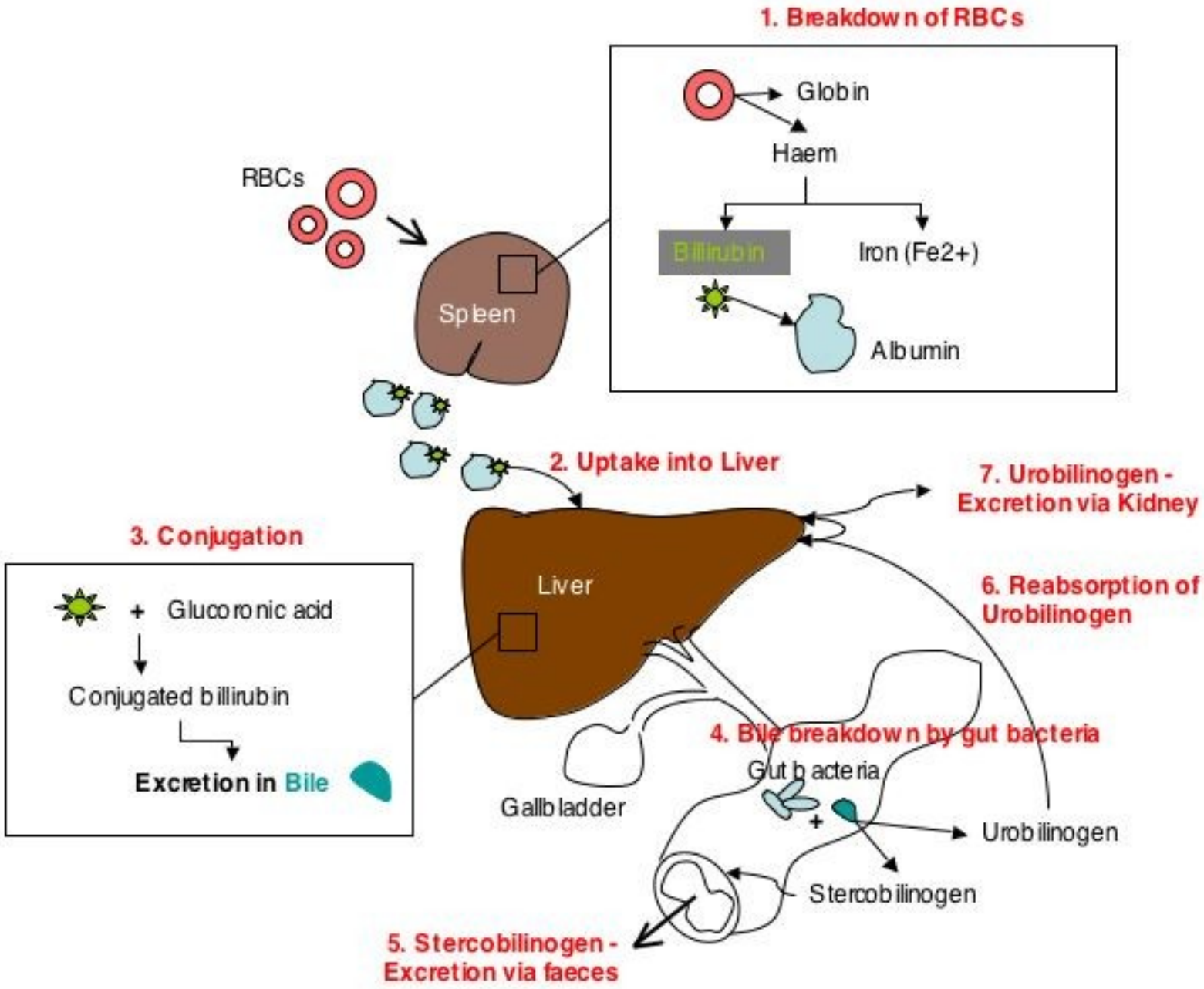
Date[20/10/2016]

Examination	Results	Reference Range
Albumin	4.2	3.5-5.2 gm/dl
Alkaline Phosphatase	71	42-128 IU/L
ALT	Not done	<45 IU/L
Bilirubin direct	0.3	<.4mg/dl
Bilirubin Total	0.7	<1.3 mg/dl
Bilirubin indirect	0.4	<1.3 mg/dl
Calcium	8.6	8.6-10.2 mg/dl
Cholinesterase	**129**	**3700-13400 IU/L**
Creatinine	0.6	.8-1.3 mg/dl
Pottasium	**2.57**	**3.5-5.1 mmol/L**

- **Albumin** -One type of plasma protein. It is water soluble, synthesized in liver, it decreases in liver and kidney disease

- **Alanine Transaminase[ALT]** -It is found in plasma and in various body tissues but it's more common in liver

- **Alkaline Phosphatase** – It is hydrolyse enzyme responsible for removing phosphate groups from many types of molecules including nucleotides, proteins and alkaloids.


1. Breakdown of RBCs
Globin
Haem
Billirubin
Iron (Fe2+)
Albumin
RBCs
Spleen
2. Uptake into Liver
7. Urobilinogen - Excretion via Kidney
3. Conjugation
+ Glucoronic acid
Conjugated billirubin
Excretion in Bile
Liver
6. Reabsorption of Urobilinogen
4. Bile breakdown by gut bacteria
Gut bacteria
Gallbladder
+
Urobilinogen
Stercobilinogen
5. Stercobilinogen - Excretion via faeces

Cholinesterase

- Cholinesterase is an esterase that lyses choline based esters.
- Catalyses the hydrolysis of these cholinergic neurotransmitters such as breaking acetylcholine into acetic acid and choline

Location:-

1.Synaptic cleft
2.RBC
3.Blood Plasma

Pseudocholinesterase

- Cholinesterase which is present in plasma, it is called as Pseudocholinesterase.
- It is also affected in same manner as like cholinesterase which is present at synaptic cleft.

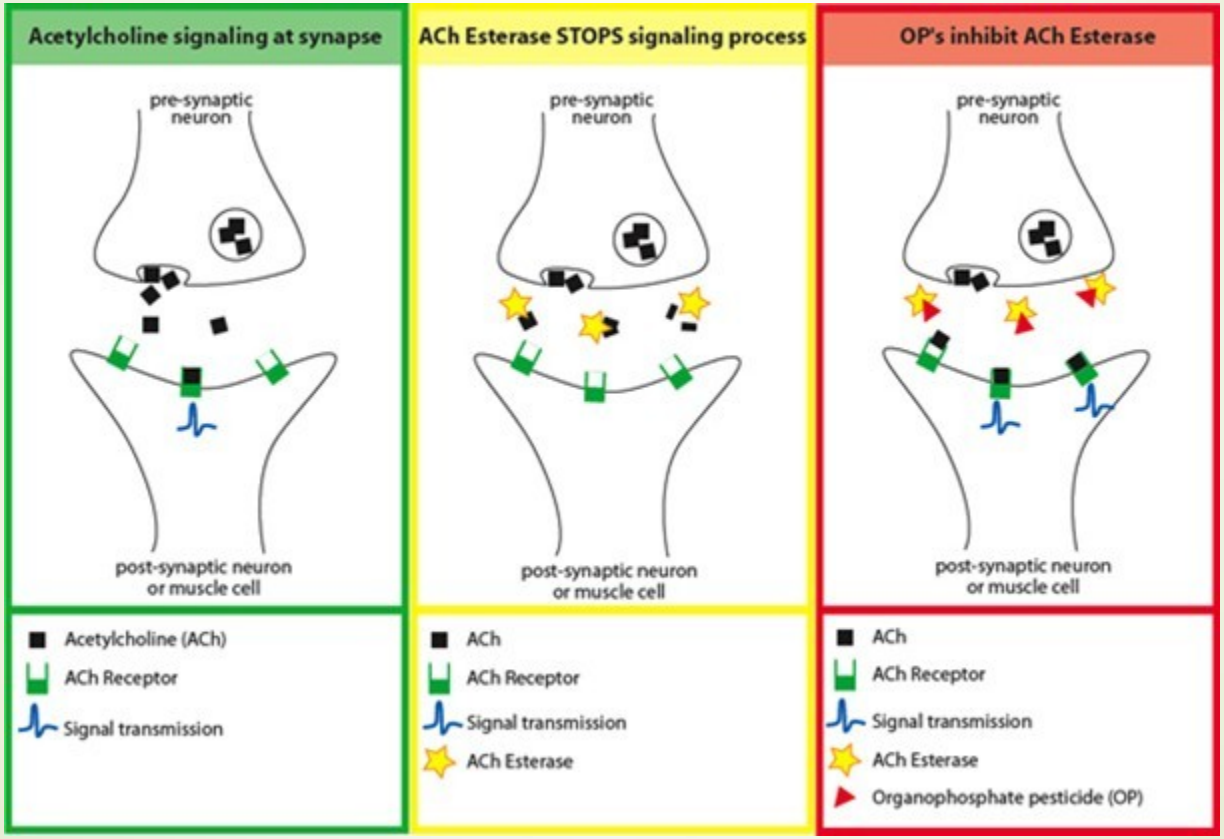
- We are measuring plasma cholinesterase or pseudocholinesterase for diagnosis because

- easy to measure
- easily available

- 50% reduction in normal values :Diagnostic [baseline values usually NA]

- Progressive increase in pseudocholiesterase with treatment

Mechanism Of Action



Date[20/10/2016]

Examination	Result	Reference Range
Potassium	3.74	3.5-5.1mmol/l
Sodium	141.97	136-145 mmol/L

Treatment given

- Gastric lavage was done and it sent to forensic science laboratory for test
- Atropine Injection
- PAM Injection[Pralidoxime injection]
  - 1-2 gm for 15-30 minutes infusion repeat in 1 hour if necessary

- The blood pressure and pupil size was monitored every hour from 2:00 AM
- It was noticed that pupil size was increasing

Organophosphate poison

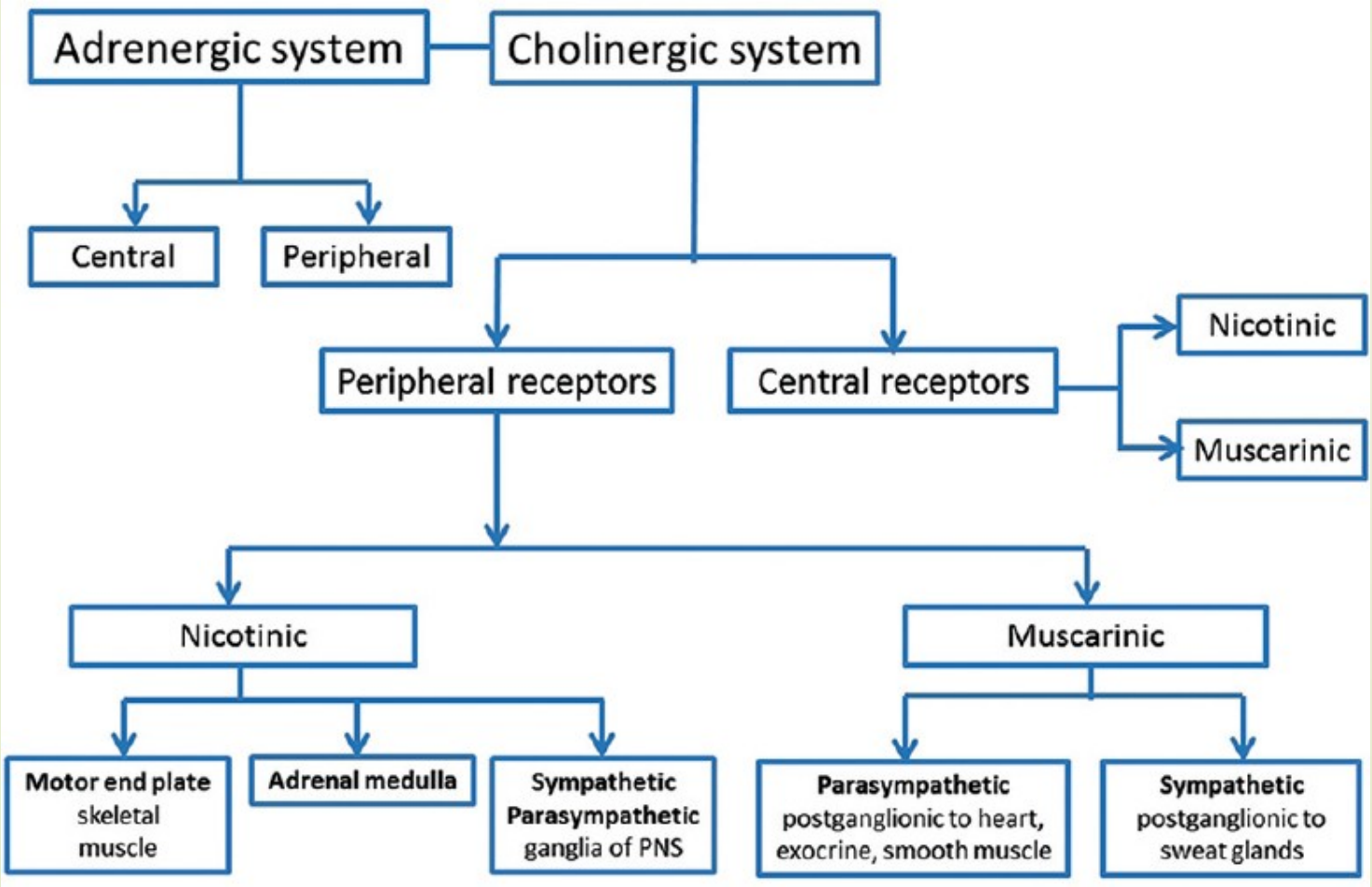
Name of Organophosphate poison

WHO CLASSIFICATION

HIGHLY TOXIC	MODERATELY TOXIC
Phosphamidon	Malathion
Ethyl Parathion	Fenthion
Methyl parathion	Temephos
Chloro thiophos	Fenithrothin
Carbo phenothion	Diazinon

Route of exposure

Autonomic nervous system



Symptoms and signs of organophosphate poisoning based on receptors involved

Type of receptor	Receptor sub-type	Action on	Manifestation
Nicotinic receptor stimulation	N1 (Nm) receptors	Neuromuscular junction	Weakness, fasciculations, cramps, paralysis
	N2 (Nn) receptors	Autonomic ganglia	Tachycardia, hypertension
		Adrenal medulla	
Muscarinic receptor stimulation	M1-M5*	Central nervous system	Anxiety, restlessness, ataxia, convulsions, insomnia
			Dysarthria, tremors, coma, respiratory depression
			Circulatory collapse
	M2 receptor	Heart	Bradycardia, hypotension
	M3, M2 receptor*	Pupils	Blurred vision, miosis
	M3, M2 receptors*	Exocrine glands	Respiratory-rhinorrhea, bronchorrhea
			Gastrointestinal-increased salivation, diarrhea
			Ocular-increased lacrimation
			Others-excessive sweating
	M3, M2 receptors*	Smooth muscles	Bronchospasm, abdominal pain, urinary incontinence

*M1 receptors play a critical role in cognitive function; M3 receptor effect predominates in the pupils, airway smooth muscles and mucus glands. Nicotinic receptors are sub-typed as N1 or Nm receptors and N2 or Nn receptors. Muscarinic receptors are sub-typed from M1 to M5

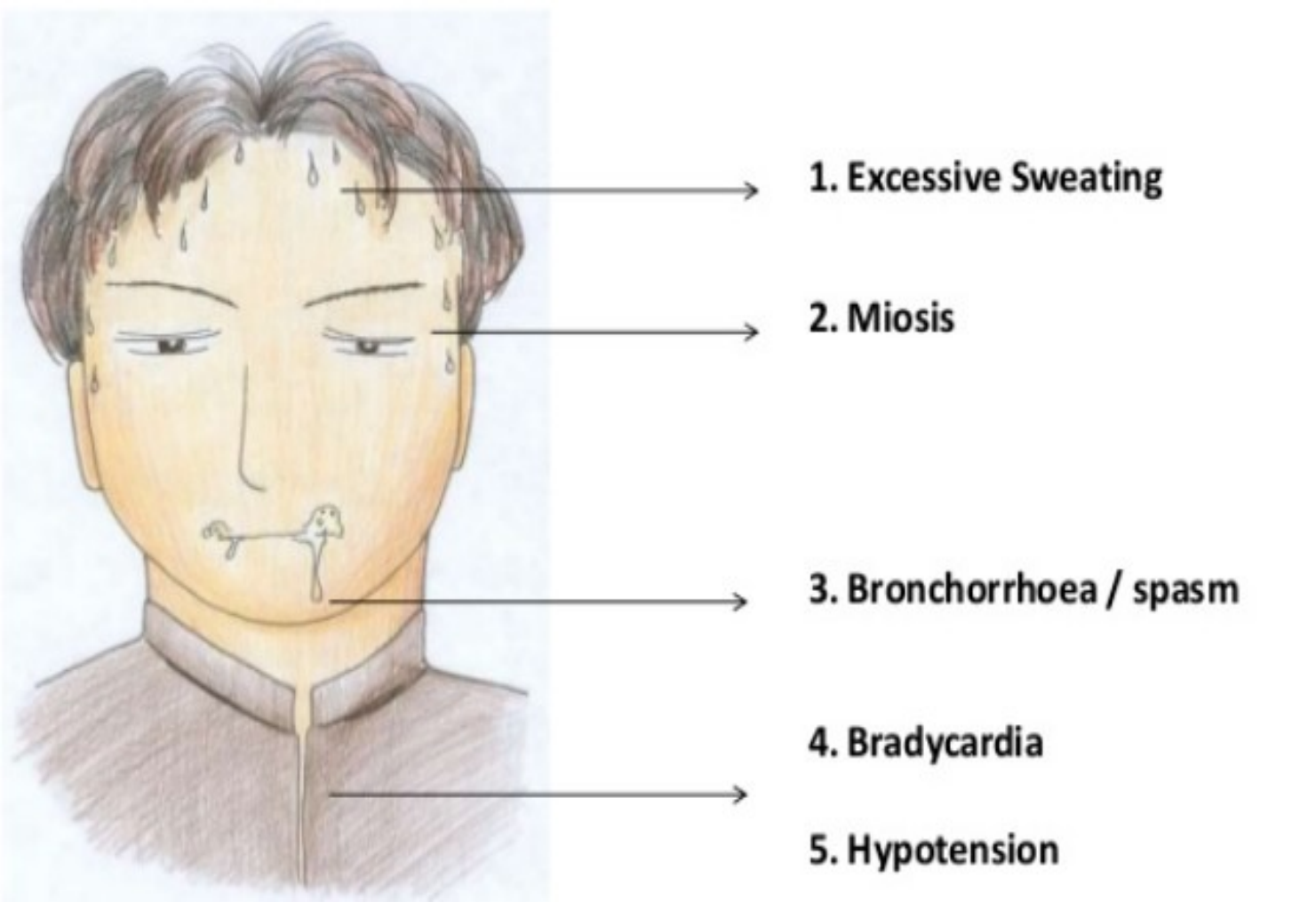
Phases Of OP Poisoning

1. Acute OP Poisoning (within 24 hour of exposure)
   - -Muscarinic Features
   - -Nicotinic Features
   - -CNS Features
2. Intermediate syndrome[1-2 days]
3. Delayed neuropathy[24hours-2 weeks]
4. Neuro psychiatric disorder[After 2 weeks]

1. Acute O-P poisoning

MUSCARININC FEATURES	NICOTINIC FEATURES	CNS FEATURES
D iarrhoea	Muscle weakness	Fatigue
U rination	Muscle fasiculations	Confusion
M iosis	Muscle paralysis	Unconsciousness
B ronchorrhea **B** ronchospasm		Seizues
E mesis	Hypertension	Ataxia
L acrimation	Tachycardia	Resp. depression
S alivation **S** weating		

MUSCARINIC EFFECT



BRONCHORRHOEA

- Early cause of mortality
- Excess fluid secretions in airway
- Obstructions of upper and lower airways
- Pulmonary edema--hypoxia--death

INTERMEDIATE SYNDROME

- 24-96 hours after poisoning after the cholinergic phase settles
- Excess Ach at neuromuscular junction cause down regulation of nicotinic receptors
- Characterized by proximal neck muscle weakness leading to respiratory distress and failure
- Lasts for few days to about 3 weeks

OPIDP
[OP Induced Polyneuropathy]

- Delayed, rare, neurotoxic effect.
- 1-5 weeks after severe acute poisoning due to slow release of OP from body fat.

Diagnosis of OP Poisoning

Diagnosis is mainly clinically based on

1. H/o-Ingestion of poison.
2. Characteristic clinical features.
3. Clinical improvement after atropine/oxime given.
4. Inhibition of cholinesterase activity.

Other Tests of Prognostic Value

A. Hyperglycemia

B. Neutrophilic leucocytosis

C. Proteinuria / glycosuria

D. Blood pH [acidosis]

Reasons of High Glucose Level

Hyperglycemia in OP Poison

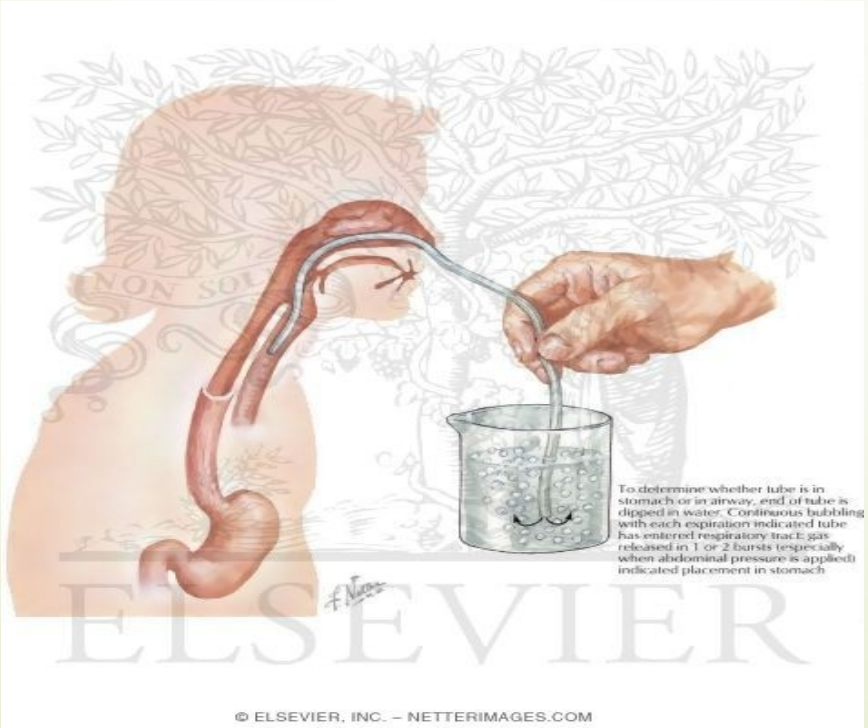
1.Oxidative stress .
2.Renal Tubular damage.
3.Stimulations of Adrenal Glands.
4.Release of catecholamines.

Treatment given

- Gastric lavage was done and it sent to forensic science laboratory for test.
- Atropine Injection
- PAM Injection[Pralidoxime injection]
  - 1-2 gm 15-30 minutes infusion repeat in 1 hour if necessary

GASTRIC LAVAGE

- It is the process of cleaning out the contents of the stomach.It has been used as a mean of eliminating poisons in stomach.



ATROPINE

- MUSCARINIC ANTAGONISTS

- AIM OF THEORY:ATROPINE

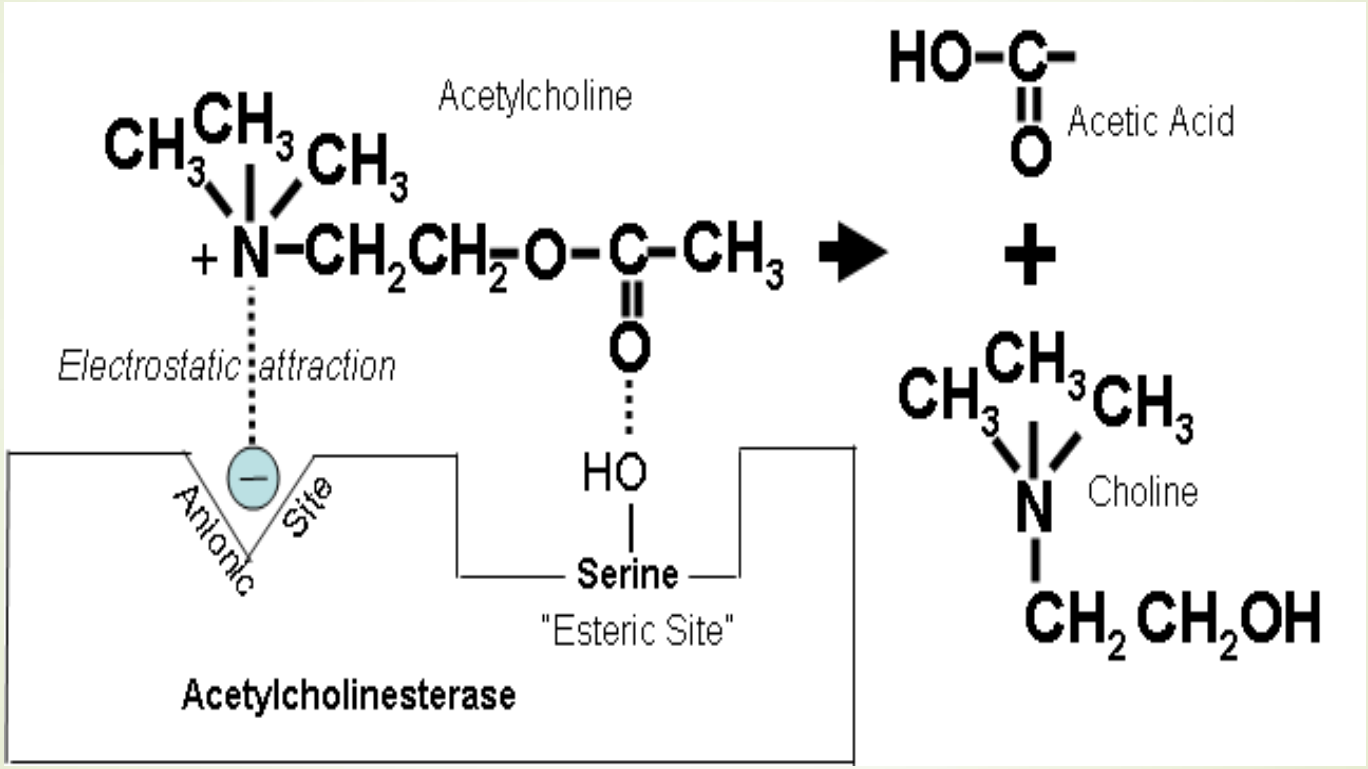
-To reverse cholingeric features

-To improve cardiac and respiratory functions

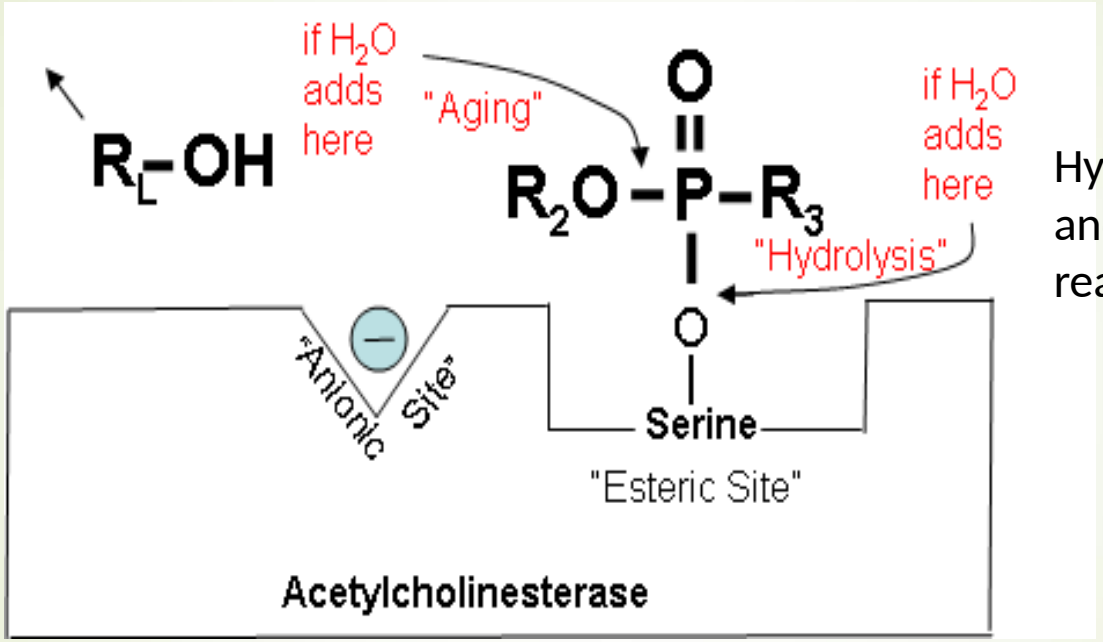
- TARGET END POINTS OF : **ATROPINIZATIONS**
  1. Drying of pulmonary secretions
     I.e-Clear lung fields on auscultation
  2. Heart Rate>80 beats/min
  3. SBP>80mmHg
  4. Pupils:No Longer pinpoint
  5. Dry Axilla
  6. Bowel sounds:just present

PAM Injection (PRALIXODIME INJECTION)

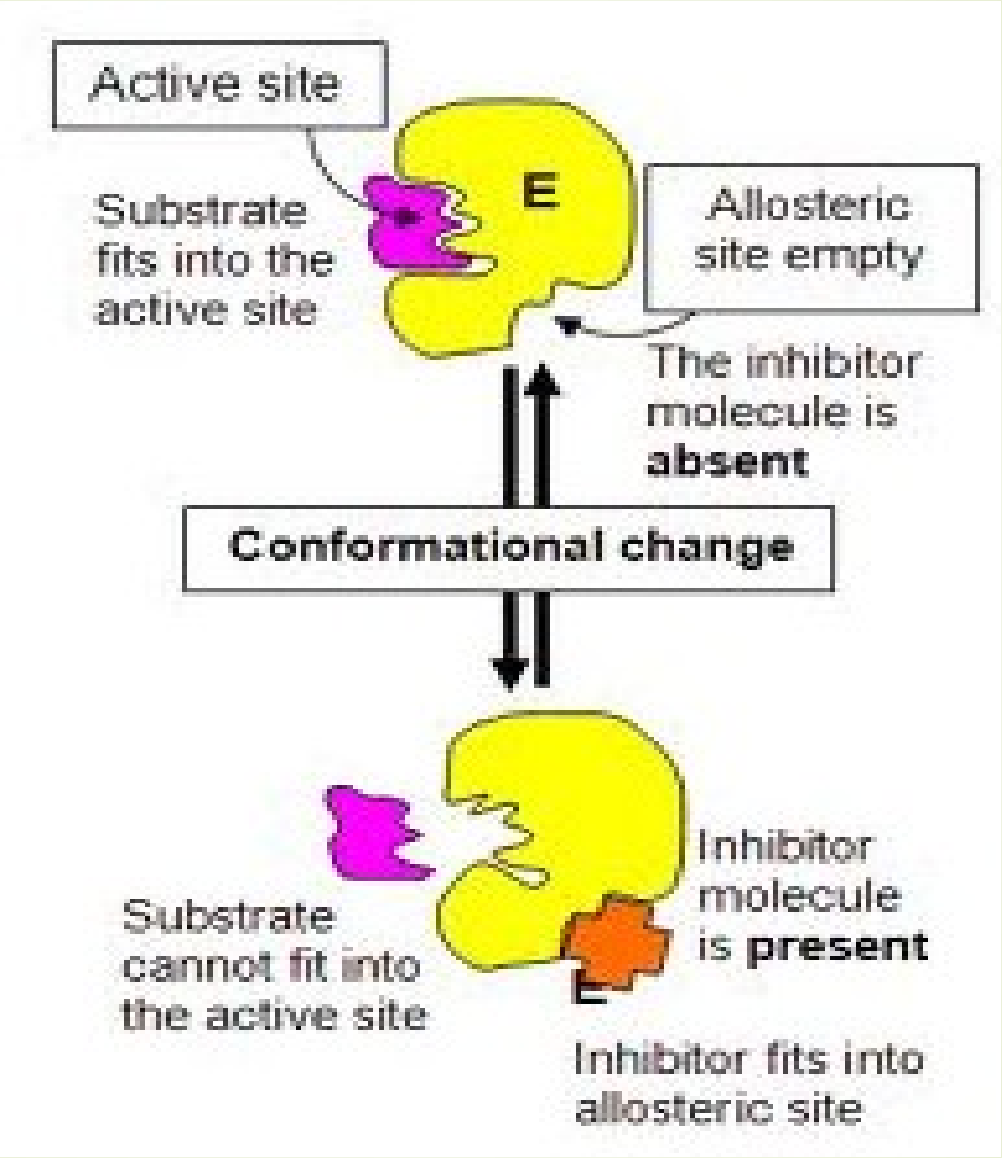
- PAM Injection belongs to group of compounds called oximes that bind to organophosphate inactivated acetylcholinesterase


Acetylcholine
Electrostatic attraction
Anionic Site
Serine
"Esteric Site"
Acetylcholinesterase
Acetic Acid
Choline

Aging occure

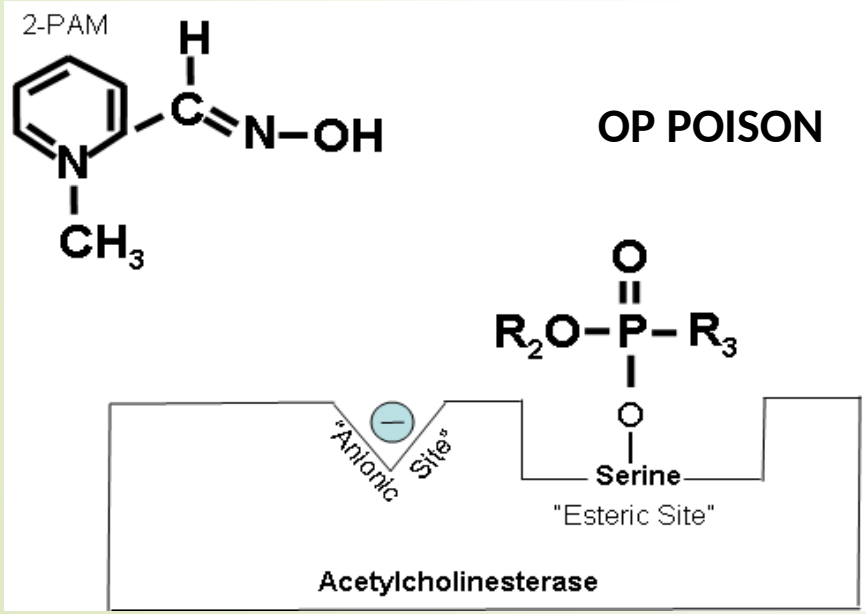


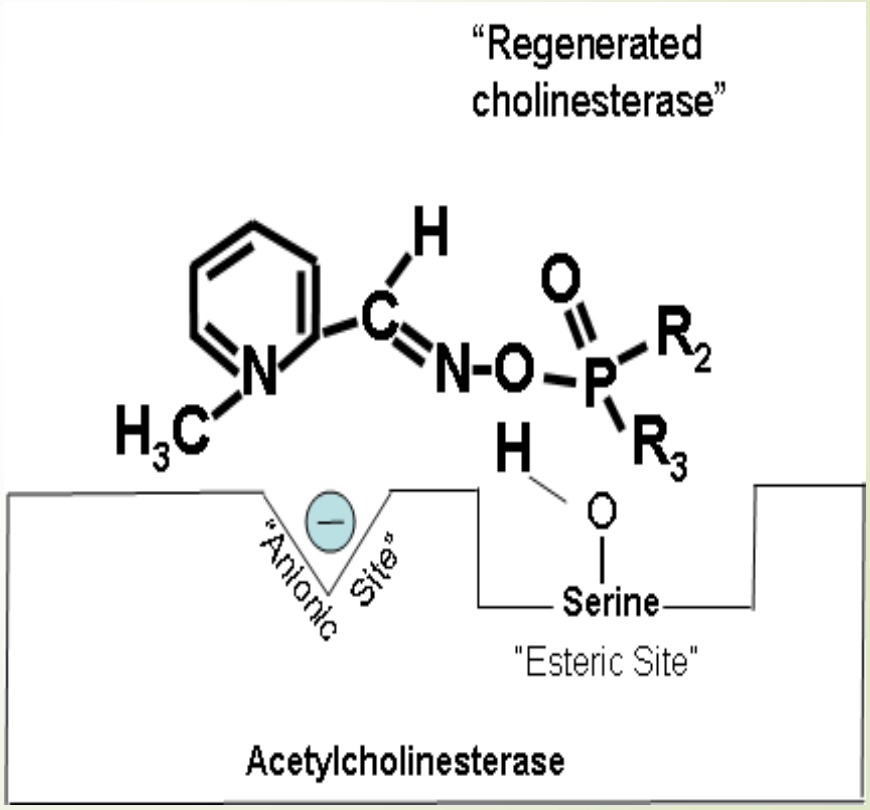
Hydrolysis occure and enzyme reactivated


Active site
Substrate fits into the active site
E
Allosteric site empty
The inhibitor molecule is absent
Conformational change
Substrate cannot fit into the active site
Inhibitor molecule is present
Inhibitor fits into allosteric site

Action Of PAM

PAM





- What are the organophosphate poison?
- What can be the reason of slurred speech and altered behaviour?
- Why Atropin was given?
- What is the role of PAM?
- What can be the reason of pin point pupil?
- What can be the reason of low cholinesterase level?
- What can be the reason of high glucose level in blood?

THANK YOU