

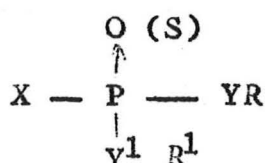
PEDIATRIC GRAND ROUNDS

Wednesday, March 9, 1960

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Organic Phosphate Ester Poisoning (Anti Cholinesterase Intoxication)

"Irreversible" or long acting cholinesterase inhibitors attack the "esteratic site" of cholinesterase, general phosphonate or thio-phosphonate structure.

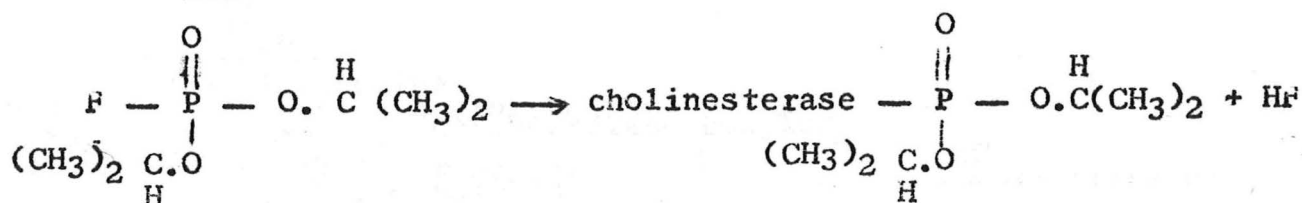


$\text{R} + \text{R}^1 =$ alkyl or aromatic residues
(or H when $\text{Y} + \text{Y}^1$ are carbon)

$\text{Y} + \text{Y}^1 = \text{O}, \text{S}, \text{N}$ or C

$\text{X} =$ organic or inorganic residue
unstable $\text{X} - \text{P}$ bond which ruptures
during complex formation with
cholinesterase.

Example: DFP



Di isopropyl fluoro phosphate (used in treatment of glaucoma).

Agricultural Insecticides

TEPP = Tetra ethyl pyro phosphate

Parathion - p - nitrophenyldiethyl thionophosphate

HETP - hexa ethyl tetra phosphate

OMPA - octa methyl prophosphor amide (also used in therapy of myasthenia gravis).

Parathion is an anti cholinesterase alkyl phosphate commonly employed as an economic poison in agriculture and is also called thiophos, niran, alphamite, genithion, mackothion, alkron, corothion, penphos, phos-kil, vapophos, plantthion, E-605, Cmp. 3422, DN & P, AAT, DPP.

Parathion and other alkyl phosphates are SUPRA TOXIC - very potent, act quickly and severely in small quantities.

Route of Absorption - multiple: via skin, mucus membranes, g.i. tract. (Direct contact, inhalation, g.i. tract.)

Symptoms - "cholinergic crisis"

Muscarinic, nicotinic and central neural excitatory effects.

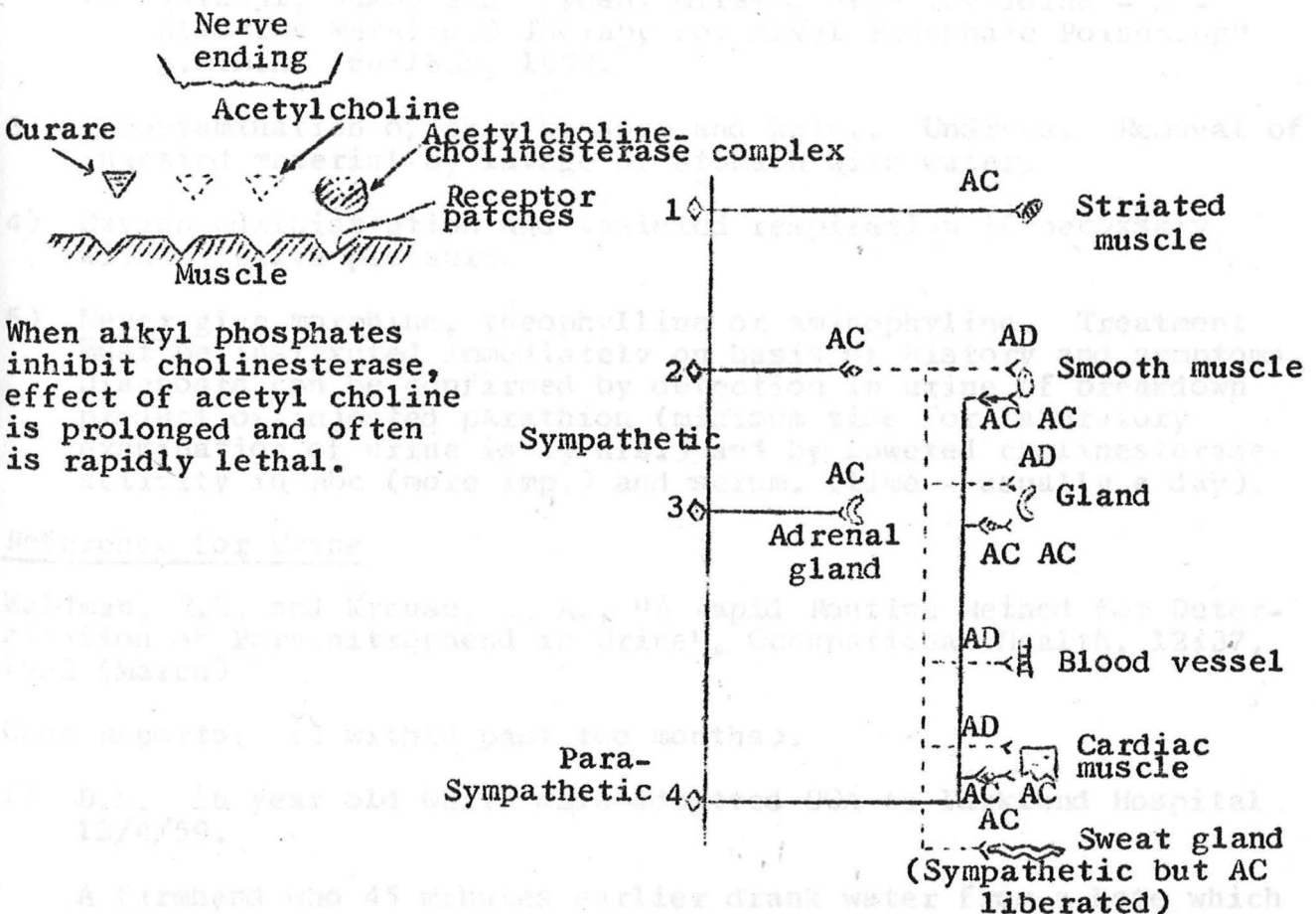
Acetylcholine when not limited in duration of action by cholinesterase throws the whole nervous system into chaos.

Nicotinic effect - contraction of striated muscle.

Muscarinic effect - stimulation of post ganglionic para sympathetic fibers smooth muscle, glands, cardiac muscles. Sweating + Pupillary constriction + decreased temperature, brady cardia, hypotension. Vomiting and diarrhea.

Stimulation is Followed by Depression

Death usually due to respiratory paralysis and may occur within 1 hour. Symptoms often begin within 15 minutes.



Acetylcholine effect on autonomic nervous system.

AC = Acetylcholine

AD = Adrenalin

Treatment

- 1) Atropine - immediate and continued atropinization, i.v. or i.m. signs of atropine effect must be present and patient watched for backslipping for 48 hours. Give repeated parenteral doses with patient under constant observation. Atropine counteracts the muscarinic and central effects of acetylcholine. Large doses of atropine may be required.
- 2) Specific Antidotes now available to interfere with the inhibition of cholinesterase than counteract the effect of acetylcholine. Thus, cholinesterase may proceed to inactivate acetyl choline.

Antidotes: conveniently named DAM - pyridine aldoxime methiodides
PAM

References:

- 1) Grob, D., and Johns, R. J. "Treatment of Anticholinesterase Intoxication with Oximes" J.A.M.A. 166:1855, 1958.
- 2) Tatusji, Namba and Kiyoshi Hiraki, "PAM (Pyridine - 2 - Aldoxime Methiode) Therapy for Alkyl Phosphate Poisoning" J.A.M.A. 166:1835, 1958.
- 3) Decontamination of skin by soap and water. Undress. Removal of ingested material by lavage of stomach with water.
- 4) Oxygen administration and assisted respiration if necessary, with positive pressure.
- 5) Never give morphine, theophylline or aminophylline. Treatment must be instituted immediately on basis of history and symptoms. Diagnosis can be confirmed by detection in urine of breakdown product of ingested parathion (minimum time for laboratory examination of urine is $1\frac{1}{2}$ hrs.) and by lowered cholinesterase activity in Rbc (more imp.) and serum. (time - usually a day).

Reference for Urine

Waldman, R.K. and Krause, L. A., "A Rapid Routine Method for Determination of Para-nitrophenol in Urine", Occupational Health, 12:37, 1952 (March)

Case Reports: (2 within past two months).

- 1) B.L. 16 year old white male admitted DOA to Parkland Hospital 12/4/59.

A farmhand who 45 minutes earlier drank water from a hose which had been immersed in a bucket in which a parathion insecticide was mixed with water before spraying. The insecticide contained parathion 25%, Xylene 65% and inert materials 10%. At 8:15 A.M. -

within a few minutes after injection, had profuse sweating, weakness, collapse. Taken to physician in Duncanville where given 1/150 gr. (0.4 mg.) atropine and sent to Parkland. Trip was said to have taken 10 minutes and patient was dead on arrival at 9:00 A.M.

Comment:

- 1) Initial recommended dose of atropine for adults is 2-3 mg. (1/32 to 1/24 gr.) to be repeated every few minutes until atropine effect noted.
- 2) Few accurate details of this case available.
- 3) Patient may have represented chronic as well as acute parathion poisoning.

2) J. F. Parkland #191978. February, 1960

Treated quickly and repeatedly with atropine im., then i.v., then im. To be discussed by Dr. Potts and Dr. Allen.

References:

- 1) Texas State Department of Health, Division of Occupational Health, Austin, "Physicians Information Bulletin", "Medical Aspects of Organic Phosphate Pesticide Exposures", O.H. - April 11, 1957. (Bulletins O.H. 3 through O.H. 10 are related and give information as to tests, precautions, testing of insecticide ingredients.)
- 2) "Clinical Memoranda on Economic Poisons" Write: Superintendent of Documents, U. S. Government Printing Office, Washington 25, D.C. (enclose 30¢).
- 3) "Phosphate Ester Insecticides", American Cyanamid. Excellent pamphlet on the symptomatology and Rx.
- 4) Spectrum, Vol. 6, May 15, 1958.
- 5) A.M.A. Archives of Industrial Health 16:330 (Oct.), 1957.
- 6) J. Pharm. and Clin. Therapy. 94:215, 1948.
- 7) Nelson, M. Textbook of Pediatrics, p. 1391
- 8) Goodman, L. S. and Gilman, A., The Pharmacological Basis of Therapeutics, The MacMillan Company, New York. 1955. pp. 458-464.

- 9) Wilson, I.B., "Molecular Complementarity and Antidotes for Akyl Phosphate Poisoning", Federation Proceedings 18:(Part I) 752-758, (July, 1959).
- 10) Saunders, B. C. "Toxic Phosphorus and Fluorine Compounds", Endeavor, 19:36-42, (January), 1960.