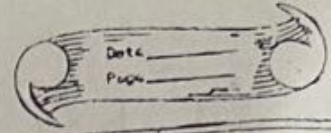
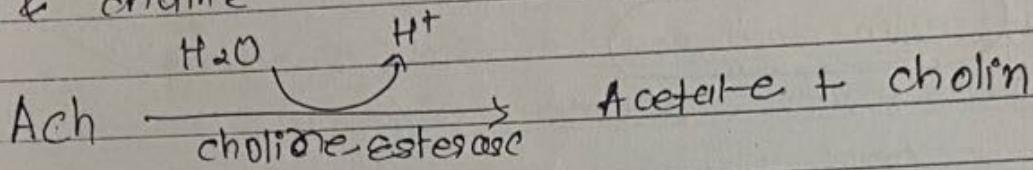


Cholinesterase



- Hydrolase enzyme
- hydrolyze Acetylcholinesterase
- Ach cause depolarization of muscle membrane
- AChE causes hydrolysis of Ach to Acetate & choline



→ 2 Types

Acetylcholinesterase

↓ (cholinesterase I)

found in RBC,

lung, spleen, nerve ending,
gray matter of brain

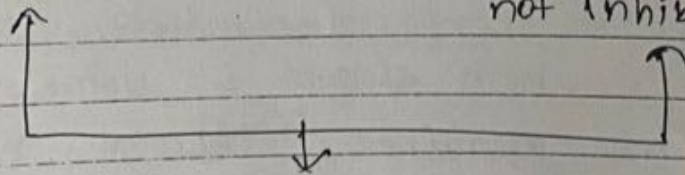
→ RBC AChE is inhibited
By Ach

Pseudocholinesterase

(Butyrylcholinesterase,
Serum CHE, cholin
-esterase II, CHE)

→ Liver, pancreas,
heart, white matter
of brain & serum

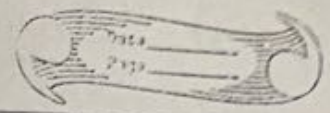
→ its activity 3 to 4 fold
higher than AChE
→ serum enzyme is
not inhibited by Ach



① Both are inhibited by alkaloids - physostigmine

∴ have quaternary Nitrogen in
their structure (also +nt in choline)

↓
So A competitive inhibition on these
both enzymes.



→ (1) Organic phosphorus like diisopropyl fluorophosphate ↓

Irreversibly inhibit enzymes

↓
Phosphoryl group binds very tightly to the enzyme site at C binding on acyl group (1) occurs

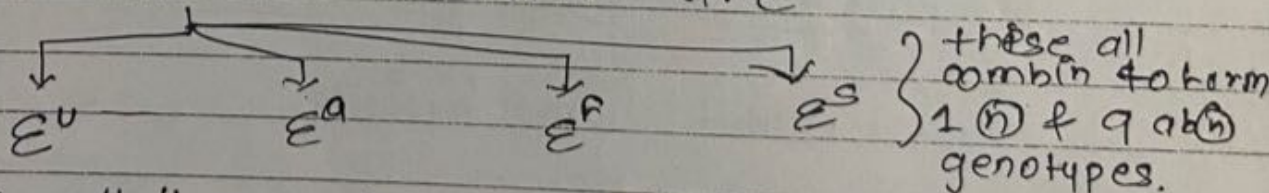
↓
Thus preventing attachment of ACh.

→ (2) Inhibited by various other compounds like morphin, bile salt, fluoside, citrate

* Genetics:- of S.CHE :-

↓
exist in many allelic forms.

↓
4 most common forms are



(1) $E^U E^U$ phenotype :- Usual gene
→ m. common phenotype

(2) $E^A E^A$ phenotype :-

→ gene E^A referred to atypical gene
→ Only weakly active toward most substrate for CHE & demonstrate ↑ resistance to inhibition of enzyme activity by inhibitors.

③ E^f gene :-

- thioside resistance
- weakly active enzyme \bar{c} ↑ resistance to thioside inhibition.

④ E^s gene :-

- -nce of enzyme or +nce of protein with minimal or no catalytic activity.

* Clinical Significance :-

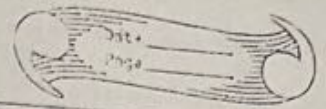
- measurement of CHE activity in serum are used (a) as an indicator of pt \bar{z} possible insecticide poisoning (b) for detection of pt \bar{c} atypical form of enzyme who are at risk for prolonged responses to certain muscle relaxants used in surgical procedures.

(a) Organic phosphorus compounds :-

inhibit CHE & Ache activity.

if enough material is absorbed to inactivate all Ache of nervous tissue, death will occur.

Activity of S. enzyme falls more rapidly than Ache.



↓
- 40% drop in CHE activity occurs before the 1st symptoms are felt

↓
drop of 80% is required before N/M effects become apparent

↓
Near zero conc. of enzyme requires emergency Rx & enzyme reactivator.

(b) Muscle Relaxant :-

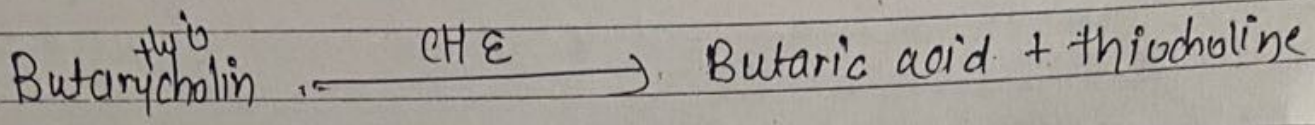
Ex: like succinylcholin & mivacurium are used as muscle relaxants & are hydrolyzed by CHE

↓
In pt with low enzyme activities or weakly active variant like AA, AS, FF, FS, SS, AF, destruction of drug will not occur rapidly enough

↓
pt may enter a period of prolonged paralysis of respi. muscle requiring mechanical ventilaⁿ until the drug effects gradually wear off.

↓ Methods :-

Various substrate - iodide salts such as Acetylthiocholin, Butyrylthiocholin, Succinylthiocholin → are used for detection of CHE activity



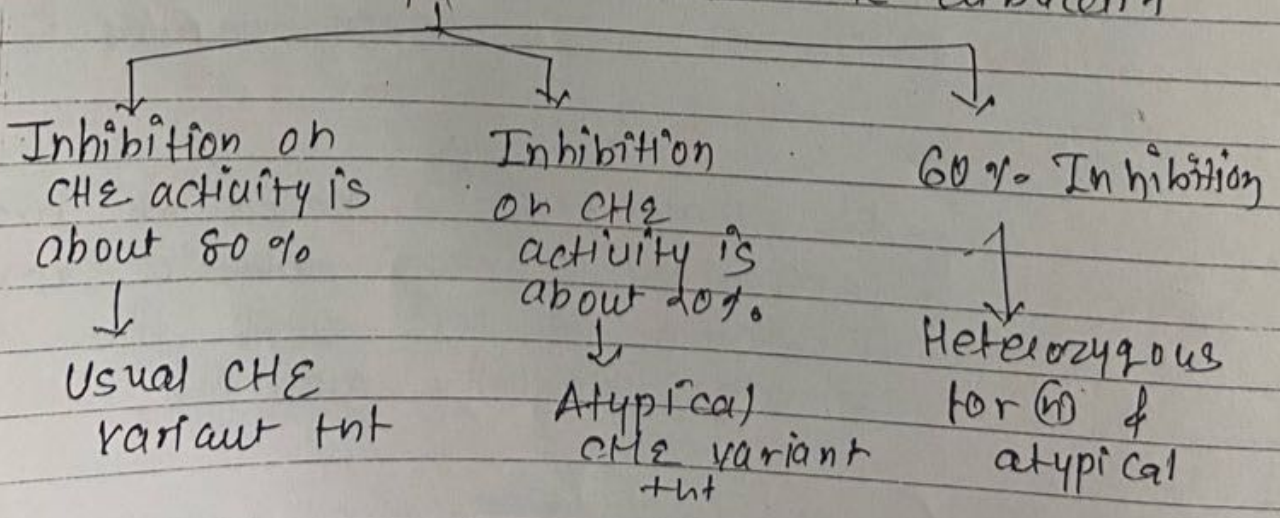
Thiocholin + 5-5 dithio-bis α Nitrobenzoate \longrightarrow
(colourless) (Ellman's reagent)
5-mersapto α -Nitro benzoic acid
 \downarrow
Coloured product measured
spectrophotometrically at 410nm

\Rightarrow Using Succinylthiocholin is a method of choice for measuring CHE to diagnose Succinylcholin sensitivity.

* Measurement of genetic variants of CHE :-

① dibucain numbers :-

\downarrow
Based on diM, such as sensitivity to inhibition by local anaesthetic dibucain



② Fluoride numbers :-

BQ

↓
Sodium fluoride is used to differentiate CHE gene variant
inhibiⁿ of CHE activity

③ Mutational genotyping :-

↓
Confirms the CHE gene abn.

* Sample type :-

↓
→ Serum
moderate

→ Hemolysis does not interfere, if separated serum has been centrifuged to remove RBC ghosts.

→ In OP poisoning → Better to investigate measure RBC → True cholinesterase

↓
As True cholinesterase +nt in RBC & Nervous tissue.

→ Di Acetylthiocholin → nonspecific → acted upon by Ache & CHE

→ Benzoylcholin / Butanilcholin → specific for Ache (pseudo)

→ Pseudocholinesterase → ~~Acetyl~~ Acetylcholine Acylhydrolase → false

→ Acetylcholinesterase → Acetylcholine, Acetylhydrolase