2000a(14): Discuss the roles of plasma esterases on drugs used in anaesthesia

General: Esterases are a heterogenous group of enzymes which hydrolyse esters through the oxygen bridge to form alcohol and alkanoic acid → inactivates ester drugs

- Found in plasma, NMJ, RBC, hepatic sinusoids
- High capacity pathway with high clearance
- Non-organ dependent metabolic pathway (except in severe hepatic disease → ↓production plasma cholinesterases)
- Metabolites are usually inactive
  - Except laudanosine (atracurium/cisatracurium) and salicylic acid → which can be active at high doses

Red Cell Esterases
Drugs metabolised:
- Esmolol
- Remifentanil (small proportion)

High capacity/high clearance

Plasma Esterases
Drugs metabolised:
- Remifentanil → predictable t½β fixed and context-independent
- Atracurium/Cisatracurium
- Etomidate → plasma and hepatic microenzymes

Independent of liver function
High capacity/high clearance

Pseudocholinesterase (plasma cholinesterase)
Drugs metabolised:
- Suxamethonium
- Mivacurium
- Ester LA (eg amethacaine)

Affected by altered physiology/co-morbidities → acquired/inherited
- Pregnancy
- Liver disease
- Inherited disorder (pseudocholinesterase deficiency) → autosomal dominant with variable penetrance → atypical 1:3000 homozygotes, 1:500 heterozygote

↓by drugs
- Anti-cholinesterases → neostigmine
- LAs → dibucaine
- Metaclopramide

NMJ acetylcholinesterase (AChE)
- Nil significant direct metabolism of drugs used in anaesthesia
- Pseudocholinesterase deficiency (↓metabolism of sux) will result in recruitment of AChE to cease effect