

## Testing for Plasma Cholinesterase Deficiency

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Plasma cholinesterase (PChE), also known as butyrylcholinesterase or pseudocholinesterase, is a glycoprotein enzyme synthesised in the liver. It is responsible for the hydrolysis of choline ester compounds, however its physiological function remains unknown.

Abnormalities in the function or quantity of PChE therefore result in delayed metabolism of compounds such as suxamethonium, mivacurium, procaine and cocaine. With suxamethonium this means a much larger quantity of intact drug will reach the neuromuscular junction, causing prolonged paralysis.

PChE deficiency may be inherited or acquired. In the anaesthetic setting testing is performed for those who have had an episode of prolonged paralysis or if a family member has been affected.

There is only one cholinesterase gene, located at the E1 locus on the long arm of chromosome 3. All inherited abnormalities of PChE are a result of mutations in this gene. Mutations may result in enzymes with reduced activity (for example the atypical and fluoride-resistant variants), enzymes with almost no activity (silent variants) or those with normal activity but reduced number of molecules (J, K, and H variants). An individual's PChE activity is determined by their two codominant alleles of this gene. Ninety-six percent of the population are homozygous for the normal allele EuEu. Heterozygotes have intermediate duration of paralysis.

Testing for PChE deficiency involves both biochemical testing and molecular genetic techniques. Biochemical testing has not changed much in over 40 years and is a two-fold process. Total PChE activity is measured using spectrophotometry. If this is reduced then the inhibition of the enzyme's activity by different substances (usually dibucaine and fluoride) is measured. The degree of inhibition is expressed as a number. Different abnormalities of PChE have different dibucaine and fluoride numbers. These numbers are then 'mapped' to match a certain genotype.

This conventional biochemical testing identifies the correct genotype in most, but not all cases. Molecular genetics has enabled precise identification of variants, some previously unrecognised. DNA samples are obtained from white blood cells, amplified using PCR techniques and compared with those of the gene for the normal enzyme. The difference in the amino acid sequence then identifies which variant is present. Molecular genetics is particularly useful in identifying combinations of mutations or multiple mutations within a single gene.

PChE testing is only performed in specialist centres. Samples should be taken in an EDTA tube and should be taken 3-4 days following paralysis to prevent interference with the assay from suxamethonium metabolites and any anticholinesterases administered.

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