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Liver Enzymes and Function Testing

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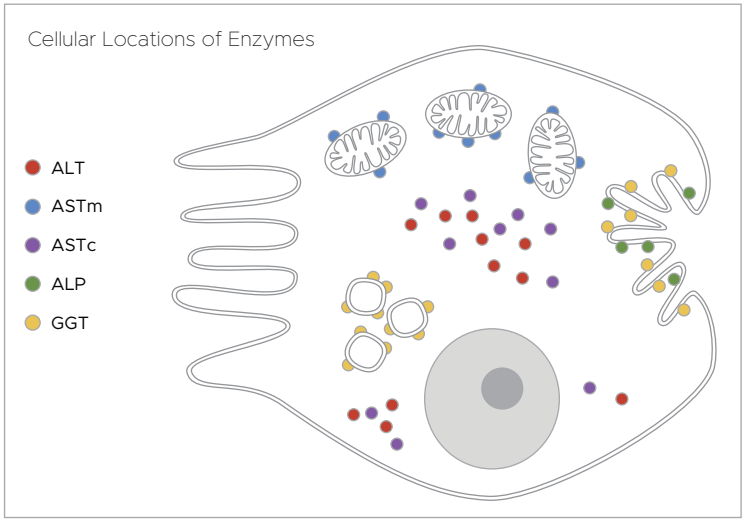
The hepatocyte is a highly complex cell containing a range of enzymes. Upon cellular damage, these enzymes may leak into plasma and therefore be utilized in determining the type of damage inflicted upon the cell.

Figure 1. Cellular Locations of Enzymes.



Alanine aminotransferase (ALT) is found within the cytosol, together with the cytoplasmic isoenzyme of aspartate aminotransferase (ASTc). When AST is measured within the laboratory setting, the assay not only reflects this fraction, but also the mitochondrial isoenzyme of AST.

Alkaline phosphatase (ALP) and gamma-glutamyl-transferase (GGT) are found predominantly on the canalicular surface of the hepatocyte, with some GGT also found associated with the microsomes.

Mechanisms of Enzyme Release

Both AST and ALT are dependent on pyridoxal phosphate (vitamin B6) as cofactor. The laboratory testing method assumes that patient serum contains sufficient amounts of vitamin B6 to facilitate the enzymatic measurement method utilized in the clinical setting.

However, if a patient is deficient, the transaminase enzymes may test falsely low. The finding of vitamin B6 deficiency is not common, however, it may be found in alcoholic patients.

Therefore, clinical correlation is always required when very low AST and / or ALT is found upon testing, which may be remedied by supplementation of the patient, followed by re-testing. In advanced alcoholic cirrhosis, a decline in these liver enzymes may again be noted as the synthetic function of the liver fails.

Membrane injury as seen with viral hepatitis or chemically induced hepatitis, results in the release of cytosolic enzymes, and therefore manifest with a significant AST and ALT predominant response.

The AST level tends to be higher in the acute phase owing to higher concentrations in the hepatocyte itself, however within 24 - 48 hours after the injury, the ALT becomes predominant due to its longer half-life. A notable exception is noted with alcoholic hepatitis which is associated with mitochondrial injury.

The mitochondrial isoenzyme of AST has a higher half-life than both cytosolic AST and ALT. The ASTm is released due to direct damage to the mitochondria by ethanol, leading to a reversed DeRitis ratio (AST / ALT quotient) of 3-4:1.

Table 1. Summary of Liver Enzyme Abnormalities

Feature	Viral hepatitis	Alcoholic hepatitis	Toxic / Ischemic hepatitis
AST / ALT ratio	<1	>2	>1
Peak AST	10 - 100	1 - 10	>100
LDH	1 - 2	1 - 2	10 - 40
Peak bilirubin (µmol/L)	5 - 20	3 - 20	<5
Prothrombin time	Not increased	Not increased	>15s

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Hepatic ALP and GGT are found predominantly on the canalicular surfaces of the hepatocyte, with ALP also being produced in bone. The membranes lining the canaliculi can be dissolved by bile acids if cholestasis occurs. Therefore, the predominance of ALP and GGT is noted with bile stasis as seen with stones, infectious processes like ascending cholangitis or space-occupying lesions.

GGT is also found on microsomes and will be increased corresponding to microsomal induction by various drugs like phenobarbital and chronic ethanol use. Using these markers in monitoring have limited use as even though GGT generally has a serum half-life of 10 days, it may be extended to 28 days in the setting of alcohol abuse.

Conclusion

The liver has significant reserve capacity prior to overt failure occurs. Functional failure is very often preceded to varying degrees with clinical and laboratory abnormalities and a clear understanding of the significance of the enzymes, their cellular location and their half-lives may serve as significant tools in the establishment of a diagnosis of liver injury.

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