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“The Metabolic Effects of Alcohol on the Liver”

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Although there has been considerable debate as to the pathways of alcohol metabolism, it still can be stated with confidence that the main enzyme responsible for ethanol oxidation is alcohol dehydrogenase. This enzyme is found in the cytoplasm of the liver cell. There are two other mechanisms for the oxidation of alcohol: 1) catalase and catalatic peroxidation; and 2) microsomal ethanol oxidation. Many laboratories including our own have attempted to determine the mechanism of microsomal ethanol oxidation and whether this system has any physiologic or clinical significance in the overall metabolism of alcohol. Most of the evidence that we have obtained would suggest that microsomal ethanol oxidation which can be demonstrated in vitro is the net result of two enzyme reactions: 1) NADPH oxidase and 2) catalase. The interactions of these two enzymes lead to the production of hydrogen peroxide which in turn serves to oxidize ethanol to acetaldehyde. Evidence for this concept as an explanation of microsomal ethanol oxidation will be presented.

One of the effects of alcohol is the production of a fatty liver. Fatty liver can be produced by: 1) increased fatty acid synthesis, 2) decreased fatty acid oxidation, 3) increased fatty acid esterification, 4) decreased formation of the apoproteins of lipoproteins, 5) increased mobilization of fatty acids to the liver and 6) decreased release of lipoproteins from the liver. Alcohol affects many of these processes. Much of the available evidence indicates, however, that decreased fatty acid oxidation is probably the most significant factor in leading to the production of the fatty liver produced by alcohol. In general the fat in the liver is present in the form of triglyceride and is present in two types of particles, a small 30–80 Å particle and the other > 200 Å. The smaller particle represents the lipoproteins which are being prepared for export. The larger particles represent the lipid being accumulated in the liver.

One of the features of alcohol on the liver is the production of hyperlipemia. This appears to be due to increased synthesis of lipoproteins by the liver and is most common in individuals who already have an elevated triglyceride level especially those with an underlying defect in type IV hyperlipoproteinemia.

Hypoglycemia occurs with alcohol but only when the glycogen stores of the liver have been depleted due to poor nutrition or fasting. The other metabolic effects of the liver will be discussed.

Finally in addition to the effects on the liver we have come to learn of important actions of alcohol on the intestine. These include: 1) increase in lipid synthesis by the intestine which contributes to the fatty liver, 2) decreased vitamin B₁₂ absorption, 3) decreased sugar and amino acid transport and 4) decrease in calcium absorption. These effects of alcohol on the intestine may contribute to the impaired nutrition seen in alcoholic subjects.