



HYPOGLYCAEMIA DUE TO ETHYL ALCOHOL

In vitro studies using human liver slices

by

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S U M M A R Y

Liver slices obtained from human subjects undergoing elective surgery were incubated in 2ml. of Krebs Ringer Phosphate or Krebs Ringer Bicarbonate in pure oxygen or 95% oxygen - 5% CO₂ respectively. The following radioactive gluconeogenic precursors were employed in concentrations of 0.01 to 10.0 micromoles per ml. (0.01 to 10.0mM). C¹⁴ - labelled L - alanine; L - glutamic acid; glycerol and D, L - lactic acid. Experimental vessels were further supplemented with 1 to 10 mM of unlabelled ethyl alcohol or sodium acetate. After 2 or 3 hours of incubation, radioactive assays were performed to assess the effects of ethyl alcohol or sodium acetate upon the disposition of each labelled gluconeogenic precursor.

The following aspects were studied:

- (a) Formation of glucose by measuring glucose-C¹⁴ in the suspending media and as tissue glycogen:
- (b) Oxidative decarboxylation by collecting C¹⁴O₂
- (c) Reductive retention as a 3 - carbon fragment by measuring the release of lactic acid - C¹⁴
- (d) Where possible, these parameters were related to the "uptake" of the C¹⁴ - labelled precursor as judged by its disappearance from the suspending media.

Ethyl alcohol (10mM) reduced the formation of glucose and the evolution of C¹⁴O₂ from all of the gluconeogenic precursors studied. "Uptake" was also decreased and the

formation of lactic acid-C¹⁴ variably augmented. The incorporation of glucose-C¹⁴ into glycogen as well as the release of glucose-C¹⁴ into the suspending medium were inhibited by ethyl alcohol indicating that gluconeogenesis had been interrupted prior to the formation of glucose-6-phosphate.

In manometric studies ethyl alcohol did not depress oxygen consumption more than 20% at the termination of 3 hour experiments indicating that some mechanism other than histotoxic anoxia was involved.

Parallel experiments using sodium acetate (10mM) failed to simulate the changes due to ethyl alcohol suggesting that the effects were not due to simple dilution with 2-carbon fragments.

An attempt is made to explain these findings of the effects of ethyl alcohol in terms of changes in the ratio of cytoplasmic ($\text{NADH}_2/\text{NAD}^+$) and the size and turnover of the 3 carbon pool.
