

The Effect of Ethanol on the Metabolism of Methanol in Man. By L. J. ZATMAN
(introduced by L. P. KENDAL)

In 1943 Røe published results of clinical investigations of methanol poisoning in which he gave case reports of some sixteen subjects. Several of these subjects, he noted, had drunk ethanol either simultaneously with or shortly after the methanol and in all such cases the symptoms of methanol poisoning were judged to be much less severe than after methanol alone. Røe therefore suggested that ethanol acts as an antidote in methanol poisoning by virtue of 'the capacity of ethyl alcohol to displace methyl alcohol from the inner surface of cells'. In the present study the effect of ethanol on the metabolism of its methyl homologue has been investigated.

In vitro experiments were carried out with alcohol dehydrogenase prepared according to Lutwak-Mann. In manometric experiments using the ferricyanide technique of Quastel & Wheatley, it was found that the dehydrogenase was able to oxidize methanol at only

about one ninth of the rate for ethanol. When these substrates were presented together to the enzyme, the rate of oxidation of methanol was assessed by estimation of the formaldehyde formed from this substrate by a method based on the one suggested by Wright for the estimation of methanol using a modified Schiff's reagent. No detectable oxidation of methanol took place when ethanol was present in equimolar concentration, and inhibition of methanol oxidation was demonstrable when the molar ratio ethanol to methanol was only about 1 to 16. The inhibition was found to be competitive in type.

If this inhibitory effect is operative *in vivo*, then one would expect a simultaneous dose of ethanol to cause diminished oxidation of ingested methanol and therefore increased excretion of methanol, both in the urine and in the expired air. Experiments on three different human subjects have shown this to be the case as regards urinary excretion. The concentration of methanol in the urine after ingestion of this alcohol (which has been shown by Haggard *et al.*, Yant & Schrenk and Eggleton to follow the blood concentration closely) was much increased when ethanol was taken together with the methanol, the latter being estimated by a method based on the one suggested by Wright.

Various authors have attributed the characteristic toxic effects of methanol to the action of oxidation products of methanol rather than to methanol itself. If their view is correct, the experimental results described above would lead one to expect ethanol to diminish the toxicity of methanol, permitting the excretion in an unchanged condition of a larger fraction of the ingested dose.

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