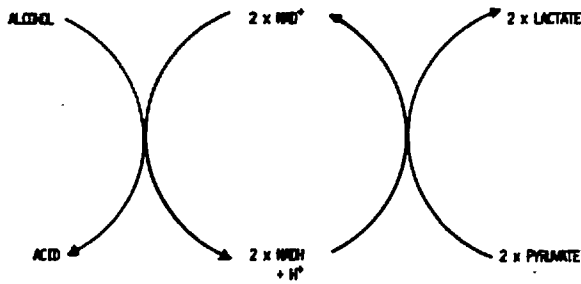


#### COMBINED FORMATE AND LACTATE ACIDOSIS IN METHANOL POISONING

SIR,—Both lactic and formic acids have been implicated in the acidosis associated with methanol poisoning but their relative contributions are uncertain. We report a case of methanol poisoning in which the levels of lactic, formic, and 3-hydroxybutyric acids were measured.

A 45-year-old man was admitted unconscious. During the previous 24 h he had complained of increasing blurred vision, dysarthria, ataxia, nausea, and drowsiness. There was no history available of drug or toxin ingestion, although 1 month earlier he had taken an overdose of flurazepam from which he had made a full recovery. He was completely unresponsive, flaccid, and areflexic

3. Zijlstra JB, Beukema J, Wolthers BG, Byrne BM, Groen A, Denkers J. Pretreatment methods prior to gaschromatographic analysis of volatile fatty acids from faecal samples. *Gas Chrom Acta* 1977; 78: 243-50.
4. Denkers J, Zijlstra JB, Wolthers BG. Volatile fatty acids in human peripheral and portal blood: quantitative determination by vacuum distillation and gaschromatography. *Gas Chrom Acta* 1981; 118: 301-07.



Biochemical explanation for lactate generation in methanol poisoning.

with fixed dilated pupils. He demonstrated Kussmaul's respiration. There was no unusual smell detected on the breath. There were no other findings of note, and funduscopy was normal. He had a profound acidosis with a hydrogen ion concentration of 210 nmol/l (pH 6.78), the reference range being 36–43 nmol/l, and a standard bicarbonate of 3.0 mmol/l. Blood gases were normal, serum sodium 136, potassium 5.5 mmol/l, and chloride 101 mmol/l. The anion gap, calculated from  $(\text{Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{HCO}_3^-)$ , was 37.5 mmol/l. The serum lactate level was 11.5 mmol/l (0–0.8 mmol/l reference range), serum formate 6.9 mmol/l, and 3-hydroxybutyrate level 0.6 mmol/l. Analysis of blood and urine was negative for salicylate and for a wide range of other drugs and toxins including biguanides and ethanol. Methanol was identified by gas chromatography in both blood and urine. Despite correction of the acidosis with large doses of intravenous bicarbonate, repeated EEGs demonstrated a complete absence of brain activity. A few hours after admission he had a cardiorespiratory arrest and died.

The anion gap in normal fit subjects is less than 18 mmol/l. The excessive anion gap in this patient was accounted for by lactate and formate anions with a minor contribution from 3-hydroxybutyrate (totalling 19 mmol/l). The lactate level was almost twice that of the formate. Thus, though formic acid plays a part in the acidosis of methanol poisoning, lactic acid makes a more significant contribution. The lactic acid probably accumulates as a result of reversal of normal oxidation of lactate to pyruvate because of trapping of  $\text{NAD}^+$  as NADH in the liver consequent upon the oxidation of methanol to formic acid (figure).

McMartin et al.<sup>1</sup> have proposed that accumulation of formic acid is the principal cause of the acidosis of methanol poisoning, the increase in blood formate in their study correlating almost exactly with the anion gap increase. These results are not confirmed by our findings. The use of ethanol to inhibit methanol oxidation to formaldehyde and formate,<sup>2</sup> while perhaps protecting from ocular toxicity due to formate, is likely to accentuate the acidosis. Haemodialysis has been proposed as an effective means of methanol and formate removal.<sup>3</sup> As acetate has direct access to the tricarboxylic acid cycle independent of hepatic NAD/NADH ratio there would be no theoretical objection on metabolic grounds to its use as a buffering agent in the haemodialysis bath fluid.

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