METHYL ALCOHOL

Methyl alcohol (methanol, wood alcohol) is a widely used solvent in paints, varnishes, shellacs ("heads") and paint removers. It is used alone as an antifreeze fluid and with ethanol and soap as a solid canned fuel. Small amounts of methanol are found in expired breath of normal subjects (Ericksen and Kulkarni, 1963), and a possible metabolic source for endogenous methanol is recognized (Axelrod and Daly, 1965). The purpose or significance of endogenous methanol and its accumulation in alcoholic subjects during prolonged periods of drinking (Majchrowicz and Mendelson, 1971) are not yet understood.

Toxicology: Methyl alcohol is readily absorbed from the gastrointestinal and respiratory tracts. As little as 2 teaspoonsful is considered toxic if ingested. The fatal dose in man lies between 2 and 8 oz.; this range implies a high variation in individual susceptibility (Soll-

Gosselin, Robert e et al: Clinical Toxicology of Commercial Products, 4th Ed., Williams + Wilkins, Baltimore, Maryland, 1981.

mann, 1957). Death may be prompt, but it is usually delayed for several days, and the mortality rate is high. The prognosis improves if treatment is instituted before visual disturbances appear (Bennett *et al.*, 1953; Benton and Calhoun, 1953).

When methanol consumption is not accompanied by the intake of ethyl alcohol, inebriation and subsequent drowsiness are said to be mild and transient. This phase may be followed by an entirely asymptomatic interval. The characteristic signs and symptoms develop in rapid succession after a latency of 6 to 30 hours (usually 12 to 18) following the initial intake (Jacobson *et al.*, 1945; Kaplan and Levreault, 1945; Röe, 1955b). Because these late effects are produced by pure samples, impurities are thought to play no important role in the toxicity of methyl alcohol (Sollmann, 1957).

The symptoms of methyl alcohol poisoning result from a combination of factors, of which a characteristic metabolic acidosis appears to be the trigger (Röe, 1946). Central nervous depression is due partly to this acidosis and partly to cerebral edema (Kenney and Mellinkoff, 1951; Sollmann, 1957), but monkeys adequately treated with bicarbonate still die from central nervous depression (Potts, 1955). Acidosis is the result of methanol oxidation to formic acid (Bastrup, 1947; Lund, 1948), which accumulates and reduces severely the body's alkali reserve. For unknown reasons other organic acids including lactic acid are said to accumulate also (Harrop and Benedict, 1920).

The severity of essentially all symptoms in methanol poisoning is said to be proportional to the intensity of this delayed acidosis (Cooper *et al.*, 1952; Bennett *et al.*, 1953). It has been suggested on the basis of experiments in dogs that acidosis increases the ratio of cerebrospinal fluid formate to blood formate, *i.e.*, acidification of blood favors the formation of the undissociated form of formic acid and facilitates its penetration into the cerebrospinal fluid (Herken *et al.*, 1969). In contrast to human exposures, a long latent period, relatively high toxicity, acidosis, and ocular injury are *not* features of methyl alcohol intoxication in nonprimate laboratory animals (Gilger and Potts, 1955; Röe, 1955a). There is even some doubt as to whether acidosis is a feature of methanol intoxication in the monkey (Cooper and Felig, 1961). Apparently, monkeys of different species react differently.

Visual disturbances, which are the most distinctive aspect of methanol poisoning in man, may become evident soon after severe acidosis begins. Dilated, unreactive pupils and dimness of vision are characteristic. The ocular lesion, which involves chiefly the ganglion cells of the retina, is a destructive inflammation followed by atrophy. In the acute phase the retina is congested and edematous, and the edges of the optic disk may be blurred. The result is bilateral blindness, which is usually permanent unless treatment is prompt and energetic. Even if complete blindness is avoided, residual scotomata are common (Benton and Calhoun, 1953; Röe, 1948). The electroretinogram is said to have diagnostic and prognostic significance in methyl alcohol poisoning (Ruedemann, 1962).

Except for optic atrophy, permanent neurologic sequelae are exceedingly rare. Motor dysfunction with rigidity, spasticity and hypokinesis of unknown etiology, however, has been reported. Levodopa provided some functional relief (Guggenheim *et al.*, 1971).

It is generally agreed that metabolically formed formaldehyde is responsible for the ocular lesions (Potts and Johnson, 1952; Pragay *et al.*, 1955). Since ocular damage has yet to be reported in cases of formaldehyde poisoning, it would appear that formaldehyde must be generated at the site of the lesion to produce damage (Kini *et al.*, 1962). The contrast between primates and nonprimates is probably due not to a difference in retinal sensitivity but rather to a difference in the rates of formaldehyde production and perhaps of its elimination (Kini and Cooper, 1960). Actual measurements of formaldehyde in body tissues and fluids during human methanol intoxication are rarely encountered in the literature, but Closs and Solberg (1970) claim to have detected high levels in urine in one case.

Ethyl alcohol, when consumed at the same time as methyl alcohol, prolongs the latent period before toxic symptoms appear. It has also been observed that even severe symptoms of methanol poisoning are alleviated by the ingestion of ethanol, and for this reason the recommended treatment includes ethanol in small quantities (*e.g.*, whiskey, 1 oz. every 3 to 4 hours by mouth or stomach tube). A blood ethyl alcohol level of about 0.1% is regarded as optimal. In extreme cases the ethanol may be given intravenously as a dilute solution in bicarbonate or saline (Agner *et al.*, 1949).

The mechanism of this protection lies in the ability of ethyl alcohol to inhibit the metabolic oxidation of methanol, even though this rate is inherently slow (Gilger *et al.*, 1956, 1959; Zatman, 1946). Like ethanol, the metabolism of methanol proceeds at a rate that is constant and independent of concentration within wide limits. In some species, *e.g.*, man and monkey, both substances are acted upon by the same enzyme, alcohol dehydrogenase (Kini and

effects in poisoned dogs and deserve a clinical trial.

Laboratory: Check blood alcohol level and arterial blood pH or plasma CO_2 combining power (or urine acidity) at repeated intervals (preferably every hour, since relapses are common). Measure serum amylase (see text). Hypokalemia of severe proportions has been reported (Tonning *et al.*, 1956). Blood methanol concentrations in 6 fatal cases ranged from 1.1 to 2.4 mg./ml. (Harger *et al.*, 1938).

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METHYL BROMIDE

Methyl bromide and methyl chloride are gases at ordinary temperatures whereas methyl iodide is a volatile liquid. The iodide is encountered infrequently, but it is an intermediate in