disulfiram — formaldehyde — 157

REVIEW

BIOHAZARDS OF METHANOL IN PROPOSED NEW USES

Herbert S. Posner

National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, North Carolina

In the past few years methanol has been proposed for use as an energy source in the place of potentially more scarce natural products. It was also proposed for use as a bacterial feedstock for production of feed protein and the denitrification of waste water. Methanol has a variety of biohazards for the human, most of which have been recognized since the early part of the century. These are discussed in eight categories: hazard at young ages; of potential interactions of several types; abuse; delayed and irreversible toxicity; inhalation and dermal hazard, as well as that due to oral exposure; toxicity of formaldehyde, its product of incomplete combustion; nearly invisible flame; and a larger storage space requirement than for an equivalent energy yield from gasoline. It is proposed that where a safer compound is available, methanol should not be utilized. However, some of the conditions for reducing the human hazard to methanol are presented. These must be taken seriously and without delay because of the proposals for large-scale use, some in rather general environmental situations.

INTRODUCTION

Methanol has been recognized as a serious human toxic agent since the end of the nineteenth century (Wood and Buller, 1904; Buller and Wood, 1904a-d). Many new uses of methanol are now being proposed, some of which would involve its use in the general environment and some in other nonindustrial settings. Most methanol is now used in generally restricted situations. It is not sufficiently recognized that methanol can produce delayed and irreversible effects on the nervous system, as will be described later, by inhalation, skin absorption, and ingestion. This can occur at widely varying levels of exposure and at rather low levels. It is not correct to view methanol as a representative alcohol with regard to human exposure, thinking only of the narcotic effect. While narcosis is obtained in most species including the human, the metabolic acidosis and the nervous system effects, which occur primarily on the retina and some of the other organs of vision, are usually limited to human and nonhuman primates.

Proposed uses of methanol are given in Table 1; the present use pattern is shown for comparison. It is seen that eight of the ten proposed uses are for direct or indirect production of energy, one for the bacterial synthesis of feed protein and one for the bacterial denitrification of waste water.

Its use as a fuel is not new (Reed and Lerner, 1973). It was used in France during the last century where wood was dry distilled in the provinces

Requests for reprints should be sent to Herbert S. Posner, National Institute of Environmental Health Sciences, National Institutes of Health, P.O. Box 12233, Research Triangle Park, North Carolina 27709.

Journal of Toxicology and Environmental Health, 1:153–171, 1975

TABLE 1. Present and Proposed Uses of Methanol

Present[a]	Percent	Proposed[b]
Formaldehyde	45	Gasoline substitute
Dimethylphthalate	7	Gasoline additive
Solvents	7	Boiler fuel for power plants
Methylamine	5	Fuel cells
Polymerization inhibitors	3	Home heating
Methylmethacrylate	3	Gas turbines
Methyl halides	3	Feedstock for synthetic gas
Antidetonant for piston-type aircraft engines	2	Feedstock for bacterial synthesis of feed protein
Glycol methylethers	1	Waste water denitrification
Antifreeze, denaturant, etc.	24	Gasoline synthesis

[a] Tourtellote et al., 1974.
[b] Hiwada, 1974; Mills and Harney, 1974; Reed and Lerner, 1973; Tourtellote et al., 1974; *Chem. Wh.*, 1975.

to obtain "wood alcohol." The alcohol was used, for example, in Paris for lighting, cooking, and heating. It is used today as a fuel in a solid preparation for home and outdoor use.[1] Burning wood chips in all sorts of vehicles provided "producer gas," a mixture of methanol vapor, carbon monoxide, hydrogen, and other gases, to power vehicles during World Wars I and II in France and Germany in place of the more scarce gasoline. Many different types of fuel were discussed in a review by Egloff (1938). It is noted that in 1936 and 1937, 23% and 33%, respectively, of the alcohol used in Germany was methanol; the remainder was ethanol, which was used by many European nations as a fuel during the 1930s.

As today, Egloff's review states that

> countries . . . are conducting research feverishly to utilize their own potential motor fuel supplies from coal, vegetables, cereals, wood, natural gas and oil shale. This research is not directed solely towards producing fuel for motor vehicles such as airplanes, pleasure cars, busses, trucks and boats, but also towards the desire to become nationally self-sufficient, to keep people employed and to utilize their own resources.

The present drive for an increased use of methanol stems from three factors: a more economically competitive situation with regard to methanol vs. petroleum fuels; production of methanol from a large number of unused or discarded sources (an ecologic advantage as well); and its appropriate combustion and mixing properties. Some technical problems (Wigg, 1974),

Sterno →

[1] Sterno, "Canned Heat," contains >60% ethanol, 25% water and acetone, <4% methanol and gelling agent; the "liquid fuel" contains >90% ethanol, <4% methanol, and water, ethyl acetate, perfume, and minor components (National Clearinghouse for Poison Control Centers, 1974).

however, do exist for some of the proposed uses. Two recent symposia dealing with methanol and ethanol production (*Abstracts of the American Chemical Society*, 1975) and methanol and ethanol use as a fuel (*Abstracts of the American Chemical Society*, 1975; Society of Automotive Engineers, 1975) are noted.

It is proposed that it would be advisable, because of the severe public health hazard, to develop other chemicals or mixtures for some of the proposed uses. The areas of insufficient information and hazard will be considered individually. Toxicity was recently considerably understated as "apprehensions about its toxicity" (Hiwada, 1974). Reed and Lerner (1973) tried to consider toxicity more adequately, but they missed the point that irreversible damage and death can also occur by inhalation and by dermal exposure. The threshold limit value (TLV) for methyl alcohol includes a "skin" notation that is meant to suggest that appropriate measures be taken to prevent skin absorption and a possible invalidation of the threshold value (*Federal Register*, 1972; American Conference of Governmental Industrial Hygienists, 1974). Furthermore, benzene, trichloroethylene, and carbon tetrachloride, which Reed and Lerner selected for comparison, are not used in general environmental situations in the large volumes proposed for methanol, and octane is not as volatile as methanol [vapor pressure of octane = 10 mm at 19.2°C; methanol = 100 mm at 21.2°C (Sax, 1975) and 261 mm at 40°C, 625 mm at 60°C, bp = 65°C (McNally, 1937)].

Only a limited portion of the large literature on methanol is reviewed here. The reviews mentioned can be referred to for further information on the topics covered and for additional areas of consideration.

AREAS OF INSUFFICIENT INFORMATION AND METHANOL HAZARD

Insufficient information on exposure at young ages. Few references to exposure at the younger ages were found.

Methanol ingestion of an unknown amount occurred in a 10-wk-old infant girl when methanol was mistaken for water and mixed with her formula. She was hospitalized within 9 hr and intravenous bicarbonate and intraperitoneal dialysis was begun within an hour. The infant's condition was described as precarious for another 10 hr, after which she improved rapidly. The child was hospitalized for 7 days. At 2 wk an apparent recovery was indicated by slight weight gain, normal ocular fundi, and an obvious ability to see (Wenzl et al., 1968).

A wood alcohol lamp was burned next to the crib where a 6-month-old infant slept. The parents noted that something was wrong with the child's eyes and they thought that the child could not see. The pupils were contracted. Upon dilation, the optic discs were found to be pale, more so on the temporal sides, and the arteries were narrow. When use of the lamp was discontinued, the child improved slowly until there was full recovery (Buller and Wood, 1904b, case 8). This case is also referred to below.

"Wood alcohol" was found in the stomachs of four family members who died after drinking stolen alcohol. "It was an established custom of this family to drink anything of an intoxicating nature and it was freely given to the younger children." The dead were 8- and 22-yr-old daughters, a 2-yr-old grandson, and the 48-yr-old grandfather. An 8 lb, 8-month-old fetus was found *in utero*. An 11-yr-old son and the 44-yr-old grandmother recovered (Hoitt, 1903).

A 13-yr, 10-month-old girl attempted suicide by ingesting between 90 and 240 ml of a commercial antifreeze that contained 60% methanol, 39% potassium phosphate in water, 0.25% wetting agent and 0.25% green and yellow dye, but no heavy metals. She was brought to the hospital 9 hr after ingestion and followed with appropriate tests 10–15 hr before being transferred to an intensive care unit. Intravenous bicarbonate and ethanol were administered to correct the metabolic acidosis and competitively inhibit methanol conversion to formaldehyde and formic acid, respectively. After 5 days she was returned to a regular ward. Bilateral optic neuritis was present at this time along with a visual acuity of 20/200 OU. She was discharged at 16 days. After 4 wk the girl noted progressive tightness of the neck and limb muscles, tremulousness, deterioration of handwriting, and difficulty in walking. Neurologic examination at 6 wk revealed a broad-based, unsteady, stooped, propulsive gait. There was a tremor of the head and hands and a deficit of spontaneous movement. In the next 6 months, both the rigidity and spasticity increased and extension of the left arm was severely limited and painful. About 7½ months after ingestion, the girl entered the St. Louis Children's Hospital for further examination and treatment. Ten days after admission, treatment with levo-dopa began and the girl improved with respect to many of the symptoms. Her condition deteriorated when she stopped taking the drug during a 2-wk school vacation and improved when the drug was reinstituted (Guggenheim et al., 1971). The authors could not find another case of this type reported after methanol exposure. However, they referred to three other cases of focal neurologic deficit other than that of the well-recognized optic atrophy (Neiding et al., 1932; Orthner, 1950; Riegel and Wolf, 1966). They also referred to postmortem findings in the brain of combinations of congestion, edema, hemorrhage, multiple slit-shaped cysts, and glial proliferation, all in adult cases (Burhans, 1930; Erlanson et al., 1965; Keeney and Mellinkoff, 1951; Menne, 1938; Pick and Bielschowsky, 1912). Merren (1972) reported an adult case of complete coagulative necrosis of the lateral geniculate bodies as the cause of blindness, which appears to have occurred within a 20–30 min period.

Boys ages 14 and 15 (Buller and Wood, 1904b, cases 83 and 82, respectively) and two age 17 (Buller and Wood, 1904a, case 57; Janotka and Pancerz, 1971) and a young woman age 19 (Buller and Wood, 1904a, case 62) drank one or another preparation containing methanol, in varied amounts, to

the point of intoxication (except perhaps for the girl) and became either nearly or completely blind. Their other symptoms were noted. In the case reported by Janotka and Pancerz (1971), the boy reported that others of ages 12–17 in the correctional institution also drank the same cleaning solution (Silux) said to contain 33% methanol. They also drank several other alcoholic preparations. A boy age 16 (Buller and Wood, 1904b, case 35) drank nearly a pint of wood spirits thinking it was grain alcohol and died within 6 hr. A young man age 19 drank about 250 ml of 35–40% methanol and recovered (Bennett et al., 1953). Bennett et al. (1953) referred to their patients as being 10–78 yr old but only presented specific data for 25 individuals, none of which were below age 19.

An 18-yr-old male "hat stiffener" had to give up the work because of difficulties with vision and a 19-yr-old male type cleaner became blind, both presumably from inhalation exposure (Baskerville, 1913, Appendix C, Part 2, cases 48 and 59, respectively).

Insufficient information on the interactions of combined exposure to methanol and other chemicals or conditions. Crude wood alcohol contains acetone, methylethylketone, methyl acetate, furfural, allyl alcohol, and other components (McNally, 1937), which give it a disagreeable odor and taste and which were proposed, in earlier years, to account for its toxicity. "Deodorization" then made the product palatable and yielded a preparation that resulted in a large increase in the number of poisonings (Wood and Buller, 1904; Wood, 1912). It was not until Reif (1923) reported that a group of dock workers in Hamburg were poisoned in a similar manner by the ingestion of synthetic methanol that the toxicity of methanol itself became generally accepted.

There are marked individual differences in the response to methanol. This has been related, in part, to concurrent or otherwise ingested or administered ethanol with the resultant variation in the ratios of ethanol to methanol in the body, presence of food in the stomach, which would tend to delay absorption of the methanol, and the nutritional status of the individual (von Oettingen, 1958). A report appeared noting 60 patients addicted secondarily to "methylated spirit" [19 parts of 95% ethanol + 1 part "wood naphtha" (methanol), which was added as a denaturant at that time] after being primarily addicted to ethanol (MacDougall and MacAuley, 1956). The lower cost of the methylated spirit caused the individuals to switch. There was no evidence of optic neuritis or atrophy in these cases, probably because of the larger quantity of ethanol consumed.

MacDougall and MacAulay (1956) state that disulfiram (tetraethylthiuram disulfide, Antabuse) was not administered to their patients for fear that an excessively toxic metabolite might accumulate. In the case of methanol this might be formaldehyde. While Antabuse can have dangerous effects and is contraindicated in some instances, it is used as a preventative to discourage ethanol consumption because it exacerbates the response to a

small amount of ethanol. This may occur by a mechanism involving the biogenic amines (Majchrowicz, 1973; Walsh and Truitt, 1970). Disulfiram is also used in the rubber industry as an antioxidant.[2]

A possible interaction effect should also be sought between methanol and other compounds reported, in some cases, to give an abnormal response when combined with either ethanol or compounds related to ethanol. These include carbon disulfide (Williams, 1937); tetramethylthiuram disulfide and its monosulfide, dithiocarbamates, cyanamide, and related compounds used for industrial or fungicidal purposes (Deitrich and Erwin, 1971; Hald et al., 1952; Williams, 1937); drugs such as citrated calcium carbimide (a derivative of cyanamide) (Ferguson, 1956; Marconi et al., 1961); hypoglycemic sulfonylureas (Truitt et al., 1962); and possibly metronidazole (Kalant et al., 1972; Swinson, 1971) and allopurinol (Airaksinen and Tammisto, 1968; Blake et al., 1969; Elion et al., 1966). This is an important area for careful clarification.

Shinaberger (1961) reported the case of an individual who was a Sterno[1] plus carbonated beverage drinker for 5 yr and was then finally able to afford a large quantity of the same material. The patient did not report visual symptoms despite severe acidosis, semicoma, and hypotension. The Sterno was said to contain ethanol and 15% methanol. Now Sterno is reported to contain >60–90% ethanol and <4% methanol.[1] The proportion of the methanol has been reduced, presumably to provide a greater safety factor. Kane et al. (1968) noted the low incidence of ophthalmologic symptoms in their 11 patients despite appropriate acidosis and serum methanol concentrations and a switch from ingesting a low methanol (2.5%)/high ethanol (51–61%) paint thinner to a brand of high methanol (74%)/low ethanol (0.5%) content. They suggested that they might be seeing patients with an acquired tolerance to the ophthalmologic effects and they referred also to Shinaberger's patient (1961).

[2] It was found in experimental animals that pretreatment with disulfiram increased the toxicity of methanol. It lowered the LD_{50} for methanol in the rat and rabbit (Way and Hausman, 1950) and in the mouse (Gilger et al., 1952). In the former study, the response to the combination also occurred earlier, and the survivors recovered more slowly. However, the potentiation of the methanol effect was less than that obtained in combination with ethanol. In the latter study, the LD_{50} with the combination was reported to be 5.5 g/kg, while with methanol alone it was 10.5 g/kg. Koivusalo (1956) found *in vivo* in the rabbit that disulfiram retarded the elimination of methanol from the blood; formaldehyde, however, could not be detected in blood. In the presence of guinea pig liver homogenates, disulfiram also retarded the disappearance of methanol. It slightly reduced the accumulation of formaldehyde. When the disulfiram was administered *in vivo* to the rat (Koivusalo, 1959) and liver homogenate then prepared for incubation with methanol, an accumulation of formaldehyde could again not be observed. However, liver catalase was found to be inhibited. Many other studies with disulfiram either alone or in combination with ethanol were reviewed by Koivusalo (1956, 1959) as were studies of methanol in combination with ethanol, isoniazid, semicarbazide, ATP, dinitrophenol, pyruvate, lactate, fructose, analogs of these, and some other compounds (Koivusalo, 1970).

Browning (1965) mentioned the possibilities that individual susceptibility, sensitization or a preexisting nervous disorder might enhance the expression of toxicity or pathology. A few references were offered that might support these suggestions but these possibilities are difficult to substantiate.

Bennett et al. (1953) listed nine reports indicating widely varying expression of toxicity after methanol ingestion. In their 323 patients, the lowest fatal dose was 3 teaspoons of 40% methanol (about 15 ml); the highest dose of a survivor was 1 pt (500 ml) of the same material. They state that "the striking range of methanol's effects is one of the unusual features of this type of poisoning and is not yet fully explained." A wide variation of response also occurs after inhalation and dermal exposure.

A discussion of the biochemical toxicology of methanol is not undertaken here. The review by Cooper and Kini (1962) and their report in press at the time of writing (Kini et al., 1962), as well as the reviews by Koivusalo (1970) and Tephly et al. (1974) can be consulted. These studies are aiding the understanding of the biochemical and histologic mechanisms of methanol toxicity, possible exacerbation or relief of symptoms by a variety of coexposure techniques, and may lead to further biochemically rational treatment methods.

Abuse hazard. The abuse potential of methanol was summarized well by Cooper and Kini (1962):

> A survey of the immense literature on the subject reveals a high incidence of poisoning in epidemic form, generally resulting from the sale of bootleg liquor. Thus, for example, in one period of 7 months, during the years when the sale of spirits was prohibited in the United States, there were 400 fatalities (McNally, 1937). A series of 323 cases of methanol poisoning was described in 1953 which resulted from the ingestion of adulterated liquor in the area of Atlanta, Georgia (Bennett et al., 1953). During war-time, servicemen are prone to drink whatever alcohol is available, without regard to the length of the carbon chain, and the results of this practice are evident in the estimate that 6% of all cases of blindness in the Armed Forces during World War II was caused by methanol (Greear, 1950). It should be noted that this figure takes into account only nonfatal cases; consideration of the number of deaths that resulted from methanol would considerably enlarge this statistic.

Bennett et al. (1953), Kane et al. (1968), and McNally (1937) listed most of the studies reporting the epidemics. Among the products ingested were adulterated liquor, ethanol denatured with methanol, alcohol for varnish, paint thinner, printing solution, antifreeze, duplicating fluid, Sterno, and cleaning solution.

An extreme example of abuse was presented by Mendelson et al. (1957). Their report dealt with addiction to alcohols other than ethanol and to other toxic agents; individuals who drank these were referred to as "super-alcoholics." Earlier reports of abuse of a variety of solvents were reviewed and nine cases of consumption of methyl or isopropyl alcohol described. These were the two most commonly abused followed by methyl salicylate and paraldehyde. It was concluded that for these individuals the cause "was not economic necessity, or ignorance of the danger, or desire for suicide" but "in the personality of these patients and in the psychodynamics of their alcoholism." A common characteristic of the group was "a striking degree of submissiveness and compliance. They seemed to be utterly devoid of overt hostility and agression." There was "marked dependency and unconscious guilt, self-debasement and need for punishment." Ethanol, which they also consumed copiously, "became too tame; their unconscious needs demanded severer measures, more complete obliteration, and a nearer tread toward the fearful and tantalizing brink between life and death." It is difficult to protect individuals of this type from their overbearing, self-destructive tendencies. However, most of us do not believe that we are in this category, and indeed we are not. On this basis, there would be expected to be an overall population benefit derived from the organization and enforcement of preventive schemes for chemicals of this type.

Delayed and irreversible toxicity. The early and transient effects of methanol are those of its narcotic, inebriation effect. Roe (1955) states that those who drink methanol are disappointed in the slight intoxicating effect and that frequently patients have been able to continue their normal activities for several hours before onset of the later symptoms. The latent period ranged from 40 min (for 500 ml of 40% methanol) to 72 hr (for 250 ml of the same mixture) in the cases reported by Bennett et al. (1953). There was little relationship between the dose and either the length of the latent period or severity of the later symptoms or between the length of the latent period and the severity of the symptoms.

Symptoms include weakness, dizziness, headache, nausea, and abdominal pain followed by vomiting, dyspnea, acidosis, visual disturbances, convulsions, coma, and death. All or some might be present and some variations in the sequence have been observed. Bennett et al. (1953) gave detailed information for 25 of their patients and compared their 323 cases with those of many other studies. The latent phase discourages the individual from seeking medical care, thus making diagnosis of methanol poisoning more difficult. The metabolic acidosis of methanol might be exacerbated, for example, in individuals with diabetes.

Baskerville (1913) wrote that between 1899 and 1913 there were nearly 1,000 cases of poisoning attributed to methanol. He tabulated 725 of reported ingestion, 64 of reported inhalation, and 60 additional cases of inhalation that were heard before a federal congressional committee. Of the 725, 390 died, 90 were permanently blind, 85 had persistent impairment of

vision, and 6–10 were temporarily blind; of the 64 reported cases of inhalation, 6 died, 16 were permanently blind, 25 had permanent impairment of vision, and 8 were temporarily blind.

Bennett et al. (1953) stated that visual disturbance was a very frequent complaint. All of their 115 patients who were markedly acidotic when first admitted to the hospital retained some visual impairment, while at least half of those whose plasma bicarbonate was within normal limits noted a transient difficulty seeing. In their chart for 25 patients, 6 were noted as blind. The detailed ocular effects (Benton and Calhoun, 1953) and pancreatitis of the patients (Bennett et al., 1952) were reported separately.

More recently, peritoneal dialysis and hemodialysis have been utilized in cases of this type of poisoning. A rather well-controlled study was that of Keyvan-Larijarni and Tannenberg (1974). Six individuals drank the same printing solution that contained 60% methanol and were brought to two emergency rooms about 24 hr after ingestion. On admission, serum methanol concentrations were similar in five (171–198 mg/100 ml) and lower in one (96 mg/100 ml).[3] All the patients received bicarbonate and ethanol, as required, and the acidosis was quickly correctable. Three were treated at a hospital where peritoneal dialysis was performed and three at a hospital where hemodialysis was available. With hemodialysis, the serum methanol declined more rapidly. After about 10 hr hemodialysis was instituted in the three on peritoneal dialysis, thus rapidly decreasing their serum methanol values. The major finding was that the three treated initially with hemodialysis required less bicarbonate and ethanol, experienced shorter hospitalization, and did not show residual complications. In the group treated first by peritoneal dialysis, one became blind and one died. There have been many additional reports utilizing hemodialysis (Austin et al., 1961; Closs and Solberg, 1970; Cowen, 1964; Erlanson et al., 1965; Felts et al., 1962; Jorgensen and Wieth, 1963; Marc-Aurele and Schreiner, 1960; Pfister et al., 1966; Setter et al., 1967; Shinaberger, 1961; Wieth and Jorgensen, 1961), peritoneal dialysis (Kane et al., 1968; Setter et al., 1967; Stinebaugh, 1960; Wenzl et al., 1968), or both simultaneously (Humphrey, 1974; Setter et al., 1967). The method of choice appears to be hemodialysis along with administration of ethanol and bicarbonate as necessary (Hussey, 1974; Keyvan-Larijarni and Tannenberg, 1974).

The problems and benefits of hemodialysis, in general, have been discussed elsewhere (Prescott, 1974). Hemodialysis gains much prominence in the treatment of individuals with end-stage kidney disease. While it is becoming more common, most medical centers do not have large numbers of

[3] Because methanol is metabolized and eliminated much more slowly than ethanol, as documented below, repeated analyses should be performed to assure that ethanol treatment and dialysis have been conducted long enough to prevent a second large increase in serum methanol as it is released from body water spaces. Many studies have reported serum methanol concentrations. In the report by Bennett et al. (1953) it ranged from 0 to 400 mg/100 ml.

the units available for potential epidemic poisonings. Fixed-bed charcoal cannisters—a less expensive and more portable technique—in conjunction with hemodialysis are being tested for rapid treatment of other poisonings. It has been used with 13 humans to date (Koffler et al., 1975; *Wall St. J.*, 1975). However, when a large amount of methanol is consumed, the capacity of one or several of these cannisters in series could be quickly exceeded (J. B. Hill, personal communication).

Many reports indicate that methanol is metabolized and eliminated more slowly than ethanol in a variety of species. For example, oral doses of 1 g/kg in the rat of [^{14}C]methanol (Bartlett, 1950) and [^{14}C]ethanol (Bartlett and Barnet, 1949) were converted to expired $^{14}CO_2$ at rates of 25 and 175 mg/kg rat/hr, respectively (Bartlett, 1950). Leaf and Zatman (1952) administered oral doses of 3–7 ml of methanol diluted with water to 100 ml to an individual and determined urinary excretion of unchanged methanol over 14 hr. Then, 4 ml of methanol was first administered to another individual followed by a single 15-ml oral dose of ethanol (presumably also diluted) when the methanol was in a linear phase of urinary excretion. The ethanol only briefly slowed methanol excretion because the ethanol is eliminated rapidly. Four additional 7.5 ml doses of ethanol half-hourly only slowed methanol excretion over a $5\frac{1}{2}$ hr period, after which the methanol was then excreted at the preethanol rate. Finally, Majchrowicz and Mendelson (1971) determined the clearance of "endogenous" methanol (discussed below) in the blood of humans after the administration of large quantities of ethanol. The methanol clearance rate was 0.29 mg/100 ml/hr, said to be in agreement with the blood clearance data for administered methanol obtained by Leaf and Zatman (1952). The ethanol clearance rate, however, was 27.2 mg/100 ml/hr, in agreement with two previous studies (Westerfeld and Schulman, 1959; Mendelson et al., 1965).

This slower metabolism and elimination of methanol may account for several of the findings: the latent period after inebriation and before expression of the metabolic acidosis and pathology; evidence of effects upon chronic exposure (due to accumulation); relapses observed with respect to the acidosis and visual effects; and a rise in blood "formaldehyde–formate,"[4] perhaps derived from endogenous, inadvertent exogenous, and enterogenous methanol[5] (Eriksen and Kulkarni, 1963; Gadsen et al., 1966; Jansson and

[4] It is unclear which was measured or if both were present (Magrinat et al., 1973). This compound nomenclature should not have been used. No methodology was presented, and the two references given for the method (Goldbaum et al., 1964; Steinberg et al., 1965) show a gas chromatographic peak for formaldehyde in nonbiologic solution but not for formic acid. While formic acid or formate has been detected in body tissues and fluids, except for a few reports (Benton and Calhoun, 1953; Closs and Solberg, 1970; Keeser, 1931a, b; Shinaberger, 1961), formaldehyde has been generally undetectable.

[5] This methanol may be derived from metabolic reactions (though this is unclear at the present time) (Axelrod and Daly, 1965; Dilberto and Axelrod, 1974; Kim, 1974), dietary sources (Carroll, 1970; Casey et al., 1963; Oppermann et al., 1973; Self et al., 1963), tobacco (Grob, 1965), and

Larsson, 1969; Majchrowicz and Mendelson, 1971; Pieper and Skeen, 1973) over several days following withdrawal at a detoxification center (Bennett et al., 1953; Browning, 1965; Magrinat et al., 1973).

Inhalation and dermal exposure hazard; hazard of siphoning. Methanol can be hazardous by inhalation and skin absorption, as well as by ingestion (Browning, 1965; Henson, 1960; Leaf and Zatman, 1952). Chronic inhalation has produced conjunctivitis, headache, giddiness, insomnia, gastrointestinal disturbance, fatigue, and a gradual failure of vision that may or may not be irreversible (Browning, 1965), as well as death.

Tyson and Schoenberg (1914) remarked that by 1912 about 100 cases of diminished vision and death from inhalation were reported and that this appeared to be a small part of the total. Usually, exposure was in more confined spaces with poor ventilation. To be sure, Buller and Wood (1904b) and Tyson and Schoenberg (1914) recognized that taking a drink from the supply of alcohol was a common habit among the varnishers. Those using products that contained methanol included painters, glaziers, varnishers, launderers, boot and shoemakers, barbers, printers and lithographers, woodworkers, harness makers, hat makers, leather workers and tanners, and metal workers (Tyson and Schoenberg, 1914).

Henson (1960) notes that as recently as 1955 headaches occurred among employees using methanol in duplicating machines in small, poorly ventilated rooms. This was considered in detail as part of the Advisory Center on Toxicology's report on methanol (1959). The air concentrations were calculated for two unventilated sizes of compartment and two types of Ditto fluid (one that contained 5% and the other 45% methanol, though some fluids had contained up to 100% methanol) (McAllister, 1954; Advisory Center on Toxicology, 1959). Air concentrations from evaporation of 1 pt of fluid were as follows: 510 and 1,000 ppm with 5% solution for 1,000 and 512 ft^3 rooms, respectively; 4,500 and 8,870 ppm with 45% solution for the same rooms, respectively. The human tolerance values for exposure to methanol were then determined. These are shown in Table 2. The guiding principles used in determining these values were to prevent accumulation of methanol and its metabolites in the tissues and to be somewhat conservative. Further documentation for the TLV of 200 ppm for an 8-hr day, 40-hr workweek is presented elsewhere (American Conference of Governmental Industrial Hygienists, 1971).

As indicated above, there are reports of toxic symptoms associated with the use of alcohol lamps in which methanol was used as the fuel. These involved a 35-yr-old woman who denied drinking any kind of alcohol and a

---

intestinal bacterial metabolism. Majchrowicz and Mendelson (1971) found "endogenous" methanol to be <0.1 mg/100 ml in the individuals that they studied. Under conditions of strong inhibition of its metabolism by large quantities of ethanol, serum methanol then increased to a maximum of 4 mg/100 ml, less than that usually seen in cases of methanol poisoning.

TABLE 2. Estimated Tolerance Values for Methanol[a]

Duration	Estimated tolerance value (ppm)
Single but not repeated exposure	
1 hr	1,000
8 hr	500
24 hr	200
40 hr[b]	200
168 hr	50
30 days	10
60 days	5
90 days	3
Single or repeated exposures	
1 hr out of every 24 hr	500
Two 1-hr exposures every 24 hr or One 2-hr exposure every 24 hr	200

[a] Advisory Center on Toxicology, 1959.
[b] Based on five, 8-hr working days.

6-month-old infant (Buller and Wood, 1904b, cases 4 and 8, respectively). Because a toxic combustion product may be involved, it is mentioned again below.

Reports also indicate diminished vision or blindness from skin application of methanol or of preparations that contain methanol for the relief of pain (Campbell, 1915; Eulner, 1954; Woods, 1913), for removal of varnish from the skin (Buller and Wood, 1904b, case 9; 1904d, case 25), as well as following accidental exposure by spillage (Brown, 1910). In some of these cases it is hard to isolate the skin exposure from possible inhalation effects. In the case reported by Brown, the following description is given. A workman

> spilled a gallon or so of alcohol down his leg, soaking his clothes and filling his shoe. He allowed the clothes to dry without changing them, but soon became dizzy and went home. He returned to work the next day but again had to leave for home and go to bed on account of dizziness. Four hours later he awoke to find himself completely blind. Vision, however, gradually improved from day to day, so that four months later he considered returning to work, but his vision again got worse in the fifth, sixth and seventh months, and has practically not changed since then.

McCord (1931) applied methanol soaked pads to the abdominal skin of rats, rabbits, and monkeys under a gas-tight cover to prevent inhalation exposure. All 29 animals died and methanol could be distilled from the tissues of all. The lowest dose causing death in a monkey was 0.5 ml/kg applied four times daily; 1.3 ml/kg applied once produced dilated pupils in 2

hr. Using the data from the monkey, he estimated that 1 oz, absorbed through the skin, might be a hazard to the human. Eulner and Gedicke (1955) studied skin absorption on the backs of rats and rabbits and in a dog, also under conditions where evaporation and inhalation were avoided. Within 30 min the rats showed signs of ataxia and then narcosis. Those rats that did not die within 24 hr survived for at least 7 days. With rabbits, an absorption rate of 0.015 ml/cm^2/hr was obtained with exposures from 12 to 30 min. With an exposure of 60 min, the rate decreased to 0.010 ml/cm^2/hr. The rate of absorption in the dog was similar to that in the rabbit. No toxic effects were observed in 8 wk of exposure of the rat tail to methanol.

Inhalation and skin exposure could occur in a variety of ways in the proposed uses of Table 1. For example, in the present system of pumping gasoline, evaporative loss occurs and, given the design of the tube to the fuel tank, fuel sometimes splashes or overflows before the flow stops. If the automatic cutoff is not used or excess gasoline is removed with a rag, this is further opportunity for either inhalation or skin exposure. Siphoning gasoline, which has become more of a problem since the gasoline shortage and increased prices of the winter of 1972–1973, could be a source of exposure via the mucosa of the mouth and, perhaps, by ingestion.

Potential for toxic products by incomplete combustion. McNally (1937) states that when methanol is burned, the odor of formaldehyde is easily detected. Toxicity due to the burning of alcohol lamps with wood alcohol (Buller and Wood, 1904b, cases 4 and 8) may, therefore, be due to methanol or to product(s) of combustion.

The TLV for formaldehyde is 2 ppm; for formic acid, 5 ppm (American Conference of Governmental Industrial Hygienists, 1971, 1974). Both are considerably lower than that for methanol, 200 ppm.

Some closed circulatory air purification systems draw the air over a heated catalyst bed in order to oxidize organic impurities to CO_2 and H_2O. There were reports (Advisory Center on Toxicology, 1959) that oxidation of methanol was occasionally incomplete; in such cases traces of formaldehyde could be detected. A 50% failure of the burner, with an air concentration of 200 ppm of methanol, would give 100 ppm of formaldehyde. Graphs were drawn showing the theoretical amounts of formaldehyde that would occur from a given percent failure of the burner at any concentration of methanol.

Methanol has been used as a fuel for racing cars and in aviation fuels. It has been considered again in recent years for automobiles, other vehicles and other uses and was the partial or sole subject of ten reports at a recent meeting of the Society of Automotive Engineers (1975).

Ebersole and Manning (1972), using a one-cylinder research engine, compared "straight" methanol vs. isooctane. They found that leaner air–fuel mixtures could be used and that emissions of unburned hydrocarbons, CO, and NO were lower while aldehyde was higher with methanol. This and other studies suggested that the proposed fuel emission standards could be met by using methanol. Fleming and Chamberlain (1975) compared pure methanol

and gasoline in a one-cylinder research engine and also in four- and eight-cylinder engines. They found that emission of CO was similar after burning the two fuels but that with methanol, unburned hydrocarbon was 77% and NO 46% of the amount obtained with gasoline at what they considered appropriate conditions for comparison. The aldehyde emitted from methanol should be formaldehyde and the unburned hydrocarbon methanol. The tests provided emission concentration patterns for air–fuel ratios of 5.5–10. These patterns vary for each emittant, and as such, blends of methanol and gasoline would give an altered set of patterns. Similarly, an engine firing improperly would give other than the expected concentrations of the emissions.

Reed and Lerner (1973) outlined the benefits of methanol and methanol–gasoline blends in the internal combustion engine and of "straight" methanol for a variety of other uses. Wigg (1974) offered a critique, listing problems with the use of methanol as a blend in gasoline for automobiles, and concluded that "straight" methanol might be useful for other purposes, such as in gas turbines for electric power generation.

Nearly invisible flame. Methanol burns with a blue, nearly invisible flame. This has been a hazard in the past and would again be a problem where pure methanol is utilized.

For the same energy yield, twice the storage space is required. As in the paragraph above, storage space would have to be taken into consideration where pure methanol was to be utilized. The storage space involved pertains to the vehicle, the storage facilities, and the power generation facilities.

PROTECTION AGAINST METHANOL POISONING

Methanol has been proposed for many new uses. It is known to produce delayed and irreversible effects. For these two reasons, it is felt that the conditions and standards of its use should be promptly reconsidered. Indeed, the National Institute for Occupational Safety and Health requested information to be used in the preparation of a criteria document (*Chem. Eng. News,* 1975). However, it is also proposed for use in the general environment. The considerations should include open places such as gasoline stations, the air along highways, the air of urban communities, sometimes poorly ventilated areas (such as underground garages and long tunnels), and waste water.

Methanol is a difficult chemical to control and its use should be avoided when possible. Some steps to reduce its hazard, however, might include the following: handling methanol in sealed systems and the redesign of delivery systems; inclusion of an intense and repulsive color, an emetic in the case of accidental or other ingestion and a colorant in the case of burning; antisiphoning methods—a solution difficult to enforce in older vehicles; adequate enforcement of the appropriate workroom air and emission standards to prevent the release of excessive or accumulating amounts of

methanol, formaldehyde, or formic acid; and labeling perhaps with such an unusual phrase as "cannot be made nonpoisonous" (von Oettingen, 1943) or some alternate form because of the well-known abuse potential.

REFERENCES[6]

Abstracts of the American Chemical Society. 169th National Meeting, April 6–11, 1975, Philadelphia, Division of Fuel Chemistry, papers No. 24 and 25.

*Advisory Center on Toxicology. 1959. Report on methanol. In *Toxicity evaluation of potentially hazardous materials,* part III, pp. 82–103. Washington, D.C.: National Research Council–National Academy of Sciences.

Airaksinen, M. M. and Tammisto, T. 1968. Toxic actions of the metabolites of halothane: LD_{50} and some metabolic effects of trifluoroethanol and trifluoroacetic acid in mice and guinea pigs. *Ann. Med. Exp. Fenn.* 46:242–248.

American Conference of Governmental Industrial Hygienists. 1971. *Documentation of the threshold limit value for substances in workroom air,* 3rd ed., pp. 155–156, 118–119, 119–120. Cincinnati.

American Conference of Governmental Industrial Hygienists. 1974. *Threshold limit values for 1974.* Cincinnati.

Austin, W. H., Lape, C. P. and Burnham, H. N. 1961. Treatment of methanol intoxication by hemodialysis. *N. Engl. J. Med.* 265:334–336.

Axelrod, J. and Daly, J. 1965. Pituitary gland: Enzymic formation of methanol from *S*-adenosylmethionine. *Science* 150:892–893.

Bartlett, G. R. 1950. Combustion of C^{14} labelled methanol in intact rat and its isolated tissues. *Am. J. Physiol.* 163:614–621.

Bartlett, G. R. and Barnet, H. N. 1949. Some observations of alcohol metabolism with radioactive ethyl alcohol. *Q. J. Stud. Alcohol* 10:381–397.

*Baskerville, C. 1913. *A report on the chemistry, technology and pharmacology of the legislation pertaining to methyl alcohol,* 2nd rep., vol. 2, pp. 921–1042. New York: Factory Inspection Commission.

Bennett, I. L., Jr., Nation, T. C. and Olley, J. F. 1952. Pancreatitis in methyl alcohol poisoning. *J. Lab. Clin. Med.* 40:405–409.

*Bennett, I. L., Jr., Cary, F. H., Mitchell, G. L., Jr. and Cooper, M. N. 1953. Acute methyl alcohol poisoning: A review based on experiences in an outbreak of 323 cases. *Medicine* 32:431–463.

Benton, C. D., Jr. and Calhoun, F. P. 1953. The ocular effects of methyl alcohol poisoning: Report of a catastrophe involving 320 persons. *Am. J. Ophthalmol.* 36:1677–1685.

Blake, D. A., Cascorbi, H. F., Rozman, R. S. and Meyer, F. J. 1969. Animal toxicity of 2,2,2-trifluoroethanol. *Toxicol. Appl. Pharmacol.* 15:83–91.

Brown, E. V. L. 1910. Discussion of Fridenberg, P. *Trans. Am. Ophthalmol. Soc.* 12:513–525.

*Browning, E. 1965. *Toxicity and metabolism of industrial solvents,* 3rd ed., pp. 311–323. New York: Elsevier.

*Buller, F. and Wood, C. A. 1904. Poisoning by wood alcohol: Cases of death and blindness from Columbian spirits and other methylated preparations. *J. Am. Med. Assoc.* 43:a) 1058–1062, b) 1117–1123, c) 1213–1221, d) 1289–1296.

Burhans, E. C. 1930. Methyl alcohol poisoning: A clinical and pathological study of 11 fatal cases. *Ill. Med. J.* 57:260–263.

Campbell, J. A. 1915. Wood alcohol amblyopia—A case. *J. Ophthalmol. Otol. Laryngol.* 21:756–761.

Carroll, R. B. 1970. Analysis of alcoholic beverages by gas-liquid chromatography. *Q. J. Stud. Alcohol. Suppl.* 5:6–19.

Casey, J. C., Self, R. and Swain, T. 1963. Origin of methanol and dimethyl sulphide from cooked foods. *Nature* 200:885.

Chem. Eng. News. Concentrates. March 3, 1975, p. 9.

[6]Asterisk (*) signifies an extensive review.

Chem. Wk. Gas from coalaward. February 12, 1975, p. 14; Technology newsletter. June 18, 1975, p. 39; Technology newsletter. June 25, 1975, p. 43.

Closs, K. and Solberg, C. O. 1970. Methanol poisoning. *J. Am. Med. Assoc.* 211:497–499.

*Cooper, J. R. and Kini, M. M. 1962. Biochemical aspects of methanol poisoning. *Biochem. Pharmacol.* 11:405–416.

Cowen, D. L. 1964. Extracorporeal dialysis in methanol poisoning. *Ann. Intern. Med.* 61:134–135.

Deitrich, R. A. and Erwin, V. G. 1971. Mechanism of the inhibition of aldehyde dehydrogenase in vivo by disulfiram and diethyldithiocarbamate. *Mol. Pharmacol.* 7:301–307.

Dilberto, E. J., Jr. and Axelrod, J. 1974. Characterization and substrate specificity of a protein carboxymethylase in the pituitary gland. *Proc. Natl. Acad. Sci. U.S.A.* 71:1701–1704.

Ebersole, G. D. and Manning, F. S. 1972. Engine performance and exhaust emissions: Methanol vs iso-octane. Paper No. 720692. Warrendale, Pa.: Society of Automotive Engineers.

*Egloff, G. 1938. Motor fuel economy of Europe. *Ind. Eng. Chem.* 30:1091–1104.

Elion, G. B., Kovensky, A., Hitchings, G. H., Metz, E. and Rundles, R. W. 1966. Metabolic studies of allopurinol, an inhibitor of xanthine oxidase. *Biochem. Pharmacol.* 15:863–880.

Eriksen, S. P. and Kulkarni, A. B. 1963. Methanol in normal human breath. *Science* 141:639–640.

Erlanson, P., Fritz, H., Hagstam, K.-E., Liljenberg, B., Tryding, N. and Voight, G. 1965. Severe methanol intoxication. *Acta Med. Scand.* 177:393–408.

Eulner, H.-H. 1954. Methanolvergiftung bei äuszerlicher Anwendung. *Arch. Toxikol.* 15:73–76.

Eulner, H.-H. and Gedicke, K.-H. 1955. Über die Hautresorption von Methylalkohol. *Arch. Toxikol.* 15:409–414.

Fed. Reg. 1972. 37:22139–22144.

Felts, J. H., Templeton, T. B., Wolff, W. A., Meredith, J. H. and Hines, J. 1962. Methanol poisoning treated by hemodialysis. *South. Med. J.* 55:46–47.

Ferguson, J. K. W. 1956. A new drug for alcoholism treatment. *Can. Med. Assoc. J.* 74:793–795; see also Armstrong, J. D. *Ibid.* 74:795–797 and Bell, R. G. *Ibid.* 74:797–798.

Fleming, R. D. and Chamberlain, T. W. 1975. Methanol as automotive fuel. Part 1: Straight Methanol. Paper No. 750121. Warrendale, Pa.: Society of Automotive Engineers.

Gadsen, R. H., Kinard, F. W., Risenger, K. B. H. and Hay, M. G. 1966. Methanol in dog breath. *Fed. Proc.* 25:566.

Gilger, A. P., Potts, A. M. and Johnson, L. V. 1952. Studies on the visual toxicity of methanol. II. The effect of parenterally administered substances on the systemic toxicity of methyl alcohol. *Am. J. Ophthalmol.* 35(II):113–126.

Goldbaum, L. R., Domanski, T. J. and Schloegel, E. L. 1964. Analysis of biological specimens for volatile compounds by gas chromatography. *J. Forensic Sci.* 9:63–71.

Greear, J. N., Jr. 1950. The causes of blindness. In *Blindness: Modern approaches to the unseen environment*, ed. P. A. Zahl, p. 568. Princeton: Princeton Univ. Press.

Grob, K. 1965. Gas chromatography of cigarette smoke. Part III. *J. Gas Chromatogr.* 3:52–56.

Guggenheim, M. A., Couch, J. R. and Weinberg, W. 1971. Motor dysfunction as a permanent complication of methanol ingestion. *Arch. Neurol.* 24:550–554.

Hald, J., Jacobsen, E. and Larsen, V. 1952. The Antabuse effect of some compounds related to Antabuse and cyanamide. *Acta Pharmacol. Toxicol.* 8:329–337.

*Henson, E. V. 1960. The toxicology of some aliphatic alcohols. Part II. *J. Occup. Med.* 2:497–499.

*Hiwada, R. 1974. International supply and demand for natural gas and methanation. *Chem. Econ. Eng. Rev.* 11:7–15.

Hoitt, E. G. 1903. Poisoning of the Underwood family by wood alcohol. *Boston Med. Surg. J.* 148:62–63.

Humphrey, T. J. 1974. Methanol poisoning: Management of acidosis with combined haemodialysis and peritoneal dialysis. *Med. J. Australia* 1:833–835.

Hussey, H. H. 1974. Methanol poisoning. *J. Am. Med. Assoc.* 229:1335–1336.

Janotka, H. and Pancerz, S. 1971. Vision damage after "Silux" fluid poisoning. *Wiad. Lek. Warsz.* 24:2235–2238.

Jansson, B. O. and Larsson, B. T. 1969. Analysis of organic compounds in human breath by gas chromatography–mass spectrometry. *J. Lab. Clin. Med.* 74:961–966.

Jorgensen, H. E. and Wieth, J. O. 1963. Dialyzable poisons. Hemodialysis in the treatment of acute poisoning. *Lancet* 1:81–84.

Kalant, H., LeBlanc, A. E., Guttman, M. and Khanna, J. M. 1972. Metabolic and pharmacologic interaction of ethanol and metronidazole in the rat. *Can. J. Physiol. Pharmacol.* 50:476–484.

Kane, R. L., Talbert, W., Harlan, J., Sizemore, G. and Cataland, S. 1968. A methanol poisoning outbreak in Kentucky: A clinical, epidemiological study. *Arch. Environ. Health* 17:119–129.

Keeney, A. H. and Mellinkoff, S. M. 1951. Methyl alcohol poisoning. *Ann. Intern. Med.* 34:331–338.

Keeser, E. 1931a. Ätiologie und therapeutische Beeinflussbarkeit der spezifischen toxischen Wirkungen des Methylalkohol. *Naunyn-Schmiedeberg's Arch. Exp. Pathol. Pharmak.* 160:687–691.

Keeser, E. 1931b. Über die Ursache der Giftigkeit des Methylalkohol. *Dtsch. Med. Wschr.* 57:398–399.

Keyvan-Larijarni, H. and Tannenberg, A. M. 1974. Methanol intoxication: Comparison of peritoneal dialysis and hemodialysis treatment. *Arch. Intern. Med.* 134:293–296.

Kim, S. 1974. *S*-Adenosylmethionine: Protein carboxyl methyltransferase from erythrocyte. *Arch. Biochem. Biophys.* 161:652–657.

Kini, M. M., King, D. W., Jr., and Cooper, J. R. 1962. Biochemistry of methanol poisoning. V. Histological and biochemical correlates of effects of methanol and its metabolites on the rabbit retina. *J. Neurochem.* 9:119–124.

Koffler, A., Hill, J. and Barbour, B. H. 1975. Treatment of drug overdose with a fixed bed of charcoal. *Clin. Res.* 23:221A.

*Koivusalo, M. 1956. Studies on the metabolism of methanol and formaldehyde in the animal organism. *Acta Physiol. Scand.* Suppl. 131, 39:1–103.

Koivusalo, M. 1959. Effect of disulfiram (tetraethylthiuram disulphide) on the metabolism of methanol in rat liver homogenates. *Acta Physiol. Scand.* 45:271–277.

*Koivusalo, M. 1970. Methanol. In *International encyclopedia of pharmacology and therapeutics*, sec. 20, vol. 2, *Alcohols and derivatives*, pp. 465–505. New York: Pergamon Press.

Leaf, G. and Zatman, L. J. 1952. A study of the conditions under which methanol may exert a toxic hazard in industry. *Br. J. Ind. Med.* 9:19–31.

MacDougall, A. A. and MacAulay, K. 1956. Addition to methylated spirit. *Lancet* 1:498–500.

Magrinat, G., Dolan, J. P., Biddy, R. L., Miller, L. D. and Korol, B. 1973. Ethanol and methanol metabolites in alcohol withdrawal. *Nature* 244:234–235.

Majchrowicz, E. 1973. Alcohol, aldehydes and biogenic amines. *Ann. N.Y. Acad. Sci.* 215:84–88.

Majchrowicz, E. and Mendelson, J. H. 1971. Blood methanol concentrations during experimentally induced ethanol intoxication in alcoholics. *J. Pharmacol. Exp. Ther.* 179:293–300.

Marc-Aurele, J. and Schreiner, G. E. 1960. The dialysance of ethanol and methanol: A proposed method for the treatment of massive intoxication by ethyl or methyl alcohol. *J. Clin. Invest.* 39:802–807.

Marconi, J., Solari, G. and Gaete, S. 1961. Comparative clinical study of the effects of disulfiram and calcium carbimide. *Q. J. Stud. Alcohol.* 22:46–51.

McAllister, R. G. 1954. Exposure to methanol from spirit duplicating machines. *Am. Ind. Hyg. Assoc. J. Q.* 15:26–28.

McCord, C. P. 1931. Toxicity of methyl alcohol (methanol) following skin absorption and inhalation. *Ind. Eng. Chem.* 23:931–936.

*McNally, W. D. 1937. *Toxicology*. pp. 613–631. Chicago: Industrial Medicine.

Mendelson, J., Wexler, D., Leiderman, P. H. and Solomon, P. 1957. A study of addiction to nonethyl alcohols and other poisonous compounds. *Q. J. Stud. Alcohol.* 18:561–580.

Mendelson, J. H., Stein, S. and Mello, N. K. 1965. Effects of experimentally induced intoxication on metabolism of ethanol-1-^{14}C in alcoholic subjects. *Metabolism (Clin. Exp.)* 14:1255–1266.

Menne, F. R. 1938. Acute methyl alcohol poisoning: A report of 22 instances with postmortem examinations. *Arch. Pathol.* 26:77–92.

Merren, M. D. 1972. Bilateral lateral geniculate body necrosis as a cause of amblyopia. *Neurology* 22:263–268.

*Mills, G. A. and Harney, B. M. 1974. Methanol—The "new fuel" from coal. *Chemtech* 4:26–31.

National Clearinghouse for Poison Control Centers. 1974. Sterno Canned Heat, 85th suppl. (August); Sterno liquid fuel, 86th suppl. (September). Washington, D.C.

Neiding, M., Goldenberg, N. and Blank, L. 1932. Die Neurologie der akuten Methylalkoholvergiftung. *Arch. Psychiatr. Nervenkr.* 96:24–35.

Oppermann, J. A., Muldoon, E. and Ranney, R. E. 1973. Metabolism of aspartame in monkeys. *J. Nutr.* 103:1454–1459.

*Orthner, H. 1950. *Die Methylalkoholvergiftung.* Berlin: Springer-Verlag.

Pfister, A. K., McKenzie, J. V., Dinsmore, H. P. and Edman, C. D. 1966. Extracorporeal dialysis for methanol intoxication. *J. Am. Med. Assoc.* 197:1041–1043.

Pick, L. and Bielschowsky, M. 1912. Über histologische Befunde im Auge und im Zentralnervensystem des Menschen bei akuter tödlicher Vergiftug mit Methylalkohol. *Klin. Wschr.* 49:888–893.

Pieper, W. A. and Skeen, M. J. 1973. Changes in blood methanol concentrations in chimpanzees during periods of chronic ethanol ingestion. *Biochem. Pharmacol.* 22:163–173.

Prescott, L. F. 1974. Limitations of hemodialysis and forced diuresis. In *The poisoned patient: Role of the laboratory,* Ciba Foundation symposium No. 26, pp. 269–282. New York and Amsterdam: Elsevier.

*Reed, T. B. and Lerner, R. M. 1973. Methanol: A versatile fuel for immediate use. *Science* 182:1299–1304.

Reif, G. 1923. Über die Giftigkeit des Methylalkohols. *Dtsch. Med. Wschr.* 49:183–184.

Riegel, H. and Wolf, G. 1966. Schwere neurologische Ausfälle als Folge einer Methylalkoholvergiftung. *Fortschr. Neurol. Psychiatr.* 34:346–351.

*Roe, O. 1955. The metabolism and toxicity of methanol. *Pharmacol. Rev.* 7:399–412.

Sax, N. I. 1975. *Dangerous properties of industrial materials,* 4th ed., pp. 908, 981. New York: Van Nostrand Reinhold Co.

Self, R., Casey, J. C. and Swain, T. 1963. The low-boiling volatiles of cooked foods. *Chem. Ind.* 863–864.

Setter, J. G., Singh, R., Brackett, N. C., Jr., and Randall, R. E., Jr. 1967. Studies on the dialysis of methanol. *Trans. Am. Soc. Artif. Intern. Organs.* 13:178–182.

Shinaberger, J. H. 1961. Treatment of methanol poisoning by extracorporeal dialysis. *Arch. Intern. Med.* 108:937–939.

Society of Automotive Engineers. 1975. Papers No. 750118–750125, 750419, 750420. Warrendale,

Steinberg, M., Nash, J. B. and Walker, J. Q. 1965. Quantitation of alcohols using gas chromatography and a 15% Hallcomid column. *J. Forensic Sci.* 10:201–206.

Stinebaugh, B. J. 1960. The use of peritoneal dialysis in acute methyl alcohol poisoning. *Arch. Intern. Med.* 105:613–617.

Swinson, R. P. 1971. Long-term trial of metronidazole in male alcoholics. *Br. J. Psychiatr.* 119:85–89.

*Tephly, T. R., Watkins, W. D. and Goodman, J. I. 1974. The biochemical toxicology of methanol. In *Essays in toxicology,* vol. 5, pp. 149–177. New York: Academic Press.

*Tortellotte, J., Bongiorne, S. and Shah, D. 1974. Methanol concept. *Chem. Econ. Eng. Rev.* 11:34–37.

Truitt, E. B., Duritz, G., Morgan, A. M. and Proutz, R. W. 1962. Disulfiram-like actions produced by hypoglycemic sulfonylurea compounds. *Q. J. Stud. Alcohol.* 23:197–207.

Tyson, H. H. and Schoenberg, M. J. 1914. Experimental researches in methyl alcohol inhalation. *J. Am. Med. Assoc.* 63:915–922.

*von Oettingen, W. F. 1943. *The aliphatic alcohols: Their toxicity and potential dangers in relation to their chemical constitution and their fate in metabolism,* USPHS Bull. No. 281, pp. 1–28. Washington, D.C.: Department of Health, Education, and Welfare.

*von Oettingen, W. F. 1958. *Poisoning: A guide to clinical diagnosis and treatment,* 2nd ed., pp. 425–427. Philadelphia: Saunders.

Wall St. J. March 19, 1975, p. 2 (N.Y. ed.).

Walsh, M. J. and Truitt, E. B., Jr. 1970. Acetaldehyde mediation in the mechanism of ethanol-induced changes in norepinephrine metabolism. *Mol. Pharmacol.* 6:416–424.

Way, E. L. and Hausman, R. 1950. Effects of tetra-ethyl thiruamdisulfide (Antabuse) on toxicity of methyl alcohol. *Fed. Proc.* 9:324.

Wenzl, J. E., Mills, S. D. and McCall, J. T. 1968. Methanol poisoning in an infant: Successful treatment with peritoneal dialysis. *Am. J. Dis. Child.* 116:445–447.

Westerfeld, W. W. and Schulman, M. P. 1959. Metabolism and caloric value of alcohol. *J. Am. Med. Assoc.* 170:135–141.

Wieth, J. O. and Jorgensen, H. E. 1961. Treatment of methanol and ethanol poisoning with hemodialysis. *Dan. Med. Bull.* 8:103–106.

*Wigg, E. E. 1974. Methanol as a gasoline extender: A critique. *Science* 186:785–790.

Williams, E. E. 1937. Effects of alcohol on workers with carbon disulfide. *J. Am. Med. Assoc.* 109:1472–1473.

Wood, C. A. 1912. Death and blindness from methyl or wood alcohol poisoning: With means of prevention. *J. Am. Med. Assoc.* 59:1962–1966.

*Wood, C. A. and Buller, F. 1904. Poisoning by wood alcohol: Cases of death and blindness from Columbian spirits and other methylated preparations. *J. Am. Med. Assoc.* 43:972–977.

Woods, H. 1913. Wood-alcohol blindness. *J. Am. Med. Assoc.* 60:1762–1764.

Received April 28, 1975
Accepted June 12, 1975