

# METHYL ALCOHOL POISONING \*

Human  
poison

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THE purpose of this paper is to reëxamine some of the cardinal features of methyl alcohol poisoning in the light of 23 cases recently studied in an Army hospital in Korea.

Methyl alcohol ( $\text{CH}_3\text{OH}$ ), properly known as methanol, and more commonly called wood alcohol, also passes under a large number of other names, such as Columbian spirit, Manhattan spirit, pyroxylic spirit, "derail" and "sterno." Methanol is an important industrial solvent and the major ingredient of many inexpensive anti-freeze preparations.

Acute or chronic poisoning may be produced by ingestion, cutaneous absorption or inhalation. Atmospheric concentrations of 0.2 per cent may cause systemic complaints<sup>13</sup> and pose a serious industrial problem. The erroneous use of methyl for ethyl alcohol as a skin rub, or its criminal incorporation in cheap hair tonics or hand lotions, may produce grave poisoning.<sup>9</sup> Most commonly, as in our cases, intoxication occurs after using it for a spirit beverage.

There is extreme variability in individual tolerance to this agent, but permanent blindness has been reported after ingestion of as little as 4 c.c.<sup>3</sup> and death has occurred after drinking 30 c.c.<sup>16</sup>

## FATE OF METHANOL IN THE BODY

Chronic poisoning is due to the cumulative effect made possible by slow elimination. Whereas ethyl alcohol is quickly and completely oxidized to harmless  $\text{CO}_2$  and water, methanol is slowly and incompletely oxidized to products more toxic than the original compound. The metabolism of methanol proceeds about five times more slowly than that of ethanol.<sup>14</sup> About 40 per cent of the assimilated dose may be oxidized to formic acid, which is six times more toxic than methanol. This is one of the stronger organic acids, more than 10 times as strong as acetic acid.<sup>2</sup>

It is presumed that formaldehyde is produced in vivo from methanol oxidation, because the reaction is known to occur in vitro. Formaldehyde is 30 times more toxic than is methanol, and individuals poisoned with it may become profoundly acidotic. Formates are found in their urine.<sup>6</sup> However, formaldehyde has not been reported in the urine of methanol patients,<sup>4</sup> and the known promptness of formaldehyde reactions with protein makes its determination in the tissues almost impossible.<sup>14</sup>

One-third of the assimilated dose of methanol may remain in the body unaltered for 48 hours,<sup>12</sup> and traces may persist for a week in serious cases.<sup>9</sup>

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Twenty to 70 per cent is excreted unaltered through the lungs.<sup>6, 16</sup> Three per cent is excreted unaltered through the kidneys.<sup>6</sup>

Formic acid is also excreted through the kidneys and will reduce Fehling's solution. This reaction can produce a false test for glycosuria and, in comatose cases, contribute to an incorrect diagnosis of diabetes mellitus.

### MECHANISM OF POISONING

Methyl alcohol produces poisoning in two ways: (1) There is direct destruction and irritation of tissues by methanol or its products. (2) Acid-base balance is disturbed by the organic acid oxidation products of methanol.

The direct tissue toxicity is proportional to the concentration of methanol at various sites. All human cells are susceptible to the poison, but its distribution is largely proportional to the water content of the tissues. Methyl alcohol has unlimited miscibility with water but a very low solvent power for fats.<sup>4, 9, 14</sup>

Among all body fluids, the aqueous and vitreous of the eye have the highest percentage of water. Pooled horse aqueous is 99.6921 per cent water, and pooled horse vitreous is 99.6813 per cent water. Both of these liquids are fat-free.<sup>3</sup> The gastric juices follow a close second, with 99.5 per cent water.

Among the solid tissues of the body, unmedullated nervous tissue has the greatest water content, approximately 85 per cent. White matter, with its fatty myelin sheath, is 70 per cent water.

Thus it happens that intraocular fluid and unmedullated nervous tissues are sites of greatest clinical damage from methanol. Von Oettingen<sup>14</sup> corroborates this scheme of distribution, and has shown that in both poisoned rabbits and dogs the eyes contain greater methanol concentration than that found in any other organ analyzed.<sup>14</sup>

Some investigators have claimed "selective-toxicity" for certain neural structures,<sup>1, 6, 12</sup> and it is possible that the delicacy of highly differentiated cells contributes to the disproportionate destruction of the retina. But Friedman<sup>4</sup> and others<sup>14</sup> seem to be on firmer ground in challenging "selective toxicity," since one need search no further than the water-content of tissues to find an explanation for "susceptibility."

Autopsy findings will be discussed below, but suffice it to say at this point that the direct local action of methanol and formic acid damages the gastrointestinal tract (especially the stomach), the lungs, the kidneys, the liver, the pancreas, the brain and, most markedly, the eyes.

In addition to these local effects, and more important from the standpoint of therapy, methanol poisoning produces acidosis. This is thought to be due largely to the formation of formic acid, and perhaps secondarily to the accumulation of CO<sub>2</sub>. The latter is a consequence of the alveolar damage of methanol. Harrop<sup>7</sup> has alleged that excessive amounts of lactic and

other organic acids are produced in this metabolic disturbance, although the reasons for this process are obscure. Under "Treatment and Results" (below) a possible additional factor, ketosis, is discussed.

### CLINICAL MATERIAL

The 23 cases of methyl alcohol poisoning upon which these observations are based were soldiers or merchant seamen who had ingested "bootleg" sake. The first five of these patients died of respiratory arrest after several hours of coma. They were sporadic cases who had ingested relatively huge amounts of both ethyl and methyl alcohol. The sixth case was brought to the hospital in profound shock and died within four hours. The remaining 17 cases were all victims of the same batch of liquor that had killed the sixth patient, and were treated with alkalis. None died or sustained permanent injury. The pertinent laboratory data are contained in tables 1 and 2.

### SYMPTOMS AND SIGNS

In general, patients who are candidates for therapy are those surviving sudden blindness and precipitous death from overwhelming doses. In common with most other observers, we found these patients seeking or being brought for medical care about 36 hours after ingestion of the methanol.

Mild cases were indistinguishable from patients suffering the aftermaths of ordinary ethyl alcoholism. The "hangover" consisted of headache, dizziness, nausea, lassitude and slight abdominal pain.

Some of the patients complained of violent epigastric pain. Other features were vomiting, delirium and various degrees of blindness.

TABLE I

Admission Summary of Cases Received 36 Hours after Intoxication from Drinking Korean Liquor Containing 16 Per Cent Methyl Alcohol

A. Cases treated as out-patients in mild acidosis with negative blood methanol determinations and no acetonuria:

1 through 10

Urinary pH ranged from 5.5 to 7.5

B. Cases hospitalized in moderate acidosis but with negative blood methanol determinations:

	Urinary pH	Acetonuria	Hospitalized
11	4.0	++++	2 days
12	4.5	++	2 days
13	4.0	+++	2 days
14	5.5	++	1 day

C. Cases hospitalized in severe acidosis with positive blood methanol levels:

	Urinary pH	Acetonuria	Hospitalized	Methanol
15	4.0	+++	3 days	12.0 mg. %
16	5.0	++++	18 days	5.0 mg. %
17	3.5	++++	55 days	39.7 mg. %

D. Case dying in profound acidosis, cyanosis, and shock:

18	5.5	++++	3½ hours	15.6 mg. %
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TABLE II

Blood Alcohol Determinations at Time of Death in Autopsied Cases  
(See Reference 5 for Method)

Case	Methyl Alcohol	Ethyl Alcohol
A	150 mg. %	185 mg. %
B	96 mg. %	400 mg. %
C	60 mg. %	Unknown
D	60 mg. %	300 mg. %
E	45 mg. %	197 mg. %
F	15.6 mg. %	375 mg. %

Sometimes the usual symptoms of inebriation would partially clear, giving a false impression of recovery in the face of impending coma. Coma was frequently accompanied by Kussmaul breathing. Some of the patients then lapsed into a stage of cyanosis, with noisy gurgling respirations and, usually, respiratory arrest before circulatory collapse.

The distinctive odor of methyl alcohol or acetone was usually detected on the breath.

The eye findings show wide variation and are not correlated with the blood methanol level or other clinical signs or symptoms. Without exception we have found the pupils to be dilated and sluggish in response to light in serious cases. The conjunctivae were injected, and there was photophobia if the patient was sufficiently alert. A frequent complaint was reduced central vision, developing 24 hours after ingestion. This was usually in the form of a negative, central scotoma of the relative type. In more severe cases the scotomata may be absolute or multiple and may occur anywhere in the visual fields according to the particular ganglion cells or axon fibers involved. Night blindness, color impairment and yellow vision have been reported by others.<sup>4, 8</sup>

Generalized constriction of the visual fields is not seen in acute cases, and we found no impairment of accommodation as tested on seven surviving serious cases. The fundi may show generalized hyperemia. The disk may be hyperemic and the borders blurred due to papillitis. Here again the lack of correlation with other findings is marked. Funduscopy in one case shortly before and after death failed to reveal *any* objective change, although the pupils were widely dilated and totally unresponsive to light. Two cases admitted with definite papillitis and mild fundic hyperemia had only mild relative, negative, central scotomata on first examination, and on the following day visual acuity was 20/20 and J-1 in all eyes. Secondary optic atrophy has been described in patients whose vision had improved for four to six weeks, with eventual deep, glaucomatous-like cupping of 4 to 6 d.<sup>10</sup> No such changes occurred in our patients.

#### TREATMENT AND RESULTS

Combating the intense acidosis is the most important single feature of therapy. Between 1912 and 1920 much contradictory literature<sup>14</sup> came

from the field of laboratory experiment. Various animals showed highly different acid-base changes. Even after Harrop and Benedict<sup>7</sup> in 1920 emphasized the important rôle of acidosis in man, descriptions of therapy remained cluttered with regimens which are ineffective and sometimes contraindicated. The report of Merritt and Brown<sup>12</sup> in 1941, in which the authors felt alkalization was life-saving in one case, was feebly accepted by standard textbooks. It remained for Chew<sup>1</sup> in 1946 to emphasize forcibly this keystone in treatment. McNally's text,<sup>11</sup> published in 1939, cites a collection of 725 reported cases in which 390 (54 per cent) died, 90 (12.4 per cent) were left totally blind, and 85 (11.7 per cent) were left with visual impairment. Chew, with intensive alkali treatment of 31 cases in 1945, reports five deaths (16 per cent), no total blindness, and only two cases (6.4 per cent) of mild residual visual impairment.

During the period of our first five autopsies, and prior to the epidemic of 18 cases, intensive alkali therapy was not practiced here. The latter patients, however, were managed with primary attention to acidosis. In this group there was only one death and no blindness or residual visual impairment. All of the victims were enlisted men from the same unit who had been drinking Korean sake from the same source. Samples of this beverage were examined and found to contain 16 per cent methyl alcohol. The patients were received on a Sunday morning following the Friday night drinking party. Blood methanol determinations and urinalyses were immediately done on each patient.

Ten, with only mild symptoms of intoxication and urinary pH's of 5.5 or higher, had negative blood methanol tests and no acetonuria. These patients were treated with 6 gm. of sodium bicarbonate every two hours until all urinary pH's reached 7.5. Each of these men returned to duty the following morning, and none had sequelae.

Four other cases, with mild epigastric discomfort, moderate acidosis, but negative blood methanol determinations and no subjective eye difficulties, were hospitalized for a period of two days. Admission urinalyses showed pH between 4.0 and 5.5, with 2 plus to 4 plus acetone. These patients were treated by immediate gastric lavage with 4 per cent sodium bicarbonate, and 500 c.c. of the solution were allowed to remain in the stomach. Urinalyses were repeated every two hours, and sodium bicarbonate was given in doses of 6 to 8 gm. by mouth every two hours. The patients were encouraged to eat heartily, and fluids were forced by mouth. All acetonuria permanently disappeared within 10 hours after admission. The sole ophthalmoscopic finding in this group was 2 plus hyperemia of the disks in one case, and that disappeared by the second day.

Three cases (15, 16, and 17), with serious acidosis, blurring of central vision and marked congestion of the optic disks, were hospitalized with blood methanol levels of 5, 12, and 39.7 mg. per cent, respectively. Urinary pH ranged between 3.5 and 5.0. Contrary to the statement of Voegtlin,<sup>15</sup>

all of our seriously ill patients showed 3 plus or 4 plus acetonuria. Although further work is necessary to clarify the point, we should like to suggest that ketosis may be an additional factor in the production of acidosis and in central nervous system depression. It is postulated that glucose may be a valuable adjunct to alkalization. The mechanism of ketosis is speculative at present. It is possible that hepatic damage may be a factor.

Patients 16 and 17 had blurring of their disk borders. Patient 17 was comatose for an hour, and semi-comatose for 10 hours, and urine specimens were obtained by means of an indwelling catheter. Gastric lavage was performed in each case, and sodium bicarbonate given hourly by Levine tube until the patients were sufficiently cooperative to take oral medication.

Patient 17 was given 200 gm. of sodium bicarbonate in 26 hours before his urine became alkaline, although it is probable that some of the alkali was lost in the stools. Five per cent glucose in normal saline was given intravenously in doses of 3,000 c.c. daily to each patient. It is noteworthy that in patient 17 acetonuria disappeared following each daily glucose infusion for three consecutive days, only to return each night when sodium bicarbonate alone, and no glucose, was being administered.

Reducing substances were not excreted in sufficient amounts to give a positive Benedict's test at any time. Blood methanol levels in all three patients were negative on the day following admission, i.e., about 60 hours after ingestion. Cephalin flocculation tests were only 1 plus and 2 plus in patients 16 and 17, respectively. Patient 15 recovered entirely by the third day and was discharged with no eye findings. Patients 16 and 17 were discharged entirely well after hospitalization of 18 and 55 days, respectively.

The most severe case, 18, had a blood methanol level of 15.6 mg. per cent. He had previously complained of blindness, but was deeply comatose and in profound shock on admission. The urinary pH was 5.5 and Benedict's test was negative, but there was 4 plus acetonuria. Blood sugar was 123 mg. per cent. The eye grounds were negative. Intravenous plasma, glucose and saline were administered, along with oxygen by mask, but respirations ceased three and one-half hours after admission, and heart action became inaudible a few seconds later.

In treating methyl alcohol poisoning, a few other points should be borne in mind. The Levine tube may perforate an acute gastric ulcer, which may appear due to the poisoning, and the tube should not be inserted farther than the cardium. Intravenous solutions of sodium bicarbonate or sixth molar sodium lactate have been well recommended, but unfortunately were not available to us at the time. Aspiration of the trachea and administration of oxygen may be life-saving in view of the frothy bronchial secretions. Plasma seems to be the best agent in combating shock.

Stimulants such as epinephrine and coramine are only transient aids to the basic therapy. Narcotics, frequently advised in the older literature because of the abdominal pain, should be avoided because of their central

nervous system depression. The use of ethyl alcohol on the hypothesis that it displaces methyl alcohol has not been proved to be efficacious, and is contraindicated in view of its depressant action and the fact that these patients may also be severely intoxicated with ethyl alcohol at the outset.

Older clinicians have advised protecting the eyes from light during the acute intoxication or longer-lasting neural inflammation. While we have no proof that this procedure is beneficial, it would seem wise on the basis of resting any organ during a period of inflammation. We used complete occlusion until all signs of acute reaction had disappeared to ophthalmoscopic examination.

#### AUTOPSY MATERIAL

The essential pathologic findings in six autopsied cases were as follows: The brains showed edema and hyperemia. All cases showed varying degrees of gastritis, and one had multiple acute duodenal ulcers. The lungs uniformly showed varying degrees of congestion, edema, patchy atelectasis, and frothy debris within the bronchial passages. In two cases there was desquamation of bronchial epithelium, and one of these had moderate bronchopneumonia. The kidneys in four cases showed marked congestion of the glomerular tufts and cloudy swelling of the convoluted tubules. One of these had desquamation of epithelium in the collecting tubules. Five of the livers were grossly fatty and histologically contained lipoid vacuoles. There was cloudy swelling in the cord cells in two of these. In only one case was the pancreas affected. The changes consisted of mild congestion and parenchymal hemorrhage. The splenic pulp was congested in four cases.

#### SUMMARY

1. Cardinal features in the mechanism, pathology, symptomatology and therapy of methyl alcohol poisoning are reviewed in the light of a series of 23 cases.
2. The two basic mechanisms of poisoning are direct chemical irritation of tissues and systemic acidosis. The former is influenced by the unlimited miscibility of methanol with water and the distribution of water in the tissues of the body.
3. Acidosis is the most important therapeutic consideration. Alkalinization should be prompt and vigorous. It is suggested that ketosis may play a rôle in acidosis and depression, and that intravenous glucose may be an important adjunct to treatment.

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