METHYL ALCOHOL POISONING: DIAGNOSIS AND TREATMENT

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POISONING by methyl alcohol has long been recognized as causing either death or blindness in a large number of cases. As far back as 1880 methyl alcohol was known to be toxic regardless of the portal of entry, including the skin. The tolerance of the individual determines the amount of methyl alcohol necessary to produce poisoning. One man drank 1 pint of a 10 per cent mixture daily without ill effects.[1] A single dose of 4 cc of methyl alcohol was toxic in another individual.[2] Peterson and colleagues have recorded that 10 cc,[3] 30 to 60 cc, and 180 to 240 cc repeatedly caused death.[4] On the other hand, much larger quantities have been taken without temporary or permanent injury. Poisoning by methyl alcohol prior to 1898 was uncommon; however, since then its incidence has increased, especially during the years of the federal prohibition act. A large number of cases resulted then from the criminal sale of adulterated beverages.

Methyl alcohol (CH_3OH), which occurs in wood alcohol, columbian spirits, colonial or manhattan spirits, eagle spirits, wood naphtha, methanol, carbinol, methyl hydroxide, standard wood spirits, green wood spirits, "derail," "sterno," etc., is a light, colorless liquid with an aromatic odor and boils at 64.1° C. It is usually prepared by the destructive distillation of wood or molasses. It may contain such impurities as furfurol, methyl and dimethyl acetate, allyl alcohol and ethyl dimethyl ketone. It is used as an adulterant of ethyl alcohol in methylated spirits, as a solvent of varnishes and at time in the preparation of essences, and in the preparation of Jamaica ginger and peppermint.[5] It has no medicinal uses.

Some form of methyl alcohol is used in making paint, shellac, wood products, rubber, linoleum, leather, soap, photographs, felt hats, aniline dyes, rubbercement, and antifreezes. It is also used in collar-fusing, in printing, in dry cleaning and in many other industries. Acute or chronic poisoning may follow ingestion, inhalation or cutaneous absorption. Applications of rubbing solution containing methyl alcohol to the skin may result in methyl alcohol poisoning as can its incorporation in hair tonics or hand lotions. The maximum allowable concentration for an eight-hour working day is 200 parts per million. Cases of methyl alcohol poisoning are largely accidental and are classed as technical homicides.[5] Sporadic cases occur because methyl alcohol has been inadequately labelled as a poison. Occasionally many persons may be poisoned at the same time when they have maintained a large quantity of it and used it as a beverage.

Fate of Methyl Alcohol in the Body and Mechanism of Poisoning

Whereas ethyl alcohol is readily oxidized and excreted within 24 hours, methyl alcohol may remain in the body for days. The metabolism of methanol is five times slower than that of ethanol. Methanol is not fully oxidized but broken down to formaldehyde and formic acid. Formic acid has been found in abnormal amounts eight days after the ingestion of methyl alcohol. About 40 per cent of the assimilated dose may be oxidized to formic acid, which is six times more toxic than methanol.[7] The B10-degradation of methanol has been assumed to be: methanol to formaldehyde to formate to carbon dioxide. Formaldehyde has not been detected in appreciable quantities but has been assumed to be an intermediate and oxidized to formate as rapidly as formed. Formaldehyde has not been reported in the urine cases of methanol poisoning perhaps because the prompt reaction of formaldehyde with protein makes its detection in tissues almost impossible. The combustion of C-14 labeled methanol in comparison with ethanol has been studied in rats and the more rapid metabolism of the latter was demonstrated.[8, 9]

The retention of the intermediate products undoubtedly explains some of the delayed toxic effects in methyl alcohol poisoning, especially the prolongation of coma for several days,[5] the profound acidosis, resulting from the formation of formic acid and to the CO_2 accumulation, is the direct cause of death. Methanol and its products also directly irritate and destroy tissues, and the by-products of their organic acid oxidation disturb acid balance. The associated acidosis has long been recognized but was not fully appreciated until recently. Ketosis has been suggested as an additional factor in the production of acidosis and in central nervous system depression. Formaldehyde or formic acid has been assumed to be responsible for the nerve injury: the toxic substances reaching the optic nerve by way of the central retinal vessels are rapidly absorbed by the tissues where these substances come in contact with the papillomacular bundle. The retinal ganglion

Important Statement

100% MeOH
↓
60% H_2CO
40% HCOOH

HCOOH is 6x more toxic than MeOH

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cells undergo irreversible degenerative changes.

The direct tissue toxicity of tissue 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. Among all body fluids, the aqueous and vitreous of the eye have the highest percentage of water, and among the solid tissues of the body non-myelinated nervous tissue has the greatest water content, approximately 85 per cent.[7] The eye and non-myelinated nervous tissues show the greatest damage from methanol and in experimental animals show at least the greatest methanol concentration.

Signs and Symptoms

Methyl Alcohol is more deleterious to the human body than ethyl alcohol, as its action is more prolonged and its products of decomposition are more toxic. The effects are depression of the central nervous system, acidosis, cerebral edema, and specific toxic action upon the optic and vagus nerves and the respiratory center. Individuals vary greatly in their susceptibility. Some may be only slightly affected and may completely recover after ingesting a larger amount than killed others. There is no correlation among the clinical picture, the amount ingested, level of plasma carbon dioxide combining power or the eye changes.[11] Tolerance is not acquired. Symptoms of methyl alcohol poisoning usually are delayed for 1 to 72 hours, during which time some individuals may be able to carry on normally. Such patients are usually in good physical condition until they pass into a coma, which directly precedes death. However, symptoms may appear soon after ingestion, and death may occur within two hours. Like ethyl alcohol but slower in action, methyl alcohol can produce intoxication. In general, however, the latent period of methyl alcohol poisoning is not attended by inebriation.

In contrast to the initial stimulation produced by grain alcohol, methyl alcohol causes a primary depression of the central nervous system. As one of the survivors of a methanol drinking party of eight men remarked: "No one was drunk, nor even felt elated, so the whole thing was rather a failure." There may be headaches, dizziness, weakness, temporal pain, dimness of vision, nausea, vomiting, diarrhea, drowsiness, epigastric and or back pain, stupor progressing to coma, dyspnea of the kussmaul type and cyanosis. Occasionally the sequence is delirium, maniacal behaviour, convulsions, coma and death. The abdominal pain and guarding of the muscle may be severe enough to simulate an acute condition within the abdomen. Pains of the back or flank may be similar to renal colic. Smooth spasm of the muscle is believed to be the mechanism responsible for this pain. Headache may be severe and be accompanied by nuchal rigidity. If death does not occur the coma may persist for several days before improvement occurs.

Ingestion of methyl alcohol frequently leads to some degree of optic atrophy and permanent blindness, although not all individuals are so affected. In general, however, the eyes are usually involved in patients who suffer severe systemic symptoms. During World War II, methyl alcohol became an official problem for the armed forces. Many who drank beverages containing methyl alcohol were permanently blinded, but not all were sick or suffered any visual disturbances. Bilateral visual impairment is the most distressing sequel of methyl alcohol poisoning and may occur as an early or late complication of acute intoxication. Symptoms which may begin within a few hours or days include pain on moving the eyes, tenderness to touch, and mild photophobia, followed by or associated with blurred vision or reduced central vision and total blindness within 10-24 hours. Indistinct vision, variously described is the most frequent complaint. If total blindness is present the prospect of any recovery is poor. If blindness is not complete, there is considerable contraction of the field of vision, night blindness, color impairment and yellow vision. If there is a permanent partial loss of vision, the usual finding is a central scotoma. Visual impairment may also result from chronic exposure to the poison.

Diagnosis

The diagnosis of methyl alcohol poisoning is usually made in the presence of a toxic state and acidosis following exposure to methyl alcohol or ingestion of an alcoholic beverage, after which ocular disturbances and symptoms listed exist. There may be loss of vision, supraorbital or retrobulbar pain, dilated and sluggish pupils, mild hyperemia of the retina and disc margins, blurring of the disc due to papillitis, and engorgement of the blood vessels. The odor of methyl alcohol may be detected on the breath. The diagnosis of an individual case may be difficult in the absence of a history of ingestion. A toxicologist may be able to demonstrate an excess of formic acid in a submitted urine specimen from a suspected clinical case. Normally about 0.251 grams of formic acid is excreted each 24 hours,[5] and to diagnose methyl alcohol poisoning one should demonstrate a considerable ex-

less quantity of this substance in the urine. The urine may be strongly acid and contain albumin, numerous hyaline and granular casts, acetone and ketone. Formic acid excreted in the urine will reduce Fehling's solution. Since it can falsely produce a positive test for glycosuria, one may incorrectly diagnose a comatose patient as being in a diabetic coma. Examination of blood may demonstrate the presence of methyl alcohol. A simple "bedside" technique for the determination of the serum carbon dioxide is available.

Illustrative Cases

Case I: P.B., a 28-year-old white man, with three other individuals (see below), drank a solution which they thought to be an intoxicating beverage. (It was found on subsequent analysis to contain 90 per cent methyl alcohol.) He consumed 7½ ounces (225 cc.) in two equally divided doses over a 24-hour period, following which he was admitted to the hospital semi-stuperous. He complained of a staggering gait, pain on moving his eyes, blurred vision, nausea, vomiting, severe occipital headache and dizziness. He was admitted to the hospital semi-comatose and in acidosis. (CO_2 combining power 18 vols. %) twenty-four fours after admission, he was completely blind. Therapy included gastric lavage, oral and intravenous sodium bicarbonate and sodium lactate. He recovered but remained totally blind.

Case II: F.L., a 29-year-old white man, drank 8 ounces (240 cc.) of the same solution as case I within a similar period. Twenty-four hours later he noted some mild pain when he moved his eyes and minimal blurring of vision. He did not seek hospitalization. Without therapy, he recovered completely, with no visual impairment. No systemic or residual visual abnormalities could be detected on subsequent examinations.

Case III: J.K., a 36-year-old white man, drank 5 ounces (150 cc.) of the same solution as case I. Almost immediately thereafter he vomited several times. He took a tablespoonful of sodium bicarbonate to "settle my stomach" and subsequently noted no further symptoms. He did not seek hospitalization, and no residual systemic or visual abnormalities could be detected on subsequent examinations.

Case IV: E.L., a 32-year-old white man, drank 4 ounces (120 cc.) of the same solution as case I and ate a hearty meal immediately thereafter. He noted no effect whatsoever. He did not seek hospitalization, and no residual systemic or visual abnormalities could be detected on subsequent examinations.

Therapy

In the initial stage, within a reasonable time after the poison has been ingested, gastric lavage should be instituted and repeated at frequent intervals. The levin tube must be inserted cautiously so as not to perforate an acute gastric ulcer which may have been induced. Lavage with a 4 per cent solution of sodium bicarbonate is recommended. Although the efficacy of sodium bicarbonate in treating methyl alcohol poisoning has been known theoretically for many years, it has only recently been employed. As far back as 1920, Harrop and Benedict observed that patients suffering from methyl alcohol poisoning showed marked acidosis and were successfully treated with intravenous sodium bicarbonate.[11] The treatment of acidosis should not be delayed pending the identification of methyl alcohol. Rather as soon as the plasma CO_2 combining power is shown to be 40 volumes per cent or less, sodium bicarbonate should be administered. It may be given by mouth or by intravenous injection or a sterile 3 to 5 per cent solution in distilled water or 5 per cent glucose. Intravenous alkali may also be administered in the form of 1/6 molar sodium R-lactate in isotonic solution of three chlorides; the amount given depends upon the plasma carbon combining power, as determined by repeated anaylses. Prompt treatment to correct the existing acidosis by intravenous sodium lactate and oral bicarbonate has been reported repeatedly with good results.[7, 10, 11] Besides correcting the acidosis, one should keep the patient warm. Intravenous glucose is also advisable, as some degree of hepatic insufficiency is often present. Administration of stimulants such as metrazol, camphor in oil, coramine, caffeine-sodium-benzoate and epinephrine is only of ephemeral aid. If there is abdominal pain, one should avoid using narcotics despite recommendation in older literature because they effect cerebral depressant. If cerebral edema is present, a 50 per cent solution of sucrose may be helpful. Roe has observed that patients who had more or less simultaneously consumed methyl alcohol and ethanol were less severely toxic[12] than those who had drunk just methyl alcohol. Roe postulated that ethanol blocked the formation of toxic oxidation products and allowed excretion of unchanged methanol. On that basis, ethanol was recommended in addition to the treatment of the acidosis and good results were reported.[12] This treatment has not been generally accepted however, and some authors believe it is contraindicated.[7] Except for damage to the eyes, most abnormalities from chronic exposure usually disappear. In treating

Ignorance is bliss

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NEW BOOKS

As an accommodation to our readers, the following books or any medical book published in America will be delivered prepaid in the United States or Canada, if the order is sent to the Radiologic Review Publishing Co., P. O. Drawer 110, Quincy, Illinois, and accompanied by a check for the published price.

ESSENTIALS OF PUBLIC HEALTH

William P. Shepard, B.S., M.A., M.D., Clinical Professor of Public Health and Preventive Medicine, Stanford University School of Medicine. With the Collaboration of Charles Edward Smith, M.D., D.P.H.; Rodney Rau Beard, M.D., M.P.H.; and Leon Benedict Reynolds, B.A., Sc.D. Second Edition. 581 pages, with 20 illustrations and 27 charts. Price $6.50, J. B. Lippincott Co., 1952.

THE second edition of this book should be particularly useful to the physician in private practice and to all professional people interested in community health. From the founding of the U.S.P.H. Service as the Marine Hospital in 1798, this department has developed into one of the most efficient and potent public health forces in the world. The Public Health Department was placed under the Treasury Department when Alexander Hamilton was Secretary of the Treasury. Even if we think we have eradicated a disease, we must maintain our "stand-by" defense and equipment. The author emphasizes the great need for medical stabilization of the health education program devoted to nutrition. When the teacher and the physician understand each other's language and agree precisely as to what they should do for the child's health, more rapid progress will be made in the school health program. Better delineation of the duties of the public health nurse and the school nurse will result in more cooperation and less duplication of work. The three most important health agencies in any community are the health department, the schools, and the medical profession. In the industrial world, the physician's role is fairly well defined. He is the arbiter between the disabled workmen and the employers. Since management and labor unions are poorly equipped to negotiate and administer plans for medical care without advice, the physician has an essential place in industry. The reader is constantly kept aware of the fact that public health education is to improve health behavior.

—E. M. Hulse

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the visual impairment, hot packs, subconjunctival and retrobulbar saline injections and retrobulbar injection of atropine have been tried without success. Short wave diathermy treatment of the eyes to produce hyperemia with increase in local metabolism has been recommended and reported as beneficial.[13] The eyes should be protected from light during the acute intoxication and during the ensuing period of neural inflammation, until all signs of acute reaction have disappeared to ophthalmoscopic examination. ACTH or cortisone has not been of benefit.

Pathological Findings

At postmortem examination, there is moderate lividity, cyanosis, and congestion of the viscera. There is edema, congestion and patchy atelectasis of the lungs, and hemorrhage into the subpleural and subepicardial tissues. The mucous membranes of the stomach, duodenum and bladder may be congested and show numerous petechial hemorrhages and ulcerations. Edema and hyperemia of the brain are outstanding features. There is degeneration of the ganglion cells of the retina as well as of nervous tissue throughout the body. Histologic examination of the eyes reveals a massive exudation from the choriocapillaries, defects in the pigment epithelium, and detachment of the retinal layers; retinal vessels show evidence of increased permeability, perivascular edema, and edema of the whole nerve layer. Parenchymatous degenerative changes may be seen in the myocardium, tubular changes in the kidneys, fatty changes in the liver and mild congestion and parenchymal hemorrhage of the pancreas.[7] The pathologic lesions are not characteristic, and therefore reliance must be placed on toxicologic examination. As a rule in methyl alcohol poisoning, there is no distinctive odor to the organs.

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DETECTION, SELECTION AND REFERRAL OF PATIENTS FOR SURGERY OF ACQUIRED HEART LESIONS

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cardial infarction (possibly on an embolic basis) is a rare finding except in individuals with advanced aortic valvular lesions. Seldom do these coronary disturbances complicate the candidate for commissurotomy.

Special Tests

Cardiac catheterization, angiocardiography, ballistocardiography, roentgenkymography and orthodiagraphy are superfluous in evaluating candidates for surgery for acquired heart disease, in my experience of over 500 cases.

Other Considerations

Age, of itself, is no contraindication to surgery. Since arteriosclerotic changes are statistically more preponderant in patients with a rheumatic background, obviously there will arise the problems of coronary disease, intra-atrial and intra-auricular thromboses of fragile material, and of heavily calcified valves. These cannot, and need not, be appreciated adequately and are inherent risks of the procedure.

Rheumatic activity is a definite contraindication to surgery. Bacteremia of any type, including subacute bacterial endocarditis, nullifies the possibility of operation.

Previous peripheral embolism is more of an indication to operate than not. Prevention of these conditions by intra-atrial thrombectomy and/or auricular appendectomy (routinely done at commissurotomy) may be life-saving.

Recommending Surgery

If technical evaluation indicates that mitral commissurotomy is the therapy of preference, can you **recommend** it to your patient? In this, as in other references, your professional reputation in the community lies in a degree of jeopardy should the result be less than satisfactory! Your patient, too, will want to know his chances of actual survival, length of morbidity, probable degree of improvement. In short, he wants the prognosis.

In properly selected cases, the **surgical-anesthesiological mortality rate** for mitral commissurotomy does not exceed 5 per cent. This rate compares very favorably with statistics relative to many other less dramatic operations; it is a rate far below that for certain hazardous procedures, such as intracranial neurosurgery.

Acute morbidity is a matter of two weeks—the same period required for the herniorrhaphy patient of 10 years ago. After the period of acute morbidity, the patient should have a protracted convalescence of at least 30 days and may gradually resume his activity up to the point of **tiredness.**

Long-term **prognosis,** it must be emphasized, depends heavily on how well the convalescent protects his newly-won gains by staying within his bounds of exercise-tolerance. **Tiredness,** always short of **fatigue,** must be his delimiting factor.

Armed with this information for your candidate for commissurotomy, you can avoid the embarrassing situation of being unable to answer his queries about an operation which he has been reading so much about in lay periodicals.

Choose your case well, prepare him psychologically, and follow his course with assurance and satisfaction.

The Figures (A and B)

These two cases with superficial similarities are striking contrasts of young individuals who should **not** be operated on and of middle-age persons who **should** be referred for surgery. Special attention is called to those considerations in the text under the heading, "Choosing the Lesion."

Note particularly that the decisive factors in evaluating each of these cases required no prohibitively specialized techniques. The general practitioner can readily make such appraisal in his office or in the community hospital.