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THE OCULAR EFFECTS OF METHYL ALCOHOL POISONING:

Report of a Catastrophe Involving Three Hundred and Twenty Persons

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BY INVITATION
and

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ATLANTA, GA.

ON OCTOBER 20, 1951 a large quantity of bootleg whiskey containing 35 per cent methyl alcohol and 15 per cent ethyl alcohol was distributed in Atlanta, Georgia. During the succeeding seven days, three hundred and twenty persons sought emergency medical care at Grady Memorial Hospital because of symptoms attributable to the ingestion of this mixture. Twenty-four persons died before or shortly after reaching the hospital and thirteen died on the medical wards, making a total of thirty-seven deaths. A general report of these cases has been published elsewhere.⁵

Ophthalmic observations were made by one of the authors (Benton) on a large proportion of the patients immediately upon their acceptance to the hospital emergency room. Data were recorded concerning the amount of contaminated whiskey consumed and the date thereof, onset and character of symptoms, the vision, pupillary reaction to light, visual fields (confrontation method) and ophthalmoscopic appearance of the fundi. Every patient admitted to a hospital bed was examined daily until the time of his discharge and then at gradually longer intervals in the eye clinic. Measurements of visual acuity and central visual fields and ob-

servations of the ocular fundi were made at each visit during the eight month follow-up period. Patients who were never admitted to the hospital were asked to report to the eye clinic for examination. One hundred and twenty-three patients returned for re-examination.

The symptoms of acute methyl alcohol poisoning usually develop eighteen to forty-eight hours after ingestion, but in a few instances transitory symptoms were noted within one hour. The patients complained of visual disturbances, weakness, abdominal pain, nausea and vomiting, headache, dizziness, and shortness of breath. Some patients had consumed as little as 90 cc. of the alcoholic mixture and others had drunk as much as 750 cc. Within this range there was no close correlation between the severity of symptoms and the quantity of methyl alcohol consumed.

The initial visual symptoms ranged from spots before the eyes to complete blindness. Many patients complained of whitish or grayish misty vision. The visual acuity was either normal or markedly reduced. The patients with severe visual loss could count fingers only in the mid-periphery of their visual field. Three patients who were conscious had no light perception in either eye. Characteristically, the initially reduced vision showed an early recovery which was in some cases only transitory. Many patients experienced full return of vision

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during the first hour of treatment by intravenous alkaline fluids. All patients who regained and retained normal visual acuity did so within six days after treatment was begun. If the vision did not return to normal in six days, it invariably dropped again to a very low level. Only 3 patients, all nearly or completely blind at the time of hospital admission, failed to exhibit any permanent or temporary improvement in vision.

In the acute phase of poisoning, diminution of the pupillary reaction to light occurred in all patients with impaired vision and in many patients with normal vision. The degree of impairment of the pupillary light reflex proved to be of considerable prognostic value. Patients with dilated, fixed pupils usually died; if they recovered they always had severe visual damage. Lesser degrees of impairment in the pupillary response to light were indicative of a more favorable outcome and no patient with normally reacting pupils had permanent visual loss. These findings are illustrated in figure 1.

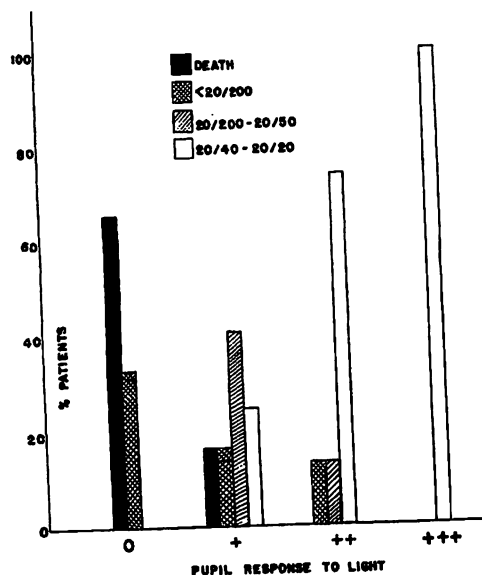


FIG. 1.—Correlation of pupillary response to light with fatality and final vision (+++ equals normal reaction).

The ophthalmoscopically visible fundus changes were always identical in type and sequence of appearance and varied only in intensity from one patient to the next. A hyperemia of the optic disc could be seen at the time symptoms of visual loss developed. The reddish color of the papilla persisted from one to seven days. From six to twenty-four hours after the hyperemia became visible, there developed a whitish striated edema of the disc margins and adjacent retina. Edema was most extensive along the course of the major retinal vessels, and it persisted for ten to sixty days. The peripapillary retinal edema appeared to be chiefly in the nerve fiber layer. Engorgement of the retinal veins usually accompanied the retinal edema and followed a similar course. These characteristic fundus changes were seen in 87 per cent of patients with initial visual loss and in every patient who later showed permanent impairment of vision. Mild or moderate retinal edema was followed by complete recovery of vision in some cases, blindness in others. It was found, however, that all patients who had severe retinal edema and most patients with moderate retinal edema had some degree of permanent visual loss.

In patients with severe ocular damage an atrophy of the optic disc became visible in thirty to sixty days. Usually the optic nerve atrophy was identical in appearance to so-called primary optic atrophy, although occasionally a cupping of the nerve head that simulated glaucoma was seen.

In 5 patients there was a striking difference between the visual acuity of the two eyes, even though the ophthalmoscopic changes were always bilaterally equal. In 4 of the 5 such cases, the left eye was the most severely impaired. The shape of the scotomas offered the explanation of this difference in visual acuity. In the central field of the better

ACUTE METHYL ALCOHOL POISONING

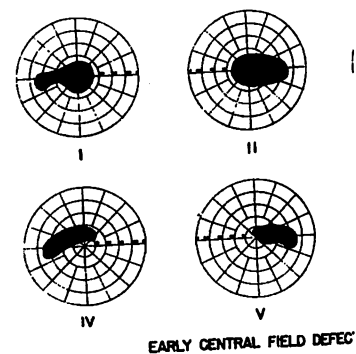


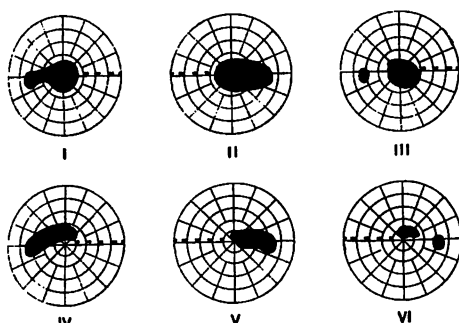
FIG. 2.—Acute methyl alcohol poisoning. Early central field defects (5/1000 form).

eye, the scotoma extended blind spot like an open mouth to engulf the fixation area. In the worse eye a complete cecocentral scotoma obliterated the area of vision. After four to six months visual acuity in the better eye declined and approached the level of the worse eye.

The typical alteration of the central field was a cecocentral scotoma of considerable density. Frequency of scotoma was incomplete, arching above or around the point and did not impair visual acuity. A few patients had a paracentral scotoma with the blind spot (fig. 3). In these patients the peripheral field was restricted in the early stages for four months various and atypical defects of the fiber-bundle type appeared in the peripheral field. These defects eliminated all or most of the peripheral field (fig. 3). The symptoms described above are similar to those reported previously by others.^{2,3,4,6,10,14,17,20,21}

Chemical studies revealed the presence of methyl alcohol in the urine, spinal fluid, aqueous humor, and the humors of the eye. The

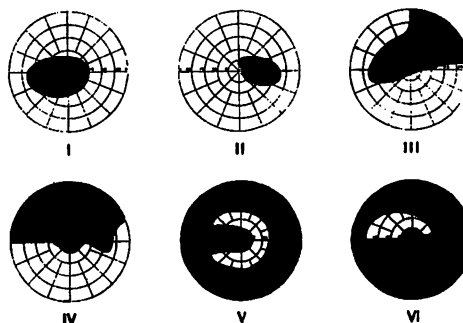
ACUTE METHYL ALCOHOL POISONING



EARLY CENTRAL FIELD DEFECTS

FIG. 2—Acute methyl alcohol poisoning. Early central field defects (5/1000 form).

ACUTE METHYL ALCOHOL POISONING



LATE CENTRAL FIELD DEFECTS

FIG. 3—Acute methyl alcohol poisoning. Late central field defects (5/1000 form).

eye, the scotoma extended from the blind spot like an open mouth preparing to engulf the fixation area. In the opposite eye a complete cecocentral scotoma obliterated the area of critical vision. After four to six months, the visual acuity in the better eye began to decline and approach the level of the other eye.

The typical alteration of the visual field was a cecocentral scotoma of considerable density. Frequently this type of scotoma was incomplete so that it arched above or around the fixation point and did not impair central visual acuity. A few patients had a pericentral or paracentral scotoma not connected with the blind spot (fig. 2). In only 2 patients was the peripheral field constricted in the early stages. After two to four months various and bizarre alterations appeared in the visual fields. Defects of the fiber-bundle type and peripheral constriction usually combined to eliminate all or most of the field of vision (fig. 3). The symptoms and signs described above are similar to those reported previously by other authors.^{2,3,4,6,10,14,17,20,21}

Chemical studies revealed the presence of methyl alcohol in the blood, urine, spinal fluid, aqueous and vitreous humors of the eye. The concentration

was always greater in the vitreous than in the aqueous of the eight eyes tested. A trace of formaldehyde was found in the vitreous of one eye. Formic acid was not detected in the aqueous or vitreous of either eye in one fatal case.

The most important alteration in the biochemical status of persons poisoned with methyl alcohol occurs in the carbon dioxide combining capacity of the blood. The blood carbon dioxide was measured on every patient immediately upon his acceptance into the emergency clinic. The degree of acidosis proved to be an invaluable guide to diagnosis, therapy, and prognosis. This point has been repeatedly stressed by Røe and others since 1943.^{4,7,14-17} The blood carbon dioxide was normal (above 26 milliequivalents per liter, or 55 volumes per cent) in 188 patients. Not one patient in this group had genuine symptoms or signs of methanol poisoning and undoubtedly many of these patients drank none of the contaminated whiskey. No treatment was given any patient who had a normal blood carbon dioxide. Follow-up studies were done two to six months later on 94 or 50 per cent of this group of patients, and not one had evidence of any visual damage from methyl alcohol. The blood carbon dioxide was 25 milliequivalents per liter or below in the re-

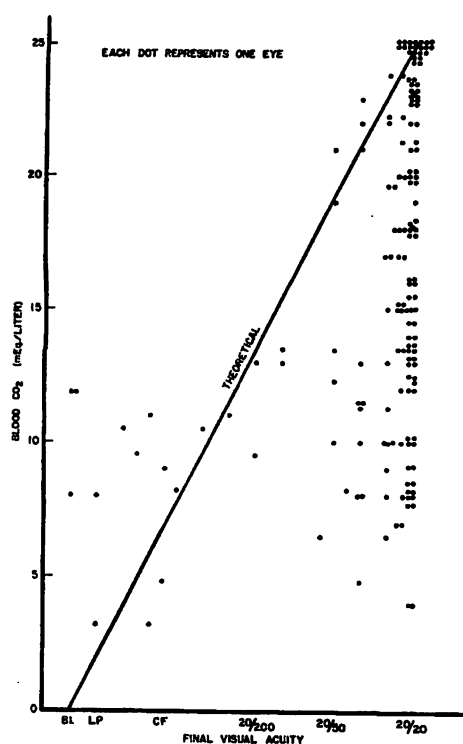


FIG. 4.—Correlation of initial blood carbon dioxide with final visual acuity. (The wide scattering of the dots on the graph does not conform to the theoretical correlation as represented by the diagonal line.)

maining 132 patients. Thirty-seven of these patients died. All fatal cases had a severe acidosis with the blood carbon dioxide usually below 10 milliequivalents per liter. Death was always characterized by cessation of respiration from medullary paralysis. Convulsions were common. The heart usually continued to beat for several minutes after respirations stopped. When it was possible to obtain a history on the patients who died, it was learned that they were always blind or nearly blind before their final loss of consciousness. Ninety-five patients with a low blood carbon dioxide survived the poisoning. Sixty-two of these patients had visual symptoms. Objective ophthalmoscopic findings were present only in patients with visual symptoms, and occurred in 87 per cent

of those. The relation of blood carbon dioxide before treatment to the final visual acuity showed that chances of restoration of complete vision was possible at almost any carbon dioxide level, but patients with a very low carbon dioxide level frequently had permanent loss of vision. No patient with a carbon dioxide level above 12 milliequivalents per liter had a final visual acuity worse than 20/200 in either eye. These findings are illustrated graphically in figure 4.

Treatment was directed toward the elimination of acidosis in those patients with a low blood carbon dioxide. Bicarbonate of soda was taken by mouth in patients whose symptoms were mild and whose blood carbon dioxide was between 20 and 25 milliequivalents per liter. Patients with a very low carbon dioxide and severe symptoms were given soda bicarbonate intravenously. The available supply of already prepared alkaline solutions for intravenous administration was quickly exhausted. New solutions were readily prepared by dissolving the dry powder from clean, previously unopened boxes of bicarbonate in flasks of sterile glucose, saline, or distilled water. Several hundred such solutions containing 25 to 50 grams of bicarbonate per liter were given intravenously with no ill effects. Symptoms of alkalosis rarely developed even though the blood carbon dioxide rose to 40 or 50 milliequivalents per liter in some patients. Because of the strong tendency for acidosis to recur, it was found that alkali therapy had to be continued for a minimum of three days, with constant check of the blood carbon dioxide or urine pH. This was strikingly demonstrated in 4 patients who were treated in the emergency clinic and failed to follow instructions to take soda bicarbonate orally at home. They were brought back the next day in severe acidosis and died.

Adequate correction of acidosis in patients with severe methemoglobinemia will not invariably result in vision. If the acidosis is persisted for several hours result in spite of energetic treatment if the patient survives. A marked loss of vision.

Also, inadequate alkalinization result in a prolonged state of moderate acidosis and permanent vision. These observations are treated by the following cases.

Cases 6, 7 and 8 demonstrate prolonged acidosis as the result of inadequate alkalinization.

Case 6. This Negro boy aged 12 consumed a half pint of the mixture two days before admission. Vision reduced to 20/200 in the right eye and counting in the left eye. The blood carbon dioxide was 9 milliequivalents per liter. Sixty grams of soda bicarbonate intravenously quickly elevated the blood carbon dioxide to 27 mEq. per liter, but by the next day it had dropped to 17 mEq. per liter. Administration of 16 grams of soda bicarbonate returned the blood carbon dioxide to 27 mEq. per liter. The final visual acuity was 20/30 and O.S., fingers at 18 inches. A central scotoma persisted in the right eye whereas a pericentral scotoma spared the fixation area.

Case 7. This 26-year-old Negro consumed a half pint of the mixture 18 hours before admission. The vision became blurred and he did not seek treatment for another 24 hours. At that time his vision was reduced to counting at 10 inches. The blood carbon dioxide was 13 mEq. per liter. Sixty grams of soda bicarbonate intravenously elevated the blood carbon dioxide to 30.5 mEq. per liter. The following day the blood carbon dioxide had fallen to 16 mEq. per liter. Administration of 16 grams of soda bicarbonate by mouth brought the blood carbon dioxide up to 22 mEq. per liter. The final visual acuity was O.D., 20/100.

Case 8. This 40-year-old Negro consumed a half pint of the mixture. Dimness of vision developed after 12 hours. The blood carbon dioxide was 13 mEq. per liter.

Adequate correction of acidosis in patients with severe methyl alcohol poisoning will not invariably save life or vision. If the acidosis is severe or has persisted for several hours, death may result in spite of energetic treatment, or if the patient survives, he may have marked loss of vision.

Also, inadequate alkali therapy may result in a prolonged state of mild or moderate acidosis and permanent loss of vision. These observations can be illustrated by the following examples:

Cases 6, 7 and 8 demonstrated prolonged acidosis as the result of inadequate alkalization.

Case 6. This Negro boy aged 19, had consumed a half pint of the methanol mixture two days before admission. Visual acuity was reduced to 20/200 in the right eye and finger counting in the left eye. The blood carbon dioxide was 9 milliequivalents (mEq.) per liter. Sixty grams of soda bicarbonate intravenously quickly elevated the blood carbon dioxide to 27 mEq. per liter, but the following day it had dropped to 17 mEq. per liter. The administration of 16 grams of soda by mouth returned the blood carbon dioxide to 28 mEq. per liter. The final visual acuity was O.D. 20/30 and O.S., fingers at 18 inches. A cecentral scotoma persisted in the left central field whereas a pericecal scotoma in the right field spared the fixation area.

Case 7. This 26-year-old Negro male drank a half pint of the poisoned whiskey. Within 18 hours the vision became blurred. He did not seek treatment for another 18 hours, at which time his vision was reduced to finger counting at 10 inches. The blood carbon dioxide was 13 mEq. per liter. Fifty grams of soda bicarbonate intravenously elevated the blood carbon dioxide to 30.5 mEq. per liter. The following day the blood carbon dioxide had fallen to 16 mEq. per liter. Thirty-five grams of soda by mouth brought the blood carbon dioxide up to 22 mEq. per liter. The final visual acuity was O.D., 20/200 and O.S., 20/100.

Case 8. This 40-year-old Negro man had consumed a half pint of the methyl alcohol mixture. Dimness of vision was experienced after 12 hours. The blood carbon dioxide was

15 mEq. per liter. For four days the blood carbon dioxide remained below 20 mEq. per liter in spite of an initial dose of 50 grams of bicarbonate of soda intravenously followed by oral doses of 30 to 45 grams daily. Although this patient could count fingers accurately at 10 inches at the time of admission, he became and remained totally blind.

Cases 3 and 5 show the tendency for acidosis to recur after initial correction.

Case 3. This Negro woman, aged 34, became blind 48 hours after consuming a half pint of the contaminated bootleg whiskey. The initial blood carbon dioxide was 9 mEq. per liter. Soda bicarbonate was given intravenously in doses of 35 grams and later 20 grams. The blood carbon dioxide remained above 20 mEq. per liter the following 36 hours and then fell to 23 mEq. per liter. No further treatment was given. The final visual acuity was O.D., 20/200 and O.S., fingers at 6 inches. A cecentral scotoma persisted in the left field whereas the right fixation area was spared by a pericecal scotoma.

Case 5. This 37-year-old Negro man drank "a little bit" of the methyl alcohol whiskey eight hours before being brought to the hospital. Amblyopia was severe and the blood carbon dioxide was 5 mEq. per liter. After 75 grams of soda intravenously the blood carbon dioxide became normal and remained so during the following day. Twenty-four hours later the blood carbon dioxide had dropped to 16 mEq. per liter but was again elevated to normal by the oral administration of 30 grams of soda. The final visual acuity was O.D., 20/40 and O.S., fingers at 18 inches. Again the difference in visual acuity between the two eyes was due to a cecentral scotoma in the left eye and a pericentral scotoma in the right eye.

The poor vision in cases 2 and 4 is evidence that adequate alkali therapy will not always prevent blindness.

Case 2. This 43-year-old Negro man drank a moderate quantity of the poisoned whiskey over a two-day period. Blurred vision was experienced one day later. The patient was not brought to the hospital until the following day, at which time he was blind. The blood carbon dioxide was 8 mEq. per liter. One hundred and twenty grams of soda intravenously elevated the blood carbon dioxide to 50 mEq. per liter, where it remained for at least two

days. Inspite of this he gained vision and then again became blind

Case 4. A 47-year-old Negro drank a half glass of the poison There was headache, nausea and six hours followed the next day of vision. The blood carbon dioxide time of hospital admission was 3 liter. After 40 and 30 grams of venously the blood carbon dioxide over 40 mEq. per liter for two visual acuity improved in two more 20/100 and O.S., fingers at 6 dropped to finger counting in the and light perception in the left.

Normal vision may result in face of initially low blood carbon dioxide if treatment is prompt.

Case 1. This 20-year-old Negro experienced abdominal pain and 10 hours after drinking a half glass leg whiskey. The blood carbon 4 mEq. per liter. After 100 gr. intravenously the blood carbon well above normal for at least two visual acuity quickly returned to both eyes and has remained the

ACTH was given to for with no beneficial effect. Spin change therapy was carried times on 3 patients who had ual loss.^{11,12} No improvement from this treatment. Ethyl a given intravenously to only 1 Although definite improvement served, this is not given because in favor of the belief alcohol should be used in the of methyl alcohol poisoning.¹

Histologic examinations removed six to eighteen hours death showed degeneration of glion cells of the retina, slight the nerve fiber layer near the degeneration of the rod and with accumulation of a small albuminous fluid under the the disc. All these changes been the results of normal p degeneration, particularly

CASES

DAY		1 L.R.	2 D.N.	3 R.F.	4 L.S.	5 W.G.	6 R.H.	7 W.M.	8 W.R.M.
1	CO ₂ Soda CO ₂ Soda	4 100 gm. 42	8 120 gm. 52	9 35 gm. 30 20 gm.	3 40 gm. 33 30 gm.	5 75 gm. 26	9 60 gm. 27	13 50 gm. 30.5	15 50 gm. 22
2	CO ₂ Soda	43	49	36	42	38	17 16 gm.	16 35 gm.	12 45 gm.
3	CO ₂ Soda			23	45	16 30 gm.	28	22 20 gm.	19 30 gm.
4	CO ₂ Soda					35			19 30 gm.
Final Vision	O. D. O. S.	20/20 20/20	L.P. Blind	20/200 C.F.	C.F. L.P.	20/40 C.F.	20/30 C.F.	20/200 20/100	Blind Blind

days. In spite of this he gained only a little vision and then again became blind.

Case 4. A 47-year-old Negro woman drank a half glass of the poisoned whiskey. There was headache, nausea and vomiting in six hours followed the next day by blurring of vision. The blood carbon dioxide at the time of hospital admission was 3.2 mEq. per liter. After 40 and 30 grams of soda intravenously the blood carbon dioxide remained over 40 mEq. per liter for two days. The visual acuity improved in two months to O.D., 20/100 and O.S., fingers at 6 inches, then dropped to finger counting in the right eye and light perception in the left.

Normal vision may result even in the face of initially low blood carbon dioxide if treatment is prompt.

Case 1. This 20-year-old Negro girl experienced abdominal pain and poor vision 24 hours after drinking a half glass of the boot-leg whiskey. The blood carbon dioxide was 4 mEq. per liter. After 100 grams of soda intravenously the blood carbon dioxide was well above normal for at least two days. The visual acuity quickly returned to normal in both eyes and has remained the same.

ACTH was given to four patients with no beneficial effect. Spinal fluid exchange therapy was carried out several times on 3 patients who had severe visual loss.^{11,19} No improvement resulted from this treatment. Ethyl alcohol was given intravenously to only one patient. Although definite improvement was observed, this is not given here as evidence in favor of the belief that ethyl alcohol should be used in the treatment of methyl alcohol poisoning.^{1,2,14-17}

Histologic examinations on six eyes removed six to eighteen hours after death showed degeneration of the ganglion cells of the retina, slight edema of the nerve fiber layer near the disc, some degeneration of the rod and cone layer with accumulation of a small amount of albuminous fluid under the retina near the disc. All these changes could have been the results of normal post-mortem degeneration, particularly since the

changes were more prominent in those eyes removed at eighteen hours than in those removed at six hours after death. Other investigators have presented considerable evidence that degeneration of the retinal ganglion cells is a specific toxic effect of methyl alcohol.^{6,8,14-17}

Other pathologic findings of interest were a mild to moderate edema of the brain and an acute pancreatitis. Studies of cerebral blood flow were done on five patients with severe poisoning. The average arterial oxygen saturation was 92 per cent. Cerebral blood flow was reduced 33 per cent and cerebral oxygen consumption was diminished 35 per cent. Serum amylase determinations on several patients showed moderate to marked high levels, therefore it was felt that acute pancreatitis was often the cause of the severe abdominal pains in these patients.⁵

Many theories have been advanced to explain the mode of toxic action of methyl alcohol in the human body.^{6,9,13,14-18} It is unfortunate that laboratory animals do not respond to this agent in a manner similar to the human. Acidosis almost never develops and the animals do not often appear to go blind. Fink⁶ and also McGregor⁸ have described degeneration of the retinal ganglion cells in animals poisoned with methyl alcohol, but this has been denied by Røe.¹⁴⁻¹⁷ Conclusions from experiments on animals should be applied to humans with great caution and reservation.

Apparently methyl alcohol breaks down slowly in the body to formaldehyde and formic acid. It appears unlikely that any of these chemicals acts directly on the retina or other nerve tissue. Methyl alcohol is rapidly distributed throughout all body fluids but symptoms of poisoning rarely develop in less than eighteen hours after ingestion. According to the theory of Rohr,¹³ methyl alcohol or one of its breakdown products

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Visual Damage Not Symmetric (often)

C. D. BENTON, JR. AND F. P. CALHOUN, JR.

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slowly combines with the iron catalyst of the oxydase system rendering it inactive and causing a tissue anoxia. This process is accelerated in the presence of acidosis.¹⁴⁻¹⁷ Because the retina has the highest oxygen requirement per unit concentration of iron of any body tissue, it is not surprising that this delicate ocular membrane should be damaged in methyl alcohol poisoning. An indirect toxic action, as just described, offers a ready explanation for the parallelism of ocular symptoms and signs of methanol poisoning with the amblyopia of lead, arsenic, thallium, or carbon disulfide poisoning or even that of severe malnutrition.¹² Recently Potts and Johnson⁹ found evidence that the proximal toxic agent in methanol poisoning may be formaldehyde, a potent inhibitor of retinal oxidation and glycolysis. The acidosis does not appear to be the cause of amblyopia but it does act as an accelerating force. If acidosis can be corrected before permanent ocular damage has resulted, a return of normal visual acuity can be expected. If retinal tissue hypoxia has existed long enough for irreversible degeneration of the ganglion cells to occur, treatment may prevent death but visual impairment will be permanent. Until a specific chemical is found that will prevent or release the combination of methyl alcohol or its products with the iron oxydase system, rapid, intense, and prolonged alkalinization appears to be the most important phase of treatment for acute methyl alcohol poisoning.

SUMMARY

Clinical and pathologic observations on a group of three hundred and twenty patients with acute methyl alcohol poisoning are reported. There were thirty-seven deaths.

Visual symptoms, occurring eighteen to forty-eight hours after ingestion of methanol, included blurred vision, loss

of central vision and complete blindness. The pupils reacted sluggishly or not at all to light. Absence of the pupillary light reflex was a sign of poor prognosis for life or eventual restoration of visual acuity. The visible retinal changes were hyperemia of the optic nerve head and superficial edema of the papilla and surrounding retina, and later a simple atrophy of the optic nerve. All patients with severe retinal edema had some degree of permanent visual loss. The earliest central field defect was usually a cecentral scotoma. Later more complex types of visual field defects appeared.

Acidosis was present in every severely poisoned patient. The degree of acidosis paralleled the severity of general and ocular symptoms.

Partial or complete recovery of the initially reduced visual acuity was observed in most patients. If the visual acuity did not return to normal within six days after treatment was begun, it invariably dropped again to a very low level. The final vision was 20/200 or less in both eyes of six patients and in one eye of three patients.

Histologic studies on six eyes enucleated after death revealed changes consistent with post-mortem degeneration.

On the basis of the results obtained in this series of cases, the most effective treatment of acute methyl alcohol poisoning consists of intensive and prolonged alkalinization. Alkalinization

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Stage 1
Stage 2
Stage 3
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DISCUSSION

ALBERT M. POTTS, M.D., Cleveland, Ohio (by invitation): It is at once a great pleasure and privilege to be asked to discuss this report of Drs. Benton and Calhoun. They are without doubt the two living ophthalmologists with the greatest experience in clinical methyl alcohol poisoning and the observations which they made have the virtue of high significance because of the large number of cases observed.

The importance of methanol poisoning as an ever-present menace lies in the very fact that such a catastrophe as the one reported could occur within the past year. Its seriousness is underlined by the statistic that of all cases reported here showing any symptoms 28 per cent, or one for every three and one half patients, died (320 less 188 symptom-free = 132 cases of which 37 deaths = 28 per cent). Of the survivors an equal proportion had some measurable visual damage and 10 per cent of the survivors were made blind, retaining vision of 20/200 or less.

Although the number of individuals involved in this instance is an unprecedentedly high one, instances of smaller outbreaks of methyl alcohol poisoning are still not uncommon among the civilian population. In the Armed Forces, where access to ethyl alcohol is restricted, methanol is a constant hazard as some of Dr. Calhoun's earlier papers testify. In one series of World War II veterans, methanol poisoning accounted for 6 per cent of blindness from all causes and this may be considered a representative figure.

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chrome-cytochrome oxidase system, is much less sensitive to formaldehyde than is glycolysis. Subsequent work, as yet unpublished, shows that the hexokinase system which phosphorylates glucose is the actual site of inhibition. Thus the chemical site of action is actually at the beginning not at the end of the metabolic cycle. There is no evidence that retinal hypoxia is a feature of methanol poisoning.

The caution of the authors about the use of experimental animals is well taken. Methanol poisoning is obviously not the same in experimental animals as it is in humans. One need only examine the lethal dose for rats as compared to humans to realize that in grams per kilogram of body weight the dose to kill a rat is some ten times higher than that for man and that on this weight basis methyl alcohol is no more toxic to a rat than ethyl alcohol. Actually one must be observing a narcotic type organic solvent poisoning in the rat and a specific metabolic product poisoning in the human—two very different effects. Nevertheless opportunities to observe human cases as numerous as this series come once in a lifetime, and when they come they must be instantaneously used to advantage or the opportunity is forever lost. What is more, the pressure to institute life-saving measures is so great that controlled experimentation is out of the question. For this reason the Western Reserve laboratory has made every effort to locate a suitable experimental test object. This effort is being prosecuted in several directions. With the help of the electroretinogram a survey of visual methanol toxicity in lower animals is being made with particular emphasis on cone retinas and mixed retinas and the utilization of lower primates. In addition human biopsy and autopsy material is being employed for in vitro work. It is hoped that by some such approach the necessity of waiting for disasters may be short-circuited.

When such an event as the one under consideration does occur, we are most fortunate if we have individuals like the authors available to seize the opportunity and make the most of it. I believe that they should be congratulated for their handling of the situation and for extracting from it the data presented here.

F. PHINIZY CALHOUN, JR., M.D., Atlanta, Ga.: A catastrophe of this magnitude provides the chance of a lifetime to observe the acute and late eye manifestations of this condition. Dr. Benton was able to devote practically his

full time to recording and evaluating the eye findings during the acute stages. The analyses given today, therefore, are the results of hundreds of eye examinations of these patients made during the acute and follow-up stages of the condition.

It may be worth while to mention the panic and terror which characterized the catastrophe. Among the consumers of so-called "alley" whiskey, hysteria mounted as news of the poisoning spread. The sidewalks outside the hospital became crowded day and night with worried relatives. The emergency clinic became swamped with victims, both real and otherwise, and some method of rapid screening of these patients became necessary. Although the commonest symptom was some disturbance of vision and the only useful physical signs in screening patients for treatment were the ophthalmoscopic findings of disc hyperemia and retinal edema, occasionally severely poisoned patients failed to show these changes. Fortunately there was at hand a new bedside method of determining the carbon dioxide combining power of the blood which required simple equipment and produced a highly accurate reading in a few minutes. This test then became a quick, reliable method of screening patients for treatment and of following therapy.

The actual poisoning agent and the significance of the acidosis in this condition are still unsettled problems. Although the acidosis may have nothing to do directly with the visual loss it remains a fact that in many cases, relief of symptoms with sodium bicarbonate therapy was prompt and satisfactory; with correction of acidosis, there was return of consciousness, disappearance of pain and nausea and improvement in subjective visual complaints. A few, however, despite return of the carbon dioxide combining power to normal remained comatose and died in a few days. It was the strong clinical impression that the massive alkalinization utilized in the treatment of this series of patients prevented a greater loss of life and vision than actually occurred.

Answering Dr. Potts' question, according to local newspaper accounts the offending bootlegger and plainly marked drum of methanol were soon found. The man was tried, convicted, sentenced to life, and is at present appealing for a retrial.

Figures of the time factors in the acidosis are given in the paper. We are well aware of Dr. Potts' recent beautiful work in this condition and believe that he is very close to a solution of the entire problem.

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Thomas G. Perkins,* 1856, p. 23

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THE OCULAR EFFECTS OF METHYL ALCOHOL POISONING:*

REPORT OF A CATASTROPHE INVOLVING 320 PERSONS

CURTIS D. BENTON, JR., M.D.
Fort Lauderdale, Florida

AND

F. PHINIZY CALHOUN, JR., M.D.
Atlanta, Georgia

On October 20, 1951, a large quantity of bootleg whiskey containing 35 percent methyl alcohol and 15 percent ethyl alcohol was distributed in Atlanta, Georgia. During the succeeding seven days, 320 persons sought emergency medical care at Grady Memorial Hospital because of symptoms attributable to the ingestion of this mixture. Twenty-four persons died before or shortly after reaching the hospital and 13 died on the medical wards, making a total of 37 deaths. A general report of these cases has been published elsewhere.⁵

Ophthalmic observations were made by one of us (C.D.B.) on a large proportion of the patients immediately upon their acceptance to the hospital emergency room. Data were recorded concerning the amount of contaminated whiskey consumed and the date thereof, onset and character of symptoms, the vision, pupillary reaction to light, visual fields (confrontation method), and ophthalmoscopic appearance of the fundi.

Every patient admitted to a hospital bed was examined daily until the time of his discharge and then at gradually increasing intervals in the eye clinic. Measurements of visual acuity and central visual fields and observations of the ocular fundi were made at each visit during the eight months' follow-up period. Patients who were never admitted to the hospital were asked to report

to the eye clinic for examination; 123 patients returned for re-examination.

SYMPTOMS

The symptoms of acute methyl alcohol poisoning usually developed 18 to 48 hours after ingestion, but in a few instances transitory symptoms were noted within one hour. The patients complained of visual disturbances, weakness, abdominal pain, nausea and vomiting, headache, dizziness, and shortness of breath. Some patients had consumed as little as 90 cc. of the alcoholic mixture and others had drunk as much as 750 cc. Within this range there was no close correlation between the severity of symptoms and the quantity of methyl alcohol consumed.

The initial visual symptoms ranged from spots before the eyes to complete blindness. Many patients complained of whitish or grayish misty vision. The visual acuity was either normal or markedly reduced. The patients with severe visual loss could count fingers only in the midperiphery of their visual field. Three patients who were conscious had no light perception in either eye.

Characteristically, the initially reduced vision showed an early recovery which was in some cases only transitory. Many patients experienced full return of vision during the first hour of treatment by intravenous alkaline fluids. All patients who regained and retained normal visual acuity did so within six days after treatment was begun.

If the vision did not return to normal in six days, it invariably dropped again to a very low level. Only three patients, all nearly or completely blind at the time of

* From the Department of Ophthalmology, Emory University School of Medicine, and the Grady Clay Memorial Eye Clinic, Grady Memorial Hospital, Atlanta, Georgia. Presented at the 53rd annual meeting of the American Academy of Ophthalmology and Otolaryngology, Chicago, 1952.

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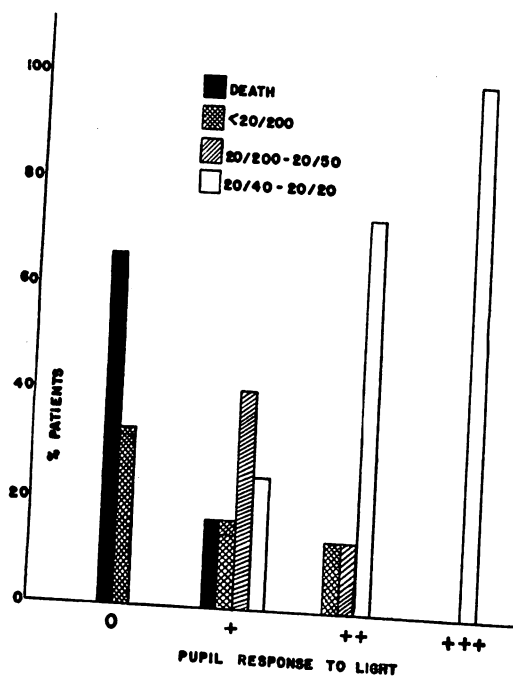


Fig. 1 (Benton and Calhoun). Correlation of pupillary response to light with fatality and final vision (+++ equals normal reaction).

hospital admission, failed to exhibit any permanent or temporary improvement in vision.

In the acute phase of poisoning, diminution of the pupillary reaction to light occurred in all patients with impaired vision and in many patients with normal vision. The degree of impairment of the pupillary light reflex proved to be of considerable prognostic value. Patients with dilated, fixed pupils usually died; if they recovered, they always had severe visual damage. Lesser degrees of impairment in the pupillary response to light were indicative of a more favorable outcome and no patient with normally reacting pupils had permanent visual loss. These findings are illustrated in Figure 1.

The ophthalmoscopically visible fundus changes were always identical in type and sequence of appearance and varied only in intensity from one patient to the next. A hyperemia of the optic disc (color plate, fig. a) could be seen at the time symptoms

of visual loss developed. The reddish color of the papilla persisted from one to seven days.

From six to 24 hours after the hyperemia became visible, there developed a whitish striated edema of the disc margins and adjacent retina. Edema was most extensive along the course of the major retinal vessels, and it persisted for 10 to 60 days. The peripapillary retinal edema (color plate, figs. b and c) appeared to be chiefly in the nerve fiber layer. Engorgement of the retinal veins usually accompanied the retinal edema and followed a similar course.

These characteristic fundus changes were seen in 87 percent of patients with initial visual loss and in every patient who later showed permanent impairment of vision.

Mild or moderate retinal edema was followed by complete recovery of vision in some cases, blindness in others. It was found, however, that all patients who had severe retinal edema and most patients with moderate retinal edema had some degree of permanent visual loss.

In patients with severe ocular damage, an atrophy of the optic disc became visible in 30 to 60 days. Usually the optic nerve atrophy (color plate, fig. d) was identical in appearance to so-called primary optic atrophy, although occasionally a cupping of the nerve head that simulated glaucoma was seen.

In five patients there was a striking difference between the visual acuity of the two eyes, even though the ophthalmoscopic changes were always bilaterally equal. In four of the five such cases, the left eye was the most severely impaired.

The shape of the scotomas offered the explanation of this difference in visual acuity. In the central field of the better eye, the scotoma extended from the blindspot like an open mouth preparing to engulf the fixation area. In the opposite eye, a complete centrocecal scotoma obliterated the area of critical vision. After four to six months, the visual acuity in the better eye began to decline and approach the level of the other eye.

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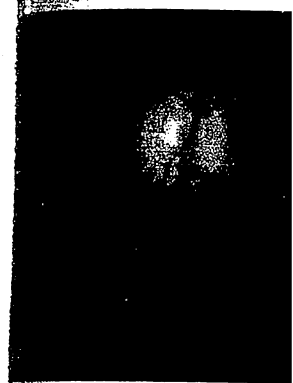


FIG. A



FIG. C

FIGS. A TO D (BENTON AND CALHOUN). A) STAGE I. HYPEREMIA OF THE OPTIC DISC. B) STAGE II-A. MILD PERIPAPILLARY RETINAL EDEMA. C) STAGE II-B. SEVERE PERIPAPILLARY RETINAL EDEMA. D) STAGE III. OPTIC ATROPHY.

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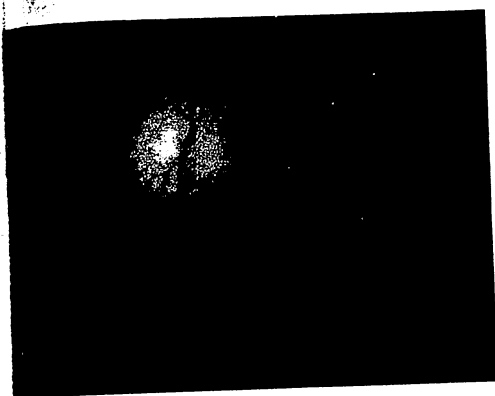


FIG. A

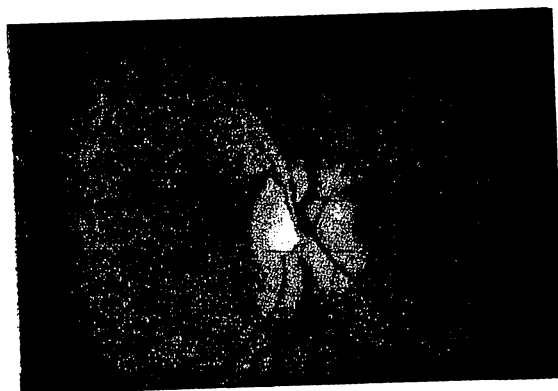


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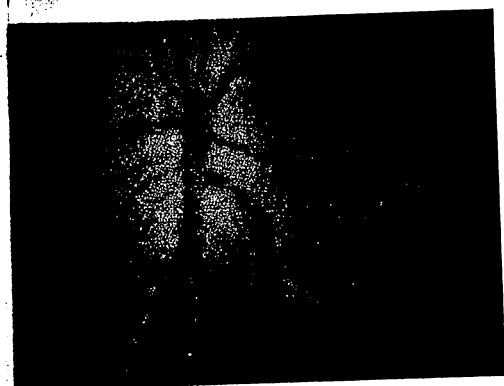


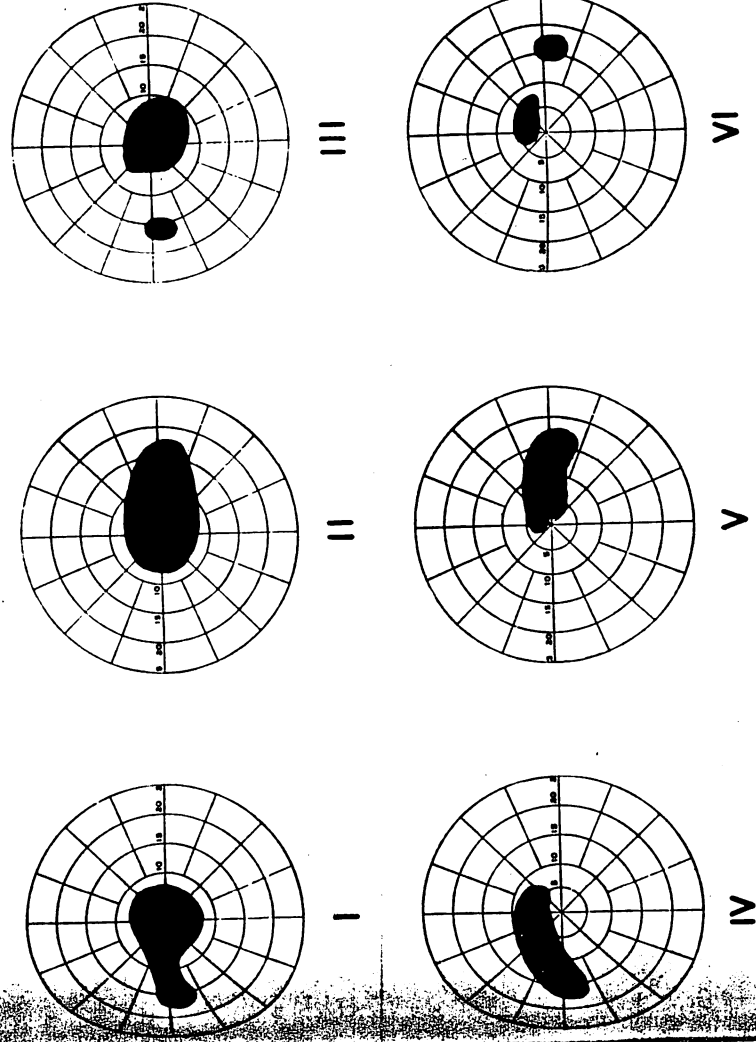
FIG. C



FIG. D

FIGS. A TO D (BENTON AND CALHOUN). ACUTE METHYL ALCOHOL POISONING.
 (FIG. A) STAGE I. HYPEREMIA OF THE OPTIC DISC.
 (FIG. B) STAGE II-A. MILD PERIPAPILLARY RETINAL EDEMA.
 (FIG. C) STAGE II-B. SEVERE PERIPAPILLARY RETINAL EDEMA.
 (FIG. D) STAGE III. OPTIC ATROPHY.

ACUTE METHYL ALCOHOL POISONING



EARLY CENTRAL FIELD DEFECTS

Fig. 2 (Benton and Calhoun). Acute methyl alcohol poisoning. Early central field defects (5/1,000 white test object).

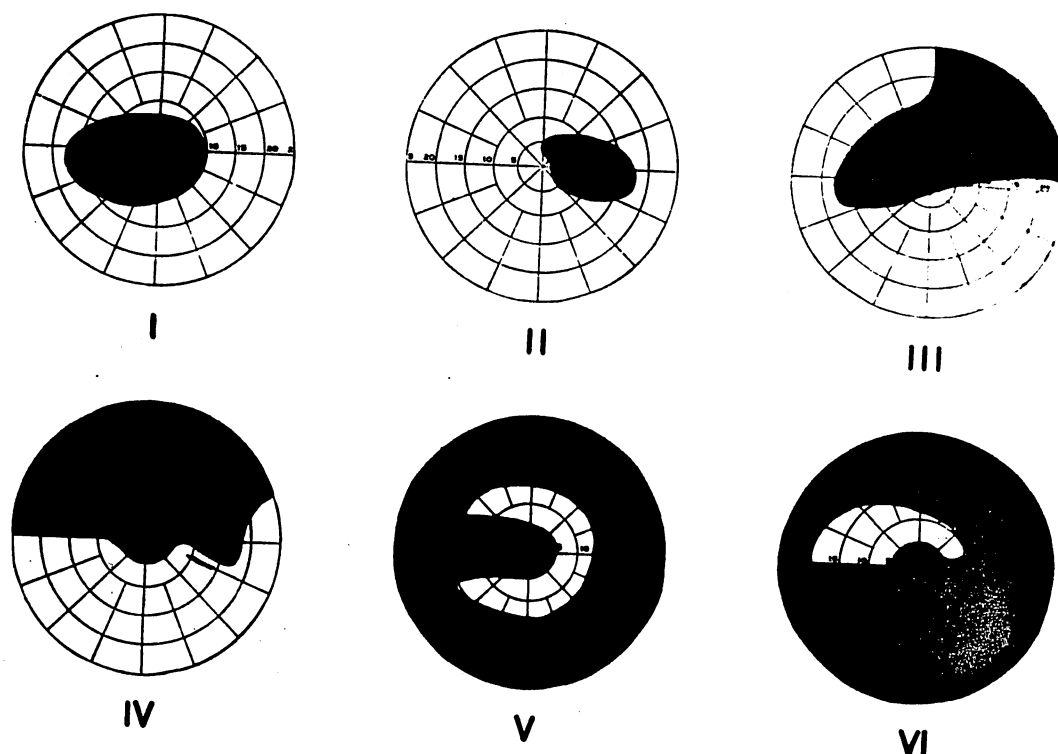
The typical alteration of the visual field above are similar to those reported previously by other authors.^{2-6,10,14,17-18}

CHEMICAL STUDIES

Chemical studies revealed the presence of methyl alcohol in the blood, urine, spinal fluid, aqueous, and vitreous humors of the eye. The concentration was always greater in the vitreous than in the aqueous of the eight eyes tested. A trace of formaldehyde was found in the vitreous of one eye. Formic acid was not detected in the aqueous or vitreous of either eye in one fatal case.

The most important alteration in the biochemical status of persons poisoned with methyl alcohol occurs in the carbon-dioxide

ACUTE METHYL ALCOHOL POISONING



LATE CENTRAL FIELD DEFECTS

Fig. 3 (Benton and Calhoun). Acute methyl alcohol poisoning. Late central field defects (5/1,000 white test object).

combining capacity of the blood. The blood CO_2 was measured on every patient immediately upon his acceptance into the emergency clinic. The degree of acidosis proved to be an invaluable guide to diagnosis, therapy, and prognosis. This point has been repeatedly stressed by Roe and others since 1943.^{4, 7, 14-17}

The blood CO_2 was normal (above 26 milliequivalents per liter, or 55 volumes percent) in 188 patients. Not one patient in this group had genuine symptoms or signs of methanol poisoning and undoubtedly many of these patients drank none of the contaminated whiskey. No treatment was given any patient who had a normal blood CO_2 .

Follow-up studies were done two to six

months later on 94, or 50 percent, of this group of patients, and not one had evidence of any visual damage from methyl alcohol.

The blood CO_2 was 25 milliequivalents per liter or below in the remaining 132 patients. Thirty-seven of these patients died. All fatal cases had a severe acidosis with the blood CO_2 usually below 10 m.e.q./liter. Death was always characterized by cessation of respiration from medullary paralysis. Convulsions were common. The heart usually continued to beat for several minutes after respirations stopped.

When it was possible to obtain a history on the patients who died, it was learned that they were always blind or nearly blind before their final loss of consciousness. Ninety-

patients with a low blood CO_2 level had no visual symptoms. Sixty-two of the patients had visual symptoms.

Objective ophthalmoscopic examination was present only in patients with severe acidosis and occurred in 87 percent of the patients. The relation of blood CO_2 level to the final visual acuity showed that the occurrence of complete visual loss was almost any CO_2 level, but that very low CO_2 frequently had a better prognosis of vision. No patient with a blood CO_2 level of 12 m.e.q./liter had a final visual acuity better than 20/200 in either eye. This is illustrated graphically in Figure 3.

TREATMENT

Treatment was directed toward correction of acidosis in those patients with a low blood CO_2 . Bicarbonate was given by mouth in patients who were mild and whose blood CO_2 was above 20 and 25 m.e.q./liter. In very low CO_2 and severe symptoms, sodium bicarbonate intravenously was given. The available supply of alkaline solutions for intravenous use was quickly exhausted. Solutions were readily prepared by adding dry powder from clean, previously sterilized flasks of bicarbonate in flasks of sterile saline or distilled water.

Several hundred such solutions were prepared, containing 25 to 50 gm. of bicarbonate per liter, and given intravenously with no untoward symptoms of alkalosis rarely developing, though the blood CO_2 rose to 40 m.e.q./liter in some patients.

Because of the strong tendency for acidosis to recur, it was found that treatment had to be continued for a few days, with constant check of blood CO_2 or urine pH. This was illustrated in four patients who were brought to the emergency clinic and failed to follow instructions to take soda bicarbonate at home. They were brought back to the hospital in severe acidosis and died.

patients with a low blood CO_2 survived poisoning. Sixty-two of these patients had visual symptoms.

Objective ophthalmoscopic findings were present only in patients with visual symptoms and occurred in 87 percent of those. The relation of blood CO_2 before treatment to the final visual acuity showed that chances of restoration of complete vision was possible at almost any CO_2 level, but patients with a very low CO_2 frequently had permanent loss of vision. No patient with a CO_2 above 12 m.e.q./liter had a final visual acuity worse than 20/200 in either eye. These findings are illustrated graphically in Figure 4.

TREATMENT

Treatment was directed toward the elimination of acidosis in those patients with a low blood CO_2 . Bicarbonate of soda was given by mouth in patients whose symptoms were mild and whose blood CO_2 was between 20 and 25 m.e.q./liter. Patients with a very low CO_2 and severe symptoms were given soda bicarbonate intravenously.

The available supply of already prepared alkaline solutions for intravenous administration was quickly exhausted. New solutions were readily prepared by dissolving the dry powder from clean, previously unopened boxes of bicarbonate in flasks of sterile glucose, saline or distilled water.

Several hundred such solutions containing 25 to 50 gm. of bicarbonate per liter were given intravenously with no ill effects. Symptoms of alkalosis rarely developed even though the blood CO_2 rose to 40 or 50 m.e.q./liter in some patients.

Because of the strong tendency for acidosis to recur, it was found that alkali therapy had to be continued for a minimum of three days, with constant check of the blood CO_2 or urine pH. This was strikingly demonstrated in four patients who were treated in the emergency clinic and failed to follow instructions to take soda bicarbonate orally at home. They were brought back the next day in severe acidosis and died.

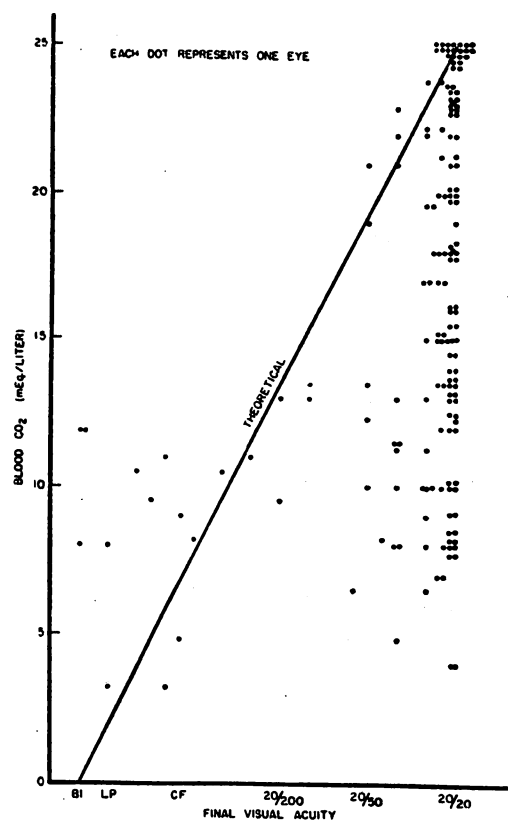


Fig. 4 (Benton and Calhoun). Correlation of initial blood CO_2 with final visual acuity. The wide scattering of the dots on the graph does not conform to the theoretic correlation represented by the diagonal line.

Adequate correction of acidosis in patients with severe methyl alcohol poisoning will not invariably save life or vision. If the acidosis is severe or has persisted for several hours, death may result in spite of energetic treatment, or, if the patient survives, he may have marked loss of vision.

Also, inadequate alkali therapy may result in a prolonged state of mild or moderate acidosis and permanent loss of vision. These observations are illustrated in Table 1.

CASE REPORTS

Cases 6, 7, and 8 demonstrated prolonged acidosis as the result of inadequate alkalization.

Case 6. This Negro, aged 19 years, had consumed one-half pint of the methanol

TABLE 1
RESULTS OF ALKALI THERAPY

Day	Case	1 L. R.	2 D. N.	3 R. F.	4 L. S.	5 W. G.	6 R. H.	7 W. M.	8 W. R. M.
1	CO ₂ Soda CO ₂ Soda	4 100 gm. 42	8 120 gm. 52	9 35 gm. 30 20 gm.	3 40 gm. 33 30 gm.	5 75 gm. 26	9 60 gm. 27	13 50 gm. 30.5	15 50 gm. 22
2	CO ₂ Soda	43	49	36	42	38	17 16 gm.	16 35 gm.	12 45 gm.
3	CO ₂			23	45	16 30 gm.	28	22 20 gm.	19 30 gm.
4	CO ₂					35			19 30 gm.
Final R.E. Vision L.E.		20/20 20/20	L. P. Blind	20/200 C. F.	C. F. L. P.	20/30 C. F.	20/20 C. F.	20/200 20/100	Blind Blind

mixture two days before admission. Visual acuity was reduced to 20/200 in the right eye and finger counting in the left eye. The blood CO₂ was 9 m.e.q./liter. Sixty gm. of soda bicarbonate intravenously quickly elevated the blood CO₂ to 27 m.e.q./liter, but the following day it had dropped to 17 m.e.q./liter. The administration of 16 gm. of soda by mouth returned the blood CO₂ to 28 m.e.q./liter. The final visual acuity was: R.E., 20/30; L.E., counting fingers at 18 inches. A centrocecal scotoma persisted in the left central field, whereas a pericecal scotoma in the right field spared the fixation area.

Case 7. This 26-year-old Negro drank one-half pint of the poisoned whiskey. Within 18 hours the vision became blurred. He did not seek treatment for another 18 hours, at which time his vision was reduced to finger counting at 10 inches. The blood CO₂ was 13 m.e.q./liter. Fifty gm. of soda bicarbonate intravenously elevated the blood CO₂ to 30.5 m.e.q./liter. The following day the blood CO₂ had fallen to 16 m.e.q./liter. Thirty-five gm. of soda by mouth brought the blood CO₂ up to 22 m.e.q./liter. The final visual acuity was: R.E., 20/200; L.E., 20/100.

Case 8. This 40-year-old Negro had consumed one-half pint of the methyl alcohol

mixture. Dimness of vision was experienced after 12 hours. The blood CO₂ was 15 m.e.q./liter. For four days the blood CO₂ remained below 20 m.e.q./liter in spite of an initial dose of 50 gm. of bicarbonate of soda intravenously followed by oral doses of 30 to 45 gm. daily. Although this patient could count fingers accurately at 18 inches at the time of admission, he became and remained totally blind.

Cases 3 and 5 show the tendency for acidosis to recur after initial correction.

Case 3. This Negress, aged 34 years, became blind 48 hours after consuming one-half pint of the contaminated bootleg whiskey. The initial blood CO₂ was 9 m.e.q./liter. Soda bicarbonate was given intravenously in doses of 35 gm. later 20 gm. The blood CO₂ remained above 30 m.e.q./liter the following 36 hours and then fell to 23 m.e.q./liter. No further treatment was given.

The final visual acuity was: R.E., 20/200; L.E., counting fingers at six inches. A centrocecal scotoma persisted in the left field whereas the right fixation area was spared by a pericecal scotoma.

Case 5. This 37-year-old Negro drank "a little bit" of the methyl alcohol whiskey eight hours before being brought to the hospital. Amblyopia was severe and the blood CO₂ was 5 m.e.q./liter.

After 75 gm. of soda in blood CO₂ became normal the following day. The blood CO₂ had dropped but was again elevated by administration of 30 gm. of soda. Visual acuity was R. counting fingers at 18 inches. The difference in vision between the two eyes was due to a scotoma in the left eye and a scotoma in the right eye.

The poor vision in Case 4 was due to the fact that adequate alkali therapy prevented blindness. **Case 2.** This 43-year-old patient received a moderate quantity of the mixture over a two-day period. He experienced one day later when he was brought to the hospital. The day at which time the blood CO₂ was 8 m.e.q./liter. Soda intravenously elevated the blood CO₂ to 50 m.e.q./liter where it remained for two days. In spite of this he had little vision and then became blind. **Case 4.** A 47-year-old patient drank half glass of the poisoned whiskey. He had headache, nausea, and vomiting. Hours followed the next day when he became blind.

The blood CO₂ at the time of admission was 3.2 m.e.q./liter. 50 gm. of soda intravenously elevated the blood CO₂ to 40 m.e.q./liter. The visual acuity improved to 20/100, right eye, counting fingers at six inches, left eye, counting fingers at 18 inches in the left.

Normal vision may be restored after initially low blood CO₂ is promptly corrected.

Case 1. This 20-year-old patient experienced abdominal pain 12 hours after drinking one-half pint of bootleg whiskey. The blood CO₂ was 5 m.e.q./liter. After 100 gm. of soda intravenously the blood CO₂ was 30 m.e.q./liter. The visual acuity was 20/20, right eye, counting fingers at 18 inches, left eye, counting fingers at 18 inches.

After 75 gm. of soda intravenously, the blood CO_2 became normal and remained so during the following day. Twenty-four hours later the blood CO_2 had dropped to 16 m.e.q./liter but was again elevated to normal by the administration of 30 gm. of soda. The final visual acuity was R.E., 20/40; L.E., counting fingers at 18 inches.

Again the difference in visual acuity between the two eyes was due to a centrocecal scotoma in the left eye and a pericentral scotoma in the right eye.

The poor vision in Cases 2 and 4 is evidence that adequate alkali therapy will not always prevent blindness.

Case 2. This 43-year-old Negro drank a moderate quantity of the poisoned whiskey over a two-day period. Blurred vision was experienced one day later. The patient was not brought to the hospital until the following day at which time he was blind. The blood CO_2 was 8 m.e.q./liter; 120 gm. of soda intravenously elevated the blood CO_2 to 50 m.e.q./liter where it remained for at least two days. In spite of this he gained only a little vision and then again became blind.

Case 4. A 47-year-old Negress drank one-half glass of the poisoned whiskey. There was headache, nausea, and vomiting in six hours followed the next day by blurring of vision.

The blood CO_2 at the time of hospital admission was 3.2 m.e.q./liter. After 40 and 30 gm. of soda intravenously the blood CO_2 remained over 40 m.e.q./liter for two days. The visual acuity improved in two months to 20/100, right eye, and finger counting at six inches, left eye, then dropped to finger counting in the right eye and light perception in the left.

Normal vision may result in the face of initially low blood CO_2 if treatment is prompt.

Case 1. This 20-year-old Negress experienced abdominal pain and poor vision 24 hours after drinking one-half glass of the bootleg whiskey. The blood CO_2 was 4 m.e.q./liter. After 100 gm. of soda intra-

venously the blood CO_2 was well above normal for at least two days. The visual acuity quickly returned to normal in both eyes and has remained the same.

ACTH was given to four patients with no beneficial effect. Spinal fluid exchange therapy was carried out several times on three patients who had severe visual loss.^{10, 18} No improvement resulted from this treatment. Ethyl alcohol was given intravenously to only one patient. Although definite improvement was observed, this is not given here as evidence in favor of the belief that ethyl alcohol should be used in the treatment of methyl alcohol poisoning.^{1, 2, 14}

HISTOLOGIC STUDY

Histologic examinations on six eyes removed six to 18 hours after death showed degeneration of the ganglion cells of the retina, slight edema of the nerve-fiber layer near the disc, some degeneration of the rod-and-cone layer, with accumulation of a small amount of albuminous fluid under the retina near the disc.

All these changes could have been the results of normal post-mortem degeneration, particularly since the changes were more prominent in those eyes removed at 18 hours than in those removed at six hours after death. Other investigators have presented considerable evidence that degeneration of the retinal ganglion cells is a specific toxic effect of methyl alcohol.^{8, 9, 14}

Other pathologic findings of interest were a mild to moderate edema of the brain and an acute pancreatitis. Studies of cerebral blood flow were done on five patients with severe poisoning. The average arterial oxygen saturation was 92 percent. Cerebral blood flow was reduced 33 percent and cerebral oxygen consumption was diminished 35 percent. Serum-amylase determinations on several patients showed moderate to marked high levels. It was felt that acute pancreatitis was often the cause of the severe abdominal pains in these patients.⁵

TOXIC ACTION

Many theories have been advanced to explain the mode of toxic action of methyl alcohol in the human body.^{8, 9, 13-15} It is unfortunate that laboratory animals do not respond to this agent in a manner similar to the human. Acidosis almost never develops and the animals do not often appear to go blind. Fink⁸ and also McGregor⁹ have described degeneration of the retinal ganglion cells in animals poisoned with methyl alcohol, but this has been denied by Roe.¹⁴ Conclusions from experiments on animals should be applied to humans with great caution and reservation.

Apparently methyl alcohol breaks down slowly in the body to formaldehyde and formic acid. It appears unlikely that any of these chemicals acts directly on the retina or other nerve tissues. Methyl alcohol is rapidly distributed throughout all body fluids but symptoms of poisoning rarely develop in less than 18 hours after ingestion.

According to the theory of Rohr,¹³ methyl alcohol or one of its breakdown products slowly combines with the iron catalyst of the oxydase system rendering it inactive and causing a tissue anoxia. This process is accelerated in the presence of acidosis.¹⁴

Because the retina has the highest oxygen requirement per unit concentration of iron of any body tissue, it is not surprising that this delicate ocular membrane should be damaged in methyl-alcohol poisoning. An indirect toxic action, as just described, offers a ready explanation for the parallelism of ocular symptoms and signs of methanol poisoning with the amblyopia of lead, arsenic, thallium, or carbon disulfide poisoning or even that of severe malnutrition.

Recently, Potts and Johnson⁹ found evidence that the proximal toxic agent in methanol poisoning may be formaldehyde, a potent inhibitor of retinal oxidation and glycolysis, and expressed the belief that the role of acidosis was a highly questionable one.

In methyl-alcohol poisoning, the acidosis does not appear to be the cause of amblyopia but it does act as an accelerating force. If acidosis can be corrected before permanent ocular damage has resulted, a return of normal visual acuity can be expected. If retinal hypoxia has existed long enough for irreversible degeneration of the ganglion cells to occur, treatment may prevent death but visual impairment will be permanent.

Until a specific chemical is found that will prevent or release the combination of methyl alcohol or its products with the retinal enzyme systems, rapid, intense, and prolonged alkalinization appears to be the most important phase of treatment for methyl alcohol poisoning.

SUMMARY

Clinical and pathologic observations on a group of 320 patients with acute methyl alcohol poisoning are reported. There were 37 deaths.

Visual symptoms, occurring 18 to 48 hours after ingestion of methanol, included blurred vision, loss of central vision, and complete blindness. The pupils reacted sluggishly or not at all to light. Absence of the pupillary light reflex was a sign of poor prognosis for life or eventual restoration of visual acuity.

The visible retinal changes were hyperemia of the optic nervehead and superficial edema of the papilla and surrounding retina, and later a simple atrophy of the optic nerve. All patients with severe retinal edema had some degree of permanent visual loss.

The earliest central field defect was usually a centrocecal scotoma. Later more complex types of visual defects appeared.

Acidosis was present in every severely poisoned patient. The degree of acidosis paralleled the severity of general and ocular symptoms.

Partial or complete recovery of the initially reduced visual acuity was observed in most patients. If the visual acuity did not

normal within six days after it had begun, it invariably dropped to a low level. The final visual acuity was less in both eyes of six patients. Pathologic studies on six eyes at death revealed only changes

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Histologic studies on six eyes enucleated
death revealed only changes consistent

with post-mortem degeneration.

On the basis of results obtained in this
series of cases, the most effective treatment
of acute methyl alcohol poisoning consists
of intensive and prolonged alkalization.

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