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ACUTE METHYL ALCHOHOL POISONING

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In January of 1966, 4 patients of North American Indian extraction suffering from acute methyl alcohol poisoning were admitted to The Winnipeg General Hospital after consuming a 'fruit juice cocktail'.

Case Reports

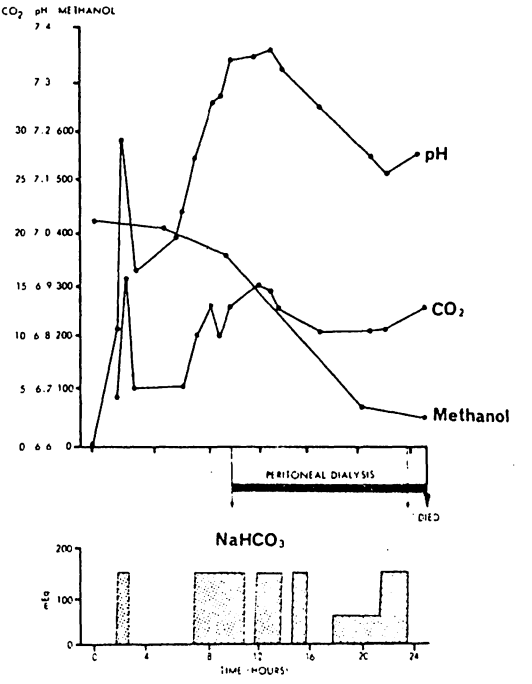
CASE No. 1:

Mrs. S., a 39 year old woman complained of hazy vision and inability to walk, 18 hours following the ingestion of approximately 260 ml. of methyl alcohol.* Six hours after the onset of these symptoms she was admitted to hospital (7:00 p.m. January 17, 1966) in a comatose state. On examination the patient was cyanosed and the pupils were fixed and dilated (blood pressure 70 systolic and pulse 50/min.). Exposure keratitis and extensive retinal edema were noted.

Biochemical investigation revealed severe acidosis with a blood pH of 6.63, carbon dioxide level of 3.9 mEq/L. The blood alcohol was in excess of 588 mg.%, of which 428 mg.% was methyl alcohol. Immediate intubation and intensive treatment of her acidosis with intravenous sodium bicarbonate and peritoneal dialysis elevated the blood pH and carbon dioxide level to 7.33 and 15.5 mEq/L., respectively, (Table I). The patient died 23 hours after admission. (i.e. 47 hours after the ingestion of the methyl alcohol) without regaining consciousness.

An autopsy was performed which included examination of the eyes. The pertinent findings were marked edema (perivascular and pericellular) of the brain and severe congestion and edema of the lungs. The kidneys showed toxic changes most

TABLE I (Case 1)



A graphic representation of the blood pH, CO_2, and methanol values. The amount of $NaHCO_3$ administered intravenously and by peritoneal dialysis is also shown.

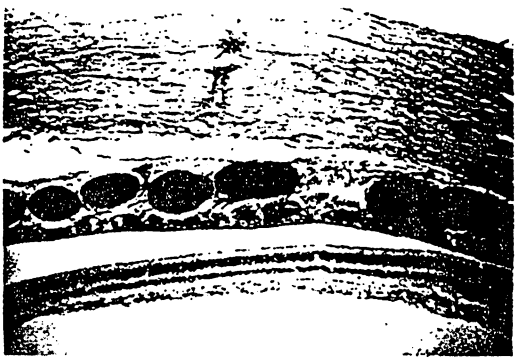


Fig. 1.—Case 1. Photomicrograph of histopathological section of the eye showing marked choroidal vascular congestion in Sattler's layer.

*The autopsy and methanol estimations were carried out by Dr. Hugh Ross, Department of Pathology, Winnipeg General Hospital.

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evident in the proximal convoluted tubules and accompanied by capillary distension.

On sectioning the eye, the retina was pale and contained many folds. Microscopically the axial area of the cornea was denuded of epithelium. There was intense choroidal vascular congestion, more marked at the posterior pole (Fig. 1). Peripapillary edema and subretinal exudation were noted. Pyknosis of the ganglion cells was present but autolytic changes could not be excluded since enucleation was performed about 8 hours after death.

CASE No. 2:

Mrs. P., age 24. Upon awakening 10 hours after ingestion of approximately 132 ml. of methyl alcohol, the patient noted a 'bit of a hangover' and that 'everything looked white'. After a hurried housecleaning she accompanied her friend Mrs. H. (Case No. 3), to the local beer parlor. During the bus ride she was unable to read street signs and people were becoming figures without faces. Increasing nausea and generalized weakness made it impossible for her to join her friends in a 'pint'. Following an episode of vomiting a pinkish stained fluid, she dozed in her chair while her companions spent the remainder of the afternoon drinking beer.

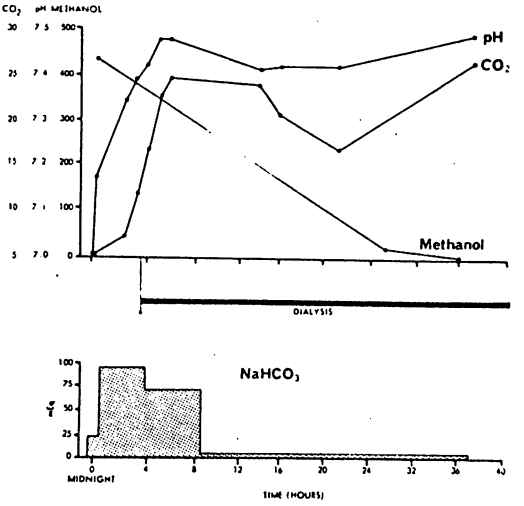
Twenty-three hours after drinking the methyl alcohol mixture, she was alarmed at what, by this time, had become almost a complete loss of vision, and was taken to The Winnipeg General Hospital by a friend.

On admission to the hospital January 18th, 1966, at 12:10 a.m. the patient was conscious, blood pressure 120/80, and the respiration rate 26 per min. Ocular examination revealed fixed, dilated pupils, and visual acuity of counting fingers at 6 feet. The fundi showed marked retinal edema. Bilateral central scotomata were present on confrontation.

Biochemical investigations reported a blood methanol of 400 mg.%, pH 6.8, and carbon dioxide 4.6 mEq/L. The patient was given intravenous ethanol and sodium bicarbonate in the casualty department. Three hours later, peritoneal dialysis with 1.5% sodium bicarbonate was begun (Table II), and her acidosis and general condition improved.

The patient's visual acuity improved from an initial counting fingers at 6 feet to 20/400 in each eye by the second day, and to 20/200 after 2 weeks. Four months after the incident her vision was 20/400 in both eyes.

TABLE II (Case 2)



A graphic representation of the blood pH, CO_2, and methanol values. The amount of $NaHCO_3$ administered intravenously and by peritoneal dialysis is also shown.

An electroencephalogram on admission was reported as follows: "Occasional bursts of slow activity and excess of fast activity without lateralization. These patterns probably represent dysfunction at the cerebral level as well as at the deep midline structures of the brain". The electroencephalogram was repeated after 3 days and was then within normal limits.

CASE No. 3:

Mrs. H., age 25. Following the admission of Cases 1 and 2, and the diagnosis of acute methyl alcohol poisoning, Cases 3 and 4 were brought to the hospital by police escort on January 18, 1966, at 1:00 p.m. Mrs. H., who apparently had drunk 10 to 15 ounces of methanol mixture had a blood methanol level of zero, normal pH, and normal carbon dioxide combining power. She had been admitted 36 hours following the drinking incident and it is interesting to note that she had spent all the afternoon of the day prior to admission drinking beer with Mrs. P., Case No. 2.

A mild epigastric upset and blurred vision was noticed on the morning of January 18, but on admission she had no complaints. Her pupillary reactions were normal and visual acuity was right

20/400, left 20/70-2 with contracted visual fields by confrontation Fundi showed minimal peripapillary edema with some hyperemia of the discs as well as changes consistent with a myopic fundus. Refraction on the following day revealed a vision of 20/30-2 with a myopic astigmatic correction which had not changed significantly from an examination performed eight years previously. She had no visual or physical sequelae, and was discharged 3 days later without complications following intravenous and oral sodium bicarbonate therapy. No pathology was found when re-examined two weeks after discharge.

CASE No. 4:

Mr. S., age 45, the host of the party had a visual acuity of 20/20 on admission at 3:15 p.m., January 18, 1966. His pupils reacted normally and no visual defect was found. Slight hyperemia and haziness of the supranasal quadrant of the optic discs were visible on fundus examination. A blood methanol level of 544 mg.%, the highest recorded in the series, was present. It was calculated that he had consumed 265 ml. of methanol. The blood carbon dioxide level was 14 mEq/L. and pH 7.37. After intravenous and oral administration of sodium bicarbonate over a period of 3 days the carbon dioxide was 26 mEq/L, pH 7.44 and the blood methanol was negative. No toxic sequelae were evident on discharge.

Discussion

McFarlan in 1856[1] published one of the earliest articles on toxicity of methanol. In 1896, Rymowitsch[2] described the histological changes in the retina of a man who died of chronic methyl alcohol poisoning. Schmiedeberg in 1912[3] first postulated acidosis as a factor, citing Pohl[4] and Bongers[5] who had studied the metabolism of methanol in experimental animals. Alkali therapy was first used clinically by Harrop and Benedict in 1920[6].

The clinical picture of methanol poisoning has been well documented in the literature.[7, 8, 9, 10, 11, 12] Gilger et al[20] have described methyl alcohol poisoning as a 'threefold disease', disease I — Narcosis, disease II — Metabolic Acidosis, disease III — Specific Nervous System Involvement (retinal edema, fixed dilated pupils, blindness, and basal ganglion necrosis). Disease I was thought to be due to the toxic effect of alcohol itself, whereas diseases II and III are due to the oxidation products of methanol (either formaldehyde or a formaldehyde complex).

The characteristic latent period prior to ocular symptoms and signs of acidosis varies from 6 to 24 hours. Prolongation of this latent period, minimization of acidosis, and a wide variation in individual tolerance to methanol are accounted for by the consumption of ethyl alcohol.[15] The work of Roe,[15] substantiated by experimental evidence on rhesus monkeys[20] suggests that ethyl alcohol, by appropriating enzymatic sites of methanol oxidation, allows only minimal oxidation of methanol which is excreted as such (being less toxic than formaldehyde).

General symptoms vary from a mild headache to nausea, vomiting, and abdominal pains or cyanosis, coma, respiratory failure and death.

Visual symptoms may be absent, or vary from blurred vision to blindness. Fixed and dilated pupils usually indicate severe visual loss and impending death. All patients with acidosis have visual complaints although these may only be transient.[13] The visual fields initially may show a central or a centrocecal scotoma which is bilateral, and peripheral contraction may occur at a later date with the development of primary optic atrophy.

The fundi may show no pathological changes in the very early stages or in mild cases. However, hyperemia of the optic disc, blurring of the disc margin, peripapillary edema spreading along the course of the major vessels to involve other retinal areas, and tortuous venous engorgements are all

of serious import. Primary optic atrophy and arterial attenuation may occur in 30 to 60 days. Cupping of the optic disc has been commonly noted.

Comments

Visual Acuity: The accurate assessment of visual acuity in the early stages of acute methyl alcohol poisoning is complicated by intoxication, exposure keratitis, mydriasis, and occasionally central nystagmus. Initial visual improvement is usually noted during the first hour of alkaline therapy and all patients who regained and retained normal vision did so within 6 days after treatment was begun.[8]

The duration of the initial visual loss is an important prognostic factor since, if prolonged, a secondary decline is likely to follow due to a narrowing of the blood vessels, optic atrophy, and peripheral contraction.[15] This was the situation in Case No. 2. Symptoms may vary from 'spots' and misty vision to blindness, due to central scotoma. All patients with acidosis complained of some visual loss, however transient, e.g. Cases 3 and 4.

Pupils: Mydriasis and impairment of the light reaction is a grave prognostic sign.[7, 8, 14] Decreased visual acuity is invariably present, e.g. Case No. 1 who died, and Case No. 2 who had severe visual loss.

Visual Fields: A bilateral, dense, central, or centrocecal scotoma accounts for the early visual loss. This may be accompanied by a change in color values, e.g. the 'white vision' in Case No. 2. Peripheral field contraction may follow and usually accompanies primary optic atrophy and arterial attenuation; however, in our case, pallor of the optic disc was not evident 4 months after the incident. Visual fields were recorded at 10 days, 2 weeks, and 4 months (Fig. 2). Case No. 3 showed temporary peripheral contraction to confrontation on the day of admission.

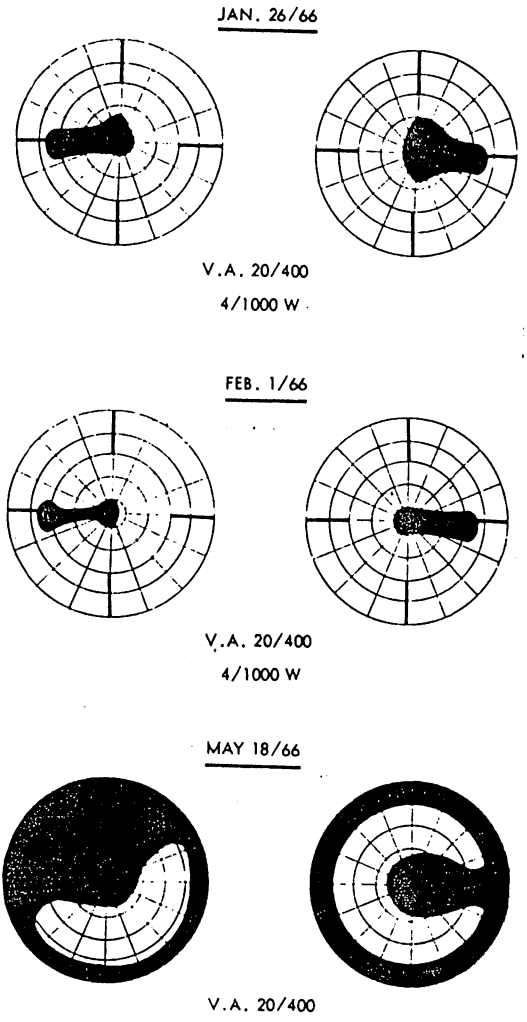


Fig. 2.—Case 2. The visual field changes as recorded at 10 days, 2 weeks, and 4 months.

Ophthalmic Examination

The fundus examination may be negative in mild cases. Hyperemia of the optic disc followed by blurring of the disc margins and peripapillary edema are usually the first ophthalmoscopic signs. Extension of the edema in the nerve fibre layer along the course of the major retinal vessels to in-

volve a variable amount of retina is next noted. Venous engorgement and tortuosity usually accompany the above picture. After 6 to 12 weeks, disc pallor may be found in severe cases and precedes arterial attenuation.

Exposure keratitis made visualization and fundus photography difficult in the comatose patient (Case No. 1). However, the pale creamy edematous appearance was remarkable in this highly pigmented fundus.

The Kowa hand camera and Zeiss fundus camera were used for serial photography. The extensive retinal edema appeared to bury the peripapillary vessels in Case No. 2. This edema persisted in the region of the optic disc before clearing after a period of 2 weeks. No evidence of pallor was noted on examination after 4 months (Fig. 3).

In Cases 3 and 4, only a minimal hyperemia and blurring of the disc margins were noted without accompanying visual loss.

Fig. 3.—Fundus photographs Case 2.

A. Right eye Jan. 18, 1966 (admission date).

B. Left eye Jan. 18, 1966 (admission date).

C. Right eye Jan. 21, 1966 (3 days after admission).

D. Left eye Jan. 21, 1966 (3 days after admission).

E. Right eye May 18, 1966 (4 months after admission).

F. Left eye May 18, 1966 (4 months after admission).

Course and Prognosis

The course and prognosis depends on the dosage, tolerance, and elapsed time before treatment. There may be no visual symptoms but blurred vision of a transient nature usually accompanies acidosis. In more severe cases if normal vision is to be regained it will be apparent within 6 days. If there is persistence of retinal edema then optic atrophy usually follows in about 2 months. Roe[15] describes a primary (edema) and secondary (degenerative) decline in visual acuity. The important prognostic factors appear to be:

Early—

1) Initial visual impairment—duration
   —severity
2) Mydriasis and loss of light reflexes
3) Retinal edema—degree
   —persistence

Late—

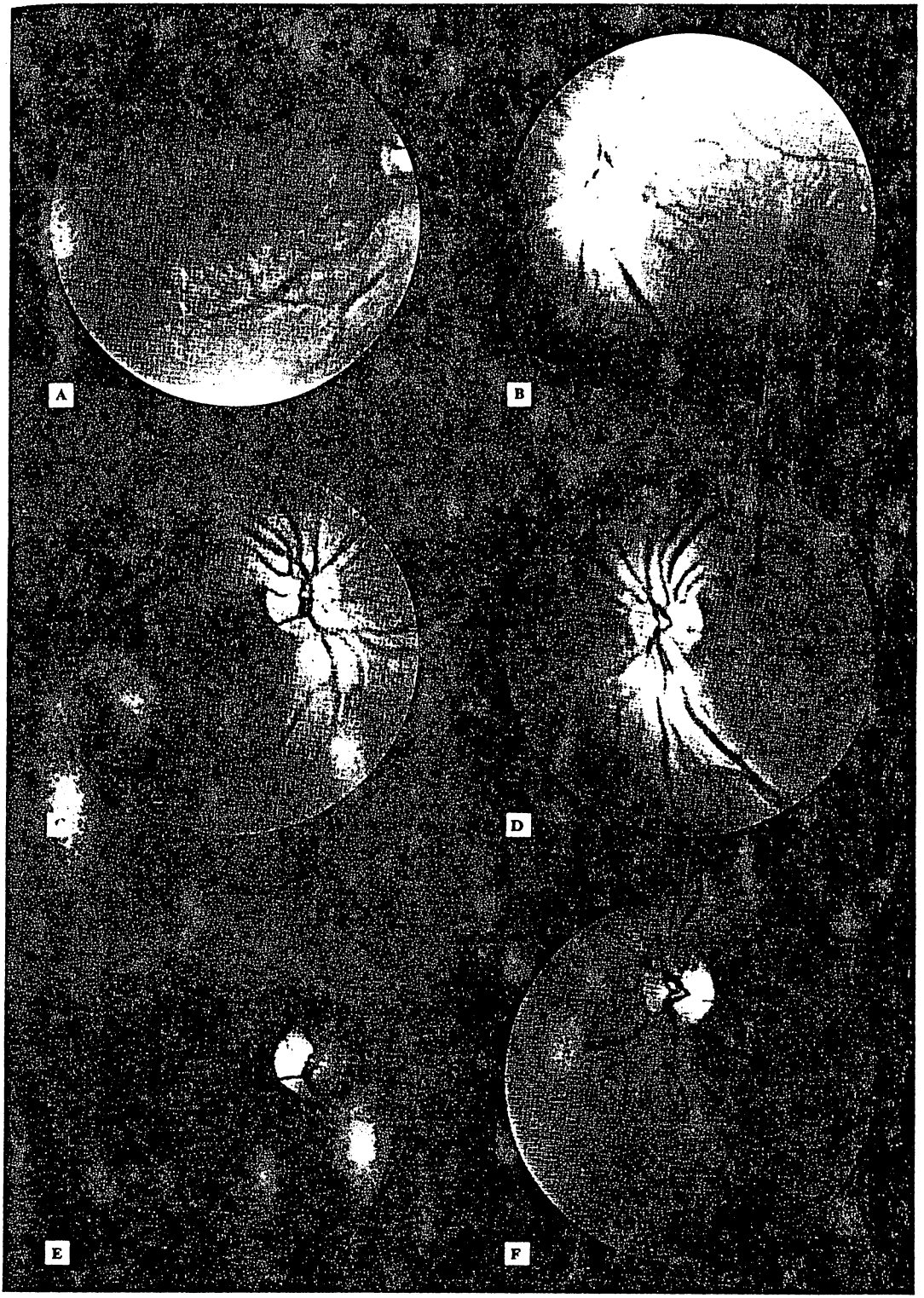
1) Central scotomata
2) Primary optic atrophy
   —arterial attenuation
   —cupping
   —peripheral field contraction

Pathogenesis and Treatment

Narcosis (disease I) due to the toxic effect of alcohol itself usually requires symptomatic treatment and indicates a search for the source of poison and hospitalization of suspected cases.

Metabolic acidosis (disease II) may be accompanied by respiratory failure and death if not treated vigorously. The toxic products of methanol oxidation are thought to be responsible for the acidosis but the exact anion depleting the alkali reserve has not been positively identified. Sodium bicarbonate orally or intravenously (5% in water containing 50 gm. or 595 mEq/L) should be maintained until the blood carbon dioxide is normal for a minimum of 3 days. Intensive care** consisting of bed rest, checking of vital signs, 2 hourly blood carbon dioxide estimations, urinary pH, intake and output charting, and blood grouping and matching

**Medical investigation and treatment by Dr. R. Cherniack and Dr. D. Levene, Department of Medicine, Winnipeg General Hospital.


A
B
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are necessary. It is interesting to note that alkalization therapy has no effect on the plasma methanol level nor does acidosis per se result in ocular degeneration (e.g. diabetic acidosis).

Ocular damage (disease III) is thought to be due to the slow oxidation of methanol to formaldehyde or a formaldehyde complex.[16, 17, 18, 19, 20] Potts et al in rhesus monkey experiments have shown that formaldehyde is a known product of methyl alcohol metabolism and is toxic to the ocular tissues at concentrations found in clinical methanol poisonings. This extremely diffusible substance affects oxidative enzyme systems resulting in tissue anoxia,[13] edema, and a varying degree of retinal degeneration. The retina is especially susceptible due to its high metabolic rate.

Early ethanol therapy (0.75 gm./kg. initially, followed by 0.5 gm./kg., 4 hourly for about 3 days) can prevent or lessen the degree of metabolic acidosis and ocular damage by pre-empting the enzymatic site of methanol oxidation and allowing methanol to be excreted as such or to be oxidized minimally.[15, 20] Experimental evidence has strongly supported this view.[16] Case No. 3 had minimal ocular symptoms and a negative blood methanol on admission after drinking beer during the day. Early ethanol therapy might be an important adjunct in acute methyl alcohol toxicity where severe general depression is absent. Gastric lavage and steroid therapy has not been generally accepted experimentally[17] or clinically.[8, 12] Precautions against exposure keratitis in comatose patients is to be recommended. The great variation in the toxic dose of methanol is illustrated by the blood methanol levels in these patients. Case No. 4 had the highest blood level but the least severe clinical course.

Pathology

Post mortem autolysis has made it difficult to evaluate the histological changes reported in the literature.[11] The acute phase is characterized by edema in the nerve fibre layer, ganglion cell degeneration (swelling, vacuolization, eccentricity of nuclei, etc.) subretinal exudation, defects in the pigment epithelium, choroidal congestion, edema and degeneration of the optic nerve. Later, optic atrophy and degeneration of the retinal elements are noted. In some reports no pathological changes have been found. In Case No. 1 the most striking features were the intense choroidal congestion, retinal edema and exposure keratitis. On sectioning the eye, marked retinal folds were noted. Since the material was fixed about 8 hours after death, interpretation of the ganglion cell changes may not be valid due to post mortem autolysis.

Summary

The ocular findings in 4 cases of acute methyl alcohol poisoning were described. Serial fundus photography and visual field examinations were correlated with the intensive medical workup. One patient died and the ocular pathology was presented. Case No. 2 had severe vision loss, whereas the remaining 2 patients were without toxic sequelae. Some comparisons have been made to previous reports of methyl alcohol poisoning. Ethanol therapy may have been responsible for the absence of toxic changes in Cases 3 and 4.

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Résumé

L'auteur fait la description de quatre cas d'empoisonnement aigu par l'alcool méthylique. Des photographies en série du fond de l'œil et des examens des champs visuels sont en corrélation avec une étude clinique intense. Un patient est décédé et on a fait l'étude de la pathologie oculaire. Dans le deuxième cas, on a constaté une perte marquée de vision alors que dans les deux autres cas on n'a pas enregistré de séquelles de toxicité. On a fait également des comparaisons avec les rapports antérieurs de cas identiques. L'on croit que la traitement à l'éthanol peut avoir prévenu la présence de changements toxiques du troisième et quatrième cas.