(1953) Jil ACUTE METHYL ALCOHOL POISONING: A REVIEW BASED ON EXPERIENCES IN AN OUTEREAK OF 323 CASES IVAN L. BENNETT, JR., M.D.,* FREEMAN H. CARY, M.D., GEORGE L. MITCHELL, JR., M.D., AND MANUEL N. COOPER, M.D. om the Department of Medicine, Emory University School of Medicine, and the Medical Service, Grady Memorial Hospital, Atlanta, Georgia CONTENTS

II.	Chemistry and Pharmacology	433		7
	1. Dosage	433		A
	2. Latent Period	434		
	3. Distribution, Metabolism, Excretion	434	- /	
	2. Latent Feriod. 3. Distribution, Metabolism, Excretion. 4. Relation to Ethyl Alcohol. 5. Acidosis.	437	15/12	
	5. Acidosis	438	لا ^ا ر 10 ا	><
v.	Symptoms	440		1
	1. Visual Disturbance	440		-
	2. Central Nervous System Manifestations	441		~ ~
	3. Gastrointestinal	441		: 'H
	4. Pain	442	1 /	ි. ලබා
	5. Dyspnea	442	hady	
V.	Physical Findings	442		(3)
	1. General	442	$\overline{}$	1.00
	2. Eyes	443	/CAB W	/ ~
	3. Cardiovascular	444	17	J 2 #
	4. Abdominal	444	,	(marga (marga (marga
	5. Neurologic	444		مسا
	6. Mode of Death 4	445		
VI.	Treatment	445	**************************************	- 5
	1. Alkalinization	445		* <u>}</u>
	2. Ethyl Alcohol	448		<u> </u>
	3. Spinal Drainage; Gastric Lavage	449		YRKGHT
	4. BAL; ACTH	449		હ્યું 🗟 🔻
	5. Other Measures	449	į	ಜ ಡ
	6. Relapses	454		NOTICE: BY COPY
II.	Laboratory Findings	455	•	
II.	Pathology	456		

INTRODUCTION

X. Discussion With Special Reference to the Mechanism of Poisoning by Methanol 457

It is the purpose of this report to describe experiences in a major outbreak of ood alcohol poisoning due to adulterated contraband whiskey and to review in etail the clinical problem of acute methanol intoxication.

Methyl alcohol (methanol, wood alcohol, Columbian spirit, Eagle spirit, Manattan spirit, Pyroxylic spirit, colonial spirit, Hastings spirit, Lion d'Or, methyl-

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the major reasons that the general recognition of the toxicity of wood alcohol was so long delayed. During Christmas week in 1911 an outbreak of 163 cases of poisoning with 72 deaths which occurred in Berlin (44, 49) provoked considerable discussion in a meeting of the Medical Society of Berlin. In the course of this. Aronson (50) described the ingestion of four liters of 40 per cent methanol by six Russian workers who had survived without ocular sequelae or other symptoms than mild gastrointestinal irritation. Wood and Buller (1) pointed out that blindness had followed the ingestion of as little as two teaspoons of methyl alcohol and Duke-Elder (51) mentions blindness after a total dose of only four ml. Uhthoff (52) stated that only 50 of 200 persons who drank the same amount of wood alcohol became ill and only 12 died. Goldflam (53) called attention to the extreme variation in dosage producing toxic symptoms and Zeigler (4) observed fatalities after as little as one ounce. Pronnie et al. (32) commented on the great variation in response after drinking wood alcohol, estimating that for each patient they saw in an outbreak at an Army installation, four others had drunk the same material and remained without significant symptoms. The smallest amount which produced a fatal result in the outbreak observed by the present authors was three teaspoons (about 15 ml.) of 40 per cent methyl alcohol. The highest dose recorded in a survivor was one pint (500 ml.) of the same mixture.

Although instances of remarkable resistance or susceptibility to many other toxic materials are well known, the striking range of methanol's effects is one of the unusual features of this type of poisoning and is not yet fully explained.

Latent period. A second peculiarity of methyl alcohol poisoning is the presence of a latent period of about 24 hours between ingestion and the development of toxic symptoms. Although many cases have been reported with a delay of less than 12 hours before development of symptoms, the usual time which elapses is 24 to 48 hours and even longer latent periods are not uncommon. In Chew's group of 26 cases, the time between ingestion and onset of symptoms was 1 to 40 hours (33). It is understandable that this latency, in combination with the aforementioned variability in response to wood alcohol caused some of the confusion in early arguments about methanol's toxicity. Among the patients in the outbreak which forms the basis of this report, the usual story was that symptoms began approximately 24 hours after ingestion. The longest lag observed was slightly more than 72 hours. Several patients noted visual disturbances in less than 6 hours and in one instance, sudden amblyopia developed in a patient 40 minutes after he had downed one-half pint of adulterated moonshine. This patient was severely acidotic within two hours after drinking wood alcohol. In our series, as in Røe's (46), the severity of poisoning generally bore little relation to the length of the lag-period, although in occasional instances, patients with rapid development of symptoms were among those most ill.

The presence of a characteristic latent period offers support for the hypothesis that most of the manifestations of methanol poisoning are effects of the breakdown products of its oxidation in the body, i.e., formic acid and, presumably, formaldehyde.

Distribution, metabolism, and excretion. After ingestion, methanol may persist

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ALCOHOLS TOXICOLOGY

by

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The quantity of food stuff in the gastro-intestinal tract and the nutritional status of the victim are important (18), however, the intake of food is less liable to interfere with methanol concentration in the blood than in the case with ethanol. Death has resulted after ingesting as little as 15 milliliters of a 40 percent methanol solution in one individual while another person survived after drinking over 33 times that amount. (19) Drinking of ethanol prior to or with methanol will usually lessen the poisonous effect. No record exists as to whether this occurred with the above mentioned individual who survived the large consumption but one would strongly expect that this might be the case. A chemical epidemiologic study of a methanol poisoning outbreak in Kentucky involving 18 people of whom 8 died indicated a correlation between severity of the poisoning and the level of ethanol in the body. Of the 26 people screened in the emergency room of the University of Kentucky Medical Center for suspected methanol poisoning, those that also had ethanol in their blood showed less acidosis than the group that had only methanol. Ethanol competes very effectively (metabolized in a competitive preferential ratio of approximately 9:1 to methanol) for the enzyme responsible for the conversion of methanol to formaldehyde and formic acid. (20, 21)

Many years ago, Roe ⁽²²⁾ attributed the toxicity of methanol to the metabolites that were produced by its metabolism. Since that time no definitive proof has been brought forth. Formaldehyde has not been found in humans or other primates during methanol poisoning but some researchers feel that is because of its high reactivity. They think that it still may be responsible for some of the toxicity that methanol exhibits. Formate is known to accumulate during methanol poisoning and correlates well with the beginning of metabolic acidosis and the usual ocular toxicity. ^(23, 24)

D. Inhalation By Humans

Inhalation of the vapor of methanol causes irritation to the mucous membrane. It also may cause headache, vertigo, tinnitis (sounds in the ear), nausea, gastric disturbances, convulsive twitchings, oppression in the chest, visual disturbances, and even loss of vision. In severe cases of exposure, tracheitis, bronchitis and blepharospasm (uncontrollable winking) may take place. (18) Because of methanol's high volatility, the vapors can easily become highly concentrated in a confined space. When at high concentrations, the vapor causes violent inflammation of conjunctiva and epithelial defects on the cornea of the eye. (25)

The permissible exposure limit is 200 ppm (260 mg/m³) and the IDLH (Immediately Dangerous to Life or Health) level is set at 25,000 ppm. It is impossible for a human to remain in an atmosphere containing 65 mg per liter of methanol for any prolonged time. (25)

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