the rapidity of reaction to a given stimulus, the height of the curve and the descent of the curve.

5. These types may be termed, respectively, the hypersecretory, hyposecretory and isosecretory types, depending on their respective reaction to such stimuli.

6. Figures approximating those commonly regarded as hyperacidity are to be found in some period of the curve in a large number of normal persons.

7. A "continued" secretion is described in normal persons which is intimately linked with alimentary and chronic hypersecretion, but can be distinguished from them.

8. The value of this method in various pathologic states is emphasized and a limited number of cases are reported together with their findings.

9. The technic commonly employed for estimating gastric function is entirely inadequate, inasmuch as it indicates but one phase in a constantly changing cycle, and that phase is by no means always the high point in the digestive curve.

10. We would insist on the great advantages of this method which, correlated with the various tests performed on different samples as well as the special tests described elsewhere, enables us to make a more perfect study of the digestive cycle than has hitherto been possible.

We wish to thank Drs. McCrae, Hare and Cohen of the medical staff of the Jefferson Hospital, as well as Drs. Livingood and Wayland, the resident physicians, for their interest and cooperation in this work.

EXPERIMENTAL RESEARCHES IN METHYL ALCOHOL INHALATION *

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Notwithstanding the earnest efforts of the ophthalmologists and the various committees for the prevention of blindness, to disseminate the knowledge of the poisonous qualities and effects of methyl alcohol, it is still a lamentable fact that many members of the medical and legal professions and the vast majority of the laymen, especially the workers using it, are either ignorant of or do not acknowledge the truth. The effect on the eyes and general health from drinking wood alcohol has been proved experimentally in animals, and has been corroborated in clinical practice; but the effect from its inhalation alone on the eyes has never heretofore been demonstrated experimentally.

Although many clinical data have been collated tending to show an effect similar to the one obtained from its imbibition, many doubt and some dispute its power to affect the human organism deleteriously through inhalation alone. The wish to prove this fact, coupled with a desire in the interest of humanity to lessen the number of the blind and to conserve life, by advocating proper preventive or precautionary measures for

workers using it, induced us to undertake these experiments.

Before giving them in detail, it may be of interest briefly to refer to the importance of the subject to the body politic.

We have found that there have been about one hundred cases of amblyopia and death from inhalation of wood alcohol recorded in the literature to 1912, and we are of the opinion that this constitutes a very small percentage of the total number of cases which have actually occurred, as a great many either have not been recorded, or have gone unrecognized. Of those that have appeared in the literature, the question whether inhalation alone produced the condition, has usually arisen. In conducting our investigations, we have endeavored to exclude all possibility of the entrance of the wood alcohol into the system except by inhalation, and we feel sure that we have succeeded in producing amblyopia and death in that manner, as we contemplated at the beginning of these researches.

In 1880 about 400,000 gallons of wood alcohol were manufactured, while in 1910 the amount had increased to over 8,000,000 gallons; consequently it appears that the industry has become firmly established. That being true, it is for the chemists and medical profession so to arrange for its use or composition that, while it may serve its purpose in the arts and industries, it shall not levy too heavy a toll on the artisans, and indirectly on the state by causing blindness or death. Its use is extensive, about 2,000,000 people working in trades are using it in the United States alone, and as the foregoing figures indicate, its use is increasing annually.

According to the 1904 United States Census, the following industries and trades were using wood alcohol.

Painters, glaziers and varnishers...	278,000 workers
Launderers	386,000 workers
Boot and shoemakers.....	208,000 workers
Barbers	131,116 workers
Printers and lithographers.....	155,000 workers
Woodworkers—piano, furniture, etc.	112,000 workers

About 500,000 workers divided among dye-work operators, brass-workers, cabinet-makers, gold and silver workers, harness-makers, hat-makers, leather-workers and tanners, metal-workers, photographers, book-binders, chemists, etc.

The subject is one of increasing importance on account of the new employers' liability law in New York and other states. At present it is not even mentioned specifically as a hazard, but when the importance of the effect of its inhalation is realized, cognizance of this omission must surely follow.

The manufacturers assert that even admitting that commercial wood alcohol is poisonous, the refined product known as Columbian Spirits is not. We have proved conclusively that the refined spirit is quite as dangerous as the unrefined; and indirectly more likely to destroy vision and life on account of the absence of the disagreeable odor to warn one of its presence.

Our original intention was to note the effect of methyl alcohol inhalation in chronic cases, that is, in those which had been exposed to its influence in small quantities over a long period. But the time allowed in which to prepare our paper for the meeting was most inadequate to conduct our investigations along these lines, so we were obliged to confine our attention principally to the more acute phases of the matter under consideration.

* Read before the Section on Ophthalmology at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

* Because of lack of space this article is abbreviated in THE JOURNAL by the omission of several experiments. The complete article appears in the Transactions of the Section and in the authors' reprints.

The apparatus used in our investigations consisted of a wooden box which was 32 cm. wide, 47 cm. long and 63 cm. deep (high) with an opening on each end about 1 cm. in diameter. In one end a mica valve was very delicately adjusted, allowing air to pass out. At the other end was an attachment for tubing which could be connected with an air-tank, or copper coil, and which acted as an inlet for fresh air. The top, in which were two square glass windows, could be fastened down by eight thumb-screws. The temperature of the air in the box for the experiments averaged about 68 F., while the hygrometric readings indicated an average of about 60 per cent., thus to a certain extent constituting conditions similar to those in which some of the workers with methyl alcohol use it, for example, varnishers in beer-vats, etc.

The wood alcohol used in the experiments consisted of both the commercial and the Columbian Spirits, and they were obtained from Eimer and Amend, chemists of New York City.

RESEARCHES IN METHYL ALCOHOL INHALATION IN ANIMALS

EXPERIMENT 1.—Acute poisoning in dog. Dec. 3, 1913: A dog, male, weight 4 kg., 700 gm. (about 10 pounds), fed one hour before experiment. At 4:15 p. m. was placed in the box with 2 ounces of wood alcohol on a sponge; inlet and outlet of box open for fifteen minutes during which time dog jumped and barked, then openings were closed. Room temperature 64 F. Interior of box temperature 70 F. Dog at 4:50 p. m. was lying quietly on his side. At 5:30 p. m. box was opened, dog appeared intoxicated; fell on attempt to walk. Moved his head from side to side.

December 5: Breakfast: meat and bread, at 11:30 a. m. At 4:30 p. m. dog was placed in box with 4 ounces wood alcohol on two sponges and box closed. At 4:40 p. m. dog was lying down, abdomen up, breathing heavily. At 4:50 p. m. dog's mouth was slightly open, tongue projecting and body in a position of opisthotonos, abdomen upward, animal moving fore feet feebly. At 5:05 p. m. dog unconscious, respiration 50 per minute. At 5:25 p. m. box opened; dog taken out apparently dying.

December 8: Dog recovered in thirty-six hours, and whereas on the 5th he was dull, he now appeared lively and well. Was placed in box with 5 ounces wood alcohol; box closed at 5:10 p. m. At 5:50 p. m. dog was taken out intoxicated, breathing heavily.

December 9: Dog appeared lively and well, and remained so.

December 30: Dog was placed in box with 5 ounces wood alcohol at 1:50 p. m. At 5:10 p. m. was observed lying on right side with tongue protruding and twitching of fore legs; was taken out of box. Examination: Temperature 90 F.; eye tension, Schiötz tonometer 26 mm. Hg, although its palpation seemed much lower, tonometer reading possibly little higher due to pressure of eyelids and to contraction of lid muscles; respiration 29 per minute, labored; blood-serum not alkaline to phenolphthalein; slightly alkaline to litmus; aqueous humor not alkaline to phenolphthalein; slightly alkaline to litmus; twitching of eyelids; cornea only slightly hazy; pupils 3 mm., no light reaction; fundus of eye, optic disk congested with edema; veins dark and dilated, arteries small.

December 31: Dog apparently dying; respiration 10.

Jan. 2, 1914: Dog found dead in morning.

Remarks.—This dog had four exposures to wood alcohol inhalation, spread over a period of one month. He died after the fourth exposure. It is interesting to note the continuous movements of the head from

side to side, which we venture to attribute to an irritation of the semicircular canals of the internal ear.

EXPERIMENT 5.—Effect of methyl alcohol inhalations, with and without ventilation. Dec. 18, 1913, at 4:05 p. m., a dog, weight 3,980 gm. (about 9 pounds), lively, eyes normal, was placed in box with inlet and outlet working. Through inlet air is pumped in at rate of 28 pumpings per minute under 2 pounds pressure. The air passes through a Woulfe bottle, which contains 3 ounces of Columbian Spirits. The vapor is thus forced through a copper spiral or coil placed in a pail of water, under which is a Bunsen burner to heat water and coil. After passing through coil it enters box warmed. At 5:05 p. m. dog was taken out of box lively and apparently unaffected.

December 20: Dog placed in box for twelve minutes. Experiment as before, allowing vapor to pass directly from Woulfe bottle into box without being warmed. Air-pressure $2\frac{1}{2}$ pounds—26 pumpings per minute. At 5 p. m. hygrometer in box, 40. After remaining in box $5\frac{1}{2}$ hours dog was lively, showing no apparent effect of vapor.

December 22: Condition as before. Dog in box from 12 m. to 3:30 p. m. having had 5 ounces of Columbian Spirits pumped in with no apparent effect.

December 27: Placed in box at 11:55 a. m. with $2\frac{1}{2}$ ounces wood alcohol pumped in under $2\frac{1}{2}$ pounds pressure; taken out at 5 p. m. lively; no apparent effect.

December 29: Through error of attendant, dog placed in box with 5 ounces wood alcohol without free ventilation. Examination at 4 p. m. found dog lying on right side, with tongue protruding, frothing at mouth, hair moist; was taken out of box. Respirations 20 per minute; deep reflexes absent; unable to stand; comatose.

December 30: Dog still comatose, lying on right side. Respiration shallow, irregular 50 per minute. Temperature 90. Eyes: tension from 6 to 8 mm., both corneae only faintly hazy; sensibility slightly diminished; pupils 3 mm. light reaction; aqueous humor not alkaline to phenolphthalein, neutral to litmus; fundus, optic disks red and edematous; arteries small, veins dark red and dilated. Blood-serum not alkaline to phenolphthalein, slightly alkaline to litmus.

December 31: Dog found dead in morning by attendant.

Remarks.—This experiment is a striking illustration showing the diminished resistance to the inhalation of Columbian Spirits when a very free ventilation was abolished. Moreover, we believe that the repeated exposures to the inhalation of Columbian Spirits (even with free ventilation) did have some effect on the dog, and that the last exposure had a quick fatal effect on account of the previous exposures.

EXPERIMENT 6.—Acute poisoning in rabbit. Dec. 13, 1913, a rabbit, weight 1,600 gm. ($3\frac{1}{2}$ pounds), was placed under a large bell jar with 5 ounces Columbian Spirits, and three minutes later was rubbing its nose. Respirations 50 per minute. Every seven or eight respirations spasmodic contraction of diaphragm resembling hiccup. At 4:55 p. m. respirations 32 per minute, with occasional convulsive rapid shortening of the body. Hygrometer 80. Taken from under jar at 5:05 p. m.

December 20: At 4:45 p. m. animal was placed under large jar with 5 ounces Columbian Spirits. At 5:45 p. m. respirations 40 per minute; hygrometer 70; taken out from under jar, not much effect shown.

December 23: At 3:40 p. m. animal under jar with 3 ounces Columbian Spirits. At 4:45 p. m. respirations 38; hygrometer 70; temperature in jar 68. Taken out in good condition.

December 27: At 11:55 a. m. animal under jar with 5 ounces Columbian Spirits. At 12:55 p. m. hygrometer 55; at 1:35 p. m. respirations 57. At 2:30 p. m. respirations 50. At 4 p. m. animal lying on side quietly; breathes regularly and deeply, 22 per minute. At 4:40 p. m. respirations 16;

at 4:45 p. m. respirations 4. Taken out from under jar; cornea hazy; no lid reflex; no light reflex; nose and ears cold. Temperature by rectum 90 F.

December 29: Found dead in morning. Eyes preserved in formaldehyd solution.

Remarks.—The rabbit appeared to be more resistant to the Columbian Spirits than the dog was. Coma and death came only after the fourth exposure, although relatively larger amounts of Columbian Spirits were used. The same spasmodic contractions of the body and diaphragm were noticed as in former experiments.

EXPERIMENT 8.—Acute poisoning in dog. Jan. 3, 1914, a dog, male, weight $5\frac{1}{2}$ kg. (12 pounds), was placed in box at 12:55 p. m., inlet and outlet closed; 5 ounces methyl alcohol commercial. At 1:50 p. m. animal staggered about, frothing at mouth, and at 2:50 p. m. was unable to stand; at 4:10 p. m. lying on right side; respirations 25, deep and labored. Dyspnea at 4:55 p. m.; respirations 24; pulse 150; eyes, cornea clear, sensibility diminished; pupils 2 mm. contracted; no light reaction; fundus, optic disks hyperemic, with edema; arteries small, veins dark, slightly dilated. Tension, left 18.5. Aqueous humor slightly alkaline to litmus, not alkaline to phenolphthalein. Respirations short; inspiration prolonged, expiration about as one to four. Hygrometer 55; temperature in box 66 F. Dog remained in comatose condition from January 3 to 5; was found dead the morning of the 5th, lying in same position as when examined on January 3 and 4.

Remarks.—Death was produced by one prolonged exposure (four hours). The intra-ocular pressure was not low January 3, soon after the exposure, and the animal lived more than twenty-four hours, a fact which confirms previous conclusions, namely, that when the tonometer shows a normal intra-ocular pressure, the animal, though in an apparently dying condition, will live at least twenty-four hours or more, and an intra-ocular pressure below 5 mm. Hg is a sign that death will follow within twenty-four hours.

EXPERIMENT 10.—Changes in the electroconductivity in the blood of a dog produced by methyl alcohol inhalation.

Jan. 17, 1914: Dog, weight 5 kg., 570 gm. ($11\frac{3}{4}$ pounds). Under ether anesthetization 15 c.c. of blood were obtained to which was added 5 c.c. of a 1 per cent. aqueous solution of ammonium oxalate. The electroconductivity was measured by Edelmann's Universal Widerstands Brücke: see technic.¹

(1) Sample of dog's blood mixed with ammonium oxalate 3 to 1; (2) bridge reading, 39.4; (3) resistance out, 100; (4) temperature 9 C. (48.2 F.) = 65.017 ohms resistance at 9 C.; = 54.615 ohms resistance at 17 C. (62.6 F.).

January 20: Dog kept in box three hours with fumes from 5 ounces wood alcohol. Respirations 42, labored; at end of time lies on right side unconscious. Temperature below 94 F. Eyes: cornea slightly hazy; corneal and pupillary reflex abolished; fundus, edema of disks with dark veins; arteries small.

Blood was obtained from which the bridge reading was 34; resistance out 100; temperature 17 C. = 51.515 ohms resistance at 17 C. Dog killed with chloroform; eyes and optic nerves were enucleated and preserved in formaldehyd solution.

Post-mortem Examination.—Pericardium contained large amount of colorless transparent fluid which spurted out as if under pressure when it was incised; macroscopically heart appeared normal; stomach and intestines were dilated; interior of stomach and pylorus very markedly congested; cupful of frothy mucus found in stomach; spleen very dark indigo blue.

Remarks.—This experiment showed that the electroconductivity of the serum was increased after the inhalation of wood alcohol. The difference of 3.1 ohms resistance obtained in testing the electroconductivity of the blood showed a change which might result from the breaking up of the corpuscles, from an increase in H-ion content, or from any increase in the inorganic salts. An increase in the H-ion content will produce an increase in the acidity of the blood and also conduces to an edema of the tissues. As we find evidence in the blood of acidosis, and a tendency to edema of the ocular tissues, we think that the increase of its electroconductivity, following methyl alcohol poisoning, is due to an increase in the H-ion content of the blood.

EXPERIMENT 11.—Acute poisoning by inhalation in a monkey. Jan. 22, 1914: Female monkey in good health, weight 4 kg. (8.8 pounds), 1 per cent. solution of atropin instilled into eyes. Apparently did not like the bitter taste, as it evidently passed through nasal duct into mouth. It kept expectorating and washing out its mouth; gagged several times as if nauseated. Eyes: pupils dilated quickly and at maximum; fundi, periphery very dark, uniformly pigmented, no abnormalities; disks appear normal and are oval, long diameter vertical.

January 29: Temperature 102 F. per rectum. Monkey placed in box with 3 ounces methyl alcohol spread over sides of box. At 4:25 p. m. air pumped in under $2\frac{1}{2}$ pounds pressure thirty times per minute. Monkey sat in one corner opposite air inlet and no apparent intoxicating effect was produced whatever; at 5:10 p. m., wood alcohol, 1 ounce additional introduced into box; at 5:25 p. m., taken out; monkey acts normally.

February 3: General condition good. At 5 p. m., in box with 3 ounces wood alcohol; same condition; temperature 100.6; at 5:50 p. m., taken out, temperature 100.2 F.

February 4: At 1:35 p. m., in box; temperature 101.4; out at 3:15 p. m., temperature 102; staggering gait, acted dazed and slightly intoxicated. Three ounces wood alcohol used, box with open ends.

February 5: At 2:55 p. m., in box; temperature 102; out at 4 p. m., temperature 100.6. Three ounces wood alcohol used. At 3:35 p. m., animal winking; slight watery discharge from nose.

February 6: At 2:45 p. m., in box; temperature 101.6; out at 3:45 p. m., temperature 101.6.

February 7: At 3:05 p. m., in box; temperature 102; out at 4:30 p. m., temperature 102; 3 ounces wood alcohol placed on cotton, high up, near top of box; monkey not affected apparently by vapor.

February 9: At 3:15 p. m., in box; temperature 102; out at 4:15 p. m., temperature 102; no effect. Wood alcohol 3 ounces.

February 10: In box at 2:55 p. m., temperature 102; out at 4:40 p. m., temperature 100; pulse 160; optic disks hyperemic as compared with first examination; veins dark; pupils dilated, sluggish to light, acts sleepy. Wood alcohol 3 ounces.

February 11: At 3 p. m., in box; wood alcohol 3 ounces; temperature 102; out at 4 p. m., temperature 101.6; staggering gait, weak hind legs; eyes red and watery; drowsy, falls forward in attempting to walk.

February 12: At 10:20 a. m., in box; temperature 101; out at 11 a. m., temperature 99. Wood alcohol 3 ounces.

February 12: At 4:10 p. m., in box; temperature 103; out at 4:20 p. m., temperature 102; vomited, much affected, scarcely able to walk; hygrometer 65.

February 13: At 9:45 a. m., in box with 5 ounces wood alcohol; temperature 100.4; out at 10:45 a. m., temperature 100; drowsy; much affected; very weak, nausea, vomiting. At 4 p. m., temperature 98.8; acts ill, face, gray pallor, refused to eat chocolate, of which was very fond. Keeps quiet; eyes red, pupils dilated, surface of body cold;

1. Centralbl. f. Electric., 1887, p. 115.

wrapped up in covers, sits with head down between fore legs; placed in room by warm radiator.

February 14: At 8 a. m. found dead; body warm, apparently just died. No evidence of painful death. Head removed, eyes enucleated. Necropsy at 5 p. m. macroscopically. Pancreas and adrenals normal; kidneys slightly congested; liver slightly darker than normal, uniform color, no apparent degeneration; uterus and ovaries normal. Heart, pericardium slightly congested; empty; no blood clots nor fluid. Lungs normal, crepitate and float; spleen small, indigo color characteristic of wood alcohol cases; preserved in formaldehyd solution. Large intestines very much inflated containing also mass of feces and a thrombus in the intestinal mucosa. Small intestines not much bloated; empty of fecal matter but in upper part sections or links bloated with occasional dilatation of vessels; stomach contains yellowish-green tenacious semifluid homogenous mass of mucus with small pin-point hemorrhages along vessels, with dilated veins; dura markedly and pia mater slightly congested; spinal cord appeared normal.

Remarks.—The shortness of time of inhalation with free ventilation, and the small amount of wood alcohol used, explain the lack of effect on the monkey during the first two exposures. But this lack of effect was only apparent, as the animal began to show weakness of hind legs, loss of appetite, diarrhea and vomiting after the subsequent exposures. That death followed the last exposure, in which 5 instead of 3 ounces of wood alcohol were used, is very significant. We are convinced that a latent debilitated condition which was not recognized, existed, and the last dose acted fatally as an overdose. The pin-point hemorrhages on the gastric mucosa is one of the characteristics of wood alcohol poisoning.

EXPERIMENT 13.—Acute poisoning in dog by inhalation of Columbian spirits, with marked ocular hypotension. Feb. 28, 1914: Dog, weight 5 kg., 900 gm., male. At 8:35 a. m., in box with 10 ounces Columbian Spirits; temperature 102.6; out at 11:15 a. m. In box at 12 m., out at 3:20 p. m., temperature 96. In box six hours; during first hour frothed at mouth; required about one hour to be intoxicated, then comatose; at 4 p. m., respirations 28; auscultation showed short inspiration with long expiration; pulse 88 by stethoscope; temperature below 93. Some fibrillary contractions of muscles of face, mouth, neck, nose and tongue. Intra-ocular pressure less than 3.5 mm. Hg with Schiötz tonometer. Not much bleeding during enucleation, but more than when commercial wood alcohol was used; bleeding stopped readily (viscosity increased, coagulation time reduced). Died one hour later as expected, using the marked hypotension as an indication of the proximity of death. The examination of the ocular fluids showed a marked reduction in alkalinity.

EXPERIMENT 14.—Changes in chemical reaction of serum and aqueous humor. March 3, 1914: Female dog, weight 5 kg., 800 gm. Aqueous humor withdrawn by aspiration under cocain anesthesia. Four-tenths c.c. obtained from left eye. Alkaline: $48 - 47.90 = 0.10$; acid: $28.10 - 28 = 0.10$; result, neutral to phenolphthalein.

March 5, 1914, 10 a. m.: In box; temperature 101; out at 12:30 p. m. In box 12:45 p. m., with 5 ounces Columbian Spirits; out at 4 p. m., temperature 95. Eyes: pupils 3 mm.; 5 p. m.—O. D., tonometer = 3.5; O. S. = 3.5; (blood examination morning and evening). Died next day as indicated by very low hypotension.² Right eye, aqueous 0.4 c.c. Titrated with phenolphthalein as an indicator. Alkaline: $32.4 - 29.5 = 2.90$; Acid: $31.10 - 29.95 = 1.15$; Alkaline: $2.90 - 1.15$ acid = 1.75 alkaline = 4 c.c.; 4.48 tenth normal sulphuric acid to 1 c.c. Normal blood-serum 0.1 acid = 1 c.c. Blood normal 0.5 c.c. Twenty c.c. water. Alkaline:

$33 - 32 = 1.00$; acid: $31.95 - 31 = .95$; alkaline $1.00 - \text{acid } 0.95 = .05$ alkaline. One c.c. = 0.1 blood tenth normal sulphuric acid to phenolphthalein. Serum taken in morning.

Blood after exposure to Columbian Spirits vapor: Alkaline: $23 - 22 = 1.00$; acid $32.85 - 32.00 = .85$; alkaline $1.00 - \text{acid } .85 = .15$ alkaline. One c.c. blood-serum = 0.15 tenth normal sulphuric acid.

Remarks.—As we see, the serum of the dog before inhalation was 0.10 tenth normal sulphuric acid; aqueous humor was neutral; serum after inhalation was 0.15 tenth normal sulphuric acid; aqueous after inhalation was 4.48 tenth normal sulphuric acid. It is very significant that the aqueous shows more acidity than the blood.

EXPERIMENT 15.—Control. Feb. 3, 1914: Male dog, weight 3 kg., 300 gm., was placed in box as control with inlet and outlet open (no methyl alcohol vapor added). Animal was kept in box four hours. No apparent effect; was active and lively when taken out.

February 7, 9:55 a. m.: In box, temperature 103.4; out at 1:15 p. m., temperature 102.6; box closed tight, no ventilation; when taken out box contained bad (close) odor. Dog showed no bad effect.

EXPERIMENT 16.—Acute poisoning with Columbian Spirits showing acidity of aqueous humor and increased viscosity of blood. March 7, 1914: Male dog, weight 6 kg. (about 12 pounds), in box with 10 ounces Columbian Spirits. At 9:30 a. m., in box; temperature of dog 104; out at 1:45 p. m., temperature 97. At 2:45 p. m., in box; temperature 95; out at 4:15 p. m., temperature 94. Pupil contracted to 2 mm.; no reaction to light; dog comatose; aqueous withdrawn with needle, 0.7 c.c. Alkaline: $24.00 - 23.00 = 1$; acid $34.85 - 34.00 = 0.85$; alkaline, $1.00 - \text{acid } .85 = .15$; $0.7 \text{ c.c.} = 0.15$. One c.c. = 0.21 tenth normal sulphuric acid to phenolphthalein as indicator.

Remarks.—As normal aqueous showed neutral reaction, this test is interesting on account of acid reaction as determined.

March 9, 9:30 a. m.: Temperature 96.4; animal comatose; pulse 20; respiration 6. Pupils 2 mm., contracted; no light reaction. Corneal reflex abolished, anesthetic; O. D., fundus hyperemic and edema of optic disk; arteries small, veins not altered in size. At 4:30 p. m., temperature 95 F.; respiration 6; pulse 20. O. D. enucleated and placed in 5 per cent. formaldehyd solution for microscopic examination, no bleeding during operation until optic nerve was severed, then slight hemorrhage occurred, about 1 dram dark viscous blood which coagulated readily. Surface of body cold; respirations slow and deep; eyes closed; tongue dry and protruding; animal comatose; pupil, no light reaction—tonometer 3 by palpation, all reflexes abolished; animal in moribund condition.

March 10: Found dead at 8 a. m. Necropsy: Brain reddish; meninges and substance of brain (white and gray matter) congested. Lungs, pleural cavity contains about 2 c.c. sanguineous fluid, surface of left lung shows numerous small hemorrhages; lung substance slightly edematous and floats on the surface of water. Trachea, normal, not congested. Heart, full of dark blood-clots. Spleen, dark indigo-blue throughout. Liver and bile both darker than normal. Kidneys, bluish-red, very dark, much congested. Adrenals and pancreas darker than normal. Stomach, empty; numerous small punctate dark purple hemorrhages along lesser curvature. Intestines, bloated and empty, purplish-red, similar to lining of stomach.

Remarks.—The symptoms, chemical reactions of the aqueous and post-mortem findings we consider typical of acute poisoning with methyl alcohol.

2. When tension is less than 5, dog usually dies within 24 hours.

3. Blood-serum 1 c.c. = 0.05 increased acid in case after Columbian Spirits.

BLOOD-COUNT IN DOG WITH ACUTE POISONING BY INHALATION OF METHYL ALCOHOL

Before inhalation:

Erythrocytes	5,700,000
Leukocytes	11,800
Hemoglobin	90 per cent.
Polymorphonuclears	79 per cent.
Lymphocytes	21 per cent.

After inhalation (2½ hours):

Erythrocytes	7,800,000
Leukocytes	28,600
Hemoglobin	100 per cent.
Polymorphonuclears	99 per cent.
Lymphocytes	1 per cent.

Remarks.—Besides the increase in the erythrocytes, leukocytes, hemoglobin and polymorphonuclears, the very marked decrease in the lymphocytes is of decided interest.

MICROSCOPIC FINDINGS IN EYES OF DOG WITH SUB-ACUTE POISONING

HEMATOXYLIN EOSIN AND VAN GIESON

1. Choroid gives the impression of hyperemia.
2. Tapetum normal. Retina: rods and cones and the external nuclear layer normal.
3. Outer reticular layer slightly edematous.
4. Inner nuclear layer, normal.
5. Inner reticular layer, slight edema.
6. Ganglion cells swollen and surrounded by clear areas, the nuclei being displaced far toward the periphery.
7. Inner layers of the retina show some edema.

WEIGERT

1. The medullary sheath of the optic nerve takes Weigert's stain rather weakly.
2. A few vacuoles show at the ends of the rods and cones. The Marchi and Nissl specimens have not been finished, the report of these will be published later.

We consider methyl alcohol to be a true hemato-toxic. It has a decided effect on all tissues, producing degenerations, and under certain conditions amblyopia or death. In the eye it produces first a toxic edema of the tissues, which, with the increased viscosity of the blood, interferes with its free circulation. The tissues, being deprived of their nutrition and oxygen, succumb to the effect of the toxin, and degeneration of the ganglion cells and nerve fibers ensues. Acidosis occurs as indicated by the results of the titration of the aqueous and serum, and by the determination of the electroconductivity of the blood.

The tension of the eye in methyl alcohol coma may be a guide as to the immediate outcome of the case, and with more study a scale might be formulated giving exact points at which, as regards life, one could prognosticate complete recovery or death.

Hypotension of 5 mm. Hg or less indicates death within twenty-four hours, while with tension over 5 the animal lived longer; and in these cases a question arises whether or not, if proper treatment was instituted early, the animal would recover.

SUMMARY

Effects of experiments with methyl alcohol inhalation were the following:

1. In nose and mouth copious discharge and frothing.
2. Temperature: marked fall, varying from 1 to 10 degrees according to amount used, method and time of exposure to vapor.
3. Respiration: rate increased, then decreased below normal, being very low just prior to death and ceasing before heart.

4. Blood: increase in electroconductivity due to an increase in H-ion content. Increased acidity, with phenolphthalein as an indicator. Coagulation time reduced, specific gravity increased. Viscosity increased. Erythrocytes, leukocytes, hemoglobin and polymorphonuclears increased and lymphocytes decreased.

5. Necropsy findings: Stomach: empty, mucous membrane congested, punctate hemorrhages. Trachea: pale. Lungs: few minute hemorrhages on surface. Heart: muscle dark, in some cases cavities, empty. Liver: dark. Kidneys: dark purple, congested. Adrenals: hemorrhage in one case. Spleen: dark indigo-blue. Intestines: bloated, small punctate hemorrhages. Brain: marked congestion of the meninges.

Effects on the eyes were: Slight irritation producing blinking, slight haziness of cornea and no inflammation of conjunctiva. Corneal reflex retained in some animals after others had disappeared. Fundus: Hyperemia and edema of the disks, with dilated, dark veins and arteries. Pupil: Moderate contraction in coma, with loss of light reaction. Tension varies with intensity of toxemia, in mild recoverable cases being normal, and in profound coma showing marked hypotension, which when less than 5 mm. Hg by tonometer, indicated a rapid and fatal termination within about twenty-four hours.

Aqueous by titration (with phenolphthalein as an indicator) showed an acid reaction.

In one dog (Experiment 9) blindness was noticed, judging from the animal's collision with objects when attempting to walk, as he could not see to get around them.

Microscopic findings indicate an edema of the tissues with very early signs of beginning degeneration of the ganglion-cell layer of the retina.

In reviewing the results of these experiments, attention is directed to the similarity with those obtained through experimental researches and clinical observations, in the internal administration of methyl alcohol; thus demonstrating its fatal and profound toxicity irrespective of the method of its entrance into the animal organism.

The contentions of the manufacturers that the refined methyl spirits are absolutely harmless are untenable and may cause many sad results among workmen by rendering them careless in taking proper precautionary measures while working with it. Many consider its inhalation harmless under ordinary ventilation. We take exception to that supposition. Most of our inhalation clinical cases result from its toxicity under what are considered by the workmen ordinary conditions. While ventilation will diminish the intensity of the toxicity, the inhalation will not be rendered absolutely harmless thereby. Not ordinary ventilation, but the very best obtainable is required for workers using wood alcohol. At least three times the ordinary air-space allotted per person should be allowed to each workman using it. Placards warning of the poisonous properties of wood alcohol should be posted in conspicuous places about premises where it is used, and hours of labor should be so arranged as to allow for exercise in the open air at frequent intervals. In our subacute cases while the exposure to the vapor for an hour or two daily had not much apparent untoward effect at the time, it certainly did have an effect which manifested itself later by subsequent weakness, trembling and unsteady gait in the intervals between expos-

ures. We are inclined to agree with M. L. Poincaré,⁴ who found, after exposing animals to small quantities of vapor of methyl alcohol over a period of from eight to sixteen months, that considerable fatty degeneration of tissues occurred, especially in the liver, heart, muscle, epithelial cells of the uriniferous tubules, some cells of the lungs, and with congestion and slight inflammation of the meninges, and of some nerve centers. He concluded that the vapor of methyl alcohol in small quantities was dangerous.

Physicians often fail to recognize industrial and occupational diseases because of the fact that they are often masked under the form of chronic disorders, which show themselves in obscure diseases of the digestive tract and nervous system, and are attributed by patients to other causes. A number of cases of methyl alcohol poisoning, to our knowledge, have occurred in which the causes of death were given as pneumonia, meningitis, heart-disease, etc. Many of the milder cases have been treated for chronic gastritis, hepatitis, etc. It is not surprising that these unfortunate persons travel from one physician to another searching for relief, when we consider the unfortunate but sad truth that many physicians fail to grasp the true etiology of the cases.

That a difference in susceptibility to methyl alcohol exists in animals and man cannot be denied, and this can be partly explained by the rate of oxidation which takes place in the animal or person. Those in which it is rapidly oxidized experience the least effect, while those with slow oxidation feel the greater toxic effect. Harnack⁵ concluded that methyl alcohol in slow oxidation formed formic acid, while in rapid oxidation carbon dioxide and water were formed. Hence when it is rapidly oxidized, it is comparatively (?) harmless, while in slow oxidation, which usually occurs in man, it is exceedingly toxic, as the action of the formic acid thus produced in the animal organism was much stronger than that of the pure formic acid introduced into the body, as in the latter case the organism attempts to convert it with bases and thus gives rise to formates.

In 1869 Richardson⁶ suggested that methyl alcohol be inhaled as an anesthetic. He stated that 2 ounces required one hour to produce anesthesia, and pointed out that reflex irritability was not abolished by small doses, that the temperature of the body was reduced 3 degrees and that the danger from its use was practically nil; but when inhalation was forced, death was produced by simultaneous cessation of respiration and circulation. We do not know the time required for him to gain the knowledge contained in the last sentence, but trust that it was during his very early use of methyl alcohol.

It is a well-recognized fact in pharmacology that poisons which affect the highly differentiated nerve-structures very powerfully are proportionately more dangerous the more highly developed the nervous system of the animal is, hence it would be expected that man would be relatively more susceptible to such a poison as methyl alcohol than would the dog or rabbit.

The results of the experiments with the titration method agree with the conclusions formed by Greg-

nolo,⁷ who determined, after the ingestion of methyl alcohol, that there was an increase in the concentration of H-ions in the aqueous and serum, and who stated that these changes go parallel with the morphologic changes in the tissues of the eye. His experiments show, as do ours, that the substances produced in the body by poisoning with methyl alcohol are extremely diffusible and penetrate the eye readily. Our microscopic specimens having been obtained from acute cases show only the stage of edema with an indication in the ganglion cells of one of the first signs of degeneration, the location of the nucleus being far toward the periphery of the cell and most of the cells showing this change. As to the fate of methyl alcohol in the human body, Pohl⁸ found that it underwent the same change as in that of the lower animals, its administration leading to the appearance of formic acid which is slowly excreted in the urine.

R. Hunt⁹ states that experiments on the physiologic action of methyl alcohol show conclusively that, however pure the preparation may be, it is totally unfit for use as a substitute for grain alcohol in any preparation which is to be taken internally or used externally, or, we add, which may be inhaled in a concentrated form.

USE OF SPECIALLY DENATURED ALCOHOL RECOMMENDED

Only those who have had experience realize the power and intensity of the opposition encountered in endeavoring to obtain proper protective legislation for the regulation of the sale and use of methyl alcohol. When it is possible for one or two members of a legislative body working in the interests of methyl alcohol manufacturers to be able to thwart the wishes of the vast majority of the inhabitants of a great state for a just protective law regulating the safe and proper labeling of methyl alcohol, it is a most unjust and deplorable state of affairs. If the law regulating the sale of specially denatured alcohol could be amended so that manufacturers might be permitted to sell this alcohol to the individual trades using it in the various industries, which would allow them to prepare their own varnishes, etc., obtaining the consistency desired, one of the objections to its present use would be overcome. The variety of denatured alcohol which the law now compels them to use contains a denaturing agent which renders the varnish of soft consistency, and after having dried it scratches very easily, leaving a white mark. If the trades could obtain the denatured alcohol without the objectionable denaturing agent (benzin, pyradin, etc.) it would in a short time supplant the methyl alcohol to a great extent, as it is only one-tenth as dangerous, and if it is used in an exceedingly well-ventilated space, the fatal results due to the toxicity of methyl alcohol would be reduced to a minimum.

The laws relating to methyl alcohol should be enforced with a jail sentence as a penalty attached. Until the gravity of the situation is realized by our law-makers and the judges in our courts, a certain number of manufacturers who value human life cheaply will continue to be a menace to society by disregarding the law and thus causing blindness and death.

4. Poincaré: *Compt. rend. Acad. d. sc.*, 1878, p. 682.

5. Harnack: *Deutsch. med. Wchnschr.*, xxxviii, 358.

6. Richardson: *Med. Times and Gaz.*, 1869, p. 703; *London Med. Rec.*, 1875, pp. 62-77-93.

7. Gregnolo: *Klin. Monatsbl. f. Augenh.*, 1913, p. 157.

8. Pohl: *Arch. f. exper. Path. u. Pharmacol.*, 1893, p. 181.

9. Reid, Hunt: *Bull. Johns Hopkins Hosp.*, xiii, Nos. 137-138.

TREATMENT

While heretofore treatment, except in a very small proportion of the cases of methyl alcohol poisoning with amblyopia, has been considered rather hopeless, the few patients who have improved or recovered, should stimulate us in our efforts to go forward with renewed vigor in search of a plan of medication which shall yield better results. A plan of treatment based on our findings might be summed up in two words, eliminate and stimulate. Eliminators of all varieties should be used, namely, emetics, hydragogue cathartics, diuretics and diaphoretics, calomel, jalap, pilocarpin hypodermatically, hot saline baths or packs, saline infusions and high saline enemas. Stimulants such as strychnin, caffein and theobromin would produce stimulation with diuresis. Ammonia and oxygen inhalation may be used to supply the alkalines and to aid in oxidation. Sodium iodid and alkaline waters would aid in reducing viscosity of the blood and the medicinal treatment may be supplemented by applying heat to the body and extremities.

Credit is hereby given and our sincere thanks extended to Professors Lee, Scott and Pike for their kindly assistance and advice tendered in these researches, which were made in the physiological laboratory of the College of Physicians and Surgeons, Columbia University, New York, also to Mr. Edward Burchell, for his kind assistance in preparing and mounting the microscopic specimens and to Drs. Dixon and Holden for their kindness in examining our specimens.

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ABSTRACT OF DISCUSSION

DR. WARD A. HOLDEN, New York: The clinical symptoms following the inhalation of wood alcohol are so identical with those following its imbibition that it was to be expected that laboratory experiments would give the same results in each. The defense in a recent suit for damages was based on the fact that there was in the literature no experimental proof that the inhalation of wood alcohol could cause blindness. The proof has now been supplied by this painstaking investigation, and an inspection of sections of the retinas of animals so poisoned reveals the same degeneration of the ganglion cells that I found a dozen years ago in animals after the imbibition of wood alcohol. When hundreds of thousands of dollars are invested in an industry it naturally is difficult to bring about safeguards and restrictions that might in any way diminish the sales of the product. The New York Committee for the Prevention of Blindness of which I am a member, believes that in time something may be accomplished. The subject was studied at some length and then a campaign of education was started in the lay press which it was hoped would render it easier to secure the legislation we desired. Hundreds of newspapers took up the matter and many trade journals treated it editorially. The varnish trade and the brewers especially were favorable. We were attacked chiefly by the perfumery-trade journals, which was to be expected, since the great majority of perfumes and toilet preparations are made up with wood alcohol. The National Brewers Association asked us to furnish them an exhibit for their last annual meeting and they sent out to the brewers of the country some thousands of reprints of our literature. For several years past suits for damages for blindness or death in varnishers in the brewery vats have been uniformly successful, and in the last case of which I have knowledge a man in Brooklyn whose eyesight had been impaired received \$12,000 from a brewing company in settlement of his claim because they feared to have the case go to a jury. Our efforts to have wood alcohol and preparations containing it labeled poison have failed in the New York state legislature and in the New York City Board of Alder-

men. The New York Department of Health, however, of whose advisory council I am a member, is about to add an ordinance to the sanitary code to prevent the use of wood alcohol in any preparation intended for internal or external use by man, and to have wood alcohol and its preparations bear the regulation poison label. The suggestion has been made in the paper that a specially denatured grain alcohol, without benzin or pyridin, be permitted to be used in the preparation of varnishes. This would seem to be a good suggestion. The denatured grain alcohol statute has almost entirely failed of its intended purpose. Denatured alcohol has not come into general use as a cheap and relatively harmless solvent, because of the restrictions thrown about its sale and of the necessity of using denaturing agents which render it more or less unfit for use in certain industries, so that the more expensive and more toxic wood alcohol, sold everywhere without restrictions, is generally used.

DR. HIRAM WOODS, Baltimore: The difficulty in securing the conviction of persons selling wood alcohol is great everywhere. This past winter I had an experience with a man blind from wood alcohol. There was no difficulty in procuring the liquor and showing that it contained 30 per cent. of wood alcohol, sold as Sherwood whiskey. The man who sold it was arrested. The Maryland law provides that anyone who sells wood alcohol to be used as a beverage is guilty of a misdemeanor. The Italian liquor-dealer said he bought it from a jobber and had not himself put the wood alcohol in. Then the judge decided that since the saloonkeeper had said he had not done it, it was up to the State Board of Health to hunt up the jobber and trace it back. This was impossible. The man was acquitted. We should have the legal department of the American Medical Association prepare us a model law. It is a state matter, of course, but it is extremely difficult to get a law fixed without some flaw that leaves these rascals out.

EDGAR B. BURCHELL, New York: On Dr. Schoenberg's suggestion I made an investigation of the blood-count of a rabbit at various intervals after it had been given 8 c.c. of methyl alcohol subcutaneously. The results are shown in the accompanying table. You will see there is quite a difference between the blood picture of the rabbit and the dog. There was no ocular effect at all in the rabbit. By careful physical examination of the rabbit there were no discernible changes in the physical signs. The findings are based on cell-counts of 500 in each instance.

DIFFERENTIAL LEUKOCYTE COUNT

	Normal, Per Cent.	1½ Hrs. after, Per Cent.	2½ Hrs. after, Per Cent.	17 Hrs. after, Per Cent.	20 Hrs. after, Per Cent.	25 Hrs. after, Per Cent.	38 Hrs. after, Per Cent.
Sm. mononuclear	42.4	68.4	66.4	74.8	55.2	77.4	80.0
L. mononuclear	2.0	4.4	1.6	2.4	3.6	2.8	0.6
Transitional	0.0	0.0	0.6	0.2	0.8	0.2	0.0
Polynuclear	54.8	22.8	28.2	18.4	32.4	16.4	18.0
Eosinophil	0.2	2.0	3.0	2.2	6.2	2.0	0.8
Mast cells	0.6	2.4	0.8	2.0	1.8	1.2	0.6

DR. M. J. SCHOENBERG, New York: We have observed in our animals continuous movements of the head together with uncertain gait which we think are due to some changes in the internal ear, and for that reason I think it would be worth while in a case of such poisoning for some otologist to examine the function of the internal ear, which has never been done before. Another point is that rabbits exhibit greater resistance than dogs to wood-alcohol poisoning by either inhalation or imbibition, which agrees with the findings of Reid Hunt. The findings of Dr. Burchell would explain this somewhat. A dog placed in a box with 5 or 10 ounces of wood alcohol will become unconscious and remain so from twenty-four to forty-eight hours or more. A rabbit resists this. The changes in the blood of the dog compared with those in the blood of the rabbit explain partly why the dog is more sensitive than the rabbit. I think the most important point is the post-mortem findings in animals as compared to