Toxicity of Methyl Alcohol (Methanol) Following Skin Absorption and Inhalation[1,2]

A Progress Report[3]

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Participants in the discussion of the toxicity of methyl alcohol are divided into two major groups. One group maintains that the reasonable and intelligent use of methyl alcohol in industry and commerce is safe and practical and may be expected to be attended by no harm to those persons handling it. The other group maintains that reason and intelligence may not be expected from those who are exposed to or have free access to methyl alcohol. In support of this attitude, 208 deaths are cited as having occurred during the winter of 1930–31 as a result of unintelligence and free access to methyl alcohol in filling stations and other little-controlled sources.

The present report epitomizes the results from animal studies with methyl alcohols in which it is shown that by skin absorption or vapor inhalation of methyl alcohol, small quantities quickly lead to harm or death of the subjects (monkeys, rabbits, rats). Unit for unit, methyl alcohol is not less toxic by these portals of entry than by oral intake. Unlike most toxic substances finding use in industry and commerce, methyl alcohol is in the peculiar position whereby definite and widespread incentives exist to use this chemical for beverage purposes. This general situation calls for unusual protective measures for the safety of the public, including industrial workers, which measures do not now exist.

THE incentives to drink methyl alcohol, intended for legitimate uses, compound the perils of exposure to this toxic substance and place it apart from such other toxic agents as benzene, carbon tetrachloride, or carbon bisulfide. With the exception of alcohols, the deliberate imbibition of harmful fluids in industry, or in connection with commerical pursuits, is rare. Addiction to ether, castor oil, or oil of wintergreen is typical of the bizarre states exceptionally found. In the case of methyl alcohol so many duly authenticated deaths have followed the oral intake of this substance obtained from industry, filling stations, etc. (208 deaths in the winter of 1930–31 from methyl alcohol are reported by the Industrial Alcohol Commissioner) that the possible dangers from the inhalation of its vapors or absorption through the skin have been overshadowed.

MacFarlan (*21*) in 1856, was one of the first to note a toxicity of methyl alcohol under industrial conditions. He refers to eye affections among cabinet makers, hatters, and metal workers, requiring the discontinuation of the use of wood naphtha and methylated spirits. Since that time the literature on methyl alcohol toxicity has repeatedly specified poisoning following skin intake or inhalation, and from local action on the skin. Near the beginning of the present century, the quality of natural wood alcohol was much improved, in that objectionable odors were partly eliminated. That improvement led to an increased use in industry, no-

[1] Received June 3, 1931.

[2] An extended bibliography of 404 items related in some way to experimental work or to industrial poisoning from methyl alcohol has been compiled and critical abstracts made. This is too extensive for general publication, but may be made available. Funds for the preparation of this separate bibliography were provided by the Industrial Alcohol Institute.

[3] As of April 15, 1931.

tably in the stiffening of felt hats. This proved to be unfortunate, for many hatters incurred methyl alcohol poisoning. A dramatic chapter in industrial hygiene centers about the activities of the Danbury hatters in eliminating this hazard from their industry (*2*). Their efforts, together with the influence of the publications of Buller and Wood (*6*), in which long lists of deaths from methyl alcohol were included, culminated in Congressional action in 1906, providing for a tax-free ethyl alcohol for controlled industrial uses. A diminished use of methyl alcohol as such then followed, although in certain formulas ethyl alcohol was denatured by methyl alcohol until 1931.

During the earlier period of extensive use, the great majority of deaths and non-fatal poisonings from methyl alcohol followed the oral use of this substance for beverage purposes, or by mistake. A smaller number resulted from inhalation or skin contact in industry, or under conditions in which methyl alcohol was used in medicaments. The most acceptable cases are those in which the painting of vats or tanks (*6, 7, 10, 12, 24, 26, 32, 33, 35, 38*) made use of methyl alcohol as a solvent for the coating material. No observations are known to have been made at that time providing data concerning the concentrations existing at the work places where deaths or dire poisonings took place. Much animal experimental work (*3, 4, 5, 8, 11, 13–20, 22, 23, 25, 27, 28–31, 33, 34, 37, 38*) sought to establish thresholds of danger, but the results are conclusive only with respect to intake by mouth. In inhalation and skin absorption investigations vitiating factors were often permitted to enter and to jeopardize the worth of the work. For example, at least one investigator suspended sponges soaked with methyl alcohol in air-tight cages. Obviously, no facts were established as to concentrations at any one time, nor was the abnormal influence of lack of oxygen considered. For a generation the entire situation was confused because of the theory that impurities in methyl alcohol were responsible for all the harmful action attributed to the basic substance. The uninformed still, on rare occasions, maintain that highly purified methyl alcohol is harmless.

Industrial progress has recently provided synthetic methyl alcohol which in time probably may be sold at lower prices than ethyl alcohol and other liquids having similar properties. This synthetic product is, in fact, methyl alcohol, differing from the natural wood product only in the extent and nature of impurities. The intrinsic properties and the probable lower cost of this newer form of methyl alcohol will prompt an extensive use in industry and commerce. This new situation calls for fuller information as to the conditions under which, with safety, methyl alcohols may be made, purveyed, and applied. This preliminary report is based on animal experimental work conducted to that end.

Methods and Procedures

Animals Utilized—Young rhesus monkeys (31), rabbits of four breeds (58), and white rats (176) have been used in this study up to the present time. Ninety animals, mostly rats, in the general lot of 265, have been housed with experimental animals, but have not been classed as controls. The uses to which the remaining 175 animals were put in experimental work are indicated in Table I.

Table I—Distribution of Animals in Experimental Work

Type of Animal Experiment	Rats	Rabbits	Monkeys	Total	%
Controls	34	22	8	64	36.5
Inhalation	46	12	11	69	39.4
Skin absorption	9	12	8	29	16.5
Oral	12	0	1	13	7.4
Total	101	46	28	175	100.0

The rhesus monkeys were supplied to us as having been brought into this country in May or June, 1930, and until inducted into experimental work, these animals were reported as never having been caged except during necessary periods of transportation. All monkeys were approximately two years old. These monkeys were maintained upon standardized, appropriate diets. Both male and female monkeys were in the lot. One monkey died of pneumonia within 24 hours of arrival; another was killed, which exhibited at the time of death low-grade inflammation of the face. Both are included in the group of controls, for whatever value tissue examination may disclose. With a few exceptions the rats were mature adults and had earlier in life been subjected to growth-curve experiments, using normal standardized diets.

Sixty-four animals constituted the specific-control group. Control animals were subjected to the same régime as experimental animals, with the exception of actual exposure to methyl alcohol. Appropriate lots of control animals were placed in gassing chambers and exposed to the action of air for a period corresponding to similar lots of experimental animals. Some, but not all controls, for skin-absorption tests, were bandaged and corseted and at times water was deposited under the gauzes in these preparations.

Materials Employed—Synthetic and natural methyl alcohols were obtained in the open market, indirectly from the producer through intermediates, and directly from the manufacturer. Chemical and physical specifications have been supplied and attested to by the intermediate purveyor. In the case of some natural methyl alcohol obtained directly from the manufacturer, precise specifications were not obtained beyond the guarantee that the specimens supplied were natural products and as labeled, which were as follows: one lot "denaturing grade," another, "95 per cent," and a third, "pure."

Procedure with Skin Absorption Tests—Those animals devoted to skin tests were customarily, but not invariably, kept under observation prior to skin application for periods of from 1 week to 2 months. During this time urine specimens were collected and examined, and blood counts were made. At the time of the institution of the experimental work, the abdomens of the animals were clipped but not shaved. On the clipped area were laid several thicknesses of gauze pads, the size and number being determined by the amount of alcohol later to be applied. These pads were lightly held in place by a few turns of bandage. Next rubber-damming was wrapped entirely around the animal's abdomen and fixed with adhesive. Lastly a heavy canvas corset, reënforced with light metal stays, was snugly applied over the abdomen and laced in the back. With the aid of hypodermic needle and syringe, measured quantities of test chemicals were deposited upon the gauze pads beneath the rubber. No methyl alcohol escaped from this device, when properly applied; due surveillance was maintained to detect leakage. Control animals were subjected to the same form of encasement; water was substituted for the methyl alcohol, or else no fluid was deposited upon the gauze. Long-continued application of water proved to be unsatisfactory, owing to the maceration of tissues. One monkey, instead of being exposed to the action of methyl alcohol in the manner described above, was merely doused with six ounces of methyl alcohol (pure natural wood alcohol). To facilitate contact with this relatively large amount of methyl alcohol, the animal's abdomen was loosely swathed with bandage, but neither rubber sheeting nor corset was applied. For a period of seven hours this animal was placed in a gassing chamber, in order that vapors might not influence other animals. The only evidence of methyl alcohol action arising from this treatment was the dilation of the pupils, which is commonly present as the first obvious result of exposure in any form. This animal was killed on the fifth day, for tissue study.

PROCEDURE WITH INHALATION TESTS; GASSING APPARATUS—Five cages, ranging in cubic capacity from 18 to 181.5 feet, were used. These cages were of metal construction, were wired electrically for fans, for mixture of chemicals, for lights, for facilitation of evaporation, and were provided with blowers connected with gasometers for the measurement of blower output. In these air circuits, bellows types of air-pressure regulators were installed. The output from this equipment was essentially constant from day to day, but in the course of months of continuous use the output gradually diminished. On this account, the blower output was carefully observed daily, and requisite amounts of chemicals for test purposes in terms of predetermined concentrations were based on the daily blower output.

For the purposes of introducing toxic materials, the apparatus described by Yant and Frey (*36*) was utilized in some of the series. In others a water drip without mercury was utilized as a source of pressure to force over desired amounts of the test chemical. The test chemical dripped onto a piece of plate glass placed at an angle, under which an electric-light bulb was burned. A drop flowing down the incline from the top was evaporated prior to reaching the bottom. By common practice, enough of the test chemical to be utilized during the entire period was weighed out and introduced into the dripping apparatus. The animals were placed in the tank and the tank was temporarily supplied with the desired concentration of gas, and then by setting in operation the dripping apparatus, the required level was maintained throughout the test period. In order to obtain constancy of dripping, it was necessary to maintain a near constant temperature of the dripping apparatus. Complete emptying of the chamber containing the test chemical would ordinarily take place within 15 minutes of the theoretical time (7 hours or more). Variations of this sort inject a small deviation from exact concentrations. During the daily test period the dripping apparatus was under continual observation, and any detected abnormal rate of flow was at once altered.

Animals were placed in these gassing chambers for from 1 to 18 hours. At times all three types of animals were gassed at the same time in the same cage, each lot being placed in separate smaller cages. Animals refused food during gassing periods, so that neither foods nor water were provided when the gassing periods were eight hours or less. When longer than eight hours, and particularly when eighteen hours, the experiment was interrupted for a period of five or ten minutes for feeding.

AUTOPSIES—Animals were autopsied immediately after death or else packed in ice. When animals were found dead in cages in the early morning, they were discarded for full utilization unless body warmth was distinctly present. Some animals were dispatched when death seemed imminent. The methods of killing such animals and controls were never entirely satisfactory. Any traumatic procedure was often followed by changes in the lungs. A frequently used method was that of subcutaneous morphine, followed quickly by the injection of air into the heart. The morphine in no known way vitiated the results from other substances, and the time of its own action was too brief to establish any anatomical evidences of its own toxic action. After the selection of specimens for microscopic study (including, but not inevitably, eyes, brain, cord, lungs, liver, kidney, spleen, pancreas, peripheral nerve, and muscle), the major organs were ground up, macerated in distilled water, the whole acidulated and appropriately distilled for the recovery of methyl alcohol or its decomposition products. Distillation procedures were largely limited to monkeys and rabbits, as the individual organs in rats were too small to permit of successful routine distillation.

Many of the commoner tests for methyl alcohol, formaldehyde, formic acid, and formates were investigated (*1*, *9*). Neither the milk test nor the para-bromobenzyl chloride test was entirely successfully used. Haley's test using Schiff's reagent was accepted as most dependable under carefully controlled conditions.

This test is not specific for formaldehyde, and is not positive for methyl alcohol unless the latter contains some aldehyde as an impurity, is made as follows:

To 5 cc. of the distillate that may or may not contain methyl alcohol, add 2 cc. potassium permanganate acid solution, made up in the manner later described. Allow this to stand 10 minutes. Add 2 cc. oxalic acid, prepared as later described. When all color has disappeared, add 5 cc. of modified Schiff's reagent. The characteristic blue or pinkish blue color may appear within a few seconds, and at least within 10 minutes. Delicacy, 1 in 7000.

Permanganate Acid Solution—To 15 cc. 85 per cent phosphoric acid, add 3 grams potassium permanganate, and dilute to 100 cc.

Oxalic Acid Solution—Add 5 grams oxalic acid to 100 cc. 1:1 sulfuric acid.

Modified Schiff's Reagent—Add 0.2 gram rosaniline hydrochloride to 120 cc. hot water. Cool, and add 2 grams anhydrous sodium sulfite dissolved in 20 cc. water; add 2 cc. concentrated hydrochloric acid. Dilute to 200 cc. and keep in glass-stoppered amber bottle.

Every distillate from an organ or tissue that might contain substances giving color to Schiff's reagent was divided into two parts of equal amount. One was immediately tested for aldehydes, the other was oxidized to change the methyl alcohol into formaldehyde, and then tested with Schiff's reagent. The amount of color produced under standardized conditions was roughly quantitative. From more than six hundred distillations only two distillates were produced which gave rise to color after Schiff's reagent, prior to oxidation. In these two instances the color produced was barely perceptible. The inference is that neither methyl alcohol nor any other substance in life has decomposed into formaldehyde under such conditions as to be present in the distillate. This is in discord with the widely accepted theory that the secondary harm (second to the narcotic action) from methyl alcohol is due to formaldehyde as a decomposition product. On the other hand the oxidation of the distillate, under conditions that would transform methyl alcohol into formaldehyde, regularly leads to positive tests for formaldehyde. It is to be understood, however, that this formaldehyde was regularly produced outside the body. No control animal ever yielded distillates from organs giving positive tests for either methyl alcohol or formaldehyde.

OPHTHALMOSCOPIC EXAMINATION—A highly qualified ophthalmologist examined the eyes of all monkeys and all rabbits, except albinos, one or more times during the investigation. Several monkeys were examined on three occasions.

Intoxication Following Skin Absorption

The animals were subjected to the skin-absorption tests, using the kinds of methyl alcohol shown in Table II.

Table II—Distribution of Animals in Skin-Absorption Tests

TYPE OF METHYL ALCOHOL	RATS	RABBITS	MONKEYS	TOTAL
Synthetic, No. 1	5	2	3	10
Synthetic, No. 2	0	2	2	4
Synthetic, No. 3	4	6	1	11
Pure natural	0	2	2	4
Total	9	12	8	29

The several detailed protocols submitted by the author have necessarily been omitted for lack of space. These and others are available in the author's laboratory.

COMMENT—All animals subjected to the action of any amount of methyl alcohol by skin absorption have died. The lowest amount regarded as responsible for death was 0.5 cc. per kg. of weight in one monkey. Clinical findings in this animal were atypical in that much œdema developed in the

hindquarters and genitalia. Other findings, including the recovery of methyl alcohol in all organs examined, were typical.

The conditions of these experiments were such that concurrent inhalation was precluded.

The high normal temperature of monkeys (101° to 103° F.) probably favored absorption.

Rabbits, and notably black ones, are far less susceptible to the action of methyl alcohol than either monkeys or rats.

The pathology, both in the gross and from microscopic examination, duplicates, in major respects, findings from other forms of intake. Some exception may exist in the local condition of musculature in the region of absorption, as opposed to greater localized inflammation along the respiratory tract in inhalation experiments.

The regular recovery, in fluids distilled from organs of animals subjected to the skin absorption tests, of methyl alcohol, and the absence of it in control animals, clearly establishes the passage of methyl alcohol into the body through the skin.

It is noteworthy that methyl alcohol, and not formaldehyde, was the substance recovered from these and all other test animals. Although the methods of testing methyl alcohol which was recovered were not quantitative, except on the basis of depth of color, it is evident that not less alcohol is recovered from skin absorption animals than from inhalation subjects. At best, however, our quantitative methods represent approximations, and are not conclusive beyond the definite assertion that methyl alcohol was regularly recoverable and that formaldehyde was rarely detected.

Application to the skin of methyl alcohol, diluted in proportions recommended for antifreeze use, proved to be toxic. Fifteen cubic centimeters of this mixture when deposited next to the skin (monkey), four times daily, led to profound sickness on the first day, inability to stand up, and vomiting, with death on the second day thereafter.

The lower limit of harm from the continued application of methyl alcohol to the skin has not been determined. The prolonged wearing of the appliances necessary in our method of skin application eventuates in local action, thus terminating acceptable testing. Five-tenths cubic centimeters of methyl alcohol per kg. of weight, applied four times daily, led to impairment at the end of four applications and within 24 hours, and eventually to death. If, however, 1.3 cc. of methyl alcohol per kg. of weight is applied four times daily, desperate illness takes place by the end of the first day, and death on the following day. The threshold of immediate danger for monkeys, by skin absorption, is somewhere below 0.5 cc. per kg. four times daily. If these figures may be applied, on a proportional basis, to an average sized man, one ounce (31 cc.) of methyl alcohol placed in contact with the body under conditions favorable to retention and repeated four times a day constitutes a practical threat to well-being; since 1.3 cc. per kg. applied once to monkeys will produce dilated pupils within two hours, it is inferred that such an amount as 2.5 to 3 ounces (77.5 to 93 cc.) of methyl alcohol applied once to the average-sized man under conditions favorable to retention is undesirable, conducive to harm, and to be discouraged.

No one brand or type of methyl alcohol has proved to be more toxic than any other. Marked variations have indeed occurred, but difference in susceptibility of individual animals is accepted as the cause.

Intoxication Following Inhalation

The animals used for inhalation purposes were distributed as to concentration of intoxicant as shown in Table III. These same animals were redistributed in terms of nature and source of the methyl alcohol, to the action of which they were subjected as shown in Table IV.

Table III—Distribution of Animals as to Concentration of Intoxicant

Animal Concentration *P. p. m.*	Rats	Rabbits	Monkeys	Total
40,000	17	8	3	28
20,000	5	0	1	6
10,000	4	3	2	9
5,000	4	1	1	6
1,000	16	0	4	20
Total	46	12	11	69

Table IV—Distribution of Animals as to Nature and Source of Methyl Alcohol

Type of Methyl Alcohol	Rats	Rabbits	Monkeys	Total
Synthetic, Nos. 1, 2, 3	34	10	7	51
Pure natural	4	2	2	8
95% natural	4	0	1	5
Crude natural	4	0	1	5
Total	46	12	11	69

The several detailed protocols submitted by the author have necessarily been omitted for lack of space. These and others are available in the author's laboratory.

Comment—The threshold of danger from the vapors of methyl alcohol is well below 1000 p. p. m. At least this concentration has led to the death of some, but not all, animals so exposed. All animals so treated have been damaged by the methyl alcohol.

In view of the fact that the ratio between liquid methyl alcohol and its vapors with a tension equal to that of air, at room temperature and common atmospheric pressure, approximates 1 to 614, the actual volume of liquid methyl alcohol in a concentration of 1000 p. p. m. is minute.

If it be permissive to apply to an assumed average-sized man the results obtained in monkeys following the inhalation of 1000 p. p. m., one ounce (31 cc.) of methyl alcohol inhaled as vapors within a period of 41 hours, but without constant exposure, constitutes a threat to life, and at least a threat to the well-being of the assumed average man.

Short periods of exposure, such as for from 1 to 4 hours, to high concentrations of methyl alcohol (40,000 p. p. m.) vapors, are dangerous. They lead, in the case of the former exposure, to obvious sickness in animals within two or three days, and eventually to death, and in the case of the latter exposure, to prompt death.

In low concentrations the duration of exposure is a prime factor. Some animals may long withstand the action of 10,000 p. p. m. during a 7-hour exposure period for 6 days a week, but promptly succumb when this period is prolonged to 18 hours.

Marked differences in individual susceptibilities have been noted in animals of one species, and in different species. One monkey may long survive the action of 5000 p. p. m., while another is promptly killed by 1000 p. p. m. The average rabbit is far more resistant to methyl alcohol action than the average monkey under conditions of these experiments, but some rabbits quickly succumb, and some rabbits are apparently wholly uninfluenced by gross concentrations of vapors. Black rabbits are notably resistant to methyl alcohol. In one instance a coal-black rabbit was subjected to the action of 40,000 p. p. m. for 44 days. (Monkeys exposed to such concentrations rarely survive one day's exposure.) This rabbit was frequently drunk and down, during the period of exposure, but quickly recovered when removed from the gassing chamber, and presented no clinical evidence of optic atrophy. When killed on the forty-fourth day, it exhibited no gross significant pathologic manifestations beyond two small areas of atelectasis in the lungs, but did present some evidence of lipoidal degeneration in the extrinsic nerves of the eye. It is remarkable that in groups of black and light

colored rabbits (always paired), which have been subjected to the action of varied concentrations of methyl alcohol, the ratio of clinical optic atrophy for black rabbits is about one in six, while for lighter colored rabbits the ratio is approximately five in six. Clinical manifestations in general correspond to these ratios.

In the distillation of tissues removed from the bodies of animals, dead from the inhalation of methyl alcohol, and the testing of the fluid obtained thereby, methyl alcohol was regularly recovered. Although appropriate tests for formaldehyde were carried out, none was demonstrated. The methods employed were not precisely quantitative, and results are not conclusive beyond the point of maintaining a wide distribution of methyl alcohol, its regular presence, and the absence of formaldehyde.

If for man the threshold of danger approximates that for monkeys, and is in a range lower than 1000 p. p. m., a practical hazard may readily arise from any open container, such as a pan or tub, in any small closed workroom, particularly if the methyl alcohol is agitated in the processes of manipulation. For example, the practice of freely sponging women's dresses in dry-cleaning establishments, transferring methyl alcohol on a sponge from a basin of that substance, is to be regarded as a practical hazard.

Recovery from the action of methyl alcohol poisoning frequently takes place in the presence of sustained exposure. It is not unusual to observe monkeys, which to all appearances are totally blind (from ophthalmoscopic examination and general observation) and are otherwise direfully affected, clear up to the point of exhibiting no optic atrophy on careful examination, and to evince no other signs of intoxication. At a later time recurrences may take place, but not inevitably so.

In some, but not all, small animals (rabbits, rats), the cornea becomes milk-white. The entire cornea, or portions, may be involved. This condition, when present, may occur early in clinical manifestations, and be preceded only by dilation of the pupils.

Summary

A progress report is made of an experimental study of the toxicity of methyl alcohol by inhalation and skin absorption.

Two hundred and sixty-five animals have been utilized to date, including 31 monkeys, 58 rabbits, and 176 rats.

The materials for test purposes have included crude, 95 per cent, and highly purified natural methyl alcohols, and also synthetic methyl alcohols derived from three sources of manufacture.

In skin absorption experiments, methyl alcohol was applied under conditions that precluded concurrent inhalation. Methyl alcohol applied to the skin has invariably led to damage consistently like that arising from the oral intake of this substance. This evidence of absorbability of methyl alcohol has been noted in optic atrophy observed clinically by ophthalmologists, and after death as observed in lipoidal degeneration. The regular recovery of methyl alcohol on the distillation of all organs derived from skin-treated animals, and the absence of similar findings in control animals, constitutes inescapable proof of absorbability.

The threshold of danger following skin absorption of methyl alcohol is near 0.5 cc. per kg. of animal weight, applied four times daily. This quantity produces illness in monkeys within 24 hours, during which time four applications of the specified amount were made, with eventual death. One and three-tenths cubic centimeters per kg. of weight will produce death within 48 hours, when such applications are made at the rate of four per day.

If these results obtained from monkeys may be applied to man, approximately 1 ounce (31 cc.) of methyl alcohol repeatedly in contact with the human body, under conditions favorable to retention and evaporation constitutes a threat to well-being.

Inhalation experiments have been carried out with the three kinds of animals mentioned, in concentrations ranging from 1000 to 40,000 p. p. m. of methyl alcohol vapor, in gassing chambers under controlled conditions providing suitable changes of air. All of these mentioned concentrations have produced death among exposed animals. One thousand p. p. m. of air have killed some, but not all animals, the shortest exposure time being 41 hours, at the rate of 18 hours per day. Rabbits, and particularly black rabbits, are much less susceptible to the action of methyl alcohol than other animals. Marked variations in individual susceptibility have been observed.

The duration of exposure in hours per day constitutes a definite factor in the experimental toxicity from methyl alcohol. An exposure of one hour daily to 40,000 parts of methyl alcohol vapor per million of air causes scant evidence of immediate impairment among animals, but eventually kills. Four hours of such exposure promptly kills all animals. A few animals will survive for weeks when exposed for seven hours daily to 10,000 p. p. m. of air, but quickly succumb to the same exposure over 18 hours per day.

Animals subjected to the inhalation of methyl alcohol have regularly yielded methyl alcohol on distillation of organs, blood, urine, muscle tissue, etc.

The varied tests made upon the distillates from organ tissues appear to establish that methyl alcohol and not formaldehyde is the principal recoverable foreign substance. Very rarely have even traces of formaldehyde been detected. Brain, lungs, heart muscle, skeletal muscle, liver, spleen, pancreas, kidneys, blood, and urine, have consistently yielded methyl alcohol after exposure either to skin absorption or inhalation. No organs taken from control animals have yielded even traces of methyl alcohol.

The threshold of danger by inhalation is well below 1000 p. p. m. of methyl alcohol vapor. If this degree of toxicity obtained from monkeys applies to man, the vapors from one ounce of methyl alcohol entering the human body constitute a threat to life even when the exposure is distributed over 2 or 3 days.

In a later publication detailed reports will be made upon tissue pathology. Note is here made of extensive peripheral nerve damage.

On a basis of exposure, cubic centimeter for cubic centimeter, methyl alcohol is at least as toxic through inhalation or skin absorption as it is following oral intake.

In view of the very small amounts necessary to produce dire clinical conditions and death in animals most like men, it is reasonable to assume that practical hazards for human beings may be produced under conditions of apparently trivial exposures.

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