TOXICITY AND METABOLISM OF INDUSTRIAL SOLVENTS

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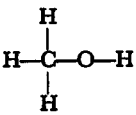
37. Methanol

Synonyms: methyl alcohol, wood spirit, wood alcohol, carbinol

Structural formula: 

Molecular formula: CH_3OH

Molecular weight: 32.042

Properties: a clear colourless, highly volatile liquid with an odour similar to that of ethyl alcohol, and a burning taste.

boiling point: 65 °C
melting point: −97.8 °C
vapour pressure: 95 mm Hg at 20 °C
vapour density (air = 1): 1.11
specific gravity (liquid density): 0.7915
flash point: 54 °F
conversion factors: 1 p.p.m. = 1.31 mg/m³
1 mg/l = 764 p.p.m.
solubility: completely miscible with water, ether and most organic solvents. Only a mild solvent for fats and oils.
maximum allowable concentration: 200 p.p.m.

ECONOMY, SOURCES AND USES

Production

(1) Natural methanol is produced by neutralisation of the products of distillation of hardwood with lime. The commercial variety contains impurities – 1 to 2% of propyl and allyl alcohol, aldehyde, methyl acetate, acetone and other organic compounds (Koelsch, 1921).

(2) Synthetic methanol is obtained by passing a mixture of CO_2 and H_2 at high pressure and temperature over a catalyst. This method now produces considerably more methanol than the natural process. The product, though practically pure, can cause poisoning as severe as that of natural wood alcohol, whose toxic action was at one time thought to be due to the impurities contained in it (Lehmann and Flury, 1943).

Industrial uses

(1) In the celluloid industry (cellophane laminating).
(2) In the boot and shoe industry (wood heel covering).
(3) In paper coating.
(4) In the manufacture of paint removers and varnishes. Paint strippers may contain methyl chloride and benzol as well as methyl alcohol, as in the fatal case reported in the Annual Report of H.M. Chief Inspector of Factories (1957), where a man engaged in removing old paint from inside a small lift was trapped inside it. The cause of death was notified as 'narcotic poisoning by inhalation'.
(5) In the production of formaldehyde and as a general solvent in organic synthesis.
(6) In the production of synthetic indigo and other dyes (Fairhall, 1957).
(7) In the straw hat industry, as a solvent for dyes (Wood and Buller, 1904; Baskerville, 1913).
(8) As a rubber accelerator.
(9) In the denaturing of ethyl alcohol.
(10) As an anti-freeze agent.

BIOCHEMISTRY

Estimation

(1) In the atmosphere

The method of estimation of methanol vapour described by Leaf and Zatman (1952) and Elkins (1959) is based on its reaction with potassium permanganate, oxalic acid and Schiff's Reagent (basic fuchsin, sodium bisulphite and concentrated HCl). The curve of transmission on a photometer is compared with that of a known amount of methanol; the sensitivity, if 10 l of air are sampled, with the midget impinger, is about 40 p.p.m. Rogers (1945) states that the midget impinger has a collecting efficiency of approximately 92% at atmospheric concentrations of 200 p.p.m. of methanol.

(2) In blood and tissues

A similar method for blood and tissues was introduced by Hine *et al.* (1947), using steam distillation. When only small amounts of blood are available (0.5 ml) the vapour may be aerated directly into the oxidising reagent.

A micro-method, using the reaction of formaldehyde with chromotropic acid, with permanganate as the oxidising agent for the methanol, was devised by Agner and Belfrage (1947).

(3) In urine

The method used by Leaf and Zatman (1952) was based on distillation of

a mixture of urine, Na_2SO_4 and sodium tungstate, followed by analysis for methanol as in their method for estimation in air.

Metabolism

The metabolism of methanol is characterised by the relative slowness of its elimination and its production of toxic metabolites. The details vary with different animal species.

(1) Absorption and excretion

Some earlier authorities such as Lewin (1912) believed that absorption of methyl alcohol is equally effective in producing its characteristic toxic symptoms whether by ingestion, inhalation or through the skin. In practice, amounts which have been found sufficient to cause death in animals by skin application (0.5 ml/kg; McCord and Cox, 1931) are not likely to resemble those found in industry (Yant *et al.*, 1931). These observers drenched the unshaven bodies of dogs for several hours, eliminating the possibility of inhalation of the vapour, without lethal effects. In non-industrial human cases however, ocular disturbances and even blindness have been reported from repeated rubbing of the skin with methyl alcohol (Wood, 1913; Campbell, 1915) and toxic symptoms were reported in a painter who spilt methyl alcohol on his feet (Ziegler, 1921), but in none of these cases was the possibility of inhalation of the vapour excluded.

In the rat, excretion is mainly by the lungs, 65% of an oral dose of 1 g/kg being eliminated as CO_2 and 14% unchanged in 48 h; only a small amount is excreted in the urine – 3% as unchanged methanol and 3% as formate (Bartlett, 1950).

In rabbits, which are relatively resistant to methanol (Lund, 1948), urinary excretion is greater – 10% unchanged – while in dogs some 15% of 2 ml/kg doses are excreted through the lungs, 10% unchanged in the urine and 20% as formate (Voltz and Dietrich, 1912).

In human beings also, after a single dose of 50 ml, both methanol and formate are excreted in the urine, the formate reaching 0.5 to 2 g/day, with a maximum 2 to 3 days after the dose, but not with a dose of 10 to 20 ml (Williams, 1959). Klauer (1938) found that in human beings suffering from methyl alcohol intoxication the amount of formic acid in the urine was greater than the normal level, which he found to range from 10 to 40 mg in 1500 ml. In some cases of fatal ingestion the level rose as high as 105 mg in 1500 ml. Other probable metabolic excretory products of methanol are choline and methyl glycuronide. With regard to the former it has been suggested (du Vigneaud *et al.*, 1950) that formaldehyde, not CO_2, is its precursor.

A slight rise in glucuronic acid in the urine of rabbits fed methanol has been observed, persisting for 2 or 3 days due to the formation of methyl glucuronide (Kamil *et al.*, 1953).

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The slowness of combustion of methanol compared with that of ethanol has been demonstrated by Bartlett (1950) using ^{14}C labelled methanol. In the rat the rate proved to be 25 mg/kg/h as compared with 175 mg/kg for ethanol.

According to Kendal and Ramanathan (1953) there is some excretion of formate in animals after small doses of methanol which can be suppressed by giving simultaneous doses of ethanol. It has been suggested by some observers (Røe, 1946; Bartlett, 1950) that ethanol exerts a favourable effect on the toxicity of methanol. The rationale of this favourable action is that ethanol depresses the oxidation of methanol and causes an increase in its unchanged elimination in expired air and urine (Leaf and Zatman, 1952). This inhibition of methanol oxidation by alcohol hydrogenase *in vitro*, even when the ratio of ethanol/methanol was as low as 1/16 had been observed by Zatman in 1946; he suggested therefore that it would be expected that ethanol would diminish the toxicity of methanol, permitting the excretion in an unchanged condition of a larger fraction of an ingested dose. (It should be mentioned that this favourable effect of ethanol has been strongly denied by Gilger *et al.* (1952) who state that in mice, ethanol increases the toxic effect of methanol and formaldehyde.)

(2) Distribution in tissues

The enzyme mechanism of decomposition of methanol is not completely explainable, but on the basis of evidence that it can be oxidised *in vitro* by means of catalase and hydrogen peroxide, it has been suggested that a similar mechanism may be effective *in vivo* (Agner and Belfrage, 1947; Jacobson, 1952). The view held by Kendal and Ramanathan (1952) is that formaldehyde itself in the presence of methanol is converted by alcohol dehydrogenase present in the liver to a volatile ester of formic acid, methyl formate, which subsequently undergoes slow hydrolysis.

It was found by Yant and Schrenk (1937) that regardless of the method of administration (oral, subcutaneous or inhalation) methanol is distributed very rapidly to all tissues, and that the amount found in any particular tissue is closely related to the amount of water which it contains. Dogs exposed to concentrations of 4000 and 15,000 p.p.m. for varying periods of time, and killed, either immediately, within one hour or some hours later, showed the highest concentration in the blood (1470 mg/100 g with 15,000 p.p.m.) followed by the heart (1200 mg), lungs stomach wall (1080 mg), liver (1040 mg) and kidneys (1038 mg). These values decreased with time – for example, some hours later the blood level had fallen to 335 mg/100 g. The bile and urine contained practically the same amount as the blood and stomach wall, and since the dogs could not ingest any methanol except by swallowing saliva, it was suggested that inhaled methanol can be secreted into the stomach and intestines, and that the amount in the body or in any particular tissue can be estimated from its determination in any tissue or fluid, preferably the blood.

In a later investigation by Sayers *et al.* (1944) it was found that when the product of concentration of vapour in air and time of exposure is a constant, even when the air concentration varies over a wide range, the same general order of methanol concentration in the blood would be attained. The blood concentration, estimated at weekly intervals, of dogs exposed to 10,000 p.p.m. (a total of 800 brief exposures)was between 6.5 and 14 mg/100 ml of blood – approximately the same as that found by these same observers in 1942 in dogs exposed for 8 h daily to 450–500 p.p.m.

TOXICOLOGY

The manifestations of acute intoxication following ingestion of methyl alcohol are similar to the well-known effects of over-indulgence in any alcoholic beverage, with the exception of the one outstanding feature of methyl alcohol poisoning – blindness. Many outbreaks of such acute poisoning have been recorded, some fatal, others with resulting blindness, from drinking brandy adulterated with methyl alcohol, from fruit juices diluted with it and from drinking it unadulterated. Severe poisoning has also occurred from inhalation of its vapour, but such cases are much rarer; of 275 cases recorded by Wood and Buller (1904) only 6 were due to industrial exposure, and in some others since reported the suspicion has existed that some of the methyl alcohol had been ingested. Symptoms of acute poisoning, which often arise after a latent period of hours, or even days, include dizziness, stupor, cyanosis, abdominal cramps, gastro-intestinal disturbance and failure of vision. Individual susceptibility with regard to the amount ingested varies greatly; Lehmann and Flury (1953) state that a dose of 5 to 10 mg is usually considered toxic, but many individuals can tolerate without apparent ill-effects a much higher intake than this.

Chronic poisoning, which may occur with repeated exposure to its vapour, may cause irritation of mucous membranes, headache, tinnitus, tremor, neuritis and its most characteristic feature, failure of vision leading to complete blindness.

Toxicity to animals

Animals show wide variation in sensitivity to methanol (Scott *et al.*, 1933) especially when given by inhalation (Loewy and van der Heide, 1914; McCord and Cox, 1931). Rats are the most susceptible and rabbits the most resistant. As early as 1895 Daremberg remarked that rabbits weighing more than 2000 g were often extremely resistant to intravenous injections of methyl alcohol.

Acute

In acute toxicity methyl alcohol has generally been found slightly less toxic than ethanol (Macht, 1920), but its later effects are much more harmful.

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(a) Lethal dose. – *(i) By stomach tube.* – For rabbits Munch and Schwartze (1925) found the lethal dose to be 18 ml/kg as compared with 12.5 ml/kg for ethyl alcohol; for mice, Weese (1928) gave the MLD as 10.5–12.0 mg as compared with 5.5–7.0 mg for ethyl alcohol. Doses too small to cause narcosis appeared to cause no injury dangerous to life, but a reversible infiltration of liver and kidney parenchyma. – *(ii) By intravenous injection.* – For cats, the MLD is given by Macht (1920) as 5.9 ml/kg, as compared with 5.0 for ethyl alcohol. – *(iii) By intraperitoneal injection.* – According to Gilger *et al.* (1952) 10.0 g/kg was usually lethal 4 days after the injection. – *(iv) By inhalation.* – The highest value is that given for mice (139,000 p.p.m., Bachem, 1927) and the lowest for monkeys (1000 p.p.m. after a few 18-h exposures; McCord, 1931).

For cats, Lehmann and Flury gave a level of 65,700 p.p.m.; when the narcotic dose reached a point where all reflexes were lost all the animals died.

Loewy and van der Heide (1914), estimating the amount of vapour inhaled by the amount absorbed by the tissues of the animals (the whole body being subjected to distillation) found that saturation took place in 2 h with levels of 0.5%. With an intake of 8.71–12.78 g/kg the animals died. They found that the process of absorption and saturation was much slower in the dog than the rat.

(b) Narcotic dose. – *By inhalation,* methyl alcohol appears also to be less narcotic than ethyl alcohol. Weese (1928) expressed the concentrations used by him in terms of the amount of alcohol in 5 l of air. He found the narcotic concentration for mice between 0.4 and 0.6 ml and the time of onset of narcosis between 8 and 18 h. The corresponding dose for ethyl alcohol was 0.2–0.6 ml/l.

For mice also Lehman and Flury (1943) gave the narcotic dose as 42,000 p.p.m. after 7 h; for rats 51,000 p.p.m. caused deep narcosis after 2½ h; for cats 129,000 p.p.m. after 6 h. They remark that concentrations which cause only slight narcosis after a single inhalation can be followed by fatal after-effects.

SYMPTOMS OF INTOXICATION

Irritation of mucous membranes, with concentrations from 7500 to 69,000 p.p.m. (Flury and Wirth, 1934); increased rate of respiration (Gradinesco, 1934); depression and drow siness followed by excitation, with inco-ordination and paralysis of the hind legs (Mashbitz *et al.*, 1936); tremor, stupor, convulsions, coma and death from respiratory paralysis (Flury and Wirth, 1934). Failure of sight and hearing (Holden, 1899) and peripheral neuritis (McCord, 1931) have also been observed.

(1) The gastric mucosa

Congestion and small haemorrhages, observed by Tyson and Schoenberg (1914), were believed by them to be characteristic of poisoning by inhalation of methyl alcohol.

(2) The eyes

Many of the earlier observers, including Holden (1899) and Birch-Hirschfeld (1901) recorded blindness in animals poisoned by methyl alcohol, usually by oral or subcutaneous administration, but some also by inhalation. McCord (1931) found that in small animals dilatation of the pupil preceded the development of a milky-white cornea, and monkeys occasionally became blind, sometimes with recovery but sometimes with recurrence.

The mechanism of blindness due to methyl alcohol is fully discussed under Effects upon the Eyes in Human Beings (see p. 321).

(3) The blood

The peripheral blood picture has been stated to show evidence of a stimulative effect of methyl alcohol on the blood-forming organs. Tyson and Schoenberg (1915) noted in the blood of animals inhaling methyl alcohol an increase in erythrocytes, haemoglobin and polymorphonuclear leucocytes. Scott *et al.* (1933) observed hyperplasia of the lymph nodes.

CHANGES IN THE ORGANISM

(1) The heart

Oedema, granular degeneration and in some instances necrosis of muscle fibres were noted by Scott *et al.* (1933) and also by Flury and Wirth (1934), while Eisenberg (1917) reported fatty degeneration of the heart muscle.

(2) The liver

Changes in the liver are essentially those of parenchymatous degeneration, sometimes developing into focal necrosis (Scott *et al.*, 1933), also fatty infiltration (Poincaré, 1878; Weese, 1928; Tyson and Schoenberg, 1914).

(3) The kidneys

Congestion and parenchymatous degeneration have been recorded by the above observers, and in mice fatty infiltration (Weese; Eisenberg; Lehmann and Flury).

(4) The spleen

A dark blue colour of the spleen was noted by Tyson and Schoenberg (1914).

(5) Lungs

Various inflammatory lesions have been noted, according to the severity of exposure. With mild poisoning Scott *et al.* (1933) reported oedema, congestion and desquamation of alveolar epithelium; in fatal cases terminal pneumonic consolidation. Patchy pneumonia in the lungs of rabbits (Eisenberg, 1917) and of mice (Weese, 1928) and petechial haemorrhages in dogs (Tyson and Schoenberg, 1914) and slight emphysema (Flury and Wirth, 1934) have also been observed.

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(6) The nervous system

Capillary congestion, oedema and patchy degeneration of the neurons, especially of the spinal cord, and some involvement of the peripheral nerves were noted by Scott *et al.* (1933). Earlier investigators (Holden, 1899, and Ruhle, 1912) had found more severe congestive lesions, while Tyson and Schoenberg (1914) noted marked congestion of the meninges of dogs.

Toxicity to human beings

(A) Non-industrial

There have been many reports of outbreaks of poisoning from methyl alcohol, causing blindness or death. One of such was the report by Monier Williams (1929) in the Ruhr in 1920 when 15 people died and 3 were totally blinded from drinking brandy adulterated with methyl alcohol; another, with similar effects, in Japan, in 42 cases, from drinking fruit juices diluted with methyl alcohol (Kaplan and Levreault, 1945) and from drinking methyl alcohol itself, with 24 deaths (Voegtlin and Watts, 1943), and another record, from the same cause, of 390 deaths and 90 cases of total and 85 of partial blindness by Baskerville in America (1913).

(B) Industrial

Following the publication of the above reports, and many others, of the highly toxic nature of methyl alcohol when taken internally, it is not surprising that the danger of its use as a solvent should have been somewhat exaggerated. It is true that cases of poisoning, accompanied by blindness, have occurred from exposure to its vapour, but the hazard is more potential than actual, especially if reasonable care is taken to keep the vapour concentrations in the working atmosphere at a level of approximately the Maximum Allowable Concentration of 200 p.pm., and to prevent workers from drinking either the methyl alcohol itself or industrial materials containing it. Some of the recorded cases have in fact carried the more or less well founded suspicion that ingestion as well as inhalation had played some part in the development of symptoms of poisoning (Gerbis, 1931; Wood and Buller, 1904). Wood and Buller remarked that "taking a drink from the supply of alcohol kept for dissolving gums in making varnishes is a very common habit among varnishers". On the other hand, surveys of workers exposed repeatedly to the vapour of methyl alcohol have sometimes revealed no harmful effects. One such survey by Yant *et al.* (1931) of men employed in the manufacture of methyl alcohol and drivers of trucks using it as an antifreeze agent revealed no harmful effects. Bertarelli (1934) has also called attention to the fact that there have been many cases of prolonged exposure to methyl alcohol without development of any symptoms.

(1) Acute

Cases of acute poisoning are especially rare from inhalation only, but have been known to occur from ingestion of various solutions containing it. Two such cases have recently been described by Stinebaugh (1960), both from drinking a paint thinner, in one case an unknown quantity, in the other 2 ounces. Both suffered from vomiting, epigastric pain, irrational behaviour, failure of vision and semi-coma. Both recovered from the general symptoms under suitable treatment, but neither recovered full vision; in one case in fact complete blindness supervened.

Other acute symptoms are related to the strongly irritant property of methyl alcohol for mucous membranes, causing conjunctivitis and bronchopneumonia. The conjunctivitis has been known to be so severe as to destroy the cornea (Grunow, 1912) and the bronchopneumonia, in a case quoted by Goldtdammer in 1878 was actually fatal.

General systemic intoxication, shown by lassitude, headache, giddiness, nausea, vomiting, pain in the gastric and lumbar region, coldness and muscle weakness, may precede or accompany the most severe toxic manifestation – blindness. Complete loss of vision, however, exhibits as a rule no premonitory symptoms but occurs suddenly in both eyes.

Koelsch (1921) stated that all these symptoms were frequent during World War I when alcohol was used widely in paints, lacquers and polishes, especially when these were handled in closed rooms in warm weather. He quotes several cases of temporary blindness and others of bilateral optic atrophy occurring in such conditions, and refers to one described by Philippi in 1906 in a painter who sprayed methyl alcohol on his feet and then continued to work for a few hours in the room; he became blind.

TREATMENT

Three methods of treatment have been tried, with varying degrees of success. *(α) Administration of alkalies.* – This method is of course based on the evidence that methyl alcohol produces formic acid, formaldehyde and possibly other unidentified acids, with formation of acidosis. It was first suggested by Harrop and Benedict (1920), and by Chew *et al.* (1946) and also Røe noted that it alleviated the symptoms and increased the survival rate. Bennet *et al.* (1953) treated a series of 323 cases due to ingestion of adulterated contraband whiskey and were convinced of the efficacy of this treatment, consisting of large amounts of sodium bicarbonate – up to 150–200 g – in the proportion of 50 g in 1000 ml of 5% glucose in water, given intravenously. They stated that return of acidosis was not unlikely following treatment by alkalisation alone, and glucose has been suggested as a useful adjunct to alkalisation on the basis of the possible role of ketosis (Keeney and Mellinkoff, 1951). Nevertheless, according to Stinebaugh (1960) correction of the acidosis does not always prevent a fatal issue either in animals (Potts, 1955) or human beings.

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(β) Administration of ethyl alcohol. – The effect of ethyl alcohol on the metabolic behaviour of methyl alcohol, by inhibiting its enzymatic oxidation into toxic metabolites has already been discussed (see p. 313). It is on this basis that ethanol treatment had been advocated (Stinebaugh, 1960; Røe, 1946), but there is no universal agreement as to its efficacy in actual cases of methanol intoxication and it is not regarded as a justifiable substitute for alkalisation.

(γ) Peritoneal dialysis. – It was shown by Blakemore and Hine (1947) that methyl alcohol could be removed by peritoneal dialysis in animals, and Stinebaugh (1960) used this evidence as a basis for this treatment, combined with alkalisation. The basic solution consists of glucose and sodium bicarbonate in water and isotonic saline and is administered through a perforated polythene tube introduced into the peritoneal cavity by an abdominal trocar. The fluid is drained after two hours and the process repeated. In one case the first specimen of dialysis fluid contained 130 mg/100 of alcohol and dialysis was continued for 18 h, at the end of which time the fluid contained none. In a second case dialysis was only begun 10 h after admission to hospital and a specimen taken 12 h later was negative. Both these cases recovered (without return of vision) but in a third case, where intoxication was due to ordinary alcoholic intake and whose dialysis specimen after two hours contained 200 mg/100 of alcohol, death took place after development of tetanic spasms. Stinebaugh suggests that the best method of treatment is a combination of all three measures.

(2) Chronic

Cases of industrial poisoning from repeated exposure to the vapour of methyl alcohol have generally been manifested by conjunctivitis, headache, giddiness, insomnia, gastro-intestinal disturbance and failure of vision.

Some of these symptoms, notably those of a narcotic nature, leading in some cases to coma, were described by Roche *et al.* (1957) in an account of a collective disturbance of health in a factory manufacturing electrical car accessories, but the presence of methyl alcohol in the compound used, which consisted chiefly of trichloroethylene, was never definitely proved. Suspicion of methyl alcohol as a contributory cause of the symptoms arose partly from the fact that the severe manifestations showed a latent period after cessation of work and that an investigation of the effects on guinea pigs exposed to a mixture of methyl alcohol and trichloroethylene also showed a longer latent period before the onset of fatal coma than those exposed to trichloroethylene alone.

It appears probable that, considering the vague character of the symptoms and the very large number of women affected, some of the manifestations may have been of emotional origin; others were quite characteristic of exposure to trichloroethylene.

Another case of industrial chronic poisoning, in which an additional factor may have been absorption through the skin, is that described by Burk in 1957.

This was a man aged 27 who had worked for 4 years in the methanol department of a chemical-pharmaceutical factory where nicotinic acid was being crystallised, the solvent being pure methyl alcohol. For two years he had complained of disturbance of vision, which was then diagnosed as slight astigmatism and corrected by glasses. At the same time he complained of weakness and numbness of his hands and arms. While cleaning a tank in which nicotinic acid and methanol had been heated, and wearing a gas mask, he thought that the methanol fume was penetrating the filter, which had become damp, and changed it for a filter intended for ammonia. During the 5-h duration of his task he felt giddy at times, but at the end had no symptoms. The next morning he vomited, but continued working, then suddenly developed spots before the eyes and dimness of vision. He also complained of loss of appetite and a sweetish taste. Blood and urine examination at that time revealed nothing abnormal; ophthalmic examination showed papilloedema of both eyes. After 5 weeks, under treatment by eye drops, ointments, vitamin B, etc., his visual acuity became normal, but after a further 5 weeks his vision became irregular. At this time his urine contained formic acid, but later the test was negative. (No quantitative estimation was made.) Earlier investigators (*e.g.* Klauer, 1938) have given the normal level as ranging between 14 and 100 mg/1500 ml.

Burk states that the amount of methyl alcohol inhaled must have been small, but that the workman had been in the habit of cleaning his hands with methyl alcohol.

In 1913 Baskerville reported 64 cases in America from the industrial use of either concentrated or 50% methyl alcohol in painters, lacquerers, coopers and chimney sweeps who cleaned the chimneys with methyl alcohol. Koelsch (1921) also mentions the case known to him of a doctor engaged in research on disinfection with methyl alcohol vapour who became completely blind. Hansohn (1944) quoted by Burk (1957) described the eventual development of bilateral optic atrophy in a man who had complained only of recurrent conjunctivitis during his 1½ years of war work involving inhalation of methyl alcohol vapour. He strongly denied ingestion of alcohol.

SYMPTOMS OF INTOXICATION

(1) Mechanism of toxic effect on the eyes

Observations on the actual toxic process of methyl alcohol on the ocular tissues have been almost exclusively discussed with regard to ingestion, but cases of ocular injury having occurred following absorption through the skin and inhalation, gradually methyl alcohol came to be regarded as a specific toxin for the retina and the optic nerve. One intensive investigation is that of Fink (1943). Like Wood and Buller (1904) and Lehmann and Flury (1943), Fink emphasised the fact that impurities in the methyl alcohol are not an influencing factor, and

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that the basic cause of the toxic action is the inability of the body to oxidise methyl alcohol to CO_2 and water, as is the case with ethyl alcohol. He brought forward evidence that formic acid is formed and suggested the possibility of formation of formaldehyde also, as a contributory factor in injury of the eye tissues. This view is also held by Kaplan and Levreault (1945), Bogen (1946), and Røe (1948), but not by Potts and Johnson (1952) who believe that the role of acidosis is questionable and that the essential toxic agent is formaldehyde.

According to Fink, the tissues predominantly affected (the optic nerve and the retina) are not equally affected, but both appear to show injury in patches, with intermediate areas of less affected cells. Oedema of nerve tissue and supporting tissue is the result of both an irritative reaction of the tissue to the toxic substance and also of a degenerative process which is proportional to the intensity of the toxic element and the susceptibility of the individual. Both the retina and the optic nerve are sensitive to metabolic disturbance and this disturbance leads to degenerative changes, which may take place simultaneously in the two tissues. In the retina the toxic effect is exerted first on the ganglion cells, then the inner nuclear layer degenerates, later the outer nuclear layer, and finally the rod-and-cone layer. In the optic nerve, degenerative changes are accompanied by varying degrees of oedema.

It has also been stated (Kendal and Ramanathan, 1952) that methyl formate can be formed from formaldehyde and methanol, and that this substance, having a preferential fat solubility, might explain the localised effects of methanol. It has also been shown, however, that formaldehyde is 25 to 75 times more active than formate in inhibiting oxygen uptake and Co_2 production, and 1000 to 30,000 times more active than methanol itself (Leaf and Zatman, 1952; Røe, 1948).

The role of skin absorption in the production of methyl alcohol poisoning has already been mentioned (as in the case of Burk, 1957), and cases of severe eye injury in which it is said to have played a predominant part are quoted by Koelsch (1921) and Eulner (1954). In Eulner's case, a woman who had applied to her body a preparation consisting almost entirely of pure methyl alcohol, the effects on the eye were attributed not only to skin absorption but also partly to inhalation.

(2) Predisposition

(a) Individual susceptibility. – Many authorities believe that individual susceptibility plays a considerable part in the variation of toxic symptoms in similar conditions, not only in poisoning by ingestion but also in industrial poisoning. In some cases one relatively slight exposure has been said to have caused blindness, while others have remained unaffected until after repeated exposure in unfavourable conditions. Koelsch (1921), who had found no specific ill-effects in the majority of workers employed in the production of wood alcohol, described the case of a woman using a shoe cement in which methyl alcohol appears to have been the chief, but not the only constituent. She was weak and anaemic, and complained

of gradual failure of vision, leading eventually to blindness, as well as headache, throat irritation and burning of the eyes. No other workers in the same room suffered from any of these symptoms except slight irritation of mucous membranes.

(b) Sensitisation. – In the case described by Burk (1957) the occurrence of slight symptoms of chronic intoxication before the development of disturbance of vision, led him to conclude that sensitisation had taken place before the crucial exposure, and to emphasise that although relatively few cases of industrial poisoning from methyl alcohol had been recorded, it is not safe to conclude that inhalation of low concentrations can do no harm.

(c) Pre-existing nervous disorder. – Symptoms indicative of chronic industrial poisoning by methyl alcohol – giddiness, headache, insomnia, gastro-intestinal disturbance, conjunctivitis and failure of vision – were observed by Schwarzmann (1934) in a man working in a straw hat factory where the synthetic fibres were hardened by formaldehyde containing 10–12% of methyl alcohol. On returning to work after a year's absence the man showed paralysis of the facial and ocular muscles. He was not definitely diagnosed as suffering from methyl alcohol poisoning but possibly as a case of multiple sclerosis, but it was suggested that the nervous system disorder rendered him more susceptible to methyl alcohol poisoning.

A similar predisposing factor, in the form of pre-existing central nervous disease, was present in a case described by Humperdinck in 1941. This man had been employed 4 years in shovelling nitro-cellulose material containing 35–40% of methyl alcohol, in conditions of poor ventilation and lighting. In addition to failure of vision this man had an enlarged liver.

One and a half hours later his pulse was very weak, he was very restless, perspired profusely and died 14 h after the end of the exposure. At autopsy the lungs showed collapse, oedema and extravasation of blood into the alveoli, and the liver fatty degeneration. Kidney sections were not available.

The second case had been exposed for 3 months to concentrations of ethylene chlorohydrin (probably mixed with sym-dichloroethane) which had caused some symptoms in other workers. His symptoms related chiefly to the central nervous system – headache, dizziness and behaviour 'of a peculiar manner'; later he had haematuria and died the following day. Autopsy was not detailed, but the kidneys showed congestion and some necrosis and the brain gross oedema of the basal ganglia and some degenerative changes.

In a case described by Cavalazzi (1942) vomiting was followed by delirium and violent excitement.

(2) Chronic or subacute

The nine non-fatal cases described by Goldblatt and Chiesman occurred during a period when a fault had developed in the plant and when the average concentration of ethylene chlorohydrin was about 18 p.p.m. The chief symptoms were nausea, vomiting and abdominal pain; in some cases a semi-comatose condition. Slight albuminuria was present in some. It was believed that the additional presence of ethylene dichloride was not the principal cause of the symptoms, since narcotic effects were very mild.

TREATMENT OF INTOXICATION

In severe acute cases Goldblatt and Chiesman state that temporary improvement is obtained by continuous oxygen administration and analeptics. With mild cases treatment is entirely symptomatic.

BIBLIOGRAPHY

Abelin, I., C. Herren and W. Berli (1938) Über die erregende Wirkung des Alkohols auf den Adrenalin und Noradrenalin-Haushalt des menschlichen Organismus, *Helv. Med. Acta*, 25:591.

Agner, K. and K. E. Belfrage (1947) A specific Micro-method for Colorimetric Determination of Methanol in Blood, *Acta Physiol. Scand.*, 13:87.

Ambrose, A. M. (1950) Toxicological Studies investigated for Use as Inhibitors of Biological Processes, *Arch. Ind. Hyg.*, 2:591.

Anker, M. (1892) Ein Fall von Amylenhydratvergiftung, *Therap. Monatschr.*, 6:623.

Annual Report, Chief Inspector of Factories, G.B. (1957) H.M.S.O. London.

Ascham, O. (1927) Zur Verwertung des Petroläthers und der Erdöl Residuen, *Chemikerztg.*, 51:4.

Atkinson, H.V. (1925) The Toxicity of Impurities in Wood Alcohol, *J. Pharmacol.*, 25:144.

Baader E. W. (1933) Gewerbemedizinische Erfahrungen, *Verhandl. Deut. Ges. Inn. Med.*, 45:318.

Bachem, C. (1927) Beitrag zur Toxikologie der Halogenalkyle, *Arch. Exptl. Pathol. Pharmakol.*, 122:69.

Baer, F. (1898) Beitrag zur Kenntnis der akuten Vergiftung mit verschiedenen Alkoholen, Dissertation, Berlin, *Arch. Anat. Physiol. Abt.*, p. 283.

Barlow, O. W. (1936) Studies on the pharmacology of Ethyl Alcohol, *J. Pharm, Exptl. Therap.*, 56:177.

Bartlett G. R. (1950) Combustion of C^{14}-labelled Methanol in the intact Rat and its isolated Tissues, *Am. J. Physiol.*, 163:614.

Bartlett, G. R. and H. N. Barnet (1949) Some Observations on Alcohol Metabolism with radioactive Ethyl Alcohol, *Quart. J. Stud. Alc.*, 10:381.

Baskerville, C. (1913) Report on Chemistry, Technology and Pharmacology of and Legislature pertaining to Methyl Alcohol *2nd. Rept. Factory Insp. Comm. New York*, 2:921.

Bennett, Jr., I. J., F. H. Carey, G. L. Mitchess Jr. and M. N. Cooper (1953) Acute Methyl Alcohol Poisoning. Review based on Experience of Outbreak of 323 Cases, *Medicine*, 32:431.

Berggren, S. M. (1938) On the Metabolism of *n*-Propyl and *n*-Butyl Alcohol in the Organism, *Skand. Arch. Physiol.*, 78:249.

Bernhard, H. (1937) Stoffwechselversuche zur Dehydrierung des Cyclohexanols, *Hoppe-Seyler's Z. Physiol. Chem.*, 248:256.

Bertarelli, E. (1934) I Pericoli practici dell' Alcool Metilico, *Ann. Igiene (Sperim)*, 44:729.

Biberfeld, J. (1918) Zur Kenntnis der Gewohnung, *Biochem. Zschr.*, 92:198.

Bijlsma, U. G. (1928) Isopropyl Alcohol, *Arch. Pharmacodyn.*, 34:204.

Bird, C. L. (1932) Auxiliary Solvents for dry-cleaning Soaps, *J. Soc. Dye Col. Bradford*, 48: 256.

Birsch-Hirschfeld, A. (1901) Experimentelle Untersuchungen über die Pathogenese der Methylalkoholamblyopie, *Arch. Ophthalm.*, 52:538.

Blakemore, W. S. and C. H. Hine (1947) (cited by Stinebaugh, 1960), The Effect of peritoneal Irrigation on experimental Methyl Alcohol Toxicity, Bumed News Letter, 10:18.

Bogen, E. (1946) Methanol Poisoning, *Calif.* [*West.*] *Med.*, 65:230.

Boruttau, H. (1921) Die Verwendung von Isopropylalkohol zu hygienischen und kosmetischen Zwecken, *Deut. Med. Wochschr.*, 47:747.

Bray, H. G., W. V. Thorpe and K. White (1951) The Formation of Benzoic acid from Benzamide, Benzyl Alcohol and Benzaldehyde, *Biochem. J.*, 48:88.

Brecher, G. A., A. R. Hartman and D. D. Leonard (1955) Effect of Alcohol on Binocular Vision, *Am. J. Ophthalm.*, 39:44.

Brezina, E. (1929) Internationale Übersicht über Gewerbekrankheiten, pp. 83 and 167, Julius Springer, Berlin.

Browning, E. (1953) *The Toxicity of Industrial Organic Solvents*, H.M.S.O. London; Chemical Publishing Co. Inc. New York.

Burger, G. B. C. and B. H. Stockman (1932) Über Urobilinurie als Folge der Einatmung von organischen Lösungsmitteln in geringer Konzentration, *Z. Gewerbehyg.*, 19:29.

Burk, M. (1957) Zur chronischgewerblichen Methylalkoholvergiftung, *Klin. Mbl. Augenheilk.*, 130:845.

Burton, K. and T. H. Wilson (1953) Free Energy Data for Dehydrogenase Systems, *Biochem. J.*, 54:86.

Butler, T. C. and L. H. Dickison (1940) The anaesthetic Activity of optical Antipodes; The secondary Butyl Alcohols, *J. Pharm. Exptl. Therap.*, 69:225.

Bush, A. F., H. K. Abrams and H. V. Brown (1949) Fatality and Illness caused by Ethylene Chlorohydrin in an agricultural Operation, *J. Ind. Hyg. Toxicol.*, 31:352.

Campbell, J. A. (1915) Wood Alcohol Amblyopia – a Case, *J. Ophth. Otol. Laryngol.*, 21:756.

Carlier, E. W. (1911) Notes on the Physiology of some of the Allyl Compounds, *Brit. Med. J.*, 2:609.

Carpenter, C. P. and H. F. Smyth Jr. (1946) Chemical Burns of the Rabbit Cornea, *Am. J. Ophth.* 29:1363.

Carpenter, C. P., H. F. Smyth Jr. and U. C. Pozzani (1949) Assay of acute Vapor Toxicity and Grading and Interpretation of Results on 96 Chemical Compounds, *J. Ind. Hyg. Toxicol.*, 31:343.

Castor, J. G. B. and J. F. Guymon (1952) On the Mechanism of Formation of higher Alcohols during Alcoholic Fermentation, *Science*, 115:147.

Cavalazzi, D. (1942) Akute und tödliche Vergiftung durch Äthylenchlorhydrin, *Samml. Vergiftungsf.*, 12:79:A. 910.

Chapin, M. A. (1949) Isopropyl Alcohol Poisoning with acute Renal Insufficiency, *J. Maine Med. Ass.*, 40:288.
Charnwood (Lord) (1950) Influence of Alcohol on Fusion, *Brit. J. Ophthalmol.*, 34:733.
Chew, W. B., E. H. Berger, O. A. Brines and M. J. Capron (1946) Alkali Treatment of Methyl Alcohol Poisoning, *J. Am. Med. Ass.*, 130:61.
Christiansen, J. (1918) On the Theory and Practice of Alcohol Disinfection, *Zschr. Physiol. Chem.*, 102:275.
Clayton, E. and C. O. Clark (1931) Modern Organic Solvents, *J. Soc. Dyers Col. Bradford*, 47:183; 247.
Cogan, D. G. and W. M. Grant (1945) An unusual Type of Keratitis associated with Exposure to *n*-Butyl Alcohol, *Arch. Ophth.*, 33:106.
Comstock, C. C. and F. W. Oberst (1952) Inhalation Toxicity of Aniline, Furfuryl Alcohol and their Mixtures in Rats and Mice (cited by Treon, 1963), *Chem. Corps. Med. Labs. Research Rep.* No. 139.
Cook, W. A. (1945) M.A.C. of Industrial Atmospheric Contaminants, *Indust. Med. Surg.*, 14:936.
Cook, C. A. and A. H. Smith (1929) The Determination of Isopropyl Alcohol in the presence of Acetone in the Urine, *J. Biol. Chem.*, 85:821.
Daremberg, G. (1895) La Toxicité des Boissons alcooliques mesurée à l'Aide des Injections intraveineuses chez le Lapin, *Arch. Méd. Expér. Anat. Path.*, 7:719.
Denigès, G. (1910) Study of Methyl Alcohol in general and especially in the presence of Ethanol, *C.R. Acad. Sci.*, 150:832.
Denny, F. E. (1928) Chemical Treatments for Shortening the Rest Periods of Plants, *J. Soc. Chem. Ind.*, 47:239.
Diack, S. L. and H. B. Lewis (1928) Studies in the Synthesis of Hippuric Acid in the Animal Organism, *J. Biol. Chem.*, 77:89.
Dierker, H. and F. Brown (1944) Study of a fatal Case of Ethylenechlorohydrin Poisoning, *J. Indust. Hyg. Toxicol.*, 26:277.
Di Luzio, N. R. (1961) Discussion on Role of Alcohol on Cirrhosis, *Am. J. Clin. Nutrition*, 9:442.
Donley, D. E. (1936) Toxic Encephalopathy and volatile Solvents in Industry, *J. Indust. Hyg. Toxicol.*, 18:571.
Doolittle. A. K. (1954) *The Technology of Solvents and Plasticisers*, John Wiley and Sons, New York.
Duchesi, V. (1915) La Colesterina del Sangue nella Intossicazione per Alcool, *Arch. di Fisiol.*, 13:147.
Dujardin-Beaumetz, and Audige (1875) Sur les Propriétés toxiques des Alcools par Fermentation, *C. R. Acad. Sci.*, 81:192.
Duke, Elder S. (1940) *Textbook of Ophthalmology*, Vol. 3, 3019, Kimpton, London.
Duncan, D. and W. H. Jarvis (1943) A Comparison of the Action on Nerve Fibres of certain Anaesthetic Mixtures and Substances in Oil, *Anesthesiology*, 4:465.
Dunlap, M. K. and C. H. Hine (1955) Toxicity of Allyl Alcohol, *Federation Proc.*, 14:335.
Dunlap, M. K., J. K. Kodama, J. S. Wellington, H. H. Anderson and C. H. Hine (1958) The Toxicity of Allyl Alcohol, *Arch. Ind. Health.*, 18:303.
Durrans, T. H. (1950) *Solvents*, 6th ed., Champan and Hall, London.
Durwald, W. and W. Degen (1956) Eine tödliche Vergiftung mit *n*-Propyl Alkohol, *Arch. Toxikol.*, 16:84.
Eberhardt, T. P. (1936) Effect of Alcohol on Cholesterol-induced Atherosclerosis in Rabbits, *Arch. Path.*, 21:617.
Eisenberg, A. A. (1917) Visceral Changes in Wood Alcohol Poisoning by Inhalation, *Am. J. Publ. Health*, 7:765.
Elhardt, W. P. (1931) The Effect of Methyl, Propyl and Butyl Alcohol on the Growth of white Leghorn Chicks, *Am. J. Physiol.*, 100:74.
Elkins, H. B. (1959) *The Chemistry of Industrial Toxicology*, Wiley and Sons, New York, Chapman and Hall, London.
Elliott, T. H., D. V. Parke and R. T. Williams (1959) The Metabolism of Cyclo [^{14}C]hexane and its Derivatives, *Biochem. J.* 72:193.
El Masri, A. M. and R. T. Williams (1956) (unpublished data, cited by R. T. Williams, 1959).

Erdmann, E. (1902) Über das Kaffeeoel und die physiologische Wirkung des darin erhaltenen Furfuralkohols, *Arch. Exptl. Pathol. Pharmakol.*, 48:233.
Eulner, H. H. (1954) Methanolvergiftung bei äusserlicher Anwendung, *Arch. Toxikol.*, 15:73.
Eyquem (1905) Du Danger des Vapeurs alcooliques dans la Fabrication de la Poudre sans Fumée, *Ann. Hyg. Publ.* Paris, 4-ième Ser., 3:71.
Fairhall, L. T., (1957) *Industrial Toxicology*, 2nd ed., Williams and Wilkins Co., New York.
Fassett, D. W. (1963) cited by Treon J. F. in *Alcohols*, F. A. Patty (Ed.), *Industrial Hygiene and Toxicology*, Vol. II, 2nd ed., Interscience, New York.
Feller, D. D. and R. L. Huff (1955) Lipide synthesis by arterial and Liver Tissue obtained from Cholesterol-fed and Cholesterol-alcohol-fed Rabbits, *Am. J. Physiol.*, 182:237.
Ficklen, J. B. (1940) *Manual of Industrial Health Hazards*. Service to Industry, West Hartford, Connecticut.
Fieser, L. L. and M. Fieser (1944) *Organic Chemistry*, Heath, Boston.
Filippi, E. (1914) Azione fisiologica e Comportamento di alcuni Derivati dal Benzene in Confronto con quelli di Cicloesano, *Arch. Farmacol. Sper.*, 18:178.
Fine, E. H. and J. H. Wills (1950) Pharmacologic Studies of Furfuryl Alcohol, *Arch. Ind. Hyg.*, 1:625.
Fink, W. H. (1943) The Ocular Pathology of Methyl Alcohol Poisoning, *Am. J. Ophthalm.*, 26:802.
Flury, F. and W. Wirth (1934) Zur Toxikologie der Lösungsmitteln, *Arch. Gewerbepath. Gewerbehyg.*, 5:1.
Flury, F. and H. Zangger (1928) *Lehrbuch der Toxikologie für Studium und Praxis*, Springer, Berlin.
Flury, F. and F. Zernik (1931) *Schädliche Gäse, Dämpfe, Nebel, Rauch- und Staubarten*, Springer, Berlin.
Fuchter, T. B. (1901) cited by Treon (1963) *Am. Med.*, 2:210.
Fuller, H. C. and O. B. Hunter (1927) Isopropyl Alcohol – an Investigation of its physiologic Properties, *J. Lab. Clin. Med.*, 12:326.
Galewski, J. and W. Alsdorf (1949) Studies on Furan Compounds: Toxicity and pharmacological Action of Furfuryl Alcohol, *Fed. Proc.*, 8:294.
Gardner, H. A. (1925) (cited by Treon, 1963), Paint Mfrs, *Ass. U.S. Techn. Circ.* No. 250:89.
Garrison, F. (1953) Acute Poisoning from Use of Isopropyl Alcohol in tepid Sponging, *J. Am. Med. Ass.*, 152:317.
Gaulejac, R. de, and P. Dervillée (1938) Sur quelques Cas d'Intoxication par les Vapeurs de Benzène et d'Alcool benzylique, *Ann. Méd. Légale*, 18:146.
Gerbis, H. (1931) Methylalkoholvergiftung, chronische, *Samml. Vergiftungsf.*, 2:171; A 160.
Gettler, A. O. and A. Tiber (1927) The Alcoholic Content of the Human Brain, *Arch. Path. Lab. Med.*, 3:218.
— (1927) The quantitative Determination of Ethyl Alcohol in Human Tissues, *Arch. Path. Lab. Med.*, 3:75.
Giardini, A. (1952) Action of Alcohol on Ability to fuse Retinal Images, Abs. in *Quart. J. Stud., Alc.*, 13:298.
Gilger, A. P., A. M. Potts and L. V. Johnson (1952) Studies on the Visual Toxicity of Methanol, *Am. J. Ophthalm. Suppl.*, 35:113.
Goldberg, L. (1943) Quantitative Studies on Alcohol Tolerance in Man, *Acta Physiol. Scand.* (Suppl. 16), 5:1.
Goldblatt, M. W. (1944) Toxic Effects of Ethylenechlorohydrin (Experimental), *Britt. J. Ind. Med.*, 1:213.
Goldblatt, M. W. and W. E. Chiesman (1944) Toxic effects of Ethylenechlorohydrin (Clinical), *Brit. J. Ind. Med.*, 1:207.
Goldtdammer, (1878) Bronchitis durch Holzgeistdämpfe, *Z. Ger. Med.*, 29:162.
Gradinesco, A. (1934) l'Action de l'Alcool sur le centre respiratoire, *J. Physiol. Path. Gén.*, 32:363.
Grande, F. and D. S. Amatuzio (1960) The Influence of Ethanol on Serum Cholesterol Concentration, *Minnesota Med.*, 43:731.
— (1923) The antiseptic and bactericidal Properties of Isopropyl Alcohol, *Am. J. Med.Sci.*, 166:261.
Grant, D. H. (1923) The Pharmacology of Isopropyl Alcohol, *J. Lab. Clin. Med.*, 8:382.
Grant, G. R. (1950) Inhibition of Methanol Oxidation by Ethanol in the Rat, *Am. J. Physiol.*, 163:614, 619.

Greenberg, L. A. and D. L
Bodies, *J. Biol. Chem.*, 1
Grilichess, R. (1913) Über
Z. Allgem. Physiol., 15:
Gruber, C. M. (1923) Pharr
— (1925) Pharmacology of
Grunow (1912) (cited by K
Guggenheim, M. and W. Lo
Zschr., 72:325.
Haag, H. B., T. Silverman
acute Respiratory Fail
Haggard, H. W. and L. A
Ethyl Alcohol; Rate o
150, 167.
Haggard, H. W., D. P. Mil
metabolic Fates and c
Hahn, E. (1937) On the D
292:148.
Hamilton, A. (1934) *Indust*
Harger, R. N. (1958) The
2199.
Harger, R. N. and H. R. J
Thomas, Springfield,
Harrop, G. A., Jr. and F.
Acidosis, *J. Am. Med.*
Henry, R. J., C. F. Kirkwo
tric Method for Deter
Fluids, *J. Lab. Clin. M*
Heuber, E. Von (1917) Ei
Hilbert (1925) cited by Le
Hine, C. H., T. A. Shea Jr.
mination of Methanol
Holden, H. C. and A. K.
Holden, W. A. (1899) Th
following Ingestion o
Hufferd, R. W. (1932) T
— (1932) Variations in p
Pharm. Ass., 21:549.
Humperdinck, K. (1941)
Gewerbepath. Gewerbeh
Huntress, E. T. (1948)
Chlorine Compounds, W
Jacobi, W. and E. Speer
Monatschr., 6:623.
Jacobs, M. B. (1941) *The*
New York.
Jacobsen, E. (1952) Met
Jacobsen K. H., W. E. R
Groff (1958) The
Am. Ind. Hyg. Ass. J.
James, V. C. (1931) Acut
Brit. Med. J., 1:539
Jetter, W. W. (1943) Syn
Death caused by or
Joffrey, A. and R. Serve
Liquides par Injecti

Greenberg, L. A. and D. Lester (1944) Micromethod for Determination of Acetone and Ketone Bodies, *J. Biol. Chem.*, 154:177.
Grilichess, R. (1913) Über die pharmakologische Wirkung kombinierte Urethane und Alkohole, *Z. Allgem. Physiol.*, 15:468.
Gruber, C. M. (1923) Pharmacology of Benzyl Alcohol and its Esters, *J. Lab. Clin., Med.*, 9:15, 92.
— (1925) Pharmacology of Benzyl Alcohol and its Esters, *J. Lab. Clin. Med.*, 10:284.
Grunow (1912) (cited by Koelsch, 1921) *Halbmonatschr. Soz. Hyg.*, 2,
Guggenheim, M. and W. Loffler (1916) Das Schicksal proteinogener Amine in Tierkörper, *Biochem. Zschr.*, 72:325.
Haag, H. B., T. Silverman and S. Kaye (1951) Relationship between Blood Alcohol Levels and acute Respiratory Failure, *J. Pharm. Expil. Therap.*, 103:344.
Haggard, H. W. and L. A. Greenberg (1934) The Absorption, Distribution and Elimination of Ethyl Alcohol; Rate of Oxidation of Alcohol in the Body, *J. Pharm. Explt. Therap.*, 52:137, 150, 167.
Haggard, H. W., D. P. Miller and L. A. Greenberg (1945) The Amyl Alcohols and their Ketones; metabolic Fates and comparative Toxicities, *J. Ind. Hyg., Toxicol.*, 27:1.
Hahn, E. (1937) On the Determination of Isopropyl Alcohol in the Respiratory Air, *Biochem. Z.*, 292:148.
Hamilton, A. (1934) *Industrial Toxicology*, Harper, New York.
Harger, R. N. (1958) The Pharmacology and Toxicology of Alcohol, *J. Am. Med. Ass.*, 167: 2199.
Harger, R. N. and H. R. Julpien (1956) *The Pharmacology of Alcohol*, (Ed.) G. N. Thompson, C. C. Thomas, Springfield, Illinois.
Harrop, G. A., Jr. and F. M. Benedict (1920) Acute Methyl Alcohol Poisoning associated with Acidosis, *J. Am. Med. Ass.*, 74:25.
Henry, R. J., C. F. Kirkwood, S. Berkman, R. D. Housewright and J. J. Henry (1948) A Colorimetric Method for Determination of Micro Quantities of Ethanol in Blood and other biologic Fluids, *J. Lab. Clin. Med.*, 33:241.
Heuber, E. Von (1917) Ein Fall von Schlafmittelvergiftung, *Münch. Med. Wschr.*, 64:216.
Hilbert (1925) cited by Lewin (1929) in *Gifte und Vergiftungen*, 4th. ed., Springer, Berlin.
Hine, C. H., T. A. Shea Jr. and W. R. Alsdorf (1947) An accurate Colorimetric Method for Determination of Methanol in Blood, Tissues and Expired Air, *Fed. Proc.*, 6:338.
Holden, H. C. and A. K. Doolittle (1935) Solvents, *Ind. Eng. Chem.*, 27:525.
Holden, W. A. (1899) The Pathology of the Amblyopia following profuse Haemorrhage and that following Ingestion of Methyl Alcohol, *Arch. Ophthalm.*, 28:125.
Hufferd, R. W. (1932) Toxicity of Aliphatic Alcohols, *J. Am. Pharm. Ass.*, 21:549.
— (1932) Variations in physiological Activity of Alcohols amoug Isomers and Homologs, *J. Am. Pharm. Ass.*, 21:549.
Humperdinck, K. (1941) Zur Frage der chronische Giftwirkung von Methanoldämpfen, *Arch. Gewerbepath. Gewerbehyg.*, 10:569.
Huntress, E. T. (1948) *The Preparation, Properties, Chemical Behaviour and Identification of Organic Chlorine Compounds*, Wiley, New York.
Jacobi, W. and E. Speer (1920) Amylenhydratvergiftung (35 gm) mit tödlichem Ausgang, *Therap. Monatschr.*, 6:623.
Jacobs, M. B. (1941) *The Analytical Chemistry of Industrial Poisons, Hazards and Solvents*, Interscience, New York.
Jacobsen, E. (1952) Metabolism of Ethyl Alcohol, *Pharmacol. Rev.*, 4:1017.
Jacobsen K. H., W. E. Rinehart, M. A. Ross, J. P. Papin, R. C. Daly, E. A. Greene and W. A. Groff (1958) The Toxicology of an Aniline-Furfuryl-Alcohol-Hydrazine Vapor Mixture, *Am. Ind. Hyg. Ass. J.*, 19:91.
James, V. C. (1931) Acute Alcoholic Poisoning due to the Application of Surgical Spirit to the Legs, *Brit. Med. J.*, 1:539.
Jetter, W. W. (1943) Symposium on Scientific Proof and Relation of Law and Medicine. When is Death caused by or contributed to by acute Alcoholism? *Clinics*, 1:1487.
Joffrey, A. and R. Serveaux (1895) Sur un nouveau Procédé de Mensuration de la Toxicité des Liquides par Injection intraveineuse, *Sem. Méd.*, 15:346.

Jones, G. W. (1938) Inflammation Limits and new practical Application in hazardous industrial Operations, *Chem. Rev.*, 22:1.
Joss, G. (1947) Contribution of Alcohol to Accident Fatalities, *Quart. J. Stud. Alc.*, 7:588.
Kamil, I. A., J. N. Smith and R. T. Williams (1953) Detoxication of Methanol and Ethanol, *Biochem. J.*, 54:390.
— (1953) The Formation of ester glucuronides of Aliphatic Alcohols during the Metabolism of 2-ethyl Butanol and 2-ethyl Hexanol, *Biochem. J.*, 53:137.
— (1953) The Isolation of Methyl and Ethyl Glucuronides from the Urine of Rabbits receiving Methanol and Ethanol, *Biochem. J.*, 54:390.
— (1953) The Metabolism of Aliphatic Alcohols; the glucuronic acid Conjugation of acyclic aliphatic Alcohols, *Biochem. J.*, 53:129.
Kaplan, A. and G. V. Levreault (1945) Methyl Alcohol Poisoning, Report of 42 Cases, *U.S. Nav. Med. Bull.*, 44:1107.
Kaye, S. and H. B. Haag (1954) Determination of Ethyl Alcohol in Blood, *J. Forensic Med.*, 1:373.
— (1957) Terminal Blood Concentrations in 94 Cases of acute Alchoholism, *J. Am. Med. Ass.*, 165:451.
Keeney, A. H. and S. M. Mellinkof (1951) Methyl Alcohol Poisoning, *Ann. Int. Med.*, 34:331.
Keith, H. M. (1931) The effect of various Factors on experimentally produced Convulsions, *Am. J. Dis. Child*, 41:532.
— (1932) Effect of Diacetone Alcohol on Liver of Rat, *Arch. Path. Lab. Med.*, 13:704.
Kemal, H. (1927) Beitrag zur Kenntnis des Schicksals des Isopropylalkohols im menschlichen Organismus, *Biochem. Zschr.*, 187:461.
— (1937) The Acetone Content of the Urine, Faeces and Organs of Dogs after Isopropyl Ingestion, *Zschr. Physiol. Chem.*, 246:59.
Kendal, L. P. and A. N. Ramanathan (1952) Liver Alcohol Dehydrogenase and Ester Formation, *Biochem. J.* 52:430.
— (1953) Excretion of Formate after Methanol Ingestion in Man, *Biochem. J.*, 54:424.
Kirk, R. E. and D. F. Othmer (1947) Encyclopaedia of Chemical Technology, *Interscience Encyclopaedia*, New York.
— (1949) Encyclopaedia of Chemical Technology, *Interscience Encyclopaedia*, New York.
— (1951) Encyclopaedia of Chemical Technology, Vol. 6, *Interscienc Encyclopaedia*, New York.
Klatskin, G. (1961) Experimental Studies on the Role of Alcohol in the Pathogenesis of Cirrhosis, *Am. J. Clin. Nutr.*, 9:439.
Klauer, H. (1938) Zum Nachweis des Methylalkoholvergiftung, *Deut. Zschr. ges. gerichtl. Med.*, 30:280.
Knipping, H. W. and W. Ponndorf (1926) On the reversible Exchange of Degrees of Oxidation of Oxy- and Oxo-compounds, *Zschr. Physiol. Chem.*, 160:25.
Kober, G. M. and W. C. Hanson (1918) *Diseases of Occupation and Vocational Hygiene*, Heinemann, London.
Kochmann, M. (1923) *Alkohol*, in A. Heffter (Ed.) *Handbuch der experimentellen Pharmakologie*, Springer, Berlin.
— (1923) *Schlafmittel*, in A. Heffter (Ed.) *Handbuch der experimentellen Pharmakologie*, Vol. I, p. 428, Springer, Berlin.
Kodama, J. K. and C. H. Hine (1958) Pharmacodynamic Aspects of Allyl Alcohol Toxicity, *J. Pharm. Exptl. Therap.*, 124:97.
Koelsch, F. (1921) Die gewerbliche medizinische Beurteiling des Holzgeistes bzw. Methylalkohol, *Zbl. Gewerbehyg.*, 9:198.
— (1927) Die Giftigkeit des Äthylenchlorhydrin, *Zbl. Gewerbehyg.*, 14:312.
— (1947) *Lehrbuch der Arbeitshygiene*, 2nd. ed., p. 281, Ferdinand Enke, Stuttgart.
Korenmann, I. M. (1932) Kolorimetrische Bestimmung von Amylalkohol und Amylazetatdämpfen in der Luft, *Arch. Hyg.*, 109:108.
Krüger, E. (1932) Augenerkrankung bei Verwendung von Nitrolacken in der Strohhutindustrie, *Arch. Gewerbepath. Gewerbehyg.*, 3:798.
Lanza, A. J. and J. A. Goldberg (1939) *Industrial Hygiene*, p. 466, Thomas, Springfield, Ill.
Larsen, J. A. (1959) Extrahepatic Metabolism of Ethanol in Man, *Nature*, 184:1236.
Larsen, J. A., N. Tygstrup and K. Winkler (1961) The Significance of the extrahepatic Elimina-

tion of Ethanol in Dete
Clin. Invest., 13:116.
Leaf, G. and L. J. Zatman (1
toxic Hazard in Industry.
Lehman, A. J. and H. W. Nev
saturated Alcohols, *J. Ph*
Lehman, A. J., H. Schwerma
Dogs, *J. Pharmacol.*, 85:6
Lehmann, K. B. and F. Flur
Wilkins, Baltimore.
— (1928) Beitrag zur allgem
132:214.
— (1928) Untersuchungen üb
kohole, *Arch. Exptl. Pathol*
Lewin, L. (1912) Über die Ver
Klin., 8:95.
— (1929) *Gifte und Vergiftunge*
Lieber, C. S. and R. Schmid
Invest., 40:394 and 1355.
Loewy, A. and R. van der He
mung, *Biochem. Zschr.*, 65:2
— (1918) Über die Aufnahme d
Lund, A. (1948) Metabolism of
4:99.
Lutwak-Mann, C. (1938) Alcoh
MacFarlan, J. E. (1855) On Met
15:310.
MacNider, W. de B. (1933) The
ring in the Liver from the U
Machata, G. (1958) Zur Method
— (1961) The Diaphorase Met
Med., 51:447.
Macht, D. I. (1918) A pharmac
aesthetic, *J. Pharmacol.*, 11:
— (1919) Further Experience,
cohol, *J. Pharmacol.*, 13:509.
— (1920) A toxicological Study
macol., 16:1.
— (1922) Pharmacological Exa
Marshall, E. K. and W. F. Frit
Therap., 109:431.
Mashkitz, N. L., R. M. Sklianska
alcohol and their mixtures.
Masoro, E. J., H. Abramovitch a
Rat Tissues, *Am. J. Physiol.*,
McCord, C. P. and N. Cox (1931
tion and Inhalation, *Ind. Eng*
McCord, C. P. (1932) The Toxic
McNally, W. D. and H. M. Co
Alcohol in Blood, *J. Lab. Cli*
Mellan, I. (1939) *Industrial Solve*
— (1950) *Industrial Solvents*, Rein
Mertens, H. (1896) Lésions anat
par le Chloroforme et par l'A
Middleton, E. L. (1930) Fatal C
12:265.

tion of Ethanol in Determination of Hepatic Blood Flow by means of Ethanol, *Scand. J. Clin. Invest.*, 13:116.
Leaf, G. and L. J. Zatman (1952) A Study of the Conditions under which Methanol may exert a toxic Hazard in Industry, *Brit. J. Ind. Med.*, 9:19.
Lehman, A. J. and H. W. Newman (1937) Comparative intravenous Toxicity of some monohydric saturated Alcohols, *J. Pharmacol.*, 61:103.
Lehman, A. J., H. Schwerma and E. Rickards (1945) Isopropyl Alcohol. Acquired Tolerance in Dogs, *J. Pharmacol.*, 85:61.
Lehmann, K. B. and F. Flury (1943) *Toxicology and Hygiene of Industrial Solvents*, Williams and Wilkins, Baltimore.
— (1928) Beitrag zur allgemeinen Pharmakologie der Narkose, *Arch. Exptl. Pathol. Pharmakol.*, 132:214.
— (1928) Untersuchungen über die Narkoseschwindigkeit homologer und isomer einwertiger Alkohole, *Arch. Exptl. Pathol. Pharmakol.*, 129:85.
Lewin, L. (1912) Über die Verwendungsgefähren des Methylalkohols und andere Alkohols, *Med., Klin.*, 8:95.
— (1929) *Gifte und Vergiftungen*, 4th. ed., Springer, Berlin.
Lieber, C. S. and R. Schmid (1961) The Effect of Ethanol on Fatty Acid Metabolism, *J. Clin. Invest.*, 40:394 and 1355.
Loewy, A. and R. van der Heide (1914) Über die Aufnahme des Methylalkohols durch die Atmung, *Biochem. Zschr.*, 65:230.
— (1918) Über die Aufnahme des Äthylalkohols durch die Atmung, *Biochem. Zschr.*, 86:125.
Lund, A. (1948) Metabolism of Methanol and Formic Acid in Rabbits, *Acta Pharmacol. Toxicol.*, 4:99.
Lutwak-Mann, C. (1938) Alcohol Dehydrogenase of Animal Tissues, *Biochem. J.*, 32:1364.
MacFarlan, J. E. (1855) On Methylated Spirit and some of its Preparations. *Pharmaceut. J. Trans.*, 15:310.
MacNider, W. de B. (1933) The acute degenerative Changes and Changes of Recuperation occurring in the Liver from the Use of Ethyl Alcohol, *J. Pharmacol. Exptl. Therap.*, 49:100.
Machata, G. (1958) Zur Methodik der ADH-Bestimmung, *Deut. Zschr. ges. gerichtl. Med.*, 48:26.
— (1961) The Diaphorase Method of Blood Alcohol Determination, *Deut. Zschr. ges. gerichtl. Med.*, 51:447.
Macht, D. I. (1918) A pharmacological and therapeutic Study of Benzyl Alcohol as a local Anaesthetic, *J. Pharmacol.*, 11:263:419.
— (1919) Further Experience, experimental and clinical, with Benzyl Benzoate and Benzyl Alcohol, *J. Pharmacol.*, 13:509.
— (1920) A toxicological Study of some Alcohols, with especial Reference to Isomers, *J. Pharmacol.*, 16:1.
— (1922) Pharmacological Examination of Isopropyl Alcohol, *Arch. Int. Pharmacodyn.*, 26:285.
Marshall, E. K. and W. F. Fritz (1953) The Metabolism of Ethyl Alcohol, *J. Pharmacol. Exptl. Therap.*, 109:431.
Mashkitz, N. L., R. M. Sklianskaya and F. I. Urieva (1936) Relative Toxicity of Acetone, Methyl alcohol and their mixtures. Their action on white mice, *J. Ind. Hyg. Toxicol.*, 18:117.
Masoro, E. J., H. Abramovitch and J. R. Birchard (1953) Metabolism of C^{14}-Ethanol by surviving Rat Tissues, *Am. J. Physiol.*, 173:37.
McCord, C. P. and N. Cox (1931) Toxicity of Methyl Alcohol (Methanol) following Skin Absorption and Inhalation, *Ind. Eng. Chem.*, 23:931.
McCord, C. P. (1932) The Toxicity of Allyl Alcohol, *J. Am. Med. Ass.*, 98:2269.
McNally, W. D. and H. M. Coleman (1944) A Micromethod for the Determination of Ethyl Alcohol in Blood, *J. Lab. Clin. Med.*, 29:429.
Mellan, I. (1939) *Industrial Solvents*, p. 205, Reinhold, New York.
— (1950) *Industrial Solvents*, Reinhold, New York.
Mertens, H. (1896) Lésions anatomiques du Foie du Lapin au cours de l'Intoxication chronique par le Chloroforme et par l'Alcool, *Arch. Intern. Pharmacodyn.*, 2:127.
Middleton, E. L. (1930) Fatal Case of Poisoning by Ethylenechlorohydrin, *J. Ind. Hyg. Toxicol.*, 12:265.

Miessner, F. (1891) Über die Wirkung des Allyl Alkohols, *Berl. Klin. Wochschr.*, 28:819.
Mohler, H. and W. Hämmerle (1941) cited by Treon (1963), *Zschr. Anal. Chem.*, 122:202; *Chem. Abstr.*, 36:4970.
Monier Williams, D. (1929) *An Outbreak of Methyl Alcohol Poisoning in the Ruhr*, Med. Off. Hlth. Memo.
Moore, W. (1917) Toxicity of various Benzene Derivatives to Insects, *J. Agric. Res.*, 9:371.
Mori, R. (1887) Über die diuretische Wirkung des Biers, *Arch. Hyg.*, 7:354.
Morris, W. J. and H. D. Lightbody (1938) The Toxicity of Isopropanol, *J. Ind. Hyg. Toxicol.*, 20:428.
Munch, J. C. and E. W. Schwartze (1925) Narcotic and Toxic Potency of Aliphatic Alcohols upon Rabbits, *J. Lab. Clin. Med.*, 10:985.
Nelson, K. W., J. F. Ege, M. Ross, L. E. Woodman and L. Silverman (1943) Sensory Response to certain industrial solvent Vapours, *J. Ind. Hyg. Toxicol.*, 25:282.
Neubauer, O. (1901) Über Glykuronsäurepaarung bei Stoffen der Fettreihe, *Arch. Exptl. Pathol. Pharmakol.*, 46:133.
— (1901) Über Glykuronsäurepaarung bei Stoffen der Fettreihe, *Arch. Exptl. Pathol. Pharmakol.*, 183:641.
Newman, H. and J. Card (1937) Duration of acquired Tolerance to Ethyl Alcohol, *J. Pharm. Exptl. Therap.*, 59:249.
Newman, H. and E. Fletcher (1941) The Effect of Alcohol on Vision, *Am. J. Med. Sci.*, 202:723.
Nicloux, M. (1896) Dosage de l'Alcool éthylique dans les Solutions ou cet Alcool est Dilué, *C. R. Soc. Biol.*, 3:841.
— (1900) *Study on Alcohol*, Univ. Thesis, Paris.
Oettel, H. (1936) Einwirkung organische Flüssigkeiten auf der Haut, *Arch. Exptl. Pathol. Pharmakol.*, 183:641.
Oettingen, W. F. Von (1943) *The Aliphatic Alcohols; their Toxicity and potential Dangers*, [U.S.] Publ. Health Rept Serv. P.H. Bull. no. 281, U.S. Govt. Printing Office, Washington.
Okubo, M. (1937) Physiological Action of 2-Furancarbinol, *J. Pharm. Soc. Japan*, 539:39.
Ørskov, S. L. (1950) Experiments on the Oxidation of Propyl Alcohol in Rabbits, *Acta Physiol. Scand.*, 20:258.
Ottley, G. B. (1933) Quick Drying Inks, *Chem. Abstr.*, 27:2830.
Overton, E. (1901) *Studien über die Narkose, zugleich ein Beitrag zur allgemeinen Pharmakologie*, G. Fischer, Jena.
Parsons, C. E. and M. E. M. Parsons (1938) Toxic Encephalopathy and "Granulopenic Anaemia" due to volatile Solvents in Industry, *J. Ind. Hyg. Toxicol.*, 20:124.
Paul, H. E., F. L. Austin, M. F. Paul and V. R. Ells (1949) Metabolism of the Nitrofurans, *J. Biol. Chem.*, 180:345.
Penniman, W. B. D., D. C. Smith and E. I. Lawshe (1937) Determination of higher Alcohols in distilled Liquors, *Ind. Eng. Chem., Anal. Ed.*, 9:91.
Perman, E. S. (1960) Effect of Ethyl Alcohol on the Secretion from the Adrenal Medulla of the Cat, *Acta Physiol. Scand.*, 48:323.
— (1961) Effect of Ethanol and Hydration on the urinary Secretion of Adrenalin and Noradrenalin and on the Blood Sugar of Rats, *Acta Physiol. Scand.*, 51:68.
— (1961) Observations on the Effect of Ethanol on the urinary Excretion of Histamine, *Acta Physiol. Scand.*, 51:62.
Pipik, O. and E. Mezheboskaya (1933) Preparing Amyl Alcohols from cracked Gasoline, Abstr. in *Chem. Abstr.*, 1934, 28:7504.
Pohl, J. (1908) Quantitative Studien über die Exhalation des Alkohole, *Arch. Exptl. Pathol. Pharmakol. Suppl.*, 427.
— (1925) Über die Giftigkeit einiger aromatischer Hydrierungsprodukte (Tetralin, Hexalin und Methylhexalin), *Z. Gewerbehyg.*, 12:91.
Poincaré, M. L. (1878) Sur les Dangers de l'Emploi de l'Alcool méthylique dans l'Industrie, *C. R. Acad. Sci.*, 87:682.
Potts, A. M. and L. V. Johnson (1952) Studies on the Visual Toxicity of Methanol, *Am. J. Ophthalm. Suppl.*, 35:107.
Potts, A. M. (1955) The visual Toxicity of Methanol, *Am. J. Ophthalm.*, 39:86.

Pratt, J. Davidson (1930) Dangerous Properties of Ethylenechlorohydrin, *Nature*, 126:995.
Quatermass, M. (1958) Amblyopia due to Ethyl Alcohol, *Brit. J. Ophthalm.*, 42:628.
Ramazzini, B. (1940) *Diseases of Workers* (Latin Text of 1713, translated by W. C. Wright), Univ. of Chicago Press.
Reid, E. W. (1934) Modern Solvent Industry, *Ind. Eng. Chem.*, 26:21.
Reid, E. W. and J. D. Beddard (1954) (cited by Dunlap *et al.*, 1958) Determination of low Bromine Absorption Values, *Analyst*, 79:456.
Robert, E. (1907) Considérations sur quelques Cas d'Intoxication par les Vapeurs d'Alcools dans la Fabrication de la Poudre sans Fumée, *J. Méd. Bordeaux*, 37:21.
Roche, L., J. Champeix, A. Échegut, A. Nicolas and A. Marin (1957) À propos d'Accidents pathologiques collectifs observés dans un Établissement industriel, *Ann. Méd. Lég.*, 37:43.
Røe, O. (1943) Clinical Investigation of Methyl Alcohol Poisoning, *Acta Med. Scand.*, 113:558.
— (1946) Methanol Poisoning, *Acta Med. Scand., Suppl.*, 182.
— (1948) The Ganglion Cells of the Retina in Cases of Methanol Poisoning in Human Beings and Experimental Animals, *Acta Ophthalm.*, 26:169.
Rogers, G. W. (1945) Sampling and Determination of Methanol in Air, *J. Ind. Hyg. Toxicol.*, 27:224.
Rost, E. and A. Braun (1926) Zur Pharmakologie der niederen Glieder der einwertigen aliphatischen Alkohole, *Arb. Reichsgesundh. Amt*, 57:580.
Ruemele, T. (1948) Isopropyl Alcohol in Perfumes and Toilet Preparations, *Mfg. Chem.*, 19:151.
Ruhle, A. (1912) Tierexperimentelle Befund im Zentralnervensystem nach Methylalkoholvergiftung, *Münch. Med. Wschr.*, 59:964.
Sander, F. (1933) *Über den Einfluss von Kohlenstoffverbindungen auf Mäuse bei cutaner Applikation*, Inaug. Diss. Köln, (cited by Von Oettingen, 1943).
Sanderson, J. McE. (1933) Solvents used in Surface Coatings, *Paint Oil Chem. Rev.*, 95:10.
Sato, K. (1928) Über die pharmakologischen Wirkungen der hydroaromatischen Verbindungen, Cyclohexen, Cyclohexan und Cyclohexanol. *Jap. J. Med. Sci. Pharmacol.*, 3:1.
Sayers, R. R., W. P. Yant, H. H. Schrenk, J. Chornyak, S. J. Pearce, F. A. Patty and J. G. Linn (1942) *Methanol Poisoning; Exposure of Dogs to 450–500 p.p.m. Methanol Vapour in Air*, Bur. Mines Report of Investigations, 3617.
— (1944) Methanol Poisoning, *J. Ind. Hyg. Toxicol.*, 26:255.
Schafforzick, R. W. and B. J. Brown (1952) Anticonvulsant Acitivity and Toxicity of Methylparafynol and some other Alcohols, *Science*, 116:663.
Schmiedeberg, O. (1881) Über Oxydationen und Synthesen im Thierkörper, *Arch. Exptl. Pathol. Pharmakol.*, 14:288.
Schumacher, H., K. Battig and E. Grandjean (1962) Die Wirkungen verschiedener Lösungsmitteldämpfe auf das Wachstum und die Spontanmortalität junger Mäuse, *Z. Arbeitsmed. Arbeitsschutz*, 12:5.
Schwarz, L. and L. Tulipan (1939) *A Textbook of occupational Diseases of the Skin*, Lea and Fibiger, Philadelphia.
Schwarzmann, A. (1934) Methylalkoholvergiftung, chronische, durch Einatmen von Methylalkohol-haltigen Formaldehyddämpfen, *Samml. Vergiftungsf.*, 5:129, A 442.
Schwenkenbecher (1904) Die Absorptionsvermögen für die Haut, *Arch. Anat. Physiol. Abt.*, p. 121.
Scott, E, M. K. Helz and C. P. McCord (1933) The Histopathology of Methyl Alcohol Poisoning, *Am. J. Clin. Path.*, 3:311.
Silverman, L., H. F. Schulte and W. E. First (1946) Further Studies on sensory Response to certain individual Solvent Vapours, *J. Ind. Hyg. Toxicol.*, 28:262.
Sisley, J. P. (1934) Solvents utilisés dans l'Industrie textile, *Reg. Gen. Mat. Col.*, 38:481.
Smith, H. M. (1927) Dewaxing Paraffin base crudes, *Oil Gas J.*, 26:146.
Smith, M. E. and H. W. Newman (1959) The Rate of Ethanol Metabolism in fed and fasting Animals, *J. Biol. Chem.*, 234:1544.
Smyth, H. F. (1956) *Cummings Memorial Lecture*, cited by Treon, 1963.
Smyth, H. F. and H. F. Smyth Jr. (1928) Inhalation Experiments with certain Lacquer Solvents, *J. Ind. Hyg. Toxicol.*, 10:261.
Smyth, H. F., Jr. and C. P. Carpenter (1945) Note upon the Toxicity of Ethylene chlorohydrin by Skin Absorption, *J. Ind., Hyg. Toxicol.*, 27:93.

— (1948) Further Experience with Range Finding Test in Industrial Toxicology Laboratory, *J. Ind. Hyg. Toxicol.*, 30:63.
Smyth, H. F., Jr., C. P. Carpenter and C. S. Weil (1949) Range finding Toxicity Data, List III, *J. Ind. Hyg. Toxicol.*, 31:60.
— (1951) Range Finding Toxicity Data, *Arch. Ind. Hyg.*, 4:199.
— (1951) Range finding Toxicity Data, *Arch. Ind. Hyg.*, 4:119.
Smyth, H. F., Jr., C. P. Carpenter, C. S. Weil and U. C. Pozzani (1954) Range finding Toxicity Data, List V, *Arch. Ind. Hyg.*, 10:61.
Smyth, H. F., Jr., J. Seaton and L. Fischer (1941) The single Dose Toxicity of some Glycols and Derivatives, *J. Ind. Hyg. Toxicol.*, 23:259.
Snapper, I., A. Grunbaum and S. Sturkop (1925) Über die Spaltung und die Oxydation von Benzyl Alcohol und Benzylestern im menschlichen Organismus, *Biochem. Z.*, 155:163.
Sollman, T. and P. J. Hanzlik (1928) *An Introduction to experimental Pharmacology*, Saunders, Philadelphia.
Starrek, E. (1938) *Über die Wirkung einiger Alkohole, Glykole und Ester* (cited by Lehmann and Flury, 1943, in *Toxicology and Hygiene of Industrial Solvents*), Williams and Wilkins, Baltimore.
Stekol, J. A. (1939) Studies on the Mercapturic Acid Synthesis in Animals, *J. Biol. Chem.*, 128:199.
Steinkoff, D. (1952) Augenschädigungen durch Butylazetat-Isobutyl Alkohol, *Z. Arbeitsmed. Arbeitsschutz*, 2:13.
Sterner, J. H., H. C. Crouch, H. F. Brockmyre and M. Cusack (1949) A ten-year Study of Butyl Alcohol Exposure, *Am. Ind. Hyg. Ass. Quart.*, 10:53.
Stinebaugh, B. J. (1960) The use of Peritoneal Dialysis in Acute Methyl Alcohol Poisoning, *Arch. Int. Med.*, 105:613.
Straus, M. (1887) Sur un Moyen de provoquer l'Anesthésie chez le Lapin, *C. R. Soc. Biol.*, 4:54.
Tabershaw, I. R., J. P. Fahy and J. B. Skinner (1944) Industrial Exposure to Butanol, *J. Ind. Hyg. Toxicol.*, 26:328.
Theorell, H. and R. Bonnischen (1951) Studies on Liver Alcohol Dehydrogenase, *Acta Chem. Scand.*, 5:1105.
Thierfelder, H. and J. von Mering (1885) Das Verhalten tertiärer Alkohole im Organismus, *Z. Physiol. Chem.*, 9:611.
Threshold Limit Values for 1962, *Am. Ind. Hyg. Ass. J.*, 1962, 23:419.
Torkelson, T. R., M. A. Wolf, F. Oyen and V. K. Rowe (1959) Vapour Toxicity of Allyl Alcohol as determined on Laboratory Animals, *Am. Ind. Hyg. Ass. J.*, 20:224.
Treon, J. F. (1963) *Alcohols*, in F. A. Patty (Ed.), *Industrial Hygiene and Toxicology*, Vol. II, 2nd ed., Interscience, New York.
Treon, J. F., W. E. Crutchfield Jr. and K. V. Kitzmiller (1943) The physiological Response of Rabbits to Cyclohexane, Methyl Cyclohexane and certain Derivatives of these Compounds, *J. Ind. Hyg. Toxicol.*, 25:199 and 233.
Tsuchiya, K. (1963) Chronic Poisoning and occupational Cancer, *Medicine (Tokyo)*, 20:86.
Tyson, H. H. (1912) Amblyopia from Inhalation of Methyl Alcohol, *Arch. Ophthalm.*, 41:459.
Tyson, H. H. and M. J. Schoenberg (1914) Experimental Researches in Methyl Alcohol Inhalation, *J. Am. Med. Ass.*, 63:915.
Uhrig, R. (1946) (cited by Treon, 1963) *Ind. Eng. Chem. Anal. Ed.*, 18:469.
Vigneaud, V. du, C. Lessler and J. R. Rochelle (1950) The biological Synthesis of "Labile Methyl Groups". *Science*, 112:267.
Voegtlin, W. L. and C. E. Watts (1943) Acute Methyl Alcohol (Methanol) poisoning, *U.S. Nav. Med. Bull.*, 41:1715.
Vollmer, H. (1931) Fortgesetzte Versuche über die Giftempfindlichkeit von Mäusen und Ratten nach Bestrahlung oder Vorbehandlung mit oxydationssteigernden Substanzen, *Arch. Exptl. Pathol. Pharmakol.*, 160:635.
Voltz, W. and W. Dietrich (1912) Die Beteiligung des Methylalkols und des Äthylalkohols am gesamten Stoffumsatz im tierischen Organismus, *Biochem. Z.*, 40:15.
Walton, D. C., E. F. Kehr and A. S. Loevenhart (1928) Comparison of the pharmacological Actions of Diacetone Alcohol and Acetone, *J. Pharmacol.*, 33:175.
Wax, J., F. W. Ellis and A. J. Lehman (1949) Absorption and Distribution of Isopropyl Alcohol, *J. Pharmacol.*, 97:229.

Webb, A. D. and R. E. Kepner (19
Mechanism of Formation of hi
Weber, H. H. and W. Koch (193
miker Z., 57:73.
Weese, H. (1928) Vergleichende U
niederer aliphatischer Alkohol
Weitzel, G. (1950) Biochemie verz
Werkman, C. H. and O. L. Osbur
tation Mixtures, *Proc. Soc. Exp*
Westerfeld, W. W. (1961) The in
Widmark, E. M. P. (1915) Konze
33:85.
— (1932) *Die theoretischen Grundlag*
holbestimmung, Urban und Sc
Williams, R. T. (1959) *Detoxicatio*
Wilson, M. M. and F. J. Worster
vents, *Ind. Eng. Chem.*, 21:592.
Wood, C. A. and F. Buller (1904)
Woods, H. (1913) Wood Alcohol
Yant, W. P. and H. H. Schrenk
19:337.
Yant, W. P., H. H. Schrenk and
ing, *Ind. Eng. Chem.*, 23:551.
Yarsley, V. E. (1933) Health Haz
3:80.
— (1934) Solvents and Plasticiser
se Acetate, *Synth. Appl. Finis*
Zangger, H. (1933) Arbeitsunfäll
Behältern, *Arch. Gewerbepath*
Zatman, L. J. (1946) Oxidation
Proc. LXVII.
Ziegler, S. L. (1921) The Ocula

Webb, A. D. and R. E. Kepner (1951) (cited by Castor, J. G. B. and J. F. Guymon, 1952) On the Mechanism of Formation of higher Alcohols during alcoholic Fermentation, *Science*, 115:147.

Weber, H. H. and W. Koch (1933) Zur Methodik der Analyse technischer Lösungsmittel, *Chemiker Z.*, 57:73.

Weese, H. (1928) Vergleichende Untersuchungen über die Wirksamkeit und Giftigkeit der Dämpfe niederer aliphatischer Alkohole, *Arch. Exptl. Pathol. Pharmakol.*, 135:118.

Weitzel, G. (1950) Biochemie verzweigter Carbonsäuren, *Hoppe-Seyler's Z.*, 285:58.

Werkman, C. H. and O. L. Osburn (1930) Determination of Butyl and Ethyl Alcohols in Fermentation Mixtures, *Proc. Soc. Exptl. Biol. Med.*, 28:241.

Westerfeld, W. W. (1961) The intermediary Metabolism of Alcohol, *Am. J. Clin. Nutr.*, 9:426.

Widmark, E. M. P. (1915) Konzentration des Alkohols in Blut und Harn, *Skand. Arch. Physiol.*, 33:85.

— (1932) *Die theoretischen Grundlagen und die praktische Verwendbarkeit der gerichtlichmedizinischen Alkoholbestimmung*, Urban und Schwarzenberg, Berlin.

Williams, R. T. (1959) *Detoxication Mechanisms*, 2nd. ed., p. 54, Chapman and Hall, London.

Wilson, M. M. and F. J. Worster (1929) Place of Synthetic Amyl Products among Lacquer Solvents, *Ind. Eng. Chem.*, 21:592.

Wood, C. A. and F. Buller (1904) Poisoning by Wood Alcohol, *J. Am. Med. Ass.*, 43:972.

Woods, H. (1913) Wood Alcohol Blindness, *J. Am. Med. Ass.*, 60:1762.

Yant, W. P. and H. H. Schrenk (1937) Distribution of Methanol in Dogs, *J. Ind. Hyg. Toxicol.*, 19:337.

Yant, W. P., H. H. Schrenk and R. R. Sayers (1931) Methanol Anti-freeze and Methanol Poisoning, *Ind. Eng. Chem.*, 23:551.

Yarsley, V. E. (1933) Health Hazards in the Lacquer and Finishing Industries, *Synth. Appl. Finish.*, 3:80.

— (1934) Solvents and Plasticisers. A Review of recent progress with special Reference to Cellulose Acetate, *Synth. Appl. Finish.*, 5:37, 57.

Zangger, H. (1933) Arbeitsunfälle und Arbeitsgefährdung bei der Arbeit in inneren geschlossenen Behältern, *Arch. Gewerbepathol. Gewerbehyg.*, 4:117.

Zatman, L. J. (1946) Oxidation of Methyl Alcohol inhibited by Ethyl Alcohol, *Biochem. J.*, 40 Proc. LXVII.

Ziegler, S. L. (1921) The Ocular Menace of Wood Alcohol Poisoning, *J. Am. Med. Ass.*, 77:1160.