Very Important
In Rats; Wood alcohol is less toxic than methyl alcohol
308-309 Chronic methanol is ~~toxic~~ much more toxic as ethanol ++

STUDIES OF CHRONIC INTOXICATIONS ON ALBINO RATS

II. ALCOHOLS (ETHYL, METHYL AND "WOOD") AND ACETONE

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INTRODUCTION

Chronic intoxication by the alcohols has been so little studied experimentally, that further data are highly desirable. The peculiar contrast between the acute and subacute toxicity ratio of ethyl and methyl alcohol adds further interest to their behavior with really chronic intoxication. It has appeared desirable to ascertain whether chronic experiments would answer the question of the relative toxicity of pure methyl alcohol and commercial "wood alcohol," and incidentally of acetone.

The experiments were conducted as described in the first paper, using three to six rats for each experiment. The alcohols were added to the drinking water, so that they were consumed continuously.

Dosage of alcohol. This is determined by the concentration of the drug and by the thirst of the animals. The mean doses are shown in table 1. The weekly variations appear unimportant. They could be calculated from the curve of fluid consumption.

The dosage, in all cases, is fairly heavy; the larger doses approaching those ordinarily acutely fatal for dogs and rabbits.

For acute poisoning by stomach, Baer, 1898, places the minimum fatal dose at 7.2 to 9 grams of methyl alcohol, and 6.25 to 7.44 grams of ethyl alcohol, per kilogram of rabbit.

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TABLE 1

Mean dosage of alcohol, and duration of experiments

CONCENTRATION OF ALCOHOL	EXPERIMENT NUMBER	NUMBER OF ANIMALS IN EXPERIMENT	DURATION	DOSAGE OF ALCOHOL PER KILOGRAM OF RATS PER DAY
			weeks	*cc.*
Ethyl, 2.5 per cent	103	3	18	2.7 (1.2–3.7)
Ethyl, 5 per cent	4798	4	21	4.8 (3.6–6.4)
Ethyl, 5 per cent	75	3 to 6	19	4.7 (1.8–6.8)
Ethyl, 5 per cent	130	3	8	6.4 (5.2–7.0)
Ethyl, 10 per cent	110	3	10	9.9 (8.6–10.9)
Ethyl, 10 per cent past 4 weeks of 5 per cent	7594	3	15	8.9 (5.8–13.5)
Methyl, 2.5 per cent	100	3	18	2.6 (1.8–3.4)
Methyl, 2.5 per cent	129	3	9	3.6 (3.2–4.7)
Wood, 2.5 per cent	6599	3	21	2.8 (2.2–3.7)
Wood, 2.5 per cent	101	2	18	3.6 (2.4–7.4)
Acetone, 2.5 per cent	102	3	18	1.8 (1.4–2.2)
Acetone, 2.5 per cent	139	3	2	3.1 (3.1–3.2)
Methyl, 5 per cent	86	5	6	3.1 (2.3–3.2)
Methyl, 5 per cent	109	3	3	3.5 (3.3–4.9)
Methyl and wood, 5 per cent	76	4	5	5.4 (4.1–6.0)
Wood, 5 per cent	87	3	6	3.3 (2.5–5.2)

TABLE 2

Mean daily consumption of fluid

ALCOHOLS	EXPERIMENT NUMBER	DURATION	FLUID CONSUMPTION PER KILOGRAM OF RAT			
			Entire period	First third	Middle third	Last third
		weeks	*cc.*	*cc.*	*cc.*	*cc.*
Ethyl, 2.5 per cent	103	18	110 (48–150)	131	109	107
Ethyl, 5 per cent	4798	21	95 (72–129)		101	95
Ethyl, 5 per cent	75	19	93 (37–136)	122	89	86
Ethyl, 5 per cent	130	8	127 (105–140)	134	127	125
Ethyl, 10 per cent	110	10	99 (86–109)	107	99	88
Ethyl, 10 per cent	7594	15	89 (58–135)	124	85	100
Methyl, 2.5 per cent	100	18	103 (72–136)	95	116	93
Methyl, 2.5 per cent	129	9	143 (126–188)	161	150	141
Wood, 2.5 per cent	6599	21	111 (89–147)		109	115
Wood, 2.5 per cent	101	18	145 (95–296)	102	144	147
Acetone, 2.5 per cent	102	18	72 (56–89)	80	70	68
Acetone, 2.5 per cent	139	2	125 (122–127)			
Methyl, 5 per cent	86	6	62 (45–63)	49		62
Methyl, 5 per cent	109	3	69 (66–97)			
Wood and methyl, 5 per cent	76	5	103 (81–119)	116		87
Wood, 5 per cent	87	6	65 (50–104)	53		76

For repeated, daily administrations, Hunt, 1902, found death to follow after three doses of 5 grams of methyl alcohol per kilogram of dog, or eight doses of 2.5 grams methyl alcohol per kilogram of rabbit (after seventeen days), i.e., a dosage approximating that which was fatal to the rats in this series. Ethyl alcohol was not fatal to rabbits after four doses of 6 grams per kilogram, but killed after six such doses. Dogs however, increased in weight after five doses of 6 grams. Our rats also tolerate this dose without trouble.

Consumption of fluid. This would presumably be affected most directly by the alcohol. Table 2 shows the mean daily consumption of fluid in each experiment; as well as the mean for the first, middle and last third of each experiment so as to indicate the influence of the continuance of the experiment.

A study of table 2 shows the following:

Ethyl alcohol. There is no material difference between the fluid consumption when this fluid contains 2.5 or 5 or 10 per cent of ethyl alcohol. In every experiment, the fluid consumption is greatest in the first third of the experiment; declines sharply in the middle third and then remains about constant in the last third. The mean of all the experiments faithfully repeats the individual experiments. It is as follows.

ENTIRE DURATION	FIRST THIRD	MIDDLE THIRD	LAST THIRD
97	123	100	97

The falling off after the first third is perhaps due to diminished muscular activity of the alcoholyzed rats, but we have no direct observations on this point.

Methyl and wood alcohol, 2.5 per cent. These have about the same mean consumption as ethyl alcohol, or rather larger. The most characteristic difference is, however, that the fluid consumption generally increases in the middle third, instead of diminishing, as with ethyl alcohol. The mean of all the experiments are:

ENTIRE DURATION	FIRST THIRD	MIDDLE THIRD	LAST THIRD
127	102	130	128

The increase in the first third is perhaps due to habituation to the taste of methyl and wood alcohol. Accordingly, the increase is greater with the wood-alcohol with which the taste is more pronounced.

Acetone, 2.5 per cent. In the one experiment with this drug that lasted sufficiently long to justify conclusions, the fluid consumption was markedly below the normal. The data resemble those of 5 per cent wood alcohol.

They are as follows:

ENTIRE DURATION	FIRST THIRD	SECOND THIRD	LAST THIRD
72	80	70	68

Methyl and wood alcohol, 5 per cent. These showed a marked decrease from the start and persisting to the early death.

ENTIRE DURATION	FIRST THIRD	SECOND THIRD	LAST THIRD
67	53		76

EFFECTS ON GROWTH

These are shown in table 3 and figures 1 to 3. In the table, data are given for the end of the experiments, and for other periods when important changes occurred in the curve.

Ethyl alcohol. With the exception of one experiment (no. 130) all the concentrations showed defective growth approaching or exceeding the extreme normal deficit (−1 per cent per week). The mean deficit for each concentration is

CONCENTRATION	DOSE	DURATION	WEEKLY DEFICIT
per cent	*cc.*	*weeks*	*per cent*
2.5	2.7	18	1 2
5.0	4.8	19	1 0
10.0	9.4	13	1 8

Consequently, 2.5 and 5 per cent ethyl alcohol or 2.7 and 4.8 cc. per kilogram per day, interfere quite considerably with growth, and to about equal degrees. Ten per cent alcohol, or 9.4 cc. per kilogram per day, produces more marked interference.

TABLE 3

Effects of alcohols and acetone on growth

DRUG AND CONCENTRATION	DOSAGE PER KILOGRAM OF RAT PER DAY	EXPERIMENT NUMBER	DURATION	OBSERVED WEIGHT	NORMAL WEIGHT	DIFFERENCE	DIFFERENCE AS PER CENT OF NORMAL WEIGHT	DIFFERENCE PER WEEK
	cc.		*weeks*	*grams*	*grams*	*grams*		*per cent*
Ethyl alcohol, 2.5 per cent	2.7	103	18	168	220	−52	−23.0	−1.2
Ethyl alcohol, 5 per cent.	4.8	4798	21	215	279	−64	−23.0	−1.0
Ethyl alcohol, 5 per cent.	4.7	75	19	192	250	−58	−23.0	−1.2
Ethyl alcohol, 5 per cent.	6.4	130	8	204	200	+4	+2.0	+0.25
Ethyl alcohol, 10 per cent.	9.9	110	10	194	220	−26	−11.8	−1.1
Ethyl alcohol, 10 per cent after 4 weeks of 5 per cent	8.9	7594	15	155	244	−89	−36.0	−2.4
Methyl alcohol, 2.5 per cent	2.6	100	18	232	248	−16	−6.0	−0.3
Methyl alcohol, 2.5 per cent	3.6	129	8	122	200	−78	−39.0	−5.0
Wood alcohol, 2.5 per cent	2.8	6599	6	178	202	−24	−11.8	−1.9
			18	155	260	−105	−41.0	−2.3
			20	163	268	−105	−40.0	−2.0
Wood alcohol, 2.5 per cent	3.6	101	7	240	340	−100	−29.0	−4.1
			18	252	336	−84	−25.0	−1.4
Acetone, 2.5 per cent.	1.8	102	2	227	229	−2	−0.9	−0.4
			3	154	229	−75	−32.0	−11.0
			18	150	230	−80	−34.0	−1.9
Acetone, 2.5 per cent.	3.1	139	2	109	100	+9	+9.0	+4.5
Methyl alcohol, 5 per cent	3.1	86	2	120	160	−40	−25.0	−12.5
			6	88	200	−112	−56.0	−9.3
Methyl alcohol, 5 per cent	3.5	109	3	203	245	−42	−13.0	−4.0
Methyl and wood alcohol, 5 per cent	5.4	76	5	84	204	−20	−9.0	−1.8
Wood alcohol, 5 per cent.	3.3	87	6	58	156	−98	−62.0	−10.0

Methyl and wood alcohol, 5 per cent. These behave alike. In dosages corresponding to 3.1 to 5.4 cc. per kilogram per day, they produce a very considerable loss of weight, starting

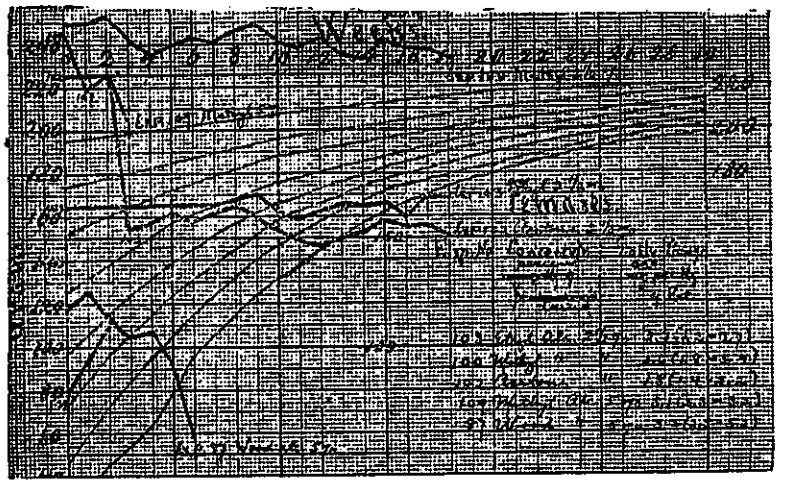

FIG. 1. EFFECT OF ALCOHOLS AND ACETONE ON GROWTH OF FEMALE RATS

The heavy lines represent the growth of the alcohol rats; the light lines represent the standard normal growth curves.

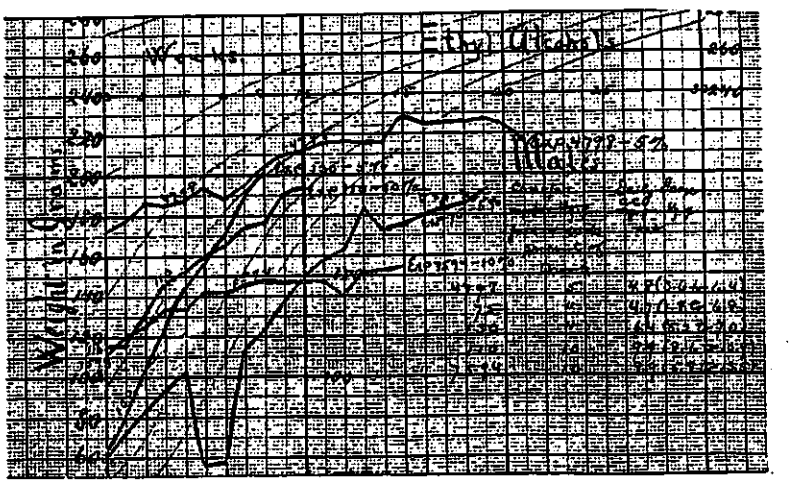

FIG. 2. ETHYL ALCOHOL ON GROWTH OF MALE RATS

within the first week of administration, and continuing until death, which occurs in a few weeks. The median weekly retardation of growth is 9 (1.8 to 12.5) per cent. The total actual loss was 17 to 51, mean 37 per cent. The loss is therefore very much greater than with 10 per cent ethyl alcohol.

Methyl and wood alcohol, 2.5 per cent. These behave alike. All experiments show considerable deficits in growth, and often

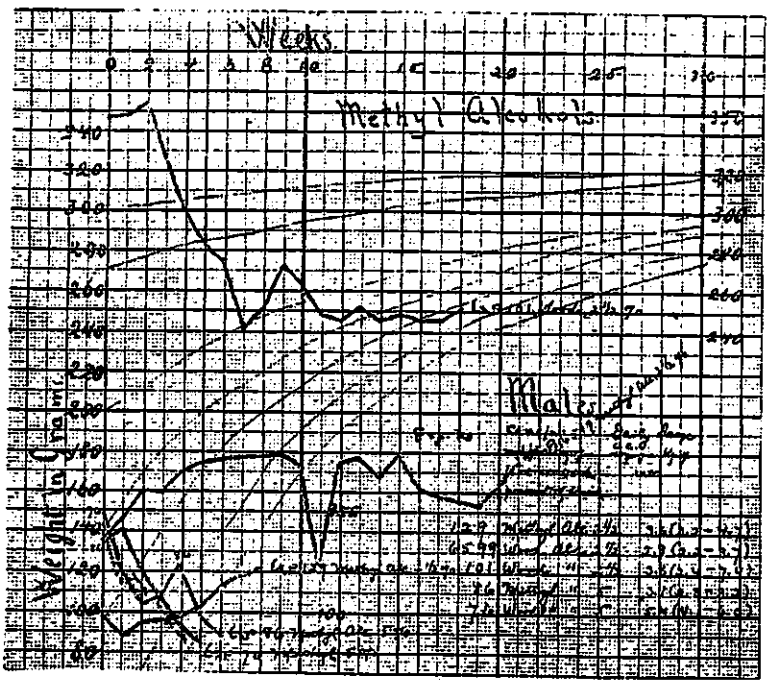

FIG. 3. METHYL AND WOOD ALCOHOLS ON GROWTH OF MALE RATS

actual loss of weight; but the extent of the growth-deficit varies widely, from 0.3 to 5 per cent per week, with a mean of −2 per cent. The observations include four experiments, with seven periods; and a mean dosage of 3.2 cc. per kilogram per day.

The largest differences were in two groups of extra large adult rats. One of these (100) had a deficit of only −0.3 per cent per week; whereas the other (101) lost 32 per cent of its original

weight between the second and the seventh week, and then remained almost stationary. This was evidently mainly a result of dosage; for table I shows that the rats of experiment 100 drank relatively lightly, while those of experiment 101 drank quite heavily, especially in the earlier periods.

In the other experiments, the retardation of growth began with the start of the experiment, and continued steadily to the end, with a tendency to keep all growth in abeyance.

The growth-interference of 2.5 per cent methyl and wood alcohol (3.2 cc. per kilogram per day) is therefore on the whole distinctly more serious than with 10 per cent ethyl alcohol (9.4 cc. per kilogram per day).

Acetone, 2.5 per cent. The one experiment (102), that is sufficiently prolonged (eighteen weeks, with mean of 1.8 cc. per kilogram per day) shows a final loss (1.9 per cent) similar to 2.5 per cent methyl and wood alcohol.

However, the form is peculiar, in that a large loss occurs between two and three weeks (32 per cent of the weight), after which the weight remains stationary. The effect resembles that of experiment 101 with 2.5 per cent wood alcohol; except that the acetone loss is more abrupt.

In principle, then the effect of acetone is allied to that of wood alcohol of the same concentration and somewhat higher dosage, but is more severe.

It should be noted that the large loss of weight cannot be attributed to nausea from the taste of the acetone or wood alcohol; for the loss starts only after two weeks.

EFFECTS ON FOOD CONSUMPTION

These are shown in table 4 and figures 4 to 8.

In interpreting the data of table 4, it must be remembered that the extreme variation of unpoisoned rats from the standard food averages lies between -0.01 and $+1.4$ gram per rat per day or -0.08 to $+19$ per cent. Practically every experiment with all the alcohols, shows a much greater deficit than the extreme for the normal experiment. In most of the alcohol experiments,

the food consumption fails to increase, as it should in normally growing animals, but remains level, or declines. There is also a frequent tendency for temporary anorexia; the food consumption being much lower on some days than on others. These sudden changes are often reflected in the growth curve. Generally they go hand in hand, i.e., the food- and growth-curves are generally parallel; but sometimes (as in experiment 101, methyl alcohol) the

TABLE 4

Food consumption

ALCOHOLS	EXPERIMENT NUMBER	DURATION OF EXPERIMENT	GROWTH, MEAN DIFFERENCE FROM NORMAL STANDARD, PER WEEK	FOOD CONSUMPTION, MEAN DIFFERENCE FROM NORMAL STANDARD PER RAT PER DAY		MEAN DIFFERENCE IN FOOD FOR SERIES
		weeks	*per cent*	*grams*	*per cent*	*per cent*
Ethyl, 2.5 per cent	103	18	−1.2	−1.6	−17	−17
Ethyl, 5 per cent	4798	21	−1.0	−1.9	−17	−10
Ethyl, 5 per cent	75	19	−1.2	−1.0	−10	
Ethyl, 5 per cent	130	8	+0.25	+0.9	+10	
Ethyl, 10 per cent	110	10	−1.1	−2.0	−19	−23
Ethyl, 10 per cent	7594	15	−2.4	−2.9	−27	
Methyl, 2.5 per cent	100	18	−0.3	−0.3	− 3	−28
Methyl, 2.5 per cent	129	9	−5.0	−4.7	−50	
Wood, 2.5 per cent	6599	21	−2.0	−3.2	−30	
Wood, 2.5 per cent	101	18	−1.4	−3.6	−26	
Acetone, 2.5 per cent	102	18	−1.9	−2.15	−23	−23
Acetone, 2.5 per cent	139	2	+4.5	+0.5	− 7	
Methyl, 5 per cent	86	6	−9.3	−7.0	−71	−52
Methyl, 5 per cent	109	3	−4.0	−3.4	−36	
Wood and methyl, 5 per cent	76	5	−1.8	−6.0	−59	
Wood, 5 per cent	87	6	−10.0	−3.6	−45	

loss of appetite sets in *after* the loss of weight. This favors the view that the appetite does not control the weight, but that both are controlled by a common cause, i.e., the general health of the animal.

Ethyl alcohol. Table 4 and figure 4 show that 2.5 per cent alcohol interferes seriously with appetite, the daily deficit averaging 17 per cent. With 5 per cent alcohol, the mean deficit happens

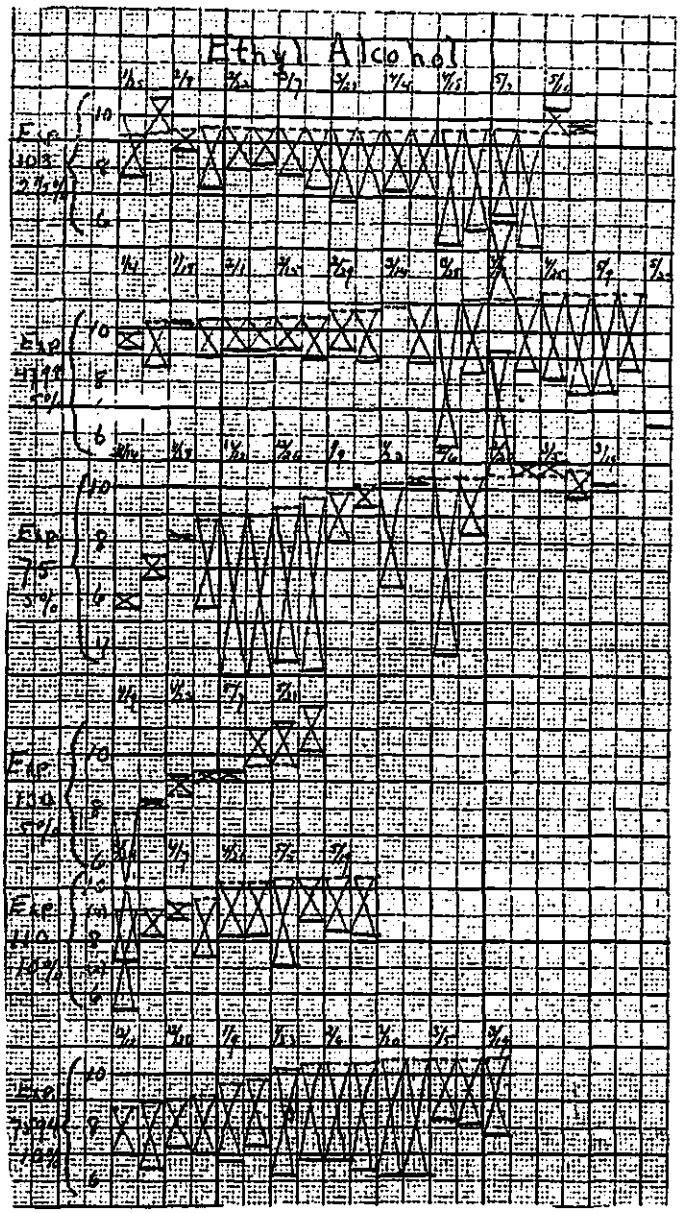

FIG. 4. ETHYL ALCOHOL ON FOOD CONSUMPTION

The numbers to the left represent grams of food consumed daily per rat. The numbers above each experiment are the dates of the observations. The dotted horizontal lines represent the standard food consumption; and the solid horizontal lines joined to the dotted lines by crossed lines represent the actual food consumption.

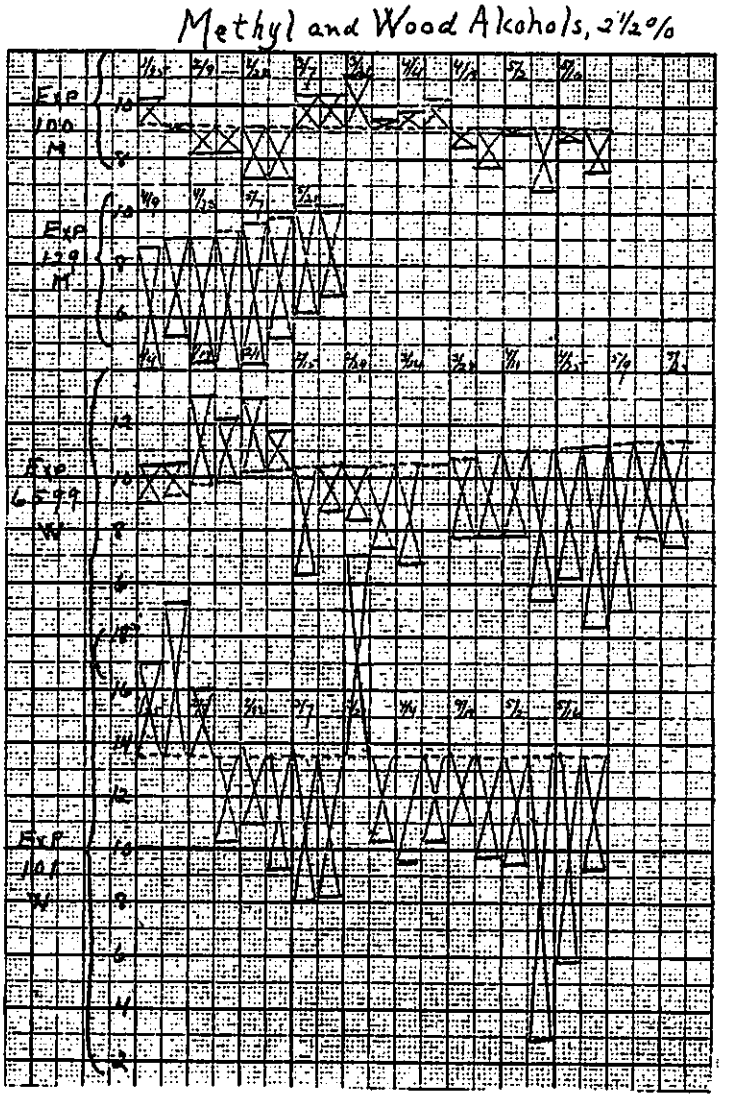

FIG. 5. METHYL AND WOOD ALCOHOLS, 2.5 PER CENT, ON FOOD CONSUMPTION

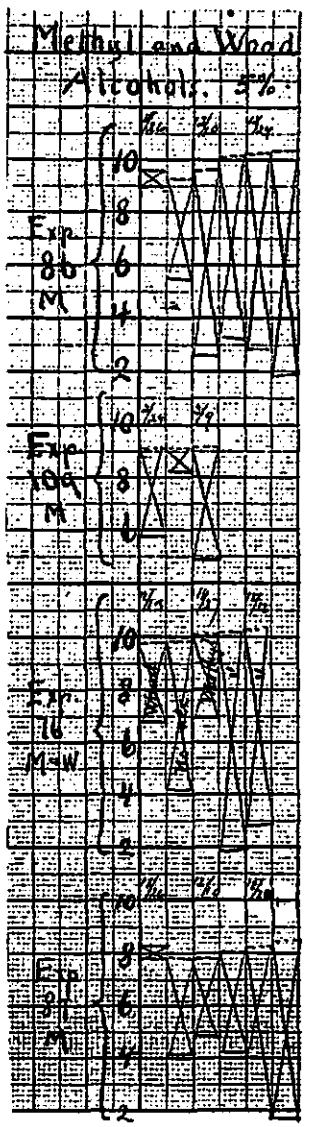

FIG. 6. METHYL AND WOOD ALCOHOLS, 5 PER CENT ON FOOD CONSUMPTION

to be a little smaller, (10 per cent; range +10 to −17); with 10 per cent alcohol, the deficit is considerably greater (−19 to −27, mean −23 per cent).

Methyl and wood alcohol. These behave alike. The deficit with 2.5 per cent (−3 to −50; mean −28 per cent) is greater than with 10 per cent ethyl alcohol (fig. 5). With 5 per cent methyl and wood alcohols the deficit is very marked (−36 to −71, mean −52 per cent).

Acetone. With the one good 2.5 per cent experiment, the food deficit (−23 per cent) is that of 10 per cent ethyl alcohol. The sharp decline in the body weight in the third week of experiment 102 is reflected in the appetite of the same week.

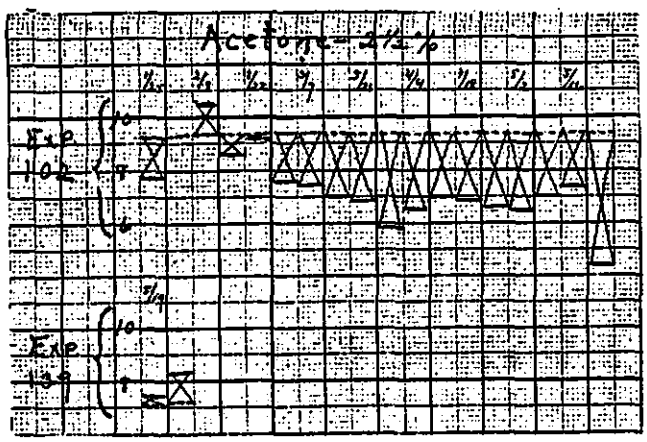

FIG. 7. ACETONE ON FOOD CONSUMPTION

MORTALITY

This is shown in table 5 for the individual experiments, and is summarized for each alcohol in table 6.

Since the duration of the alcohol administration is doubtless a very important factor in the mortality, the last column of table 6 divides the total mortality by the duration of the experiment. This factor is evidently the best measure for comparing the relative toxicity of the alcohols.

The actual sequence of this factor and its relation to the actual dosage is shown in table 7.

This table shows that 2.5 per cent alcohol and 2.5 per cent acetone can be consumed daily for over eighteen weeks, in daily doses corresponding to 2.8 cc. of absolute alcohol, or 1.8 cc.of acetone. per kilogram of rat, without mortality.

TABLE 5

Mortality

DRUG AND CONCENTRATION	DOSAGE	EXPERIMENT NUMBER	NUMBER OF ANIMALS	WEEKS OF FATALITIES	TOTAL DURATION	PER CENT OF FATALITIES
					weeks	
Ethyl alcohol, 2.5 per cent	2.7	103	3	0	18	0
Ethyl alcohol, 5 per cent	4.8	4798	4	0	21	0
Ethyl alcohol, 5 per cent	4.7	75	6	1, 13	19	33⅓
Ethyl alcohol, 5 per cent	6.4	130	3	0	8	0
Ethyl alcohol, 10 per cent	9.9	110	3	0	10	0
Ethyl alcohol, 10 per cent after 4 weeks of 5 per cent	8.9	7594	3	13	15	33⅓
Methyl alcohol, 2.5 per cent	2.6	100	3	6	18	33⅓
Methyl alcohol, 2.5 per cent	3.6	129	3	0	8	0
Wood alcohol, 2.5 per cent	2.8	6599	3	0	20	0
Wood alcohol, 2.5 per cent	3.6	101	2	0	18	0
Acetone, 2.5 per cent	1.8	102	3	0	18	0
Acetone, 2.5 per cent	3.1	139	3	0	2	0
Methyl alcohol, 5 per cent	3.1	86	5	3, 4	6	40
Methyl alcohol, 5 per cent	3.5	109	3	2, 3	3	66⅔
Methyl and wood alcohol, 5 per cent	5.4	76	4	2, 2, 5, 5	5	100
Wood alcohol, 5 per cent	3.3	87	3	7, 7	6	66⅔

With the following (doses = cubic centimeters of absolute per kilogram of rat per day) the mortality is so low that it may be accidental: Ethyl alcohol 5 per cent (4.8 cc.), methyl and wood alcohol, 2.5 per cent (3.2 cc.) and perhaps ethyl alcohol 10 per cent (9.4 cc.).

Severe fatality occurs within two to eight weeks with 5 per cent wood alcohol (3.3 cc.) and 5 per cent methyl alcohol (3.5 cc.); the methyl alcohol being distinctly more toxic than the wood alcohol.

TABLE 6

Mortality summarized

DRUG AND CONCENTRATION	DOSAGE OF ALCOHOLS, DAILY MEDIAN CUBIC CENTIMETERS PER KILOGRAM	WEEKS	MORTALITY RATIO	MORTALITY PER CENT	MORTALITY FACTOR $\frac{M\%}{WEEKS}$
Ethyl alcohol, 2.5 per cent....	2.7	18	0:3	0	0
Ethyl alcohol, 5 per cent.....	4.8	8	1:13	8	1
		13 and 19	2:10	20	1
Ethyl alcohol, 10 per cent....	9.4	10	0:6	0	0
		15	1:3	33	2⅓
Methyl and wood alcohol, 2.5 per cent.....	3.2	15	0:11	0	0
		16	1:11	9	⅔
		18	1:8	13	⅔
Acetone, 2.5 per cent.....	1.8	18	0:3	0	0
Methyl alcohol, 5 per cent....	3.5	2	3:12	25	12½
		3	5:12	40	13⅓
		4	6:12	50	12½
		5	8:12	67	13½
Wood alcohol, 5 per cent.....	3.3	6	0:3	0	
		7	2:3	67	9½

TABLE 7

Mortality and dosage

CONCENTRATION	DRUG	MORTALITY PER WEEK	MORTALITY PER GC. PER KILOGRAM PER DAY
per cent		*per cent*	
2.5	Ethyl alcohol	0	0
2.5	Acetone	0	0
2.5	Methyl and wood alcohol	⅔	0.22
5.0	Ethyl alcohol	1	0.21
10.0	Ethyl alcohol	2½	0.24
5.0	Wood alcohol	9½	2.9
5.0	Methyl alcohol	13½	4.1

Symptoms. These were observed only superficially.

Ethyl alcohol. The rats showed no effect with 2.5 per cent; with 5 per cent the animals were a trifle "wild," i.e., shy and easily frightened. With 10 per cent, they were slightly "doped" (stupid) and wild.

Methyl and wood alcohol. Two and one-half per cent, were slightly doped and with roughened fur. With 5 per cent, they were more markedly doped, weak, with eyes half closed.

Acetone. Two and one-half per cent were practically normal.

Effect of concentration on the toxicity of methyl alcohol. The great difference in mortality between 2.5 and 5 per cent methyl alcohol does not depend on a difference in the mean daily dosage, in terms of absolute methyl alcohol. This is practically alike for both concentrations, because the rats drank only half as much of the 5 per cent as of the 2.5 per cent alcohol. This reduction in fluid consumption started with the first day, in the experiment (109) in which a daily record of the first week was kept, so that the greater mortality is not explained by excessive dosage on the first day or week. It appears, therefor, that the same dosage of methyl alcohol is more toxic, in chronic experiments, when taken in 5 per cent than when taken in 2.5 per cent concentrations. This might be explained by diminished fluid and food consumption, which probably causes damage that adds itself to that produced by the methyl alcohol directly. This appears more plausible than the alternative explanation of differences in the rate of absorption: for even if they existed, they would not be expected to play an important part in chronic poisoning.

SUMMARY

Groups of rats received for drink exclusively the various diluted alcohols, for periods up to twenty-one weeks (five months).

Dosage. The mean daily consumption, cubic centimeters of absolute alcohol per kilogram of animals, ranged for the various groups as follows:

	cc.	*The equivalent dosage for a 60 kg. man would be*
Ethyl alcohol, 2.5 per cent	2.7	160 cc.
Ethyl alcohol, 5 per cent	4.8	290 cc.
Ethyl alcohol, 10 per cent	9.4	560 cc.
Methyl* and wood alcohol 2.5 per cent	3.2	190 cc.
Methyl and wood alcohol 5 per cent	3.4	200 cc.
Acetone, 2.5 per cent	1.8	110 cc.

* The methyl alcohol was the Baker brand, 95 per cent; N. V. M., 0.002 per cent; C_3H_6O, trace.

Consumption of fluid. The addition of ethyl alcohol to the drink diminished the consumption of fluid by about a fifth; possibly by diminishing the activity of the animals. There was no material difference between the various concentrations and doses used.

Methyl and wood alcohols, 2.5 per cent, at first decreased the consumption of fluid about a fifth due perhaps to the taste; but this was only temporary, the ultimate consumption being rather more than with ethyl alcohol.

With 5 per cent, these alcohols very greatly decreased the fluid consumption (by nearly half) from the start, until the early death.

Acetone, 2.5 per cent caused considerable decrease, of fluid consumption (by about a third) through the eighteen weeks of the experiment.

Growth. Ethyl alcohol interfered with the growth of the animals. The interference was considerable with 2.5 and 5 per cent; and more marked with 10 per cent.

Methyl and wood alcohols, 5 per cent, produced very considerable loss of weight (by about one-third) starting with the first week of the administration, and continuing until death, which occurred in a few weeks.

Methyl and wood alcohols and acetone, 2.5 per cent, behaved alike, and showed considerable deficits in growth, varying widely in different experiments but generally distinctly more severe than with 10 per cent ethyl alcohol; though much less than with the 5 per cent methyl alcohols.

Food consumption. Ethyl alcohol definitely diminished the consumption of food, by about one-tenth with 2.5 and 5 per cent alcohol; and by about one-fourth with 10 per cent alcohol.

Methyl and wood alcohol (and acetone 2.5 per cent) again behaved alike. The deficit was considerably greater than with ethyl alcohol; namely nearly a third for 2.5 per cent; and about half for 5 per cent.

Relation of food consumption and growth. These generally showed parallel changes, although not always in strict proportion. As the change in growth may precede the change in food consumption, the diminished appetite is evidently not the cause of the checked growth. It may be either the effect; or more likely, diminished growth and diminished appetite are both results of a common cause.

Mortality. Ethyl alcohol and acetone, 2.5 per cent may be consumed for over four months as exclusive drink and in the large dosage of this experiment without fatality.

Ethyl alcohol, 5 per cent; and methyl and wood alcohol 2.5 per cent have a slight mortality (one per cent or less per week of duration) that might be accidental.

Ethyl alcohol, 10 per cent has a higher fatality (2⅔ per cent per week) but the number of animals was limited, so that this also could have been accidental.

Methyl and wood alcohol 5 per cent have a high and prompt mortality, viz., about 10 per cent per week of duration; the methyl being distinctly more toxic than the wood alcohol.

The greater toxicity of methyl alcohol in 5 per cent concentration is probably due to the additive damage of voluntary restriction of liquid and food consumption.

CONCLUSIONS

The continuous consumption by rats of ethyl alcohol, in doses of 2.7 to 9.4 cc. per kilogram per day, interferes considerably with their growth, and diminishes the consumption of food. Little or no mortality occurs even after periods of months.

Methyl and wood alcohols and acetone are markedly more toxic than ethyl alcohol. Methyl and wood alcohol 3.4 cc. per kilo-

gram per day as 5 per cent solution produced very great loss of body weight; greatly diminished consumption of food and drink, and caused death within a few weeks. "Wood alcohol" is rather less toxic than pure methyl alcohol. The same dose, in more dilute form, i.e., as 2.5 per cent solution produced very few fatalities even after prolonged administration. Their effects on growth and food consumption are more deleterious than those of ethyl alcohol in three times the dosage.

Acetone, 1.8 cc. per kilogram per day as 2.5 per cent, is not fatal even after four months administration. Its effects on growth and food consumption are about the same as 2.5 per cent methyl alcohol.

The investigation brings out the deleterious effects of chronic alcoholism on growth.

It emphasizes that the dangers of chronic alcoholism are much greater with methyl than with ethyl alcohol.

It proves that the "impurities" of wood alcohol play only a minor part in chronic intoxication, the methyl alcohol itself being the dominant toxic agent.

REFERENCES

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