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Ethanol Elimination Rates in Normal and Ethanol Dependent Animals[1]

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SAMSON, H. H., D. C. MORGAN, C. M. PRICE, M. TANG AND J. L. FALK. *Ethanol elimination rates in normal and ethanol dependent animals.* PHARMAC. BIOCHEM. BEHAV. 5(3) 335–341, 1976. – Ethanol elimination rates were determined in rats using an intravenous route of ethanol administration after several experimental manipulations. Twenty-four hr food deprivation resulted in a 30% reduction to 35 mg/100ml blood/hr in elimination rate from a non-deprived rate of 50 mg/100 ml blood/hr. After 2 months of ethanol drinking (5% v/v), 24 hr starvation resulted in only a 10% reduction in elimination rate (45 mg/100 ml blood/hr), and did not increase the non-food-deprived rate (49.2 mg/100 ml blood/hr) over that obtained in the above animals' drinking water rather than 5% ethanol. Animals which chronically overdrank ethanol or water for 3 months on a schedule-induced polydipsia procedure, known to result in ethanol physical dependence, showed a decreased rate of ethanol elimination (37.9 mg/100 ml blood/hr for ethanol drinkers; 35.0 mg/100 ml blood/hr for water drinkers) in the non-food-deprived condition. By providing 750 mg of liver powder daily as a food supplement in the ethanol overdrinking regimen, the ethanol elimination rate remained at a rate comparable to the normal animal (48.4 mg/100 ml blood/hr).

Ethanol metabolism Ethanol intake Ethanol physical dependence Ethanol and nutrition
Schedule-induced polydipsia

THE effect of chronic ethanol administration on the rate of elimination of ethanol has been a long-standing problem (for a general review see [9]). Increases [10, 17, 29 (rat); 23 (monkey); 18 (man)], decreases [28 (rat)], and no change [14 (rat); 20 (dog); 15 (man)] in elimination have been reported. Certain nutritional factors, known to affect elimination rate, could be operating in these studies to yield the varying results. Food deprivation decreases ethanol elimination rates [6, 21, 26, 30 (rat); 13,26 (dog); 22 (man)], as does maintenance on a low protein diet [12,31 (rat); 3 (man)].

The present studies evaluate the effects of ethanol dependence on ethanol elimination rate. Recently, we developed a procedure for inducing chronic ethanol overdrinking leading to physical dependence in the rat [7,8]. This procedure maintains a high, daily blood level of ethanol. Pilot work using intragastric administration of ethanol resulted in elimination rates too variable for reliable determination. Intraperitoneal injection of 20% ethanol was ruled out since the possible tissue damage could change metabolic function. Therefore, the intravenous route was chosen since it eliminates both gastrointestinal clearance variability and tissue reactions which complicate use of the intraperitoneal route.

EXPERIMENT 1

Since food deprivation has been shown to alter elimination rates, the first experiment determined the ethanol elimination rates in control animals that had no prior ethanol exposure, under both food-deprived and non-deprived conditions.

METHOD

Animals

Nine adult, male albino rats (Holtzman strain) were individually housed in standard stainless-steel rodent cages. Food and water were available at all times prior to the start of the experiment. Animals were maintained on a 12 hr on 12 hr off light–dark cycle. The room temperature was regulated at 24.4° C ± 3.2° C.

Procedure

Ethanol elimination rate was determined under 2 experimental conditions: (1) ad lib food and water and (2) 24 hr food deprivation (water available). Determinations were made in 7 animals in the *ad lib* condition. One week later, elimination rates in 5 of these animals and in 2 additional

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animals were determined in the 24 hr food deprivation conditon. The 2 additional animals were incorporated to examine any serial effect prior ethanol administration might have on elimination rate.

To determine rate of ethanol elimination an animal was anesthetized with ether and the tip of the tail amputated by guillotine. A 100 μl blood sample was obtained and the tail ligated with nylon suture. The jugular vein was exposed and venipuncture was accomplished with a 30 gauge needle that had been removed from the needle hub and inserted into polyethylene tubing (PE 10). Ethanol infusion was at a rate of 0.33 ml/min. All animals received a dose of 1.5 g ethanol/kg body weight of 20% (v/v) ethanol which, at the given rate of infusion, required a total infusion time of 10–15 min. Anesthesia was maintained during the infusion. Following infusion, the needle was removed, light pressure was applied on the vein to prevent bleeding, and the incision sutured. The animal was returned to its cage and blood samples (100 μl) were collected from the tail by removing the ligature at 1, 2, 3 and 4 hr after the start of infusion.

Blood ethanol levels were determined by the enzymatic method [4]. The data were averaged and the best fit straight line was determined by the method of least mean squares. The slope of this best-fit line was used for the mean rate of ethanol elimination in mg ethanol/100 ml blood/hr.

Upon completion of the experiment, the animals were sacrificed and the wet liver weights obtained. The ratio of grams liver/100 g body weight was calculated in order to determine any changes in liver size due to food deprivation.

RESULTS

The animals that were not food deprived showed an ethanol clearance rate of 50.0 mg ethanol/100 ml blood/hr (see Fig. 1A). Using the linear equation, the projected T_0 blood level was equal to 227 mg ethanol/100 ml blood. The animals had a mean body weight of 481 g.

Figure 1B shows ethanol elimination for the 24 hr food deprived condition. For these animals the mean elimination rate was 35.2 mg ethanol/100 ml blood/hr with a T_0 level of 219.5 mg ethanol/100 ml blood. At the time of infusion, the mean body weight was 479 g, which was a 6.7% weight loss over the 24 hr food deprivation period. The 2 24 hr food deprived animals had the same elimination rate (35.8 mg/100 ml/hr) as the repeated-exposure animals had after their 24 hr food deprivation treatment (37.4 mg/100 ml/hr). Thus, the repeated ethanol exposure received by the 5 animals who were tested under both ad lib and food deprivation conditions could not account for the observed differences in elimination rate. Therefore, these data were combined, making a total of 7 animals in each condition.

An analysis of variance between the 2 conditions was significant ($F(1,44) = 49.4$; $p<0.01$) with the interaction between the groups also significant ($F(7,44) = 2.81$; $p<0.05$). Thus, the rate of elimination was significantly decreased by food deprivation. The T_0 blood levels were nearly the same and could not account for the observed difference in elimination rate.

The non deprived group had a mean liver weight of 3.61 ± 0.09 g/100 g body weight, while the food deprived group value was 3.06 ± 0.04. An analysis of variance between the group liver weights was significant ($F(1,8) = 39.44$; $p<0.01$), which could underlie the slowed rate of ethanol elimination following food deprivation.

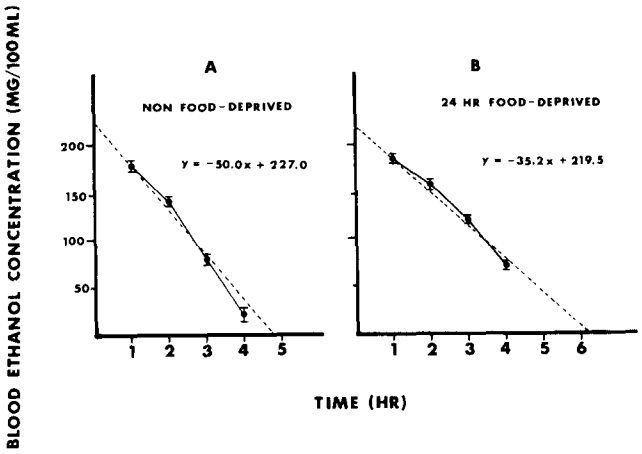

FIG. 1. Blood-ethanol elimination curves for non-food-deprived (A) and food deprived animals (B) following1.5 g/kg intravenous dose of 20% (v/v) ethanol. (Data are means ± SE)

EXPERIMENT 2

Experiment 1 showed that the lower ethanol elimination rate of 24 hr food deprived rats was accompanied by a reduced liver weight. Since chronic ethanol consumption had been reported to alter ethanol elimination rate [10], the above experiment was repeated with rats which were maintained on 5% ethanol as their sole drinking fluid rather than water.

METHOD

Animals

Nineteen adult, male, albino rats (Holtzman strain) were maintained and housed under conditions identical to Experiment 1.

Procedure

The animals were divided into 3 groups. Group 1 consisted of 5 animals maintained on ad lib food with 5% (v/v) ethanol as the only available drinking fluid for 2 months. Daily body weights and ethanol intakes were recorded. Following this 2 month period, the animals were placed on water for 24 hr, but were not food deprived. After the 24 hr on water, the rate of ethanol elimination following a 1.5 g ethanol/kg body weight dose of 20% ethanol (IV) was determined using the same procedure followed in Experiment 1. This group was therefore the same as the non deprived group of Experiment 1, except that for 2 months they had had 5% ethanol instead of water as their only available drinking fluid.

The remaining 14 animals formed the other 2 groups. Before placement on a particular feeding drinking regimen, all animals were food deprived for 24 hr, given the standard 1.5 g/kg dose of ethanol (IV) and blood ethanol elimination rate determined as in the first experiment. They then were placed into Groups 2 and 3; Group 2 was maintained on ad lib food and water (n = 5), while Group 3 was maintained on ad lib food and 5% ethanol as the only available fluid (n = 9). Following 2 months under these conditions, ethanol elimination rates were redetermined. The animals maintained on water (Group 2) were simply food deprived for

24 hr, while the group maintained on 5% ethanol (Group 3) had both food and ethanol removed and water available during the 24 hr deprivation period.

Upon completion of the experiment all animals were sacrificed, and wet liver weights were measured.

RESULTS

Group 1 (maintained on ad lib food and 5% ethanol) had a mean starting body weight of 357.8 g. The mean daily ethanol intake was 41.6 ml for the first month and 59.8 ml the second month. Weight gain over the 2 months was not significantly different from the ad lib food and water condition in Experiment 1. The mean ethanol intake in g/kg/day was 4.58 during the first month and 5.14 for the second. Ethanol eliminiation was 49.2 mg/100 ml/hr. The best fit linear equation ($y = -49.2 \times +225$) made the projected T_0 blood levels equal to 225 mg/100 ml blood. These values were not significantly different from those found for the non-food-deprived, water-maintained condition of Experiment 1 when tested with a one-way analysis of variance. Thus, the 2 month period of drinking 5% ethanol with ad lib food had no effect on the ethanol elimination rate of non-food-deprived animals. The mean g liver/100 g body weight for these animals was 3.63 ± 0.12, which was not significantly different from the non deprived conditions in Experiment 1.

Mean body weight, daily fluid intake and ethanol consumption for the remaining groups are presented in Table 1. Over the course of the experiment, no significant differences could be found between these groups on these variables. They both gained weight at the same rate and had equal fluid intakes, independent of the fluid available. Prior to the final ethanol elimination determination, but following the 24 hr food deprivation period, the ethanol exposure group was observed for withdrawal symptoms. The observation methods were as previously described (7). No signs of ethanol withdrawal were observed.

TABLE 1

MONTHLY WEIGHTS AND INTAKES FOR ANIMALS MAINTAINED WITH ONLY 5% (v/v) ETHANOL OR WATER AVAILABLE. FOOD WAS AVAILABLE AD LIB. (VALUES ARE 30 DAY MEANS ± S.E.)

	Water (Group 2)	5% ethanol (Group 3)
Body weight		
1st month	365 ± 7	357 ± 8
2nd month	438 ± 5	435 ± 11
Fluid intake†		
1st month	41.4 ± 1.7	36.5 ± 1.4
2nd month	38.0 ± 2.9	42.5 ± 2.9
Ethanol intake‡		
1st month	—	4.1 ± 0.1
2nd month	—	3.9 ± 0.2

* Body weight in g.
† Fluid intake in ml/day.
‡ Ethanol intake in g absolute ethanol/kg body weight/day.

Prior to the 2 month ethanol drinking period, the rate of ethanol elimination for the ethanol-exposure group (Group 3) was 41.5 mg ethanol/100 ml blood/hr, while the water-exposure group (Group 2) rate was 43.1 mg ethanol/100 ml blood/hr (Fig. 2). Mean body weights are

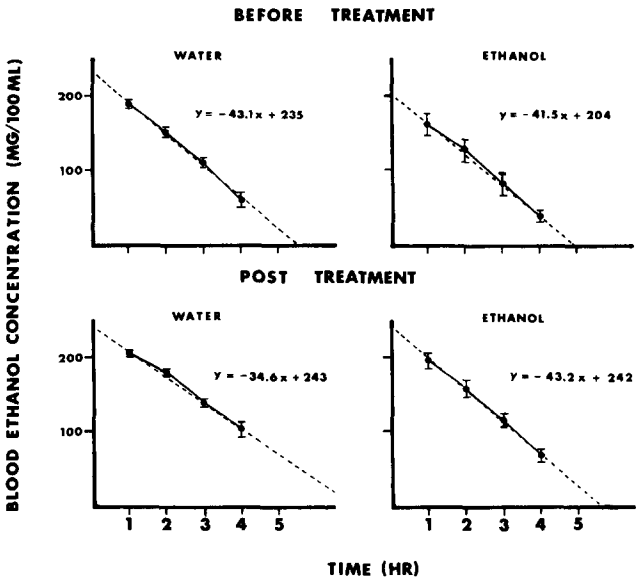

FIG. 2. Blood ethanol elimination curves before and after either daily water or ethanol drinking for 2 months. Curves are for doses of 1.5 g/kg (IV) of 20% (v/v) ethanol. (Data are means ± SE)

TABLE 2

EFFECT OF 24 HR FOOD DEPRIVATION ON BODY WEIGHT BEFORE (PRE-TREATMENT) AND AFTER (POST-TREATMENT) 2 MONTHS OF ACCESS TO EITHER WATER OR 5% ETHANOL AS THE SOLE DRINKING FLUID. (DATA ARE MEAN VALUES.)

	Water	5% ethanol
Pre-treatment		
Pre	319	304
24 hr dep.	281	264
% loss	13%	12%
Post-treatment		
Pre	465	475
24 hr dep.	432	438
% loss	7%	8%

presented in Table 2. The rate of ethanol elimination was greater than that found for the 24 hr food deprived condition in Experiment 1, but lower than the non-food-deprived condition.

Following the 2 months of either drinking 5% ethanol or water, the rates of ethanol elimination were 43.2 mg ethanol/100 ml blood/hr for the ethanol-exposure group (Group 3) and 34.6 mg ethanol/100 ml blood/hr for the water-exposure group (Group 2, Fig. 2). The only significant difference found was between the post-water-exposure and post-ethanol-exposure group (t (12) = 2.63, $p<0.05$). At this time, the body weights for the ethanol and water groups were not different (Table 2), nor were they significantly different from the groups in Experiment 1. The water-exposure group had the same rate of ethanol elimination as the similarly treated animals in Experiment 1 (food deprived condition) while the ethanol-exposure group remained at the same rate of elimination as in the pre-exposure condition (Fig. 2, right side).

The water-exposure group (Group 2) had a liver weight

of 2.75 g/100 g body weight, while the ethanol-exposure group (Group 3) had a value of 3.10. These levels were significantly different from each other (t (12) = 2.68; $p<0.01$) and were both significantly different from the normal, non deprived condition of Experiment 1 (ethanol vs Exp. 1: $t(12) = 4.40$; $p<0.005$; water vs Exp. 1: $t(8) = 7.64$; $p<0.005$).

There was no difference between the liver weights of the food deprived condition animals of Experiment 1 and the ethanol exposure animals, but the effect of food deprivation in the water animals was significantly greater than that found for the food deprived animals of Experiment 1 (t (8) = 3.69; $p<0.005$).

EXPERIMENT 3

The results of the previous experiment indicated that the ethanol elimination rate could be altered by drinking ethanol. No enhanced rate was found, but chronic drinking of 5% ethanol for a 2 month period reduced the 24 hr food deprivation effect on elimination rate. But since the animals in the ethanol-exposure condition were not physically dependent upon ethanol, the present experiment examined the effect of long-term, chronic ethanol drinking, known to produce physical dependence on ethanol (8).

METHOD

Animals

Twelve adult, male rats (Holtzman strain) were used in this study. Eight animals were placed into an ethanol over-drinking group, while the remaining 4 were treated in the same manner but drank water instead of ethanol. The animals in the ethanol group had a mean starting body weight of 315 g ± 5 g, while the 4 animals that later served as the water control weighed 411 g ± 14 g at the start of the experiment. All animals were gradually reduced to 80% of their free-feeding body weights by limiting daily food intake over the initial 2 week period of the experiment. During this period, the animals were housed under the conditions used for the previous experiments, with water available at all times.

Procedure

Following weight reduction, ethanol or water over-drinking was established by the use of schedule-induced polydipsia (for a complete procedural description see ref. 8). Briefly, each animal was housed in a Plexiglas chamber equipped with an automatic food pellet dispenser and a 250 ml graduated cylinder that served as a fluid reservoir. The cylinder was attached to a ball-bearing drinking tube (TD-300, Ancare Corp., New York, N. Y.) which prevented fluid leakage. The pellet dispenser was programmed with electromechanical switching circuitry such that for 1 hr a 45 mg food pellet (P. J. Noyes Co., Lancaster, N. H.; 4.3 kcal/g) was automatically delivered every 2 min. Then for 3 hr no pellets were delivered, followed by another hour of pellet delivery, etc. Thus, every 24 hr, 6 pellet delivery sessions occurred (180 pellets/day), with a 3 hr interval between sessions. The only available fluid was 5% (v/v) ethanol for the ethanol group, or water for the water control group.

The animals were maintained in this condition for the next 90 days. Each day, between the midmorning pellet delivery sessions, the animals were weighed, the fluid intakes recorded and reservoirs refilled. For the ethanol group, any food supplements necessary to maintain body weights at the 80% level were given at this time. For the water group, an additional, daily food ration was administered at this time to equate total daily caloric intake with the ethanol group.

On the 90th day, ethanol was replaced by water for the ethanol group, with the food delivery schedule continued. On the 91st day, elimination rates were determined for both groups as in Experiment 1. Wet liver weights were obtained for the ethanol group.

RESULTS

Over the 3 months of chronic ethanol polydipsia, the mean daily ethanol intake was 11.7 g ± 0.8/kg/day. During this time the animals had a mean weight gain of 79 g, resulting in a final mean body weight of 331 g ± 12. During the last 24 hr, in which water was substituted for ethanol, the animals lost some weight (1.2%), but as they drank less fluid, probably little actual weight loss occurred and this, therefore, could not account for any difference in ethanol elimination. The mean rate of ethanol elimination was 37.8 mg ethanol/100 ml blood/hr (Fig. 3) with an estimated T_0 blood-ethanol level of 203.5 mg/100 ml. The mean wet liver weight was 2.97 ± 0.07 g/100 g body weight.

Over the 3 months of water drinking, the control animals gained an average of 85 g with a resulting final mean body weight of 390 g ± 10 g. During the 3 months, the animals drank daily an average of 78 ml of water (first 30 day mean = 81 ± 8; second 30 day mean = 77 ± 6; last 30 day mean = 77 ± 5). Their mean rate of ethanol elimination was 35.0 mg ethanol/100 ml blood/hr. The estimated T_0 blood level was 206 mg/100 ml blood. These values were not significantly different from the ethanol group.

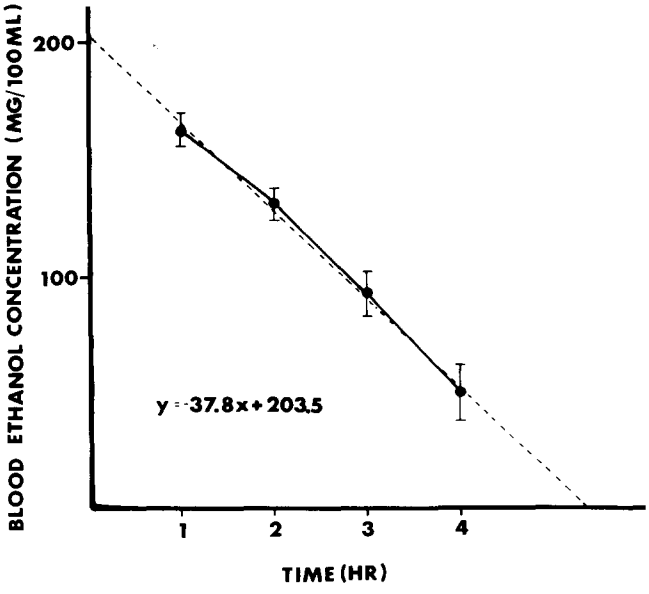

FIG. 3. Blood ethanol elimination curve for animals having ingested ethanol at levels known to produce physical dependence for three months. Curve is for a dose of 1.5 g/kg of 20% ethanol (IV). (Data are means ± SE)

EXPERIMENT 4

Experiment 3 failed to show an enhanced rate of ethanol elimination following a procedure known from previous work [8] to produce physical dependence upon ethanol. Since the water overdrinking animals had the same ethanol elimination rates as did the ethanol overdrinking animals, and since these rates were well below those found in normal, non-food-deprived animals, it seemed possible that the observed results were due to a protein insufficiency resulting from the feeding regimen used in the experimental overdrinking procedure. Low protein diets are known to decrease the rate of ethanol elimination [12,30]. Thus, Experiment 4 was conducted to determine the effect of an added daily protein supplement upon ethanol elimination rates after chronic ethanol polydipsia.

METHOD

Animals

Two adult, male rats (Holtzman strain) with a mean starting body weight of 320 g were slowly reduced to 80% of this value in the same manner as in Experiment 3. All housing and environmental conditions were the same as in Experiment 3.

Procedure

Following reduction to the 80% body weight level, animals were placed into chambers similar to those use in Experiment 3, except that each chamber had an additional food delivery chamber into which a small stainless steel food cup could be placed containing any additional food supplement that might be given. Animals were maintained on the same food delivery schedule as in Experiment 3 and ethanol (5%) was the only fluid available in the chamber.

Following the daily, midmorning fluid intake and body weight recording, a 750 mg liver powder (Nutritional Biochemical Corp., Cleveland, Ohio: lot #8924, approximately 70% protein) food supplement was given to each animal in the stainless steel food cup. One to 2 drops of water were mixed with the liver powder to assure that the animals would ingest all of the supplement. This supplement was administered daily for the duration of the experiment.

After 90 days of ethanol overdrinking, water was substituted for the ethanol for a 24 hr period while the animals were maintained on the feeding schedule, as in Experiment 3. Then, ethanol elimination rates were determined as in the preceding experiments.

RESULTS

Over the 3 month period, the animals had a mean daily intake of 10.9 g ethanol/kg body weight/day and showed an increased weight gain of 85 grams, resulting in a final mean body weight of 405 g. The mean ethanol elimination rate was 48.4 mg ethanol/ml blood/hr with a T_0 of 226 mg/100 ml. This was not significantly different from the normal non-food-deprived animals of Experiment 1 (mean rate of 50.0 mg ethanol/100 ml blood/hr), but was significantly different from the ethanol (t (8) = 2.16, $p<0.05$) or water ($t(4) = 2.90$, $p<0.05$) drinking groups of Experiment 3 (ethanol group = 37.8 mg ethanol/100 ml blood/hr; water group = 35.0 mg ethanol/100 ml blood/hr). Thus, the additional liver supplement appeared to have maintained the rate of ethanol elimination at that of the nontreated, non-food-deprived animal.

DISCUSSION

Table 3 presents a summary of the 4 experiments. The first experiment indicated that the normal rate of ethanol elimination in the rat often may be underestimated. Short-term (24 hr food deprivation produced a 30% reduction in elimination rate which agrees with previous studies [21, 26, 31]. Thus, studies using food deprivation in order to reduce the variability of ethanol absorption from the gastrointestinal tract may result in an underestimation of the rate actually operating in the nondeprived animal.

Experiments 1 and 2 were done at different times and 2B was essentially a replication of 1B. Since the results were quite comparable (Table 3), other comparisons between these 2 experiments are allowable. Chronic ethanol exposure which did not produce physical dependence, did not alter ethanol elimination rate in the non-food-deprived animal (cf. Experiments 1A and 2A). However, this exposure to ethanol did result in a smaller decrement in elimination rate occurring after food deprivation (cf. Experiments 1A and 1B vs Experiments 2A and 2C). This indicated that the 2 month exposure to ethanol attenuated the deprivation induced depression of the ethanol elimination rate. In 2 studies [17,29] claiming increased ethanol elimination following chronic ethanol consumption animals were food deprived before elimination rates were determined. Mezey [17] reported a rate of 33 mg ethanol/100 ml blood/hr for control animals, while Videla *et al.* [29] reported 33.7 mg ethanol/100 ml blood/hr. These data are closely comparable to those of Experiments 1B and 2B. Mezey [17] found a rate of 46.5 mg/100 ml blood/hr for ethanol-fed rats while Videla *et al.* [29] reported 51.3 mg/100 ml blood/hr. In the present study, the 24 hr deprived ethanol-fed group (Experiment 2C) had a comparable rate of 43.2 mg/100 ml blood/hr. while the non-food-deprived control animals (Experiment 1A) had a rate of 50 mg/100 ml blood/hr. Thus, the increases reported [17,29] apparently are not actually increases over normal elimination rates. When the non-food-deprived animals (Experiments 1A and 2A) are compared with the Mezey [17] and Videla *et al.* [29] ethanol drinking groups, no increases over the normal nondeprived rate are apparent.

Biochemical changes in the liver following ethanol consumption [2,19] could underlie the effects observed in these studies. Following chronic ethanol treatment, Morland [19] found little effect of 24 hr food deprivation upon several liver measures compared to effects found in control animals maintained on water. This could be the basis of the protective effect afforded by 2 months of drinking 5% ethanol (Experiment 2B vs 2C) on the attenuation of elimination rate induced by food deprivation.

Age-weight factors in elimination rates which have been previously reported [11] could account for the differences found between Experiment 1 and the pre-exposure rates of Experiment 2. Younger animals are reported to have a higher rate of ethanol elimination, and the animals of Experiment 2, at the time of the pre-exposure elimination rate determination, were somewhat younger.

In Experiment 3, chronic ethanol polydipsia also failed to increase ethanol elimination rate in the non-food-

TABLE 3

EFFECT OF DIET AND ETHANOL EXPOSURE ON ETHANOL ELIMINATION RATE

Experiment	Experimental condition	N	$\overline{X}$ body weight (g)	$\overline{X}$ EtOH intake (g/kg/day)	EtOH elimination rate (mg/100 ml blood/hr)
1 A.	Ad lib food and water	7	481	—	50.0
B	24 hr food deprivation	7	479	—	35.2
2 A.	Ad lib food with 24 hr water after 2 mo. 5% EtOH exposure	5	454	4.9	49.2
B.	24 hr food deprivation	5	465	—	34.6
C.	24 hr food deprivation with water after 2 mo. 5% EtOH exposure	9	475	4.0	43.2
3 A.	Scheduled food with 24 hr water after EtOH polydipsia (3 mo.)	8	331	11.7	37.8
B.	Scheduled food with water polydipsia (3 mo.)	4	390	—	35.0
4	Scheduled food with 24 hr water after EtOH polydipsia and daily liver supplement	2	405	10.9	48.4

deprived condition; rather it produced a 24% decrement from normal, non-food-deprived animals. However, the water polydipsia control also showed a decreased rate of ethanol elimination, suggesting that the ethanol itself was not the determining factor in elimination rate decrement.

One question raised by these results concerns the nutritional state of the chronically polydipsic animals. Because of a possible added demand for proteins under these feeding regimens, the standard, nutritionally adequate diet (12–14% protein) may not contain enough protein to meet possible increased metabolic needs. Maintenance on protein poor diets results in decreased ethanol elimination rates [12,31]. The results of Experiment 4 would support the contention that a major factor in the reduced ethanol elimination rates found in the feeding regimen inducing polydipsia was due to a lack of adequate protein in the diet. However, the crucial component of the added liver supplement in the maintenance of normal ethanol elimination rates in polydipsic animals remains to be elucidated.

The ethanol-food caloric intake ratio resulting from the chronic ethanol polydipsia regimen approximates that of the human alcoholic [8,16]. Increases [18], or no change [15] in ethanol metabolism in man following ethanol overdrinking have been reported. Decreased rate seems specifically related to the nutritional state of the individual [3,22]. In this respect, the effects of 24 hr of food deprivation [22] are very similar to those found in Experiment 1. Thus, the human alcoholic may actually have a decreased rate of ethanol elimination when compared to the non-food-deprived normal adult.

In general, smaller liver weight to body weight ratios were found with a decreased rate of ethanol metabolism (Pearson correlation coefficient = 0.94; Fisher $t(5) = 5.70$, $p<0.01$). However, food restriction is known to not only affect liver size but also levels of stored metabolites [1, 5, 27, 32]. Thus, moderate ethanol intake that does not result in physical dependence may alter the storage composition characteristics of the liver and provide a mechanism whereby food deprivation does not deplete essential metabolic stores needed for ethanol elimination. However, it appears that this change did not occur in the chronic ethanol polydipsia feeding regimen employed.

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