CXIII. THE EFFECT OF ALCOHOL, UNDER VARYING CONDITIONS OF DIET, ON MAN AND ANIMALS, WITH SOME OBSERVATIONS ON THE FATE OF ALCOHOL IN THE BODY.

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The relationship of the alcohol concentration in the blood of animals to varying conditions of the food content of the alimentary canal was first put on a broad experimental basis by the work of E. Mellanby [1919]. This worker used mainly dogs for his investigations in which the alcohol blood concentration curve was determined for varying conditions of the food and drink of these animals. A year later [1920] he described further results obtained with a human subject. Previous to this Weissenfeld [1898] noted that the changes produced by the ingestion of alcohol in his respiratory and circulatory system were greatest when the beverage was taken on an empty stomach. Voltz, Baudrexel and Dietrich [1912] gave moderate doses of alcohol to men and found that the content of alcohol in the urine was six times greater when the alcohol was taken on an empty stomach than when its ingestion had followed the taking of food. Hanzlik and Collins [1913] studied the absorption of alcohol from the alimentary tract of cats and dogs. Though these investigators were not primarily concerned with the influence of foodstuffs on alcohol absorption, they showed that substances such as olive oil, cholesterol and bile salts exerted a retarding effect on alcohol absorption. Vernon [1919] carried out experiments on the influence of alcohol on manual work and neuro-muscular coordination and concluded that at the height of its influence alcohol is about twice as active in upsetting neuro-muscular coordination when taken on an empty stomach as when taken with food. McDougall and Smith [1920], working independently, corroborated Vernon's results. The extensive results published from the Nutrition Laboratory of the Carnegie Institution of Washington have dealt in the main with the psychological effects of alcohol, but among these records are some which illustrate the effect of food on alcohol ingestion. Thus Miles [1924] showed that when a dose of alcohol was taken shortly after the ingestion of a full meal, the effect, as exhibited in the accuracy and speed of neuro-muscular processes involved in typewriting during a 4-hour interval following the ingestion, was very much reduced compared with the effect when no food had been taken. With the exception of Mellanby the above-mentioned authors

have not dealt mainly with the effect of foodstuffs *qua* foodstuffs on the alcohol blood concentration. The work to be described is a more detailed study of the relation of alcohol to diet in the human subject. Three men, who were moderate drinkers of alcoholic beverages, were chosen. They were J. H. B. age 53 years, weight 11st. 4 lb., an army pensioner after 23 years in the R.F.A. who continues at his trade as saddler; G. H. N. age 31 years, weight 11 st. 8 lb. and his brother W. N. age 34 years, weight 9 st. 8 lb. were foundrymen, but for the past 18 months have been unemployed. The investigations covered the period July, 1923–December, 1924. During this interval the weight of the three men remained sufficiently constant to need no change in the amount of alcohol given. Not more than one experiment was carried out per week and the routine was always the same. Their last meal on the day preceding that of the experiment was consumed between 8 and 9 p.m. Alcoholic drinks were, of course, not allowed on this day and no liquid of any kind after 9 p.m. No food or drink was taken before arrival at the laboratory on the morning of the experiment. The dose of alcohol was the same for each man and for each experiment, namely, 1200 cc. of (practically) 8 % alcohol made by adding 300 cc. of absolute alcohol to 3450 cc. of tap water, *i.e.* 96 cc. of absolute alcohol per man. This dose produced little or no evidence of intoxication. There was no difference in their ability to draw a simple diagram, to walk or run, an hour after taking the alcohol from that before the beverage was taken. No flavouring was added to the alcohol, the drinking of which was always spread over 10 minutes. The men rested in the laboratory, the temperature of which was maintained as nearly as possible at 17–18°. In those experiments in which food was taken before the alcohol, the interval between the consumption of the food and taking alcohol was always $1\frac{1}{2}$ hours with the single exception of the period (2 hours) after olive oil. The alcohol content of the blood, urine, etc., was recovered by distillation in the apparatus previously described by the author [1924] and estimated by the slightly modified Pringsheim's method described therein. Blood samples (about 10 g.) were taken at the following intervals after the completion of drinking the alcohol, 1, $2\frac{1}{2}$ and $6\frac{1}{2}$ hours. In several of the experiments the concentration of alcohol in the urine was also determined at intervals. Whether the urine was kept for estimation or not, the times for evacuating the bladder were the same in all the experiments, namely, just before the dose of alcohol, then every 20 minutes during the next $2\frac{1}{2}$ hours, then every $\frac{1}{2}$ hour.

In the accompanying table the concentration of alcohol in the blood is given in cmm. of alcohol per 100 g. blood; the concentration in the urine in cmm. of alcohol per 100 cc. urine. In some of the experiments the whole of the urine for the $6\frac{1}{2}$ hours was pooled and the mean figure for the alcohol content also determined.

The experimental results are set out in the following table:

Table I. *The variation of the alcohol concentration in the blood and urine of the resting subject with varying dietetic conditions.*

Food taken	Subject	Alcohol concentration in the blood after			Alcohol in urine		Alcohol in urine / Alcohol in blood	
		1 hr.	2½ hrs.	6½ hrs.	2½ hrs.	6½ hrs.	2½ hrs.	6½ hrs.
(*a*) No food	J. H. B	146	148	87	193	114	1·37	1·37
	G. H. N.	151	148	78	199	103	1·39	1·34
	W. N.	160	154	85	212	126	1·38	1·40
(*b*) 530 cc. water	J. H. B.	142	145	81	205	127	1·41	1·56
	G. H. N.	130	141	74	199	104	1·41	1·40
	W. N.	170	154	92	197	125	1·28	1·36
(*c*) 530 cc. whole milk previously boiled	J. H. B.	114	130	58	186	87	1·43	1·50
	G. H. N.	123	134	62	184	100	1·37	1·40
	W. N.	Lost	141	71	196	101	1·39	1·42
(*d*) 530 cc. whole milk previously boiled and 183 g. bread	J. H. B.	106	116	48	161	70	1·39	1·46
	G. H. N.	125	116	45	162	58	1·40	1·26
	W. N.	128	123	49	180	82	1·46	1·67
(*e*) 530 cc. water and 183 g. bread	J. H. B.	Lost	125	58	163	83	1·30	1·43
	G. H. N.	137	126	62	164	92	1·30	1·48
	W. N.	159	143	70	191	114	1·34	1·63
(*f*) 50 g. separated milk powder, 183 g. bread, 500 cc. water	J. H. B.	101	117	44	146	67	1·60	1·50
	G. H. N.	140	123	52	154	76	1·25	1·46
	W. N.	157	130	52	182	78	1·40	1·50
(*g*) 50 cc. olive oil	J. H. B.	143	142	79	203	114	1·43	1·44
	G. H. N.	126	146	79	217	125	1·49	1·58
	W. N.	126	155	88	226	128	1·46	1·45

The effect of diet on the concentration of alcohol in the blood (Table I).

(*b*) In these experiments there is no increased rate of absorption when water is previously taken. Mellanby found that a previous drink of water increased the absorption rate of alcohol in the case of dogs.

(*c*) The marked effect of a previous draught of milk in lowering the alcohol blood concentration curve, which Mellanby noted in his experiments is well corroborated.

(*d*) Taking a meal of bread and boiled whole milk previously has an even greater effect than milk alone in lowering the concentration curve which is given by alcohol on an empty stomach.

(*e*) Exps. (*c*) and (*e*) show that the meal of bread and water has about an equal effect to that of whole milk on the subsequent blood concentration curve under the above experimental conditions.

(*f*) This experiment was designed to simulate Exp. (*d*), the milk-fat being absent. The figures in these two experiments agree on the whole quite well. Exps. (*e*) and (*f*) suggest that fats are not the only factor tending to prevent alcohol from circulating in the blood stream.

(*g*) This experiment was carried out to see whether fats as such have any specific effect on subsequent alcohol absorption. In the case of J. H. B. it will be seen that there is little difference between the concentration curves of alcohol in the blood, on an empty stomach, after a drink of water, or after taking olive oil. In the case of the other two subjects there is evidence of delayed absorption at first, but subsequently the concentration curves after

olive oil practically coincide with the respective curves obtained when the alcohol is taken on an empty stomach. On the whole, therefore, it would seem improbable that it is the fat of milk or of bread and milk, as Mellanby [1920] suggested, which is responsible for the alcohol blood concentration curve being so depressed after these foodstuffs.

It is noteworthy that after the maximum concentration of alcohol in the blood has been reached the rate of fall in the concentration of alcohol in the blood is the same for the same individual in all these cases, provided he be kept at rest, and external conditions, especially temperature, be kept constant. This fact was noted by Mellanby in dogs. The results here suggest that within the limit of experimental error this rate of disappearance is the same for all three men, but further experiments will have to be carried out before this can be regarded as established.

This fact of the rate of disappearance of alcohol being independent of the concentration when once the maximum has been reached raises an important question, namely, the fate of a large fraction of the alcohol taken after a meal of bread and milk. For it is obvious from the table that a large fraction of the ingested alcohol after a previous meal of bread and milk never reaches the blood stream, or, if it does, disappears from this at once. The following attempts, unfortunately unsuccessful, were therefore made to trace the fate of this alcohol:

(1) The first solution that suggested itself was that a considerable fraction of the alcohol had never been absorbed, being perhaps adsorbed or retained in some way by the food. To test this, two dogs were given alcohol, one on an empty stomach, the other when a meal of bread and milk had been given 1½ hours previously. Blood samples were taken at intervals; after 2½ hours the animals were instantaneously killed, and the alcohol in the contents of the alimentary canal estimated. The gut wall was not included in this estimation. The results were as follows:

Dog A

Weight	Food taken	Alcohol given	Alcohol in 100 g. blood after	Total alcohol in
15 lb.	No food after 6 p.m. previous evening or water after 8 p.m.	9·75 cc. diluted to 122 cc.	14 mins. 152 cmm. 44 ,, 184 ,, 85 ,, 175 ,, 134 ,, 161 ,, 140 ,, dog killed	Stomach 20 cmm. Small intestine 0 Large intestine 20 cmm.

Dog B

13 lb.	33 g. bread, 250 cc. milk	8·5 cc. diluted to 106 cc.	18 mins. 90 cmm. 50 ,, 134 ,, 116 ,, 131 ,, 137 ,, 116 ,, 144 ,, dog killed	Stomach 280 cmm. Small intestine 40 cmm. Large intestine 110 cmm.

An examination of these figures shows that the amount of alcohol in the lumen of the gut of dog A at the time of killing is practically negligible. From dog B 0·43 cc. of alcohol was recovered. A set of experiments was also carried out to see whether known amounts of alcohol added to bread and milk under

conditions simulating those existing in the stomach and small intestine, could be recovered. It was found that when 10 cmm. alcohol in dilute aqueous solution were added, on the one hand, to 10 g. bread and milk with pepsin and hydrochloric acid, and on the other to 10 g. bread and milk with pancreatic extract and sodium carbonate, and each sample incubated for 2 hours at 37°, the alcohol could be recovered practically completely from both mixtures. It would appear therefore that the alcohol recovered from the contents of the alimentary canal represents the whole of that compound present. If this can be assumed then it is obvious that the presence of 0·43 cc. of alcohol in the alimentary tract of the second dog will not explain fully its low alcohol blood concentration figures compared with those of the first dog.

(2) The low figures for the alcohol content of the alimentary canal of dog A rather rule out the idea that there is a back secretion of the alcohol into the lumen of the gut. Gréhant [1903] found that when he gave large concentrated doses of alcohol intravenously to dogs there was a secretion of this into the stomach. Hanzlik and Collins [1913] found that when alcohol was placed in the stomach or in isolated loops of intestine there was a re-secretion of this compound into the intestine, though the amount was small. Previous to the experiment with the two dogs the present writer had carried out a series of experiments on rabbits to test the degree of back secretion into the alimentary tract. The animals were given no food for 2 days previous to the experiment and their drinking water was withdrawn on the evening preceding the experiment. The alcohol was given intravenously. The following results were obtained:

Rabbit	Weight	Alcohol given	Interval between the alcohol and killing	Concentration in the blood at death	Alcohol found in the alimentary canal
A	5¼ lb.	5 cc. diluted to 50 cc.	25 mins.	208 cmm.	Stomach 75 cmm. Small intestine 35 cmm. Large intestine 46 cmm.
B	5¼	5 cc. diluted to 50 cc.	4¼ hrs.	72 „	Stomach 91 cmm. Small intestine 19 cmm. Large intestine 34·3 cmm.
C	6	—	—	—	Stomach equal to 1·4 cmm. Small intestine 0 Large intestine 1·5 cmm.
D	4¾	4·8 cc. diluted to 48 cc.	8 mins.	258 „	Stomach 39 cmm. Small intestine 45 cmm. Large intestine 56 cmm.
E	5¾	5·8 cc. diluted to 58 cc.	11½ hrs.	3 „	Stomach equal to 2·8 cmm. Small intestine 0 Large intestine 0
F	4¾	4·8 cc. diluted to 48 cc.	5 hrs.	67 „	Stomach 70 cmm. Small intestine 11·7 cmm. Large intestine 44 cmm.
G	5¼	—	—	—	Stomach equal to 2·1 cmm. Small intestine 0 Large intestine 1 cmm.

It is evident that a secretion into the lumen of the gut takes place along its whole length, though not large in amount. It is curious to note here, as in

the case of the two dogs, that the small intestine contains least alcohol. This seems to point to one of two possibilities; either the absorption of alcohol is most rapid from the small intestine [cp. Hanzlik and Collins, 1913] or alcohol is being used up in this part of the tract. It will also be noted that in the case of two control rabbits C and G which were not given alcohol, the amount of volatile reducing substance obtained from the contents of their alimentary tract was negligible in spite of fermentation taking place among the contents of the never empty stomach of the fasting rabbit.

(3) The possibility that the disappearance of the alcohol might be due to some interaction or oxidation taking place during the processes of digestion or bacterial action had to be considered and tested. The following experiments were made.

(*a*) To test the effect of enzymes, well-stoppered bottles containing respectively the quantities given below were incubated for 2 hours at 37°, then the volatile contents were distilled, and the reducing substances in the distillates estimated:

Bottle 1. 10 g. bread and milk, pepsin and hydrochloric acid to make 0·2 %.
„ 2. „ „ ground up stomach mucosa and HCl.
„ 3. „ „ liquor-pancreaticus and dilute sodium carbonate.
„ 4. „ „ liquor-pancreaticus and dilute sodium carbonate and ground up small intestine mucosa.

To each of the above bottles 10 cmm. alcohol were added before incubation.

A corresponding set of bottles containing no alcohol was also put up and similarly incubated. The estimations showed that the alcohol had been recovered practically quantitatively from the contents of bottles 1–4 and that the controls contained none.

(*b*) No organism has been obtained from human faeces which could be classed with the acetic acid producing group. On the other hand the production of alcohol from carbohydrates by members of the *B. coli* group, and by *B. welchii* is a well-known fact. The following experimental evidence shows that when dilute alcohol is added to a suspension of faeces and the mixture maintained at body temperature there is a slow disappearance of the alcohol. 100 g. of freshly passed faeces were emulsified with 150 cc. water and then used in quantities of 10 cc. as follows:

Bottle 1. 10 cc. faeces emulsion + 10 cc. water.
„ 2. 10 cc. faeces emulsion + 5 cc. water + 5 cc. 0·4 % aqueous alcohol.
„ 3. Repetition of 2.
„ 4. Repetition of 2.
„ 5. 10 cc. autoclaved emulsion + 10 cc. sterile water.
„ 6. 10 cc. autoclaved emulsion + 5 cc. sterile water + 5 cc. 0·4 % aqueous alcohol.
„ 7. 10 cc. filtered faeces emulsion and 10 cc. sterile water.
„ 8. 10 cc. filtered faeces emulsion and 5 cc. sterile water + 5 cc. 0·4 % aqueous alcohol.
„ 9. 10 cc. autoclaved filtered faeces emulsion + 5 cc. sterile water + 5 cc. 0·4 % alcohol.

The emulsion of faeces used in bottles 5 and 6 was 0·4 % autoclaved for 20 minutes at 125°. The emulsion of faeces used in bottles 7, 8 and 9 was filtered through an "Imperator" candle. This filtrate was found to be sterile as regards ordinary bacteria. The well-stoppered bottles were then incubated at 37° for 4 hours with the exception of bottles 2 and 3 which were withdrawn

after 1 and 2 hours respectively. After incubation a little milk of lime was added to each bottle and the contents distilled. The alcohol discovered or produced was then estimated with the following results:

Bottle 1. Contained no volatile reducing substances.
,, 2. 1·4 cmm. (about $\frac{1}{14}$th) of the alcohol added could not be recovered.
,, 3. 2·7 cmm. (about $\frac{1}{7}$th) of the alcohol added could not be recovered.
,, 4. 5·0 cmm. (about $\frac{1}{4}$th) of the alcohol added could not be recovered.
,, 5. Contained no volatile reducing substances.
,, 6. Practically the whole of the added alcohol was recovered.
,, 7. Contained no volatile reducing substances.
,, 8. 2·6 cmm. (about $\frac{1}{8}$th) of the added alcohol could not be recovered.
,, 9. Practically the whole of the added alcohol was recovered.

There is a definite though small disappearance of the alcohol added to faeces *in vitro*—whether this process is increased or not in the colon cannot be determined. The result obtained with the contents of bottle 8 suggests that the active agent is either a filter passer or else a ferment. At the same time the possibility of the effect being due to adsorption cannot be excluded by the results obtained above, for the process of autoclaving markedly alters the physical properties of the emulsion. Thus while this evidence of the using up of alcohol by the faeces could only account for the fate of a small fraction of the alcohol ingested, it gives some explanation of the fact that alcohol cannot be found in faeces when a dose has previously been taken [Atwater and Benedict, 1902; Pringsheim, 1908].

The effect of diet on the concentration of alcohol in the urine (Table I).

It will be seen that these results for the urine corroborate and extend the work of Miles [1922], who showed that when 27·5 g. of alcohol, diluted to one litre, were given to human subjects it produced an alcohol concentration in the urine 40–50 % higher than that in the blood during the period 40 minutes to 2 hours after the ingestion of the alcohol. In the present experiments in which 96 cc. alcohol diluted to 1200 cc. were given, a similar increase in the concentration of the urine-alcohol above that of the blood was found at the $2\frac{1}{2}$ and $6\frac{1}{2}$ hour intervals after the ingestion of the alcohol. Some further determinations, not given here, gave a similar figure at the 1 hour interval. It will be seen from the table that the ratios for the $6\frac{1}{2}$ hour intervals are on the whole slightly higher than those for the $2\frac{1}{2}$ hour intervals, though in some of the individual experiments the ratios at these two intervals agree quite well. In the case where bread and water were taken previously to the alcohol (Exp. *e*) the ratios at the longer interval are distinctly higher. It is difficult to suggest a cause for this last result apart from some specific dietary effect.

The main fact which emerges from these results is that the ratio of the alcohol concentration in the urine to that in the blood keeps fairly constant over a considerable period of time after taking the alcohol and represents a value for the urine 40–50 % above that in the blood. The work of Miles showed that the contention of Widmark [1916] and Ambard [1920], that the concentration of alcohol in the urine was identical with that in the blood, only held

for the first half hour after ingestion, but that afterwards, from 40 minutes to 2 hours, the urine concentration was 30–50 % above that in the blood. The present work shows that this figure practically holds for the subsequent 4 hours as well, and with a much larger dose of alcohol and in greater concentration.

The importance of this fact is urged in view of the present need for a more reliable test for drunkenness. From the above results, as well as those of Miles, it would appear that a close approximation to the alcohol concentration in the blood can be obtained from a knowledge of the actual figure for the concentration in the urine. The alcohol concentration in the blood probably gives us the best means of gauging the intoxication of the subject. Widmark [1915] reported the results of examining the urine of 27 individuals arrested for alcoholic intoxication. The results varied from 450 to below 200 mg. of alcohol per 100 cc. of urine. Not all those arrested were suffering from gross intoxication. In the above experiments the figures for the urine concentration for the $2\frac{1}{2}$-hour period varied from 150–225 cmm. per 100 cc. of urine, and there were no signs of intoxication. Some specimens of urine from persons arrested and subsequently convicted for drunkenness in this city gave figures 360–366 cmm. of alcohol per 100 cc. of urine. Further specimens are being examined in the hope of establishing a figure for the concentration which may be of service in estimating intoxication.

Summary.

1. The effect of certain foodstuffs taken previously to alcohol on the subsequent alcohol blood concentration curve in man is shown.

2. Once the maximum concentration of alcohol in the blood has been reached, provided the subject be at rest and external conditions are maintained constant, then the subsequent rate of disappearance of alcohol from the blood is independent of the concentration.

3. The effect of a previous meal of a foodstuff such as bread and milk in depressing the concentration curve is demonstrated. This is shown not to be due to delayed absorption, but to the fact that a considerable fraction of the alcohol ingested is never manifested in the blood stream.

4. Experiments are recorded of the attempts made to trace the fate of this fraction of the alcohol which "disappears."

5. The concentration of alcohol in the urine exceeds that of the blood over a period of 1–6 hours after ingestion by about 40–50 %; the passage of alcohol through the kidney into the urine cannot, therefore, be merely a diffusion process.

6. Under the experimental conditions employed the amount of alcohol excreted in the urine varies from 3 to 5 % of that ingested.

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