THE EFFECT OF ALCOHOL ON THE ABSORPTION OF GLUCOSE FROM THE ALIMENTARY TRACT.
Part II.

By NORA EDKINS and MARGARET M. MURRAY.

(*From the Physiology Department, Bedford College, London.*)

In Part I of this communication (1) it was pointed out that the only satisfactory way of studying absorption from the alimentary tract of such substances as glucose would be to recognise the presence of the absorbed substance in the blood stream and not rely simply upon its disappearance from the gut. In the case of sugar absorption this presents difficulties when working with anæsthetised or decerebrate animals because of the attendant variations of blood sugar evoked by the technique employed. There remain two alternatives, either to work with normal un-anæsthetised animals or to use some hypnotic which does not cause variations in the blood sugar level. The first of these methods is naturally ideal, and some preliminary experiments on normal rabbits showed that giving a constant amount of glucose caused the rate of absorption, as estimated by the blood sugar level, to be greater when alcohol was simultaneously supplied. This method was however rejected since different individual animals showed considerable variations at different times. Recourse was had therefore to animals under amytal (ethyl-isoamylbarbituric acid) for the production of anæsthesia, since this substance is stated by Page (2) to maintain deep anæsthesia without producing hyperglycæmia. Moreover, it gives, according to Deuel, Chambers and Melhorat (3), after an initial fall a constant blood sugar level, slightly lower than the normal, over periods as long as six to eight hours.

In the series of experiments about to be described amytal was employed as the anæsthetic throughout.

Method.

Cats were employed after 18 hours' deprivation of food, and without any preliminary anæsthetic were given an intraperitoneal injection of a 10 p.c. solution of amytal, made by dissolving 1 grm. of amytal in 8·85 c.c. half normal NaOH with gentle heating and adding water to 10 c.c. The

dose for the production of anæsthesia in a cat was 0·8 c.c. of this solution per kilo of body weight. Almost invariably the animals went under in ten minutes. Great care was taken during the experiments to keep the animals warm by means of rubber hot water bottles and flannels kept hot by electrical means. (It may be mentioned that amytal is said to lower the body temperature.) After tracheotomy the carotid artery on one side was exposed but not ligatured. A tube was tied into the œsophagus at the neck. A canula was placed in the femoral vein by which injections could be made. Directly these operations were completed a sample of blood was taken by a syringe from the carotid artery and the hole so made closed by a clip without occlusion of the vessel, thus the cerebral circulation was in no way interfered with. After the lapse of half an hour another blood sample was taken and the glucose solution introduced. The quantity of glucose given was comparable to that of the glucose tolerance test, that is, 2 grm. per kilo body weight in a concentration of 20 p.c. This solution was administered by means of the tube tied into the œsophagus and the remains were washed in with half the volume of water or, in experiments with alcohol, half the volume of 30 p.c. alcohol. Thus a final concentration in the gut was reached of about 13 p.c. glucose. Blood samples of 0·8 c.c. were taken at definite intervals in the way described above, and were followed by the immediate injection of an equal amount of saline to make up the blood volume.

The sugar was estimated by the method of Hagedorn and Jensen, employing 0·2 c.c. of blood and performing each estimation in triplicate.

The experiments fall into three series.

Series I.

Realising that there would probably be wide differences in the amount of alimentary hyperglycæmia caused by the administration of glucose in different animals, it was anticipated that a rather large number of experiments would have to be done, in some cases with glucose alone, in others with glucose and alcohol, in order to obtain a reliable average for any conclusion to be drawn with precision. The first set of experiments were carried out as follows. Glucose was given and the blood sampled at regular intervals until the sugar level was either constant or falling slightly, then alcohol was introduced in the quantity and concentration described above and the blood sugar again determined at intervals of half an hour. The expectation was that when the blood sugar was at its maximum height alcohol would, if it aided absorption, cause a further rise. This

anticipated rise was observed to take place as shown in the table of observations and graphs annexed.

Experiment	Initial blood sugar (mg. per 100 c.c.)	Maximum blood sugar with glucose alone	Maximum after alcohol
III	136	187	326
V	138	278	318
VI	120	210	252
VII	103	193	215
XI	129	197	242
XII	163	209	255
Average	132	212	268

Graphs of the course of changes in III, V and XI are presented in Fig. 1.

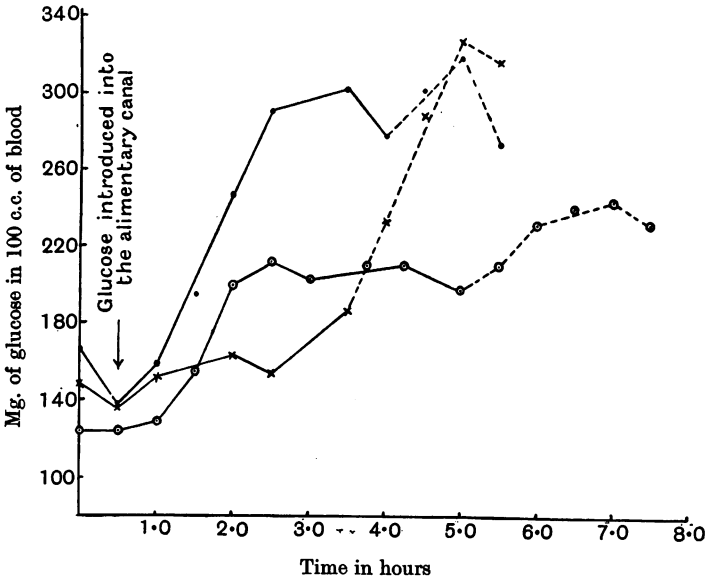

Fig. 1.

After introduction of glucose into alimentary canal ———
After introduction of alcohol into alimentary canal - - - - -

In considering these results there is first the obvious criticism that the effect of the alcohol when absorbed might have been to turn out glucose from the glycogen of the liver and muscles, and that the increase did not represent augmented absorption. If this were so, then alcohol introduced directly into the blood stream should cause a similar, or even a greater,

increase. In two cases when alcohol was introduced directly into the blood stream (*via* the carotids) a fall and not a rise was obtained. But to show definitely that the alcohol was not acting by glycogen mobilisation several experiments were made where alcohol alone was passed into the œsophagus and the effect on the blood sugar level noted. The alcohol would be very rapidly absorbed in a fasting animal (see E. Mellanby (4)). Nevertheless no marked rise resulted, as shown in the next series of observations.

Series II.

These experiments were designed to show the effect of amytal alone, and further, the effect of alcohol alone on the blood sugar level. Graphs of this series are presented in Fig. 2.

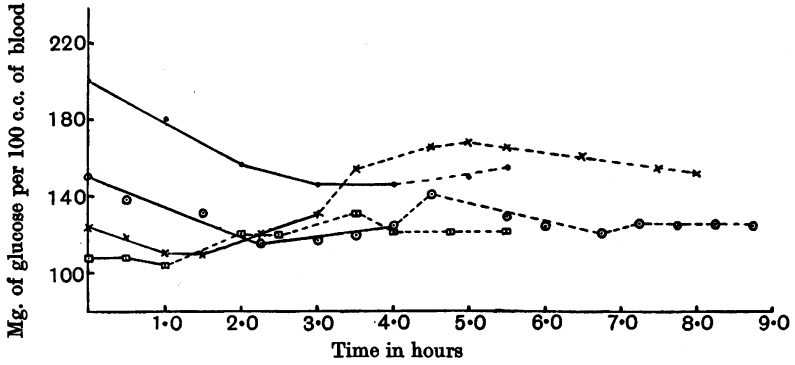

Fig. 2.

After injection of amytal ———
After introduction of alcohol into alimentary canal - - - - -

From these graphs it can be seen that the invariable effect of amytal is to produce an initial fall in blood sugar and then maintain a constant level in cats as in dogs. (See Deuel, Chambers and Melhorat (3).) The giving of alcohol alone causes but a very slight rise in the sugar level.

Series III.

Having obtained evidence that alcohol aids the absorption of glucose and that it increases postprandial hyperglycæmia, another series of experiments was performed to confirm the point definitely. In these a complete record was made of the rise of blood sugar due to giving glucose as described and, wherever possible, the return of the blood sugar to the original value. In short, these experiments were similar to the glucose tolerance tests in man. A fairly large number of experiments on these lines proved

to be necessary before any generalised statement could be made and before a standard could be fixed with which to compare results obtained in similar experiments where, in addition to sugar, alcohol was also given.

The results are best seen in the following graphs in Fig. 3.

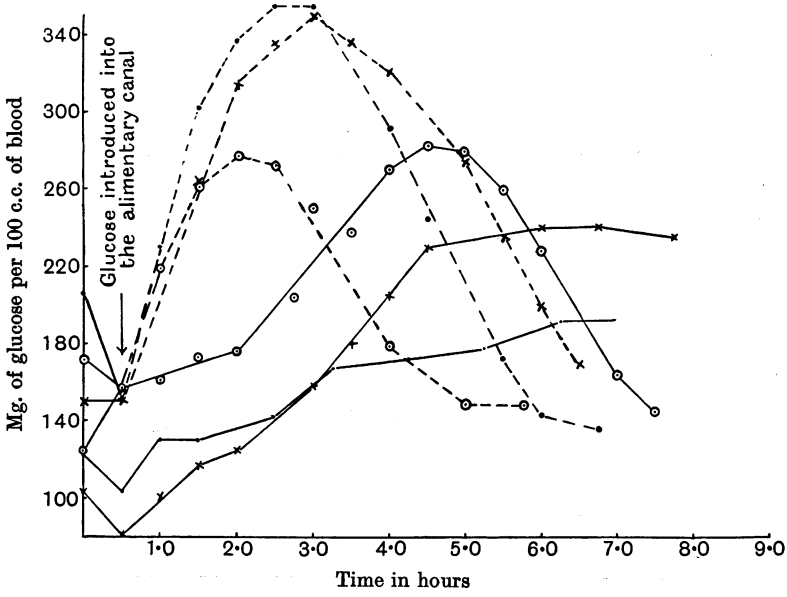

Fig. 3.

After introduction of glucose into alimentary canal ———
After introduction of glucose and alcohol into alimentary canal - - - - -

To facilitate the interpretation of these results several points require emphasis.

(1) The maximum sugar level occurs on an average (taken from a larger number of experiments than charted) four hours after the giving of the sugar, *i.e.* the absorption is slow.

(2) The average maximum figure for all experiments with glucose in the absence of alcohol is 232 mg. per 100 c.c.

(3) The fall in the blood sugar level is very slow, so slow that in most cases it was not possible in the experiments to follow the fall.

No doubt the reason of this maintenance of the hyperglycæmia is due to the lowered metabolic rate which is a characteristic effect of amytal, and also possibly to a decrease of the glycogenic function of the liver under this drug. That amytal does diminish the activity of the glycogenic function of the liver has been shown by Hindes, Boyd and Leese(5).

The experiments to be compared with these were carried out under exactly the same conditions. Proportionally the same amount of glucose was given and also a volume of 30 p.c. alcohol equal to half the volume of the glucose solution, resulting in a concentration of 10 p.c. alcohol. Again the results are presented graphically (see Fig. 3).

Emphasising the same points as before, we have: (1) the maximum sugar level occurs on an average two hours after giving sugar together with alcohol, (2) the average maximum sugar level is 311 mg. per 100 c.c., (3) the fall of the sugar level is more rapid. The explanation of the more rapid fall is not altogether clear. It might be that alcohol stimulated the metabolism and so led to a utilisation of the sugar or, that glycogen became formed. These possibilities could only be determined by observations of the metabolic rate and respiratory quotients. But leaving for the present the explanation of this more rapid fall we see that there is clear evidence of the augmentation of sugar absorption by the simultaneous administration of alcohol.

Whatever criticisms can be applied to results relating to absorption experiments obtained by estimating the rate of disappearance of the substance in question from the lumen of the gut, such criticisms cannot be applied to the experiments recorded here. The disappearance from the gut is definitely related to the appearance in the blood, and the conclusion is justified that alcohol accelerates the rate of absorption of glucose from the alimentary canal into the blood. Similar experiments are being performed along the same lines in normal human subjects.

Summary.

1. If glucose is introduced into the alimentary canal of an animal under amytal anæsthesia the blood sugar rises and reaches a maximum in about four hours after which it very slowly falls.

2. If alcohol is introduced with the glucose the maximum sugar level is reached in about two hours.

3. The average maximum level without alcohol is 232 mg. per 100 c.c. of blood; with alcohol it is 311 mg. per 100 c.c. of blood.

4. The blood sugar falls much more slowly to the normal value when alcohol is not given.

5. The influence of alcohol alone on the blood sugar level is shown to cause a slight rise.

6. Introduction of alcohol after the maximum level of alimentary hyperglycæmia with glucose alone has been reached causes a further rise in the sugar level.

7. From these observations it is concluded that the effect of alcohol is not greatly to mobilise liver glycogen but to influence directly the rate of absorption of glucose from the gut.

REFERENCES.

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