Moreover, sections from different kinds of necrobiotic tissue (tubercles, infarcts, tumors) which show a very intense plasmal reaction were equally positive with Bennett's stain, and the pattern of distribution shown by the two reactions was again identical. The same applies to myelin sheaths both in the brain and in peripheral nerves, although neither necrotic tissues nor myelin are known to be rich sources of ketosteroid hormones.

While ketosteroids under the conditions of Bennett's reaction do give phenylhydrazones similar to that of plasmal, the method is by no means specific for them, the less so as even a positive ketosteroid reaction would be completely masked by the incomparably more intense plasmal reaction. Only a ketone test which is directly positive without any previous oxidative treatment of the tissues can be accepted as a presumptive evidence for the presence of ketosteroids, if the possibility of a false positive reaction due to hydrolysis of plasmal can be ruled out.

*Summary.* Bennett's histochemical test for ketosteroids in the adrenal cortex is not a specific reaction since it merely indicates the presence of lipid bodies having aldehyde or keto groups. Lipid aldehydes, not related in any way to ketosteroids, are present in large amounts in the adrenal cortex.

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## Absorption of Carbohydrates in Humans.*

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The rate of absorption of glucose from the intestinal tract has been generally considered to be independent of both the concentration of glucose, and the absolute amount of glucose present in the intestine. However, observations on the absorption of various hexoses have revealed that the rate of absorption varies in the following order: galactose>glucose>fructose>mannose>xylose>arabinose.[1] The investigation by Cori was conducted on rats and the technic consisted of the oral administration of various carbohydrates in various dosages. After definite intervals the animals were sacrificed and the carbohydrate remaining in the intestine was determined.

In our own studies on insulin shock treatment, it was observed that the time required for the patient to rouse from coma was dependent on the concentration of glucose administered. In the ordinary procedure for insulin shock treatment, patients are awakened by the oral administration of 600 cc of 30% glucose, and they regain consciousness in about 15 to 30 min. Frequently patients failed to rouse from coma with 30% glucose and required the administration of glucose intravenously. In such patients, almost invariably, the administration of 600 cc of 5% glucose terminated the coma within a reasonable time. It was therefore thought of interest to determine the rate of absorption of glucose solutions varying from 5 to 30% concentrations.

*Method.* Patients were chosen from the wards of Bellevue Psychiatric Hospital, who were to all intents and purposes physically normal. The diagnoses of these cases included psychopathic personality and recovered reactive depressions in whom the situational defect causing the difficulty had been alleviated while the patient was in the hospital. On the morning of the experiment, patients received no breakfast and after a one-half hour rest in bed, a fasting blood sample was drawn from the antecubital vein. A 30 g dose of glucose in concentrations varying from 5 to 30% was administered by mouth and blood samples were obtained at intervals of 10, 15, 30, and 60 min. Blood sugars were

* Aided by a grant from the William R. Warner & Company Fellowship Fund.

1 Cori, C. F., *J. Biol. Chem.*, 1925, **66**, 691.

analyzed by the Wendel[2] modification of the Hagedorn and Jensen method.

With the second group of patients similar studies were made in which the total volume of fluid was kept constant and the concentration of glucose administered varied from 3 to 30%. Fasting blood samples were taken after a one-half hour rest in bed, and 200 cc of the glucose solution was administered by mouth. Blood samples were obtained subsequently at 10, 15, 30, and 60 min.

*Results.* The changes in blood sugar after the administration of 30 g of glucose in concentrations varied from 5 to 30% and are presented in Table I. It may be seen that the blood sugar rose in 10 min only with the 5 and 10% concentrations while the administration of 15 or 30% glucose showed no change. The administration of 600 cc of 5% glucose produced a maximum rise in the blood sugar in 30 min, and the rate at which the blood sugar rose exceeded the other concentrations. After the administration of 10% glucose the peak of the blood sugar did not occur within one hour, and the rise in blood sugar exceeded that observed with 15 and 30% glucose. There appeared to be no appreciable difference between the blood sugar curves after the administration of 15 and 30% concentrations. Data on experiments in which the total volume of solution administered was kept constant and the concentration varied from 3 to 30% are presented in Table II. Despite the fact that the dose varied from 60 g in the 30% concentration while only 6 g of glucose was ingested in the 3% concentration, there was no appreciable difference in the rise of the blood curve during the first 30 min at any of these concentrations. However, the one-hour specimen shows a

TABLE I.
Change in Blood Glucose After Oral Administration of Glucose (mg%)

| Pt. | 10 min | 15 min | 30 min | 60 min |
|---|---|---|---|---|
| | Dose—5% (600 cc) 30 g. | | | |
| 1 | 9 | 9 | 36 | 37 |
| 2 | 22 | 29 | 45 | 4 |
| 3 | 16 | 38 | 67 | 41 |
| 4 | 5 | 31 | 45 | 35 |
| 5 | 9 | 25 | 43 | 22 |
| 6 | 26 | 33 | 36 | 24 |
| 7 | 12 | 48 | 67 | 70 |
| Avg | 14 | 30 | 48 | 33 |
| | Dose—10% (300 cc) 30 g. | | | |
| 1 | 11 | 16 | 49 | 64 |
| 2 | 17 | 24 | 40 | 69 |
| 3 | 3 | 13 | 57 | 48 |
| 4 | 10 | 18 | 39 | 40 |
| 5 | 0 | 15 | 30 | 53 |
| 6 | 12 | 20 | 60 | 64 |
| Avg | 9 | 18 | 46 | 56 |
| | Dose—15% (200 cc) 30 g. | | | |
| 1 | 7 | 3 | 11 | |
| 2 | —2 | 3 | 22 | |
| 3 | —8 | 9 | 14 | |
| 4 | 4 | 17 | 27 | 32 |
| 5 | —2 | 1 | 44 | 19 |
| 6 | —2 | 0 | 36 | 70 |
| 7 | 5 | 7 | 36 | 24 |
| Avg | 0 | 6 | 27 | 36 |
| | Dose—30% (100 cc) 30 g. | | | |
| 1 | —4 | —6 | 22 | 13 |
| 2 | 5 | 10 | 25 | 15 |
| 3 | —3 | 6 | 10 | 24 |
| 4 | 6 | 5 | 23 | 29 |
| 5 | 1 | 3 | 18 | 49 |
| Avg | 1 | 4 | 20 | 26 |

TABLE II.
Change in Blood Glucose After Oral Administration of Glucose.

| Pt. | 10 min | 15 min | 30 min | 60 min |
|---|---|---|---|---|
| | Dose—3% (200 cc) 6 g. | | | |
| 1 | 7 | 19 | 25 | |
| 2 | 10 | 13 | 12 | |
| 3 | 3 | 3 | | |
| Avg | 7 | 12 | 19 | |
| | Dose—5% (200 cc) 10 g. | | | |
| 1 | 5 | 8 | 24 | 24 |
| 2 | 2 | 15 | 19 | —1 |
| 3 | 14 | 28 | 33 | 29 |
| 4 | —4 | 5 | 22 | 5 |
| 5 | 1 | 4 | 21 | —2 |
| 6 | 16 | 35 | 31 | 0 |
| 7 | 7 | 16 | 24 | 33 |
| Avg | 6 | 14 | 25 | 13 |
| | Dose—15% (200 cc) 30 g. | | | |
| 1 | 7 | 3 | 11 | |
| 2 | —2 | 3 | 22 | |
| 3 | —8 | 9 | 14 | |
| 4 | 4 | 17 | 27 | 34 |
| 5 | —2 | 1 | 44 | 29 |
| 6 | —2 | 0 | 36 | 70 |
| 7 | 5 | 7 | 36 | 24 |
| Avg | 0 | 6 | 27 | 39 |
| | Dose—30% (200 cc) 60 g. | | | |
| 1 | 9 | 15 | 26 | 18 |
| 2 | —3 | 7 | 33 | 48 |
| 3 | 4 | 3 | 32 | 37 |
| 4 | 10 | 10 | 9 | 63 |
| Avg | 5 | 8.5 | 25 | 42 |

[2] Wendel, W. B., *J. Biol. Chem.*, 1933, **102**, 47.

definite tendency toward a higher blood sugar with a greater dosage of glucose.

*Discussion.* The disposal of sugar in the animal body is dependent on 4 distinct processes: first, the absorption from the intestinal tract; second, the passage through the blood and its elimination in the urine; third, penetration through the tissues; and fourth, its synthesis by the tissues. There have been numerous investigations on the absorption of sugar from the intestinal tract and its passage into the blood stream. Cori[1] investigated the disappearance of glucose from the intestinal tract of rats by means of sacrifice experiments in which the amounts of glucose remaining in the intestinal tract at definite periods were analyzed. In his experiments glucose was administered in 25, 50, and 80% solution and he observed no difference in the rate of absorption of these concentrations. Similar observations on galactose, fructose and mannose revealed that the absorption of these sugars was also independent of these high concentrations in the intestine. Previous investigations on the absorption of sugars from the intestinal tract were directed towards a comparison of the various hexoses and no attention was paid to the concentration of the sugar.[3,4]

These observations are contrary to our own clinical observations on the effects of various concentrations of glucose on the time required to rouse patients from the insulin shock. The data reported in the present paper also indicated that glucose is more rapidly absorbed in the 5% solution than in the 30% solution. Since one factor involved in absorption through a semi-permeable membrane is the equilibrium established between the fluid in the intestine and the blood stream, it would seem on an *a priori* basis that differences would be observed in the rate of absorption with different concentrations of glucose in the intestine. This effect has been investigated in the animal by Darrow and Yannet[5] and Gilman.[6] These investigators found in experiments on dogs, rabbits, and monkeys that the injection of 5% glucose solution intraperitoneally resulted in the establishment of an equilibrium between the peritoneal fluid and the blood serum before absorption actually took place. During the initial period of several hours, glucose molecules passed into the blood stream while electrolytes appeared in the peritoneal fluid, and only after a considerable period was there an actual disappearance of fluid from the peritoneal cavity. In a typical example which Darrow and Yannet report in Table I on page 267, 500 cc of glucose was injected and after 6 hr they could recover 467 cc. There was a fall in serum sodium and chloride which appeared in the peritoneal fluid.

There is some indication in Cori's article that such a process may well take place in the intestinal tract. On page 706, he reports, "It was noted that the rats showed a greatly distended stomach when examined 1 to 3 hr after sugar feeding. This suggested that the stomach water was attracted by a hypertonic solution." In view of the observations of Darrow and Yannet, it seems unlikely that the only process was the attraction of the water due to the hypertonic solution but rather that there was an attempt to equilibrate the intestinal solution with the blood serum, which would involve the passage of electrolytes into the stomach and intestines with the fluid.

*Summary and Conclusions.* We have presented blood sugar curves in human patients following the oral administration of glucose solutions varying from 5 to 30%. The initial rise in blood sugar during the first 30 min was more rapid with the lower concentration. It was also noted that the administration of 5% glucose solution to patients in insulin coma produced a more rapid arousal from the coma than with the 30% ordinarily employed. These results are in contrast to earlier work indicating that the absorption of glucose was independent of its concentration in the intestine. This evidence supports the hypothesis that the absorption from the intestine is at least partially dependent on the establishment of an equilibrium between the intestinal solution and the blood serum.

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[3] Nagano, J., *Arch. Geo. Physiol.*, 1902, **90**, 389.

[4] Hewitt, A., *Biochem. J.*, 1924, **18**, 161.

[5] Darrow, D. C., and Yannet, H., *J. Clin. Invest.*, 1935, **14**, 266.

[6] Gilman, A., *Am. J. Physiol.*, 1934, **108**, 662.