THE ABSORPTION OF DEXTROSE AND WATER FROM THE CHRONIC ISOLATED LOOP IN DOGS

By

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Foreword

I wish to express my sincere appreciation for the invaluable suggestions and encouragement given me by Dr. G. E. Burget and for the help of Robert W. Lloyd in the actual experimental work performed.

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Master Thesis

Absorption of Dextrose and Water From The Large Bowel

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The Absorption of Dextrose and Water
From the Chronic Isolated Loop in Dogs

Much has been said and written on the efficacy of introducing fluids and nutrient substances into the colon. The exact date at which this procedure was first begun is uncertain, but the use of such enemas as a source of energy and fluid has been handed down to us as a time proven therapeutic method. This therapeutic procedure is used in some form in almost every large hospital and by a large percentage of the reputable practitioners of medicine. There are records of patients being kept alive for fifteen months with no other source of nutrition.[22] In spite of the long period of use, this method has, until very recently, been on an imperical basis. Many times when walking through the wards, I have observed this method in use. Upon asking the attending physician why such a method was being used and how much absorption of sugar and fluid could be expected, the answer was always a proof of the above statement as to impericism. In reviewing the literature, in an attempt to find the different mixtures of nutrient solutions and mixtures given per rectum, one is astounded at the countless types of prescriptions. Almost every conceivable substance, either alone or in combination is described. These prescriptions include meats, fruit, milk, etc. Some have lauded the use of the addition of various chemicals, such as NaCl and $NaHCO_3$, for the purpose of speeding up the absorption of water and sugar. The per cent of sugar solutions used shows wide variations.

While we realize that no one set of experiments can definitely decide this question, the following series of experiments and their results, is given with the hope that it will add to the experimental evidence already recorded.

The feasability of using the chronic closed loop of the dog's small intestine for the study of absorption has been amply shown.[28, 29, 30, 31, and 32] Using a technique, similar in major respects to that described by Martzloff[30] we have succeeded in making chronic closed loops of the colon in some twenty-two dogs. The dogs have recovered, in 75 per cent of the operations, lived a normal life and are seemingly very good experimental animals. One animal, number 9, has been used for almost one year with no change in her general condition, or in the absorbing ability of the loop. The use of narcotics has been eliminated, trauma minimized, and psychic factors avoided. Histological studies on the mucosa of the colon loops from posted dogs have not been performed. There was no demonstrable changes in the mucosa of chronic loops of small intestine,[30] and there is no reason to believe the findings would be different in the case of colon mucosa. Grossly the mucosa appears normal, even after long periods of time have elapsed between the date of operation and the sacrifice.

All the absorption experiments were performed on dogs apparently in the best of health, with a minimum of trauma, without the use of narcotics and using the chronic closed loops of the colon. This method removes the above objectionable factors, allows for controlled analysis of the substances tested, and removes the variable factors of regurgitation into the ileum and contamination by fecal material encountered in most of the previous work.

In order that the reader may have a more complete conception of the work previously reported, a more detailed review is given.

Review of Literature

Several of the earlier experiments are interesting because of the conclusions drawn on such scanty and sometimes obviously faulty experimentation. Reach[1] in 1902 concluded that dextrose was absorbed, upon injection per rectum, because of a slight increase in respiratory quotient. Hari and Halasz[2] separated the large and small bowel in the dog by ligation. They believed an actual glycosuria and increase in respiratory quotient was proof of sugar absorption. Ornstein[3] injected glucose per rectum, with and without starch. He believed that glucose was absorbed in small amounts when given alone, and almost in toto when given with starch.

Nagel[4] reports the study on patients by Czerny and Latschenberger, and refers to the experimental studies on dogs by Heile. He concluded that glucose is absorbed from the rectum and colon. Tallerman[5] has recently reported observations on human subjects free of demonstrable rectal pathology. Within thirty to ninety minutes after injection of 60 grams of glucose in 180 cubic centimeters of normal saline, an average increase of .019 per cent in the blood sugar was noted. He concluded that some glucose was absorbed.

Rubino and Varela[7] in 1922 reported studies on normal human subjects, using rectal injections in varying strengths of glucose, levulose and galactose, and found no sufficient increase in blood sugar to indicate absorption.

Franke and Wagner[8] studied blood-sugar curves of dogs after rectal injections of 25 grams of glucose in a 25 per cent solution and found no actual evidence of sugar absorption. Levi[9] studied the effects of rectal injections, using 500 cubic centimeters of glucose solution, ranging in strength from 10 to 16 per cent, with human subjects that included normals, diabetic patients and post-operative cases. Four of the eight diabetic patients studied showed no early rise in the blood sugar curves. All of the diabetic patients showed a decrease in blood sugar after the first thirty minutes following injection, with an average decrease at the end of two hours of 29 milligrams below the level of the fasting blood sugar. Levi concludes that at best only small amounts of glucose are absorbed from the colon.

Pressman[11] has published studies on seven human subjects. He has used a hypertonic glucose solution of 33-1/3 per cent strength, injecting 250 cubic centimeters into the rectum in a ten-minute period, and studied the blood-sugar curves for the succeeding four hours. None of the blood-sugar curves of his series show definite evidence of glucose absorption and, in each case, the blood sugar value at the ninety minute period after glucose injection is at, or below, the level of the fasting blood sugar figure. Pressman also shows the recovery from stool following the glucose enema of an average of 24 per cent of the total sugar injected, with the high value of 42 per cent in one instance after the sugar had been retained in the bowel four hours. Implantation tests of glucose and stool mixtures showed the loss of a large amount of the glucose through the activity of intestinal bacteria.

Cannon[12] in 1902 stated that there was little or no absorption from solutions in the colon or rectum.

McNealy and Willems,[10] in a recent report, show the results of studies on fifteen dogs, under barbitol and ether anesthesia, with isotonic glucose solutions. Loops of the ileum and of colon were isolated from the remaining bowel by ligation. After washing both loops with saline solution, from 50 to 75 cubic centimeters of five per cent glucose solutions were injected and allowed to remain one hour. They concluded that very little five per cent glucose is absorbed from the colon, but that water, water and salt are readily absorbed from the same.

In a further study[15] of the effects of chemical excitants and stimulants on the absorption rate, he experiments with 2.5 per cent dextrose in 0.45 per cent saline, 5 per cent dextrose plus 6 per cent alcohol. He concluded that a small amount of dextrose can be absorbed from a saline-dextrose solution, and infers that the presence of sodium chloride increases the rate of absorption slightly. Dextrose was not appreciably absorbed from a dextrose-sodium bicarbonate solution, and alcohol did not increase the very low absorption rate.

Smith[14] presents the above cited examples in a review of recent date. He performed no experimental work but concludes from these that there is a possibility of glucose acting in the bowel much the same as a salt that is absorbed to but little or no degree, when the salt is the main factor in excreting osmotic pressure, and that the effort to bring about osmotic equilibrium might result in a reversal flow of fluid into the bowel lumen and result in an increase, rather than a correction, of an existing dehydration of the tissues. He believes that the blood sugar can be decreased by the instillation of glucose in any strength into the bowel, and that it is possible to bring about a degree of hypoglycemia in this way in the more sensitive patient that would be sufficient to lower both blood pressure and blood volume, or disturb the acid-base balance similar to that seen in over-dosage of insulin in diabetics, with a sharp shift to an alkalosis. Further that such circulatory disturbance, without an associated chemical imbalance, may complicate and prolong postoperative convalescence.

This is a grave accusation of a time tried therapeutic measure on such inconclusive experimental data, and it is significant that Doctor Toland and Doctor Ward in the discussion of his paper have accepted his conclusions wholeheartedly and both condemn the therapeutic enema.

Varela and Rubino[16] tested the peripheral blood and the urine for sugar after the injection of large amounts of 40 per cent dextrose into the rectal ampulla. They concluded that small amounts are absorbed shortly after injection, but that the colon soon becomes irritated and expells the enema. McLester,[17] Friedenwald, and Pureah teach that glucose per rectum is valuable source of nutrition, but give no experimental basis for this.

Scott and Zweighaft[20] studied the blood sugar in man following the rectal administration of dextrose. They found no rise in the blood sugar and concluded that the slight drop in blood sugar might be due to a stimulation of pancreatic activity resulting from the absorption of slight amounts of glucose. They recovered a variable and frequently considerable amount of dextrose from the stools after a period of two and one half hours.

Ebeling[19] in a recent article on the absorption of dextrose from the colon gives the following excellent review of the literature. The references given by him, not including those previously cited in this paper will be quoted.

"Voit and Bauer performed the first systematic research on the absorptive mechanism of the colon. Their experiments were performed with albumin, and they stated that the addition of sodium chloride assisted in the absorption of that substance. Czerny and Latschenberger reported studies on two patients in whom the entire large intestine, or part of it, had been completely cut off from the small intestine. In these they obtained evidence which indicated that dextrose was absorbed. Deucher reported that he gave five enemas to a patient during nineteen hours, each containing 40 grams of dextrose. One hundred and fifty-four grams of dextrose was absorbed, constituting 77 per cent of the amount introduced. Zehmisch, working with human beings, gave 152 grams of dextrose per rectum and lost 103 grams (67.5 per cent), supposedly by absorption. Ornheim gave 50 grams of dextrose by bowel to diabetic patients. He was able to recover only 3 grams of dextrose after a period of five hours. He did not believe that bacterial action could account for the dextrose that had disappeared. Boyd and Robertson fed seven women on nutrient enemas for from six to seven days. Each day the bowel was washed out and the contents analyzed. Urinary nitrogen was used as a gage of the absorption of nitrogenous substances. They reported that in two cases 100 per cent of the introduced dextrose was absorbed. They lost as much as 61.8 and 81 Gms. of dextrose during twenty-four hours, but recovered the bulk of the protein in the rectal washings. After having incubated dextrose solutions which were contaminated with colon bacilli, they concluded that the dextrose lost by bacterial action was insignificant. They were not able to produce dextrosuria with the amounts they administered. Halasz, working with patients, placed clysters in the large bowel and, in from five to six hours, found that from 50 to 200 Gm. of the dextrose had disappeared. He accounted for only 0.5 to 1 per cent of the dextrose as lost by bacterial action. Mutch and Ryffell gave four enemas to each of several patients during a twenty-four hour period. Each enema consisted of 450 cubic centimeters of 6 per cent dextrose. When the nutrient enemas were well tolerated, they increased the dextrose to 60 Gm. to the pint of solution. Using a "washout" method of experimentation, they concluded that dextrose could be satisfactorily administered by this route to a maximum of 700 calories per day. Carpenter in two experiments on human beings, gave 30 Gms. of dextrose in 500 cc. of physiological solution of sodium chloride. Within two or three hours after the injection, the respiratory quotient changed from 0.02 to 0.05. He found that 17.5 Gm. of dextrose was absorbed in one instance, and in the other 26.3 Gm. Similarly, five hours after the administration of 60 Gm. of dextrose, he found that 34.6 Gm. had apparently been absorbed. The quantitative results were based on the "washout" method, using more than one lavage.

Bingel investigated the absorption of dextrose in diabetic patients. He concluded that only small amounts of dextrose were absorbed. One hour after having placed 35 Gm. of dextrose in the bowel, 31 Gm. was recovered from the stool. Bingel incubated fecal material with added dextrose, and claimed that the dextrose lost was almost as great as that supposed to have been absorbed.

De Takats, in 1931, gave 1,000 cc. of 5 per cent dextrose to patients under the skin, by mouth and by bowel. The blood sugar level rose after introduction of dextrose under the skin and by mouth. When the dextrose was given by rectum, the blood sugar fell during a period of two hours. He noted that no dependance could be placed on the amount absorbed by rectum, and that insulin reactions occurred when this method of entry was depended on in the diabetic person."

Perusse[21] has recently published data on the subject and believes that a 1 per cent dextrose solution is most efficient in preventing dehydration and in supplying a limited amount of nutrient.

Ebeling[19] has recently, 1933, published the result of experiments on dogs under barbitol anesthesia. His experiments are perhaps subject to less criticism than those of any other worker referred to. He checked the absorption of 5, 7 and 10 per cent solutions of dextrose in water, using dogs with normal, high and low blood sugars. The absorption of dextrose was measured in three ways; i.e., by recovery and washings, peripheral blood sugar studies, and colonic blood sugar studies. The absorption period was two hours. He concluded that dextrose solutions are absorbed at a slow rate when placed in the entire colon of the dog; that hypertonic solutions (10 per cent) are absorbed little faster than isotonic solutions; that when a marked dextrose deficit occurs in the blood, dextrose can be absorbed from the colon approximately as rapidly as it can be from a low ileal loop of the noninsulinized dog; that the presence of dextrose in the solution in the colon, in the concentrations used, causes a retardation in the rate of water absorption; and finally, that the total amount of dextrose which can be administered and absorbed from the colon under the best conditions would appear to be too small for any considerable immediate therapeutic effect.

Boas[23] believes that rectal feeding has been overestimated and that only water absorption is of any real value. Montague,[24] in a review of systemic results of drug administration per rectum, believes that in many cases it takes less of the drug as it may be absorbed by the inferior hemorrhoidal veins and so miss the liver.

In the above review of the literature one is impressed with the wide diversity of results and opinions. It seems quite evident that the clinician is still unable to critically judge the therapeutic value of the rectal enema.

Criticism of Experimental Results and Conclusions

In most instances no attempt to prevent regurgitation of material from the colon into the small bowel was made. This has been shown by Cannon[12] to be an important physiological result when the colon is distended.

Smith[14] reports that, "Diabetic patients will show a marked variation in the readiness with which liver glycogen may become mobilized in response to nervous stimulation and to mechanical pressure change in the intestinal tract. The sensitive patient can show a slight blood sugar rise from the insertion of the rectal tube, with a later and more marked increase in the blood sugar if the amount of solution introduced into the rectum is sufficient to cause pressure within the lumen of the gut. Such increases in the blood sugar do not indicate, necessarily, that glucose is absorbed. In fact, slight increases may appear in blood sugar when distilled water or simple saline solution are injected into the rectum in small amounts. The very slight increases in respiratory quotients that have been reported might be influenced by the reversal change to glycogen synthesis that could follow the increases in blood sugar from stimulation.[11] Brodie[6] and his collaborators report that distilled water instilled into the bowel will cause increased oxygen consumption."

McNealy and Willems[10] published some of the first accurately controlled experiments but used narcotized, traumatized animals and based their conclusions on a very few experiments.

Most of the solutions used were hypertonic with the blood and tissue fluids. Theoretically a 4.9 per cent solution of glucose is isotonic with a 0.9 per cent saline solution. Solutions more concentrated than 10 per cent will draw fluid into the bowel lumen and, according to Goldschmidt[13] hinder the absorption of glucose. Hausmann[18] has caused the death of rats by injecting 50 per cent glucose into the peritoneal cavity and thereby withdrawing the fluid from the tissues into the peritoneal cavity.

With the exception of a few workers, especially McNealy and Willems,[10] and Ebeling,[19] the blood sugar estimations were made only on the peripheral blood. Since the blood from the digestive tract is subject to the metabolic activity of the liver before it reaches the peripheral circulation, such determinations are not necessarily an index of absorption.

Our own work,[25] in which we analyzed the blood sugar from veins from isolated, chronic ileal and colon loops and systemic blood sugar simultaneously, would seem to indicate that the peripheral blood sugar is not an indication of intestinal absorption of small amounts of levulose or dextrose. Magee and

Reid,[26] however, believe that the systemic venous blood sugar is as good an index of intestinal absorption as portal blood sugar. Cori,[27] after the investigation of the alimentary absorption of dextrose, has concluded recently that the peripheral blood sugar is not a measure of intestinal absorption.

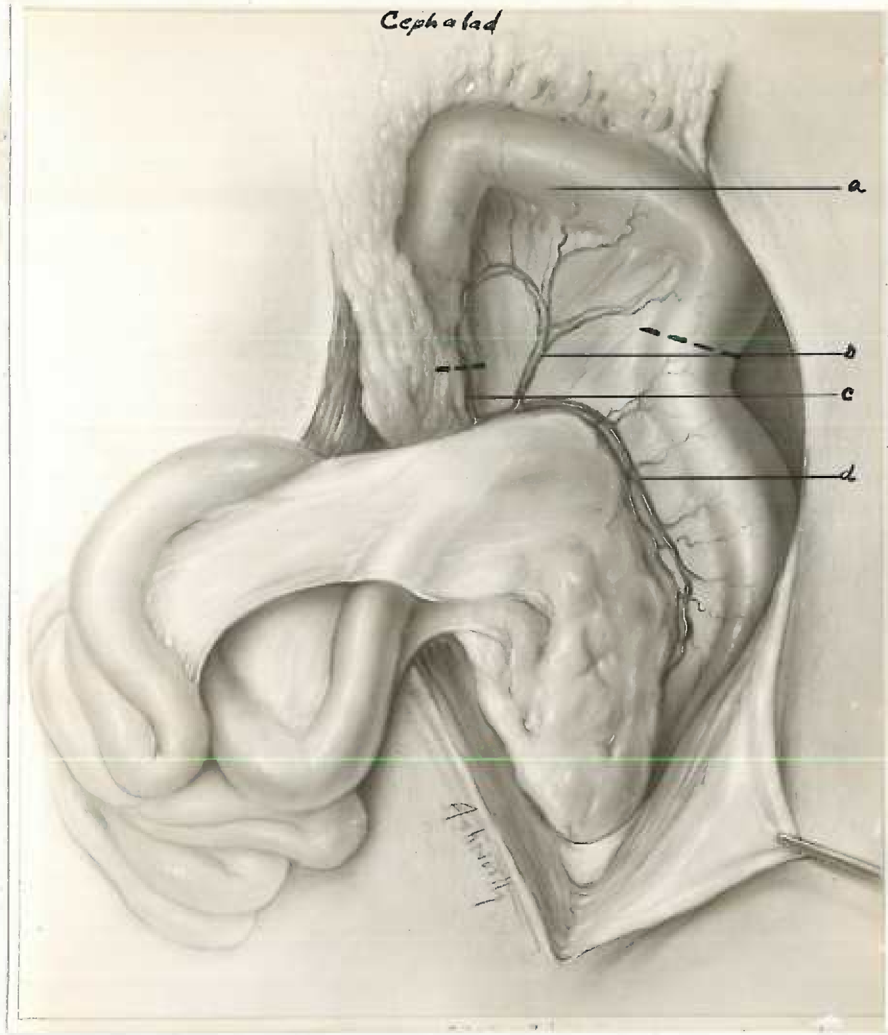
With few expections, no effort has been made to determine the effect of fermentation by the many organisms in the colon.

In a summary of the above points the important facts are: (1) That regurgitation of material from the colon into the ileum is a vital factor in the intact intestinal tract; (2) That the peripheral blood sugar is probably not an accurate indication of absorption of dextrose from the colon; (3) That changes in the respiratory quotient are not reliable as an indication of the same; (4) That varying percentages of dextrose will influence the absorption of water and probably dextrose; (5) That bacterial action on the injected sugar should be determined, especially where the absorption period exceeds one hour; (6) And finally, that narcotization and visceral trauma have been overlooked as possible factors influencing absorption of both water and dextrose in experimental investigations on laboratory animals.

Technique

I. Operative Technique

Dogs weighing 35 to 40 pounds, preferably between the ages of 1 and 3 years, and in apparent good health were selected for the operation. The dogs were starved for twenty-four hours and given an enema of soap and water immediately before operation. At least one pint of solution should be used, since it is extremely important to have the colon empty of fecal material. After expulsion of the enema we routinely gave a hypodermic of morphine (1/4 grain) and atropine (1/100 grain). Absolute surgical asepsis was maintained throughout the operation. Since the technique of the operation is fundamentally the same as that given by Martzloff[30] for loops of small intestine, I will mention only those points of difference when the large intestine is being used. A left rectus incision, 7-8 cm. long, parallel to and 2.5 cm. from the linea alba, and so situated that the umbilicus marked the midpoint of the opening, was made. The descending colon was located and carefully drawn through the incision.



a-transverse colon; b-rt. colic vessels; c-ileo-colic vessels; d-Median colic vessels. Clamps placed at dotted lines.

The descending portion of the dog's colon is supplied by the median colic artery which runs parallel to the large intestine. The transverse colon is 8 to 12 cm. in length and is supplied by the right colic artery. The short ascending portion is supplied by the ileo-colic artery. The transverse portion is isolated by clamps and separated from the remaining large intestine.

The blood and nerve supply to this segment remains intact and in the subsequent handling and attachment of the loop to the anterior abdominal wall great care should be taken to avoid torsion, undue pull or relations that may later obstruct the blood supply. Before clamping or in anyway injuring the intestine a thorough inspection of the colon should be made. (1) The colon should be free of fecal material. If the fecal material has not been entirely expelled and is not too hard, one may carefully milk this material distally until the desired segment is empty. Severe trauma should be avoided, since it results in constriction of the powerful intestinal muscle coats and manipulation following is exceedingly difficult or impossible. (2) The transverse colon should be at least 10 cm. long in the relaxed state. If shorter than this the contraction, following clamping and inversion of the ends by suture, will results in an impractical loop. (3) The mesentery to the transverse colon should be of sufficient length to allow for attachments of the loop to the anterior body wall without tension on the attachments or mesenteric pedicle. (4) The length of the proximal colon, or part supplied by the ileo-colic artery, should be at least 4 cm. Since the caecum is attached by mesentery to the peritoneal surface of the posterior abdominal wall a free transverse portion of this length is necessary for anastomosis with the descending colon. If these conditions are not all met we have considered it advisable to close the animal and select another. We have found only 3 dogs in 25 in which we decided against the completion of the operation.

The attachment to the anterior adominal wall is made with the long axis of the loop parallel to and very near to the mid-line, the anastomosed colon being kept lateral to the loop and its mesentery. The only practical difficulty we have had is at this point. Either because of the more powerful contractions of the large bowel, or because adhesions are formed with greater difficulty, the large bowel loop is much more difficult to keep snugly attached to the abdominal wall. Very little difficulty is experienced in attaching the loop of the small intestine. In attaching the loop of large bowel, traumatization of the surfaces to be opposed should be thorough, and the placing of single interrupted sutures in a slightly staggered fashion so as to bring a broad surface of intestine against the peritoneum seems of value. Even this technique will insure a permanent attachment in less than 50 per cent of the animals. Attachments may be satisfactory for several weeks. At this time a stretching of the attaching adhesions may be noted and it may be so extreme that a re-attachment becomes necessary.

Post Operative Care

This is, in most cases, very simple. The dog is allowed water four to five hours after the operation. Small quantities of ground meat, or similar low-residue food is given twenty-four hours after the operation. Full portions of low-residue food are given on the fourth day and the usual diet resumed at the end of one week. Careful observation for straining in an attempt to defecate, for stretching and for vomiting, will usually indicate loop distention. Post-operative aspiration was necessary in six of twenty-two dogs operated on. Early in the series we lost two dogs by rupture of distended, unaspirated loops. Both dogs died within six days of the operation. In the absence of the above symptoms aspiration is not advisable since the loop may be torn away from its point of attachment before adhesions are organized.

According to the general condition of the animal actual experimental work is begun ten to fourteen days after the operation. The care of the dogs from this time on is similar to that of any normal animal. Aspiration for loop distention after post-operative healing is complete, probably always means an obstruction to the venous return from the loop or some severe intra-abdominal irritation. One dog in our series was discarded because of repeated loop distention, resulting from an obstruction to the venous return from the loop.

II. Analytical technique

Pfanstiehl dextrose, having a specific rotation of + 52.5° at 20° C., was accurately weighed and dissolved in distilled water. These solutions were diluted to a standard volume in accurate volumetric flasks. As a further check on the accuracy of the solutions each new sugar solution was checked by the same method and measuring apparatus as was used in analysis of the fluid withdrawn from the loops. Where sodium bicarbonate or sodium chloride was added, the amount was accurately weighed against checked weights.

The washing of the loop and injection of material to be analyzed is very simple. The abdominal wall is shaved over the point of loop attachment and cleansed with 70 per cent alcohol. A 20 cc. glass syringe is fitted with a 19 gauge needle, 1½ inches long and both aresterilized by boiling. The needle is inserted into the loop with a quick thrust, and sterile 0.9 per cent sodium chloride, at body temperature is injected. The injection of salt solution has two purposes; first, to verify the entrance of the needle into the loop, and second, to wash out any accumulated mucosal debris. After the first few experiments on any given animal the loops of colon usually remain clean, and very little foriegn material is every withdrawn. (This is in marked contrast to the loops of the small intestine. These are liable to much greater variation in activity and consequently are much harder to keep in a useable condition.) The loop is washed and completely emptied of the fluid used for washing. The required amount of sugar solution is then accurately measured into a second syringe and injected. The syringe used for the sugar injection is then rinsed out with distilled water, the rinsings are saved and analyzed with the unabsorbed sugar aspirated from the loop. We originally analyzed the sugar rinsed from the injection syringe separately, but found the amount to be less than 0.05 Gm. We later added this to the withdrawn solution and determined this amount simultaneously. This gives a more accurate estimation of the amount absorbed and eliminates the small, variable amount which might havebeen lost by adherence to the syringe, used for injecting.

The dog is then released from the table and allowed to pursue its normal inclinations for the period allowed for absorption. At the end of this period the fluid containing the unabsorbed material is withdrawn and the amount of fluid measured. The remaining sugar in the loop is washed out by injecting and withdrawing three 15 cc. quantities of normal saline.

On a check for the accuracy of the above procedure we have injected a known quantity of sugar, immediately withdrawn and analyzed the amount of sugar aspirated. The error has been within 3 per cent.

The aspirated fluid, plus the syringe and loop washings, is diluted to a standard volume of 100 cc. in a volumetric flask. After the proper dilution of this fluid it is analyzed by the Shaffer-Hartman method as modified by Haskins and Holbrook.[33, 34] Repeated checks on known solutions have shown that in the dilutions used the small amounts of protein, sodium chloride or sodium bicarbonate do not affect the accuracy of the method in analyzing the per cent of contained dextrose. (This method may be used for the analysis of levulose and galactose by adding 10 per cent to the amount of dextrose which corresponds to the titration figure.[31,32] It is not accurate, however, for the determination of mannose.[35])

The amount of sugar as determined above, is subtracted from the known amount injected and the difference recorded as sugar absorption.

The determination of sodium chloride was by the method of Volhard.[36]

Problems and Results

1. The amount of dextrose and water absorbed from 10 c.c. quantities of a 5 per cent dextrose solution in water, in varied time intervals allowed for absorption.

This series of 29 experiments was performed in an attempt to prove or disprove the actual absorption of sugar from a solution approximately isotonic with the blood and tissue fluids. The amount of sugar absorption for the various absorption periods is shown in table 1.

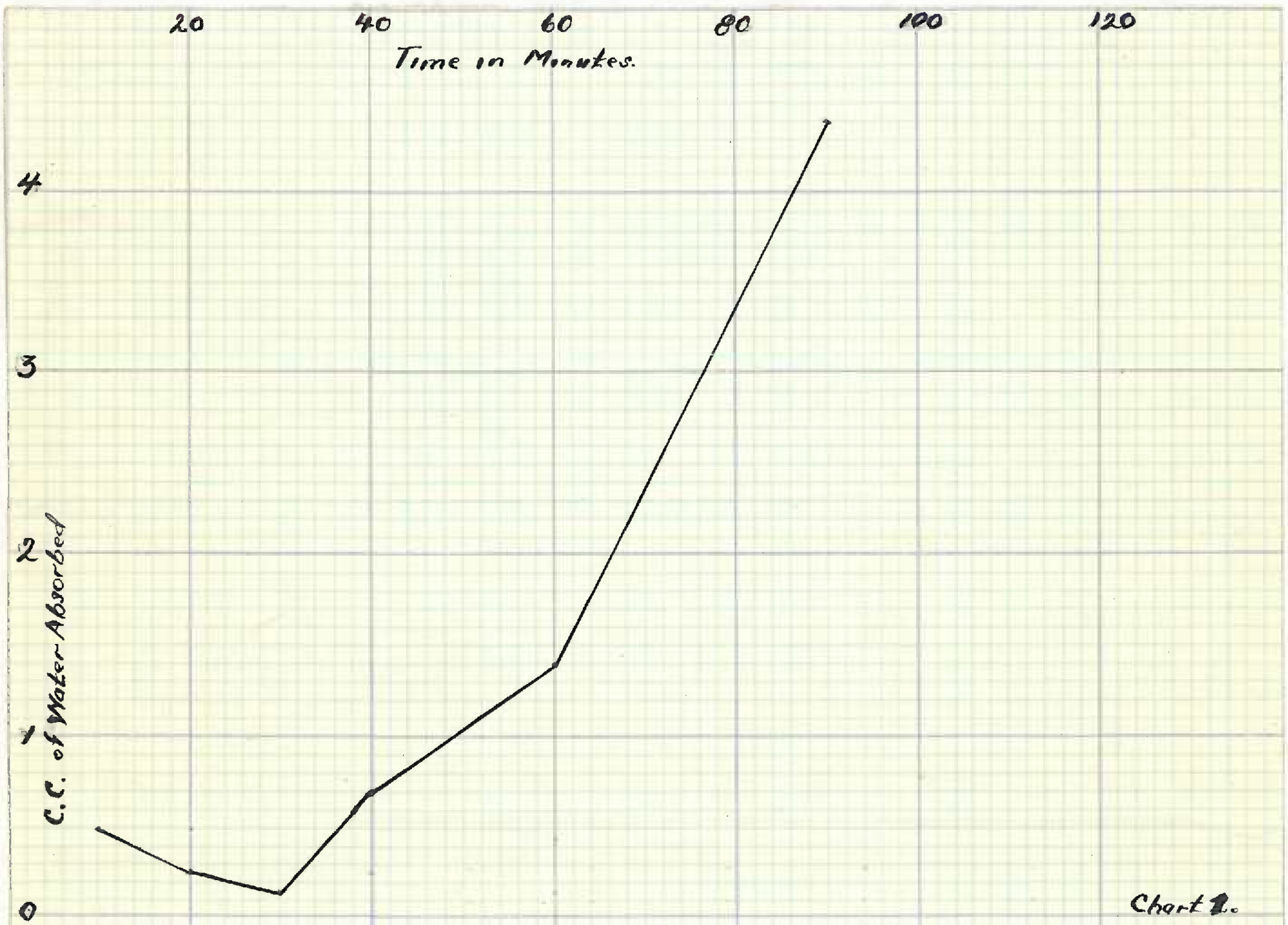
Table I

Absorption of Glucose After Injection of 10 c.c. of a 5% Solution

Time in Min.	Grams Absorbed				
	Dog 9	Dog 12	Dog 17	Dog 18	Average
10	0.07	0.10	0.05	0.08	0.07
20	0.09	0.10	0.09	0.09	0.09
30		0.12	0.09	0.08	0.10
40	0.08	0.23		0.14	0.15
60	0.12	0.22	0.14	0.30	0.19
90	0.24	0.31		0.33	0.29

In the time allowed for absorption, we believe that the loss of sugar by bacterial action is insignificant (see below). If the loss of sugar was due to poor withdrawal technique, the amount lost would not be an increasing one.

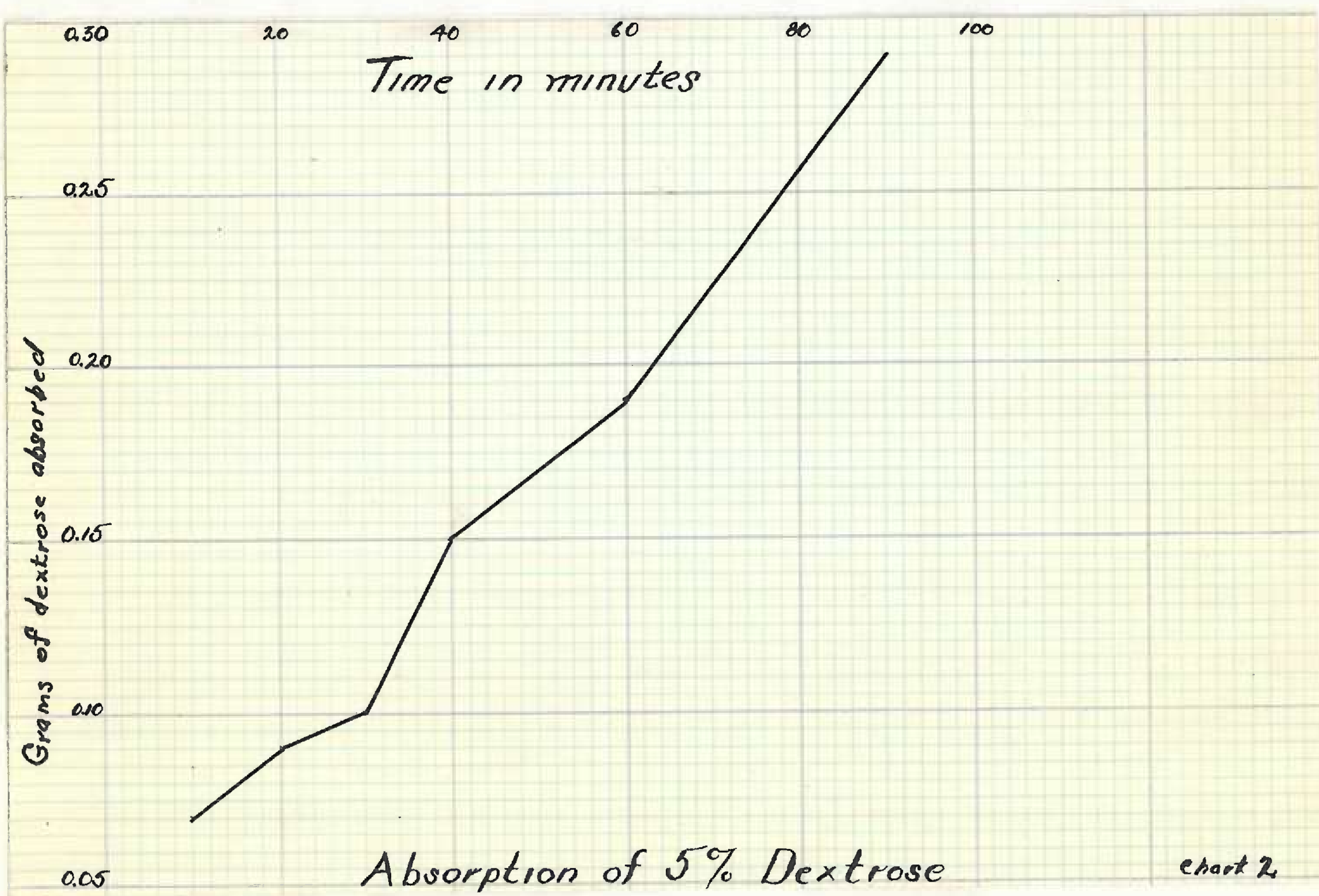
See chart of average absorption.



Absorption of Water from 10c.c. of 5% Dextrose Solution

Furthermore, this technique has been checked and found to be accurate within 3 per cent variation.

This data also lends important evidence for the active absorption of dextrose by the mucosa. If water alone is absorbed, and sugar is lost only by diffusion, then as the water was absorbed the concentration of dextrose and consequently the rate of diffusion would increase. This is evidently not true because the graph representing the absorption of water is almost a straight line. A study of the amount of water absorbed (Chart 1) shows us that this amount is not proportional to that of sugar absorption. Very little water is taken up in the first hour period, whereas almost half of the sugar is absorbed. This is strong evidence for the active absorption of dextrose regardless of the concentration of sugar.



2. The amount of dextrose and water absorbed in a one hour period from 10 c.c. of a 20% solution of dextrose in water. A total of 29 experiments were performed.

The amount of sugar absorbed is shown in Table 2.

Table II

Grams of Glucose Absorbed in one Hour Following Injection of 10 c.c. of a 20% Solution

	Dog 6	Dog 7	Dog 9	Dog 10	Dog 12
	0.75	1.34	0.39	0.38	0.52
	0.76	1.30	0.35	0.45	0.48
	0.83	1.57	0.32	0.56	0.51
	0.58	1.20	0.32	0.72	0.32
	0.78		0.36	0.73	0.34
			0.39	0.77	
			0.39		
			0.29		
			0.36		
Average	0.74	1.35	0.35	0.60	0.43

When this concentration of sugar is used the amount of fluid withdrawn at the end of a one hour period averages 20 to 25 c.c. It is evident that a considerable influx of fluid followed the injection. The distention produced by this often caused the animal to stretch and defecate. At autopsy the loop of dog number seven was found to be much larger than the average. This explains the greater absorption recorded for this animal.

3. The absorption of sugar and water, from 10 c.c. of a 10 per cent solution of dextrose in water, in one hour. Twenty-five experiments were performed. The amount of sugar absorbed is shown in Table 3.

Table III

Grams of Glucose Absorbed in one Hour from Colon Loop following Injection of 10 c.c. of a 10% Solution

	Dog 9	Dog 12	Dog 18	Dog 21	Dog 22
	0.19	0.20	0.27	0.22	0.24
	0.19	0.25	0.24	0.22	0.20
	0.20	0.22	0.27	0.19	0.22
	0.18		0.27	0.21	0.21
	0.19		0.25	0.20	
	0.18		0.22	0.18	
Average	0.20	0.23	0.25	0.22	0.22

The amount of sugar absorbed by a given animal in repeated experiments is remarkably constant. The average amount of fluid withdrawn was 12 c.c., and the animals never gave evidence of loop distention.

4. The absorption of dextrose and water from 10 c.c. of a solution containing 2.5 per cent dextrose and 0.45 per cent sodium chloride.

This solution is approximately isotonic with blood and tissue fluids. Ten experiments were performed. The total amount of sugar injected was 0.25 Gm. The average amount of sugar absorbed in dog number 9 was 0.09 Gm.; in dog number 12, 0.10 Gm.; and in dog number 18, 0.11 Gm. This is an average of 0.10 Gm. or 40 per cent of the injected sugar.

The absorption of water from this solution differs markedly from that from the 5 per cent solution of dextrose (see Chart 2). Both solutions are theoretically isotonic with the blood and tissue fluids. The average absorption of water from this solution was 7 c.c. in dog number 9, 8 c.c. in dog number 12, and 9.5 c.c. in dog number 18. Although dog number 18 has not been sacrificed I noted at operation that this loop was larger than the average, which would account for the greater amount of water absorbed by this loop. This experiment is very significant since it would indicate that the presence of sodium chloride, in an isotonic solution , facilitates water absorption, or that the presence of dextrose slows the absorption of water. The per cent, of the injected sugar, absorbed is comparable to that found in solutions of 5 per cent dextrose in water. A further discussion of this point will be found under the analysis of results.

5. The absorption of dextrose and water from a solution containing 5 per cent dextrose and 1.5 per cent sodium bicarbonate. A total of 25 experiments were performed. The results are given in Table 4.

Table IV

Grams of Dextrose Absorbed from 10 c.c. of a Solution Containing 5 per cent Dextrose and 1.5 per cent Sodium Bicarbonate.

	Dog 9	Dog 18	Dog 21	Dog 22
Gms Dextrose Absorbed	0.15	0.24	0.13	0.17
	0.11	0.15	0.12	0.17
	0.10	0.22	0.20	0.15
	0.10	0.19	0.12	0.15
	0.12	0.17	0.12	0.14
	0.10	0.17	0.12	
		0.16		
Average	0.11	0.19	0.13	0.16

The average absorption of dextrose for the four dogs is 0.15 Gm. An average of 0.19 Gm. of dextrose was absorbed where 5 per cent dextrose in water was used. There was also considerable influx of fluid into the loop as is shown in Table 5.

Table V

C.C. of Fluid Withdrawn in One Hour After the Injection of A Solution Containing 5 per cent Dextrose and 1.5 per cent Sodium Bicarbonate

	Dog 9	Dog 18	Dog 21	Dog 22
C.C. Fluid Withdrawn	17	16	15	16
	16	16	16	16
	17	16	15	14
	16	15	16	20
		16	15	
			16	
Average	16	15.8	15.5	16.5

This again is in striking contrast to the fluid balance as seen where 5 per cent dextrose in water was injected. An average of 8.6 c.c., of the 10 c.c. injected, was withdrawn, i.e. 1.4 c.c. of water was absorbed from the 10 c.c. of 5 per cent dextrose in water. The presence of 1.5 Gm. of sodium bicarbonate in 100 c.c. of 5 per cent dextrose solution rendered the solution hypertonic to the blood and tissue fluids, retarded the absorption of dextrose slightly and caused the influx of fluid into the loop. This influx averaged about 5 c.c.

6. The absorption of water and sodium chloride from 10 c.c. of a 0.9 per cent solution of sodium chloride in one hour.

An average of 8 c.c. (80%) of the fluid and sodium chloride injected was absorbed. Analysis for sodium chloride in the sample withdrawn gave percentages varying from 0.6 to 1.0 per cent, with an average very close to 0.9 per cent.

7. Blood sugar from colonic and systemic blood.

The procedure is outlined in the following. The dogs were placed on a table and the abdomen shaved. Blood was then drawn from the heart, oxalated and saved for sugar analysis. 10 to 15 c.c. of 10 per cent dextrose were injected and the time recorded. Forty minutes from the time of the injection the animal was given ether anesthesia and prepared for a laporatomy. The abdomen was opened under strict asepsis, through a left rectus incision, and blood drawn from the vein draining the colon loop. Blood was drawn almost immediately from the heart. Both specimens were oxalated to prevent clotting and kept for analysis. The time interval between injection of sugar into the colon loop, and aspiration of blood from the loop vein and the heart was one hour. The incision was then closed and the animal placed in a warm cage to recover. The entire operative time was less than thirty-five minutes.

A protein-free filtrate of the blood samples was then prepared by the method of Folin and Wu,[37] and the blood sugar determined by the Shaffer-Hartman method as modified by Haskins and Holbrook.[32 & 33] The milligrams of blood sugar corresponding to the titration figure were read from the table published by Haskins.[38]

The blood sugar, in the blood withdrawn from the colonic-loop vein, always exceeded that found in the blood drawn simultaneously from the heart. The difference averaged 7 milligrams per 100 c.c. of blood. A point of much interest is the change noted in blood sugar during ether anesthesia. In nine dogs, in which we determined the blood sugar during anesthesia, we found a doubling of the blood sugar per cent in eight animals. In one animal there was no increase in blood sugar with the anesthesia.

8. The effect of bacterial action on the injected sugar.

Although we have felt that the amount of dextrose lost by bacterial action is insignificant for a one hour period, we performed experiments to determine this. 10 c.c. of 10 per cent dextrose was injected and then withdrawn. By this procedure the bacteria of the colon loop were mixed with the sugar solution.

The sugar content in a sample of the aspirated fluid was immediately determined. The remainder was placed in a loosely stoppered flask, incubated at 37.5 degrees C. for one hour and the sugar content then determined. We were unable to detect any loss of sugar by bacterial action, since the percentages of sugar in the two samples, taken before and after incubation were identical.

V. Analysis of Results

1. Water absorption.

The effect of dextrose, in varying percentages; of sodium chloride and of sodium bicarbonate on the rate of water absorption or on the influx of fluid into the lumen of the chronic closed colon loop have been studied. The results were definite and striking. A study of Chart 1 and 2 shows that there is no definite correlation between the amounts of sugar and water absorbed from a 5 per cent solution of dextrose in water. Whereas there is a positive absorption of dextrose within 10 minutes following injection, a definite water absorption is not evident until almost forty minutes following injection. A point of major importance, however, is that with this concentration of dextrose we were unable to detect an influx of fluid into the loop at any interval in the absorption period, and that after the forty minute period the absorption of fluid proceeded at a fairly constant rate. Approximately 50 per cent of the injected fluid was absorbed in the 90 minute interval.

When 10 c.c. of a 20 per cent solution of dextrose in water was injected and aspirated in one hour, not only was no water absorbed but 10 to 15 c.c. of fluid had entered the loop in an attempt to dilute the hypertonic sugar solution. In spite of this influx of fluid positive absorption of sugar evidently occurred.

At the end of a one hour absorption period an average of 12 c.c. of fluid was withdrawn after the injection of 10 c.c. of a 10 per cent water solution of dextrose. As previously stated, the animals showed no signs of loop distention during the absorption period and, although an average increase in fluid of 2 c.c. was found at the end of the one hour period, it is evident that the influx of fluid was never large enough to cause marked distention of the loop. In this series of experiments we again found evidence of dextrose absorption in spite of the negative water balance.

Since it had been reported that the addition of sodium chloride to an isotonic solution of dextrose might influence the rate of water and sugar absorption, we performed a series of experiments injecting a solution containing 2.5 per cent dextrose and 0.45 per cent sodium chloride. If the relative osmotic pressures of the injected fluid and tissue fluids was the only factor influencing the absorption of water by the mucosa, we might expect the rate of fluid absorption to be similar to that from a 5 per cent solution of dextrose in water, since both solutions are theoretically isotonic with the blood and tissue fluids. This did not prove to be the case. The amount of water absorbed in one hour from a 5 per cent solution of dextrose in water was about 1.5 c.c. in contrast to an average of 7 c.c. absorbed in one hour from the dextrose-saline solution. Either the presence of the sodium chloride hastens water absorption, or the increased amount of dextrose in the 5 per cent water solution delayed the fluid absorption. This is even more significant when we note that the relative percentage of the injected sugar absorbed was approximately the same in both instances.

The absorption of water from a solution containing 5 per cent of dextrose and 1.5 per cent sodium bicarbonate was equally striking. By referring to table 5 it will be noted, that at the end of a one hour absorption period, an average of 16 c.c. of fluid was withdrawn after the previous injection of 10 c.c. of the dextrose-bicarbonate solution. The influx of fluid here almost equaled that found when a 20 per cent dextrose solution was injected. We know that the osmotic pressure exerted by any fluid is determined by the number of molecules in solution, that dextrose does not ionize and that sodium bicarbonate does, and finally, that the molecular weights of the two substances is markedly different. (84.01 for sodium bicarbonate and 198.11 for dextrose.) We might use these facts to explain the marked increase in fluid influx with the addition of such a small quantity of sodium bicarbonate, but the results obtained by the addition of a small quantity of sodium chloride, a highly ionized salt with a low molecular weight (58.45), were exactly the opposite as regards the fluid balance. In the latter case fluid absorption was comparatively rapid. We are forced to believe that the difference is not due to changes in relative osmotic pressures but to some effect the substances have on the activity of the colon mucosa.

It was decided to test the rate of water absorption from a third solution, isotonic with the blood and tissue fluids, in which no dextrose was present. 10 c.c. of a 0.9 per cent solution of sodium chloride was injected and aspirated in one hour. 80 per cent or 8 c.c. of the injected fluid was absorbed, compared to 5 c.c. from a 5 per cent solution of dextrose and 7 c.c. from a solution containing 2.5 per cent dextrose and 0.45 per cent sodium chloride. Again I wish to repeat that if osmotic pressure were the only factor we would expect water absorption to be greatest from the 5 per cent solution of dextrose and least from a 0.9 per cent solution of sodium chloride. The exact reverse was found. It would seem that some influence of dextrose on the activity of mucosal cells tends to slow the absorption of water.

As regards the absorption of sodium chloride from a 0.9 per cent sodium chloride solution, the following results were found. The percentage of sodium chloride in the aspirated sample was approximately the same as that of the injected fluid, i.e. 0.9 per cent. This would indicate that the absorption of sodium chloride is comparable to that of water.

In summarizing the above points it would seem that, (1) any solution containing 10 per cent or more dextrose will actually dehydrate the tissues, by causing an influx of fluid into the gut; (2) that the addition of small quantities of sodium bicarbonate (1.5 per cent) to 5 per cent dextrose will likewise result in an influx of fluid into the gut; (3) that small quantities of fluid (1-2 c.c.) are absorbed in one hour from 10 c.c. of a 5% solution of dextrose; (4) that 7 c.c. of fluid are absorbed in one hour from 10 c.c. of a solution of 2.5% dextrose and 0. 5% sodium chloride; (5) that 8 c.c. of fluid are absorbed in a similar time from 10 c.c. of 0.9 per cent sodium chloride; (6) that dextrose, in any percentage, may inhibit the rate of water absorption; and (7) finally, that osmotic pressure relationships do not seem to explain the differences in absorption rate.

2. Dextrose Absorption.

Before beginning a long series of experiments on dextrose absorption we wished to convince ourselves of actual absorption by the mucosa of the colon. We had, as previously stated, minimized all the sources of error known to us. In order to determine whether there was actual absorption the first group of experiments was performed. (See Tablel, and Charts 1 and 2) By referring to Table 1 and Chart 2, it will be noted that an average of 0.07 grams of dextrose had disappeared in 10 minutes, and that the amount of sugar lost steadily increased to 0.29 Gms. or 58 per cent of the injected sugar, at the end of 1½ hours. The rate of water absorption bears no relation to this, especially for the periods less than and up to 40 minutes. If diffusion was the only factor the rates of water absorption and sugar diffusion should be comparable. They were not. Whereas water absorption was not positive until the 40 minute period, a definite and steadily increasing sugar loss was noted at the end of a 10 minute period. This is even more significant when one considers that the dextrose solution was approximately isotonic with the blood and tissue fluids. As will be discussed below, the possibility of loss by errors in technique and bacterial action were checked and found to be insignificant. We considered these findings as indicative of actual absorption by the chronic closed colon loop.

In a consideration of the absorption of dextrose from 10 c.c. of a 20 per cent solution we find that the average for 29 experiments on 5 dogs was 0.49 Gms., or approximately 25 per cent of the injected sugar. It is apparent that the per cent of the injected sugar absorbed is much less than when a 5 per cent solution was used. The reasons for this may be several. The marked hypertonicity may have inhibited absorption by physical means of osmotic pressure relations, the capacity of the mucosal surface for absorption may have been exceeded, the blood supply to the loop may have been embarrassed by distention or there may have been an inhibitory affect excited on the mucosal cells. From the standpoint of absorption in grams it should be noted that 0.49 Gms. of the 2 Gms. injected was absorbed from the 20 per cent solution as compared to 0.29 Gms. from a 5 per cent solution.

When 10 c.c. of a 10 per cent solution was injected the average absorption in 25 experiments was approximately 0.22 Gms. or 22 per cent of the injected sugar. This percentage is approximately the same as for a 20 per cent solution. The amounts absorbed, from the 10 per cent solution in single experiments, was remarkably constant. The highest and lowest figures for any given animal did not differ by more than 0.05 Gm. All the other solutions, but especially the 20 per cent dextrose solution, showed less constancy in the absorption rates. This fact may indicate that, when considering sugar absorption alone, this volume and percentage of dextrose may be the least objectionable for studying the comparative absorption rates of various sugars.

The presence of 0.45 per cent sodium chloride in a 2.5 per cent solution of dextrose did not seem to increase the percentage of sugar absorption. 40 per cent (0.10 Gm.) of the dextrose was absorbed in a one hour period as compared with 58 per cent of the 5 per cent solution of dextrose in water. Both of these solutions are approximately isotonic with 0.9 per cent saline.

1.5 per cent sodium bicarbonate in a 5 per cent dextrose solution resulted in a lowered rate of dextrose absorption. In 25 experiments an average of 0.15 Gm., 30 per cent of the amount injected, was absorbed in one hour. 40 per cent of the saline - dextrose solution and 58 per cent of the 5 per cent dextrose solution was absorbed in the same period of time.

In summarizing we may state that: (1) the optimal percentage of dextrose solution for absorption of dextrose probably lies somewhere between 5 and 10 per cent, (2) the absorption from a 20 per cent solution is higher in grams absorbed but lower as regards percentage of sugar injected than for any other solutions tested, (3) the amount of absorption varied considerably when a 20 per cent solution was used, (4) the addition of sodium chloride in isotonic solutions apparently does not facilitate dextrose absorption, and finally, (5) that the addition of small quantities of sodium bicarbonate to a 5 per cent sugar solution resulted in a diminished rate of sugar absorption.

3. Relation of loop size to amount of absorption.

This relationship has been interesting and very constant. Dog number 7, whose loop absorbed large quantities of dextrose (Table 2) had a loop 12.5 cm. by 2.5 cm. This was noted at operation and confirmed at post. The loop of dog number 6 was measured at post and found to be 12 cm. by 2 cm. In table 2 this animal stands next below number 7 in the number of grams absorbed. Next highest in absorption (Table 2) was dog number 10. The loop was found at post to be 8 cm. by 4 cm. in dimension. Dog number 9 has consistently shown a low absorption rate. Although this dog has not been posted, we know that she has a very small loop. The size has been noted when operating for reattachment, and when fluid in excess of 12 c.c. is forcibly injected definite signs of loop distention are noted. The loop of dog number 17, when removed, measured 5 by 4 cm. This is approximately the same size as the loop in dog number 9 and these two dogs compete closely for the lowest absorption rate (Table 1).

Dogs number 18, 21, and 22, have not been posted but observations at operation and during the injection of varying amounts of fluid seem to indicate a close correlation between loop sizes and absorption rates. These observations would seem to indicate that the amount of absorption is in direct proportion to the area of the loop mucosa. The same relationship has been noted as regards fluid absorption.

4. Comparison of Absorption in the Lower Ileum and in the Colon.

In order to compare these more accurately the following table is given. These are partially reproduced from a paper previously published by Burget, Moore, and Lloyd.[31]

Table VI

Results of Repeated Experiments on Individual Dogs Expressed as Grams of Dextrose Absorbed by Closed Ileal Loops in One Hour from 10 cc. of a 20 per cent Solution of Sugar.

	Dog 61	Dog 131	Dog 132	Dog 135
	0.98	1.01	1.38	1.03
	0.97	0.97	1.11	0.97
	0.99	0.85	0.74	0.72
		0.77	0.75	0.73
		0.93	0.65	
Average	0.98	0.90	0.91	0.86

The average amount of dextrose absorbed for the four dogs is 0.91 Gms. Comparing the absorption in one hour from 10 cc. of a 20 per cent dextrose solution in the colon (Table 2) we find that the absorption rate is much higher in the ileum. An average of 0.49 Gms. being absorbed by the colon loop and 0.91 Gms. from the ileal loop, the colon loop absorbing 53 per cent of the amount absorbed by the ileal loop.

In comparing the relative absorption from 10 cc. of a 10 per cent solution we find that the low ileal loops were reported[31] to absorb an average of 0.52 Gms. as compared with 0.22 Gms. by the colon loop, as reported in this paper (Table 3). That is, the colon loop absorbed 41.5 per cent as much dextrose from an identical solution in the same time period.

The above comparisons would seem to indicate that the absorption of dextrose, under these conditions, is twice as rapid in the lower ileum as compared with the transverse colon in the dog.

In comparing the relative influx of fluids, when these two slutions were used, we find that when 10 cc. of a 20 per cent dextrose was injected that the average influx was 19 cc. in the low ileal loop and about 12 cc. in the colon loop. With the 10 per cent solution the increase was 9 cc.

for the ileal and 2 c.c. in the colon loop.

Either water is absorbed faster by the colon or there is a much greater initial influx of fluid into the ileal loop. The amount of fluid increase in the ileal loops varied from 6 to 30 cc. whereas the influx into the colon loops was very constant. The small intestine must be much more sensitive to changes in osmotic relationship and to irritating or inhibiting factors. This relative stability of the colon has been noted in all our experimental studies on absorption.

As final evidence of positive absorption we should again draw attention to the experiments where the blood sugar from the loop veins was compared with that of heart blood during an absorption period. As previously stated, we have formerly found an increase in the blood sugar from ileal loop veins as compared with that from the heart, and demonstrated this difference to be due to levulose absorbed from the ileal loop.[32] Seven experiments were performed. In the experiments reported in this paper we found that the blood sugar from the colon loop veins exceeded the amount present in the heart's blood by approximately 0.008 Gm. Sugar must have been entering the mesenteric veins from the loop. This small amount of sugar was probably removed by the liver.

In interpreting the conclusions given below, and in the application of these interpretations to clinical therapy on humans, one must remember that the absorption by the large intestine of the dog may not be similar to these activities in the human. These conclusions are the result of experimental work on the dog and should be interpretated as such.

Conclusions

1. Dextrose is absorbed approximately one half as fast by the transverse colon as by the lower ileum.

2. The optimum absorption of dextrose by the colon is from solutions between 5 and 10 per cent in strength.

3. The addition of small amounts of sodium chloride does not facilitate the absorption of dextrose.

4. Sodium bicarbonate in the amounts used retards the absorption of dextrose.

5. A definite water influx occurs when solutions containing 10 per cent or more dextrose are used. This undoubtedly produces tissue dehydration.

6. Dextrose, in percentages as low as 2.5, inhibit water absorption.

7. Small quantities of sodium bicarbonate added to an isotonic sugar solution result in a marked influx of fluid into the gut.

8. The optimal solution for water absorption is a 0.9 per cent saline solution.

9. The small intestine is more sensitive to changes in osmotic relationship, and irritative, or inhibiting factors.

10. The systemic blood sugar is not a true index of sugar absorption from the intestine.

11. The action of the bacteria found in the closed colon loop on dextrose, is not significant for a one hour period.

12. If we can apply these results to clinical application, two types of enemas should be used. A 0.9 per cent saline enema should combat dehydration most efficiently, whereas a dextrose solution of about 5 per cent should allow for a maximum of dextrose absorption. Where dehydration is to be prevented the use of dextrose enemas is not advisable.

13. The practicability of the chronic closed colon loop for studying absorption has been demonstrated.

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