

EVALUATION OF PORTACAVAL SHUNT PATENCY WITH THE DIFFERENTIAL GLUCOSE TOLERANCE TEST

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IN THE MANAGEMENT of patients in whom surgical portal-systemic shunts have been established, it may be important to know the state of patency of the anastomosis. Such information would always be of prognostic significance postoperatively. If recurrent hemorrhage occurs after the shunting procedure, this knowledge would be of utmost value in planning the therapy, since the bleeding could be either secondary to thrombosis of the anastomosis or be attributable to any of the other causes of upper gastrointestinal bleeding. Finally, it would permit a more objective evaluation of the operative results as compared with the results of nonoperative care, since technical failures could readily be detected. In the past, considerable effort has been expended to develop methods of detecting the patency of the shunt. The techniques have been limited by their inherent dangers or because complex technical or biochemical procedures were required.

An evaluation of a differential glucose technique for determining shunt patency is herein presented. In principle, it involves the ingestion of a glucose meal, following which the plasma glucose content is measured in samples obtained simultaneously from a peripheral systemic vein and from the inferior vena cava at, or just above, the anastomotic site. The method requires no special equipment or analytic determinations. In the case of a patent shunt, the vena caval sample which is mixed with portal

blood would be expected to have a significantly higher plasma glucose content than a simultaneous peripheral venous sample.

In a series of cirrhotic patients not operated upon who had portal hypertension differential glucose studies were carried out for comparison with results obtained from patients having had a portal-systemic anastomosis. Because it is frequently impossible to obtain anatomic verification of shunt patency in human beings, a companion series of dogs was prepared, and differential glucose studies carried out before and after the performance of Eck fistulas. Complete autopsy information on shunt patency was available in the latter series.

METHOD

Laboratory. Trained, fasted mongrel dogs of both sexes, weighing between 10 and 20 kilograms, were used. Under local anesthesia, a catheter was inserted into the inferior vena cava of each dog by way of a small branch of the femoral vein. After injection of 10 cubic centimeters of 50 per cent hypaque sodium, to allow pyelographic visualization of the kidneys, the catheter was positioned so that its tip would be opposite the twelfth thoracic to first lumbar interspace. This site usually coincided with the upper half of the left kidney. A second catheter was inserted into the external jugular vein. After withdrawal of 3 pairs of control samples, 50 grams of glucose were administered through a stomach tube, and simultaneous blood samples were obtained from each catheter at 15 minute intervals for 2 hours. Plasma glucose determinations were carried out with an autoanalyzer.

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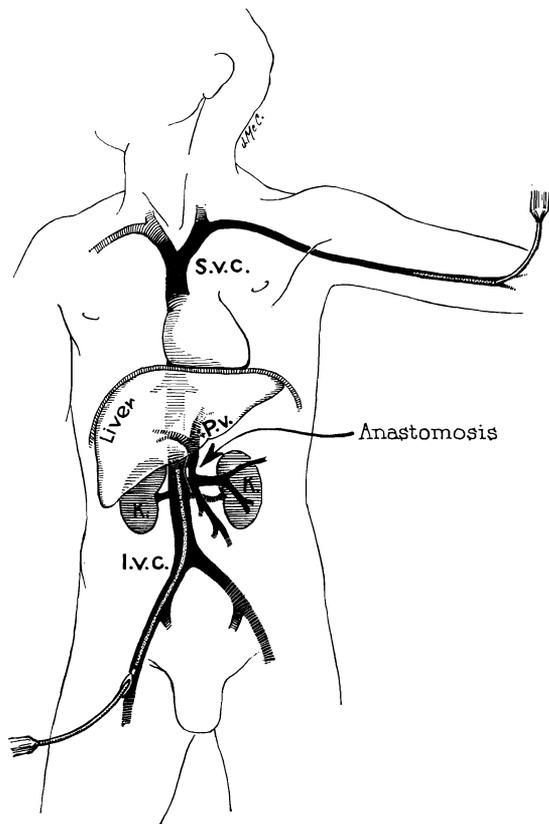


FIG. 1. Technique of sampling for differential glucose tolerance test in human beings. The inferior vena caval catheter is inserted percutaneously to, or just above, the anastomotic site. Peripheral venous samples are obtained from a vein of the arm. Samples from the 2 sites are drawn simultaneously, before and after a glucose meal.

The following day, Eck fistulas were created by fashioning a side-to-side porta-caval anastomosis cephalad to the renal veins. The portal vein was ligated between the anastomosis and the liver. Silver clips were placed around the anastomotic site for future roentgenographic identification.

Approximately 10 days postoperatively, a second glucose tolerance test was carried out, each dog, thus, serving as his own control. The tip of the inferior vena caval catheter was positioned just cephalad to the most superior silver clip. Upon completion of the test, an autopsy was performed upon each dog to ascertain the patency of the shunt. All shunts were found to be widely open. There were 9 dogs in the preshunt and

8 in the postshunt group, 1 dog having died postoperatively.

Clinical. The patients were in a fasting state at the time of the examination. A percutaneous puncture of the femoral vein was performed with a No. 13 short bevel needle. A No. 160 polyethylene catheter was inserted into the inferior vena cava through the needle (Fig. 1). The needle was then withdrawn and the catheter flushed with a heparin saline solution. Twenty cubic centimeters of 50 per cent hypaque sodium were injected into the catheter, and the tip was positioned postoperatively between the twelfth thoracic and first lumbar vertebrae or just cephalad to the level of the silver clips. The opacification of the kidneys was often a help in correctly positioning the catheter. A similar indwelling catheter was introduced into a vein of the upper extremity (Fig. 1) to obviate the necessity of multiple venipunctures. Two control samples were taken. Then 100 grams of glucose were given orally, and simultaneous blood samples of 3 cubic centimeters were withdrawn from each catheter every 10 minutes for a period of 1 hour.

RESULTS

Normal dogs. Nine normal dogs were studied. The mean plasma glucose in the jugular control samples was 104 ± 1.6 (S.E., standard error) milligrams per 100 cubic centimeters. After oral ingestion of glucose, glucose concentration in the jugular samples rose to a maximum of 180 ± 15.8 (S.E.) milligrams per 100 cubic centimeters after 60 minutes and then declined.

In the control period the plasma glucose concentration in the inferior vena caval samples was 105 ± 1.3 (S.E.) milligrams per 100 cubic centimeters. After glucose ingestion it rose to 188 ± 16.6 (S.E.) milligrams per 100 cubic centimeters after 60 minutes.

The glucose concentration differences between the inferior vena caval sample, hereinafter designated I, and the jugular sample, hereinafter designated P to indicate its peripheral origin, were not significantly

different during the control period (Fig. 2). The I-P difference was $0.4 \pm .4$ (S.E.) milligrams per 100 cubic centimeters. After glucose ingestion the I-P difference increased to a maximum of 12 ± 2.6 (S.E.) milligrams per 100 cubic centimeters at 60 minutes and then slowly declined (Fig. 2).

Dogs with Eck fistulas. Eight dogs were studied, and the mean fasting plasma glucose in the jugular samples was 102 ± 2.1 (S.E.) milligrams per 100 cubic centimeters. After the glucose meal, glucose concentration in the jugular sample rose to a maximum of 293 ± 15.8 (S.E.) milligrams per 100 cubic centimeters after 60 minutes.

Fasting plasma glucose control values in the inferior vena cava were 103 ± 2.6 (S.E.) milligrams per 100 cubic centimeters. After glucose ingestion, these values rose to a maximum of 330 ± 19.1 (S.E.) milligrams per 100 cubic centimeters after 60 minutes.

The I-P plasma glucose concentrated difference was $1 \pm .8$ (S.E.) milligrams per 100 cubic centimeters in the control period. After glucose ingestion, the I-P difference increased immediately to a maximum of 34.5 ± 8.4 (S.E.) milligrams per 100 cubic centimeters after 15 minutes. The increase in I-P difference was sustained for at least 120 minutes (Fig. 2).

Patients with cirrhosis. The 5 patients in this group all had advanced cirrhosis, proved by liver biopsy with confirmatory liver function tests. The presence of portal hypertension was proved by demonstrating esophageal varices with esophagrams or esophagoscopy or by determination of elevated hepatic vein wedge pressures.

Mean fasting plasma glucose in the control period was 90 ± 3.7 (S.E.) milligrams per 100 cubic centimeters in the samples taken from the veins of the arms. After oral ingestion of glucose, the maximum hyperglycemic response was to 180 ± 14.4 (S.E.) milligrams per 100 cubic centimeters after 60 minutes.

The fasting plasma glucose level in the inferior vena caval samples was 92 ± 3.6 (S.E.) milligrams per 100 cubic centimeters.

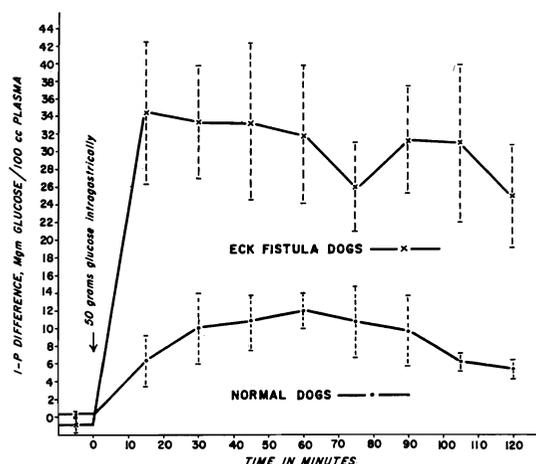


FIG. 2. Concentration differences of plasma glucose between the suprarenal inferior vena cava and the jugular vein in dogs before and after a glucose meal. The line graphs represent mean values, and the vertical cross bars are the standard errors. The lower curve represents normal dogs and the upper curve the same group of dogs after performance of Eck fistulas. "I" refers to inferior vena cava samples and "P" to the peripheral, jugular, sample.

After glucose ingestion, this rose to 178 ± 15 (S.E.) milligrams per 100 cubic centimeters after 60 minutes.

The I-P plasma glucose concentrating difference was $2.8 \pm .54$ (S.E.) milligrams per 100 cubic centimeters in the control period. After oral ingestion of glucose, the I-P difference increased to a maximum of 7.2 ± 2.5 (S.E.) milligrams per 100 cubic centimeters after 10 minutes (Fig. 3).

Patients with cirrhosis after portal-systemic shunt. Six of the 7 patients in this group had either end-to-side or side-to-side portacaval shunts, and the seventh patient had a splenorenal shunt. Cirrhosis and preoperative portal hypertension were proved in all. On the basis of radiographic, esophagoscopic, and clinical grounds, the anastomoses were thought to be patent in all 7 patients. One patient was studied both before and after operation. Several months after the study was begun a second patient died following operation for intestinal obstruction. At autopsy, the end-to-side portacaval anastomosis was found to be widely patent.

Mean fasting plasma glucose from the

arm was 90 ± 2.5 (S.E.) milligrams per 100 cubic centimeters in the control period. After orally ingested glucose, the maximum hyperglycemia was 176 ± 26 (S.E.) milligrams per 100 cubic centimeters after 40 minutes.

In the inferior vena cava, control plasma glucose was 91 ± 2.2 (S.E.) milligrams per 100 cubic centimeters. After orally ingested glucose, this figure rose to a maximum of 207 ± 33 (S.E.) milligrams per 100 cubic centimeters in 40 minutes.

The mean control I-P plasma glucose difference was $2.8 \pm .96$ milligrams per 100 cubic centimeters. After oral ingestion of glucose, the I-P concentration difference was sharply increased for the entire test period (Fig. 3) to a maximum of 31 ± 6.3 (S.E.) milligrams per 100 cubic centimeters after 20 minutes. There was no overlap in the maximum I-P difference in those not operated upon as compared to those having surgical portal systemic shunts. The highest I-P glucose difference ever observed in a patient in whom a shunt was not established was 14 milligrams per 100 cubic centimeters. The lowest I-P difference observed in a patient having a shunt was 16 milligrams per 100 cubic centimeters. This value was obtained in the only patient in this series who had a splenorenal shunt. The lowest maximum I-P difference in the patients with portacaval anastomoses was 20 milligrams per 100 cubic centimeters.

In 1 patient, glucose studies performed before and after operation were particularly helpful because of the complicated nature of the operative procedure.

REPORTS OF PATIENTS

PATIENT 1. A 36 year old male was admitted to the hospital for treatment of recurrent ascites and upper intestinal hemorrhage. Examination revealed esophageal varices and advanced liver disease. Preoperative hepatic vein wedge pressure was 31 millimeters of mercury. A side-to-side portacaval shunt was performed on 25 June 1962. The operative procedure was complicated by the necessity of performing a thrombectomy in the portal vein to remove old and recent thrombi. A satisfactory anastomosis was obtained with good flow and satisfactory pressure drop in the

splanchnic system. The postoperative course was benign. Differential glucose studies were performed 2 weeks postoperatively. Inasmuch as the maximum I-P plasma glucose concentration differential rose to 42 milligrams per 100 cubic centimeters postoperatively as compared to 14 milligrams per 100 cubic centimeters preoperatively, it was believed that the shunt was widely patent.

In another patient admitted for evaluation of her hepatic status, glucose studies were invaluable in assessing shunt patency.

PATIENT 2. This 58 year old, alcoholic female had had an end-to-side portacaval shunt in 1957. She was readmitted to the hospital in April 1962 because of jaundice and lethargy. Studies revealed advanced liver disease. A barium swallow was interpreted as demonstrating esophageal varices.

A differential glucose tolerance test was performed. This revealed a maximum I-P concentration difference of 64 milligrams of glucose per 100 cubic centimeters of plasma. Therefore, despite the roentgenographic finding of esophageal varices, the test indicated that the previously constructed shunt was still functioning. The patient died 3 months after readmission from unrelated causes. The portacaval anastomosis was found to be widely patent at autopsy.

DISCUSSION

A number of techniques have been evaluated for determining anastomotic patency after a portal-systemic shunt. Most investigators have attempted to establish a method which is applicable to all patients, gives consistent results, is simple to perform, is easy to interpret, and affords a minimal risk.

The most direct approach has been to enter the portal system in order to measure the pressure. Atkinson and his associates have recommended postoperative splenic puncture. Palmer has described needle puncture of esophageal veins through an esophagoscope. Collapse of the varices after successful decompression makes the latter method impractical. In addition, fatal hemorrhage from a torn varix has been reported by Deterling and his associates following this procedure. Attempts have also been made to enter the portal vein by retrograde catheterization through portacaval anastomoses. Dotter and his associates

reported upon 1 case, while Warren and Thompson catheterized the portal vein via the patent anastomoses in 7 patients. While useful as an investigative tool, the technical difficulties involved probably preclude the widespread acceptance of this method. It is obvious that failure to enter the portal vein is not proof that the anastomosis has closed.

There have been many reports of attempts at direct visualization of the anastomosis with the rapid injection of radiopaque dyes directly into the portal circulation. Splenoportography has become an accepted diagnostic tool, both in the preoperative, as well as postoperative, evaluation of the splanchnic venous circulation. This method suffers from the slight, but definite, danger involved in splenic puncture, the inability to carry out the examination in the absence of the spleen, as in a postoperative spleno-renal shunt, and lastly, the need for specialized technical help. Giuseffi and Largen have described a method utilizing a double balloon tube to "trap" the area of the anastomosis while the dye is being injected for roentgenographic visualization of the areas.

A different approach to this problem has been the measurement of decreased portal circulation time which exists in patients with patent shunts. Many of these methods require injection into the splenic pulp of a substance which can be readily detected when it reaches the systemic circulation. Gilsanz and his associates have employed ether, and Morrow (14) has used indocyanine green and radioactive krypton. In other studies, rectal veins have been used to gain entry into the splanchnic system. Ether has been extensively evaluated by Newman and later by Giges and Teschan but Waldstein and his associates have found it to be unreliable due to the vague end point. Deterling and his associates have instilled radioactive sodium into the rectum and measured the time of its appearance in the brachial artery by means of an external scintillation counter. There was wide varia-

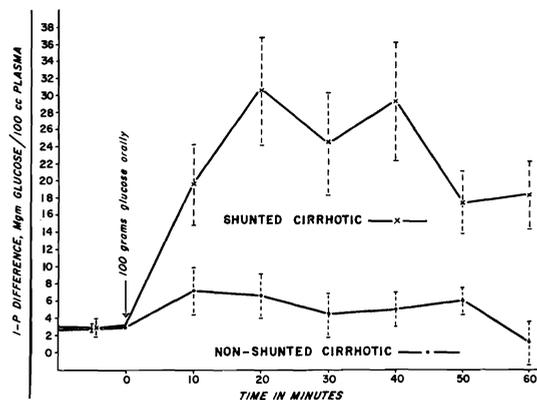


FIG. 3. Concentration differences of plasma glucose between the suprarenal inferior vena cava (*I*) and the arm veins (*P*) of cirrhotic patients before and after ingestion of 100 grams of glucose orally. Points are mean values and the vertical cross bars standard errors. The lower curve represents cirrhotic patients who were not operated upon. The upper curve represents cirrhotic patients in whom a portacaval or spleno-renal shunt had been established.

tion in normal or cirrhotic patients, but in all postoperative patients with patent shunts the circulation times were short. This method, although apparently possessing validity, necessitates a preoperative and postoperative examination as well as complex equipment.

Other methods have been described which are based upon the inability of the bypassed liver to metabolize test substances rapidly. Eiseman and his associates (8, 9) have employed oral ingestion of ammonium salts and Akita and his associates (1, 2) have used bile salts as the test drug. These techniques, besides requiring special laboratory skills, suffer from the fact that a severely impaired liver detoxifies test substances so slowly as to mimic the curve obtained in instances of a patent shunt. In addition, Levine and Rigler found in evaluating the ammonium tolerance test, that 2½ months after closure of a portacaval shunt in dogs, extensively developed collaterals caused false peripheral elevation.

The difference in postprandial plasma glucose concentration between a peripheral vein and one draining the splanchnic bed has been previously described. In 1946,

Sherlock and Walshe noted that a large glucose concentration difference was present after a test meal between the samples drawn from abdominal wall venous collaterals and the veins of the upper extremity. A similar study by Billings and DePree confirmed these findings. Subsequently, Allard and his associates reported a case in which the left renal vein was catheterized after splenorenal shunt. Simultaneous blood samples, taken from this site as well as a peripheral vein, revealed a difference in glucose concentration.

In our experience, the differential glucose tolerance test has proved to be a valuable method for assessing anastomotic patency. The reliability of the method depends upon the observance of a few details of both technique and interpretation. Proper placement of the vena caval catheter is the most important of these. If the catheter is too low, the disproportionate rise in plasma glucose in the vena caval samples will not be observed. If it is too high, the samples will be contaminated with blood from the glucose-rich hepatic veins. These errors are readily avoided, using the renal shadows, the vertebrae, or silver clip tagged anastomosis as a landmark.

The ideal application of this test would be in cases in which the preoperative determinations could be compared with those obtained after operation. In normal dogs, as well as nonshunted cirrhotic human beings, a small increase in the vena caval-peripheral vein concentration difference is observed after a glucose meal, presumably due to small splanchnic-vena caval communications. However, in patients who have not been studied preoperatively, it is still possible to obtain accurate data on the patency of the shunt. If the maximum glucose concentration difference is less than 12 milligrams per 100 cubic centimeters, it is very unlikely that the anastomosis is open and effectively decompressing the splanchnic bed. If the maximum difference exceeds 20 milligrams per 100 cubic centimeters, shunt patency is virtually assured. In this

study, all patients with portacaval shunts exhibited a glucose concentration difference exceeding 20 milligrams per 100 cubic centimeters. The single patient with a splenorenal anastomosis had a maximum glucose difference of 16 milligrams per 100 cubic centimeters. In these smaller shunts, therefore, the method may provide less accuracy.

SUMMARY

A method has been described for establishing shunt patency by determining the difference in postprandial plasma glucose levels between a peripheral vein and the inferior vena cava at or near the site of the portal-systemic anastomosis. This test was evaluated both in the laboratory with normal dogs before and after Eck fistula formation as well as in cirrhotic patients with and without shunts.

The results indicate that this test is reliable and has the advantages of safety, specificity, and ease of performance.

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