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Regional disposal of intravenously infused glucose during prolonged hyperglycemia–hyperinsulinemia

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We measured splanchnic and leg glucose uptake during prolonged (i.e., 15 hours), moderate hyperglycemia–hyperinsulinemia (clamp). Plasma free fatty acid (FFA) concentration was maintained at basal concentration during the clamp via infusion of exogenous lipids and heparin in healthy volunteers to create a metabolic profile similar to glucose intolerance (i.e., hyperglycemia–hyperinsulinemia with elevated FFA concentration). During the clamp, glucose was infused at an average rate of 49 ± 4 μmol/kg/min, which resulted in a plasma glucose concentration of 8.8 ± 0.5 mmol/L compared with a concentration of 4.4 ± 0.2 mmol/L in the basal state ($P < 0.05$*). Insulin concentration increased from 5.5 ± 1.1 μU/mL (basal) to 31.3 ± 12.7 μU/mL (clamp;* $P < 0.05$*), whereas plasma FFA concentration was similar in the two conditions (3.9 ± 0.5 mmol/L and 4.1 ± 0.5 mmol/L, basal and clamp, respectively). Glucose balance across the splanchnic region switched from net release (−5.8 ± 0.7 μmol/kg/min) in the basal state to net uptake in the clamp (19.8 ± 3.7 μmol/kg/min;* $P < 0.05$*) and accounted for approximately 40% of the infused glucose. Glucose uptake across the leg was 0.7 ± 0.2 μmol/kg/min (basal) and 5.5 ± 2.2 μmol/kg/min (clamp;* $P < 0.05$*). In summary, tissues in the splanchnic region (i.e., liver) are important for disposal of intravenously infused glucose during prolonged, moderate hyperglycemia–hyperinsulinemia. Accelerated hepatic glucose uptake may disrupt normal liver metabolism, with potentially dangerous consequences for the patient. Measures to control systemic glucose concentration may be necessary to prevent excessive glucose disposal in the liver.* (J. Nutr. Biochem. 10:547–554, 1999)

Keywords: parenteral nutrition; liver; insulin resistance; hepatic vein; splanchnic balance

Introduction

Parenteral nutrition involves administration of glucose, lipids, and amino acid mixtures of various forms and composition. Although some of the infused substrates are taken up by tissues and oxidized immediately, a significant portion are cleared from the systemic circulation and stored for future use. The relative importance of these pathways (i.e., immediate oxidation versus storage) depends on the specific physiologic condition of the patient.

Muscle and liver are considered the two quantitatively most important tissues for glucose clearance.[1] The relative importance of these two tissues in clearing ingested or infused glucose depends on a variety of factors such as the route of glucose delivery (i.e., peripheral infusion versus ingestion), glucose concentration, and hormonal milieu (i.e., insulin and glucagon concentrations). Thus, it has been suggested that raising the glucose concentration by peripheral infusion while keeping insulin and glucagon at basal levels decreases hepatic glucose output but does not cause net hepatic glucose uptake (NHGU).[2] Similarly, raising insulin while keeping glucose constant inhibits hepatic glucose output but does not significantly increase NHGU.[2] A combination of hyperglycemia–hyperinsulinemia pro-

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duces significant NHGU in humans (i.e., 1.0–1.6 mg/kg/min).[2–5] However, even under these conditions, it was estimated that the liver clears only 10 to 15% of the infused glucose.[3–5] The conclusion from the above studies is that short-term elevation in systemic glucose and insulin concentrations, alone or in combination, have minimal effects on NHGU in healthy volunteers. Furthermore, when glucose is peripherally infused, hepatic glucose uptake accounts for only a small portion of the infused glucose, with the majority cleared by non-splanchnic, peripheral tissues.

When glucose is given orally, there is a rapid switch from net output to net uptake of glucose across the splanchnic region. In this circumstance, NHGU approaches 30 μmol/kg/min,[3] which represents approximately 50% of the glucose ingested, with the remaining 50% taken up by extrahepatic tissues.[5] This response is similar to when glucose is infused directly in the portal vein,[6,7] suggesting the presence of a "portal signal" for hepatic glucose uptake, which may allow the liver to distinguish between ingested and peripherally infused glucose. Studies in the dog suggest that the portal signal rapidly activates NHGU and can cause glycogen accumulation in the liver independent of a rise in insulin.[8]

The pattern of intravenously infused glucose disposal appears to be different in insulin resistant patients than in healthy volunteers. Thus, during hyperglycemia–hyperinsulinemia, NHGU is significantly higher in insulin resistant patients than in healthy controls and accounts for approximately 47% and 27% of intravenously administered glucose, respectively.[9] The factors that contribute to this difference are not well understood. It has been suggested that the peripheral tissues of insulin resistant patients have a reduced ability to effectively clear the glucose load, resulting in higher systemic glucose concentration compared with healthy controls.[10] Therefore, glucose availability to the liver is higher in insulin resistant patients, which may accelerate hepatic glucose uptake. Plasma free fatty acid (FFA) concentration is usually higher in patients with noninsulin dependent diabetes mellitus[11] and may play a role in the reduced peripheral glucose uptake in insulin resistant patients compared with healthy adults. This is because lower FFA concentration in the healthy volunteers may stimulate peripheral glucose clearance[12] and thereby enhance the site of glucose disposal.

The goal of the present study was to evaluate the effect of a metabolic state simulating insulin resistance (i.e., hyperglycemia–hyperinsulinemia with high plasma FFA concentration) on the uptake of intravenously administered glucose by the splanchnic region and the leg. Therefore, we examined glucose balance across the splanchnic region and the leg in five volunteers in the fasting state during prolonged (i.e., 15 hours), moderate hyperglycemia–hyperinsulinemia while keeping plasma FFA concentration at basal levels. This was accomplished by the simultaneous infusion of glucose, lipids, and heparin to prevent the expected decrease in plasma FFA concentration during exogenous glucose administration. This experimentally created metabolic profile should simulate the metabolic profile of an insulin resistant patient.

Methods

Five male volunteers (age 29 ± 2 years, weight 76 ± 5 kg, height 177 ± 5 cm) participated in this study. All volunteers were healthy, as indicated by a comprehensive history, physical examination, and standard blood and urine tests, and had maintained stable weights for at least 3 months before the studies. The Institutional Review Board and the General Clinical Research Center (GCRC) of the University of Texas Medical Branch at Galveston approved the experiments. Informed consent was obtained for all procedures.

Experimental design

Volunteers were admitted to the GCRC at the University of Texas Medical Branch at Galveston and received a light meal at 5:00 PM. The meal contained 30% of energy as fat, 20% as protein, and 50% as carbohydrates. At 9:00 PM catheters were placed percutaneously into an antecubital vein for lipid and glucose infusion and into a contralateral dorsal hand vein, which was heated for sampling of arterialized blood. The catheters were kept patent by infusion of 0.9% NaCl. Background blood samples were collected after the volunteers had rested for 30 minutes and one of the following two randomly assigned experimental protocols was performed.

Protocol 1: Basal state. Blood samples were collected every 60 minutes throughout the night. At 7:00 AM, the volunteers were transferred to the Angiography and Interventional Radiology Center of the University of Texas Medical Branch, which is located in the same building as the GCRC, where femoral artery and hepatic vein catheters were inserted as described below in Procedures. The volunteers were transferred back to the GCRC 30 to 60 minutes after catheter placement. Blood samples were obtained from the artery, the hepatic vein, and the femoral vein 100, 110, and 120 minutes after returning to the GCRC.

Splanchnic blood flow was determined using a constant infusion of indocyanine green as described below in Procedures. After completion of the study, all catheters were removed and the volunteers remained in the hospital for observation until the next morning.

Protocol 2: Hyperglycemic clamp. The protocol for this group was the same as in protocol 1, except that a continuous infusion of 15 to 20% dextrose was started at 9:00 PM and maintained until the end of the study approximately 15 hours later. Dextrose was infused at a rate designed to increase blood glucose concentration to approximately 8 mmol/L. Blood glucose levels were measured every 30 minutes and dextrose infusion was appropriately adjusted to maintain blood glucose concentration at approximately 8 mmol/L. The average glucose infusion rate was 8 mg/kg/min. Insulin concentration was allowed to change freely in response to dextrose infusion. Blood potassium concentration was measured every 2 hours and a variable infusion of potassium chloride was given to maintain a constant plasma potassium concentration. Lipids were infused together with heparin (bolus of 7.0 U/kg; continuous infusion of 7.0 U/kg/h) to prevent the expected insulin-induced decline in plasma FFA concentration.

Procedures

Catheter placement. On the morning of the study, volunteers were brought to a vascular radiology suite where the right groin was prepared and draped in a sterile fashion. A lead glove was placed over the genitalia before the procedure. After patient preparation, the right common femoral vein was punctured and a 6 Fr sheath was placed. Through this sheath, a straight 5 Fr catheter with several side holes near its tip was manipulated into

the right or middle hepatic vein. This catheterization was performed using a deflecting-tip 0.035 inch guidewire within the straight catheter. After the catheter was positioned in the hepatic vein, a digital venogram was performed to verify placement, and both the sheath and catheter were infused with heparinized saline to maintain patency. The position of the catheter was confirmed again by a plain view abdominal radiograph immediately following the study. A short, straight 4 Fr catheter was then placed retrograde into the right common femoral artery and connected to a pressurized flush setup. After suturing both catheters and the sheath in place, a sterile transparent dressing was used to cover the vascular entry sites.

Blood flow. Blood flow was determined using a constant infusion of indocyanine green dissolved in 0.9% saline. The dye was infused through the femoral artery catheter at the rate of 0.5 mg/min for 55 minutes during the last hour of the study, and blood samples were taken simultaneously at 40, 45, 50, and 55 minutes from the hepatic vein, the femoral vein, and a peripheral vein. The concentrations of the dye in the infusate and in serum samples were determined using a spectrophotometer set at 805 nm. Splanchnic plasma flow was determined by dividing the infusion rate of the dye by the concentration difference across the splanchnic region (antecubital vein concentration minus hepatic venous concentration). Leg plasma flow was determined by dividing the infusion rate of the dye by the concentration difference across the leg (antecubital vein concentration minus femoral venous concentration). Splanchnic and leg blood flow were then calculated by dividing the plasma flow by 1 minus the hematocrit.

Assays

Samples for determining substrate and hormone concentrations were collected in pre-chilled tubes and plasma was immediately separated by centrifugation and frozen until further processing. Blood glucose and plasma lactate concentrations were measured on a 2300 STAT analyzer (Yellow Springs Instruments Co, Yellow Springs, OH USA). Plasma insulin concentration was determined using a radioimmunoassay method (INCSTAR, Stillwater, MN USA).

Calculations

Net glucose uptake or release across the splanchnic bed (NBspl) and leg (Nbleg) was determined by multiplying the arteriovenous glucose concentration difference by the blood flow:

$$\text{NBspl} = (\text{CGA} - \text{CGHV}) \times \text{HBF} \quad (1)$$

$$\text{NBleg} = (\text{CGA} - \text{CGFV}) \times \text{LBF} \quad (2)$$

where CGA, CGHV, and CGFV are the arterial, hepatic venous, and femoral venous blood glucose concentrations, respectively, and HBF and LBF are the hepatic and leg blood flow rates, respectively.

Likewise, net lactate uptake or release across the splanchnic bed (NBLspl) and leg (NBLleg) was determined by multiplying the arteriovenous lactate concentration difference by the blood flow:

$$\text{NBLspl} = (\text{CLA} - \text{CLHV}) \times \text{HBF} \quad (3)$$

$$\text{NBLleg} = (\text{CLA} - \text{CLFV}) \times \text{LBF} \quad (4)$$

where CLA, CLHV, and CLFV are the arterial, hepatic venous, and femoral venous blood lactate concentrations, respectively.

Net fractional extraction of glucose delivered to the splanchnic bed (ExGspl) and leg (ExGleg) was determined by dividing the arteriovenous glucose concentration by the arterial glucose concentration:

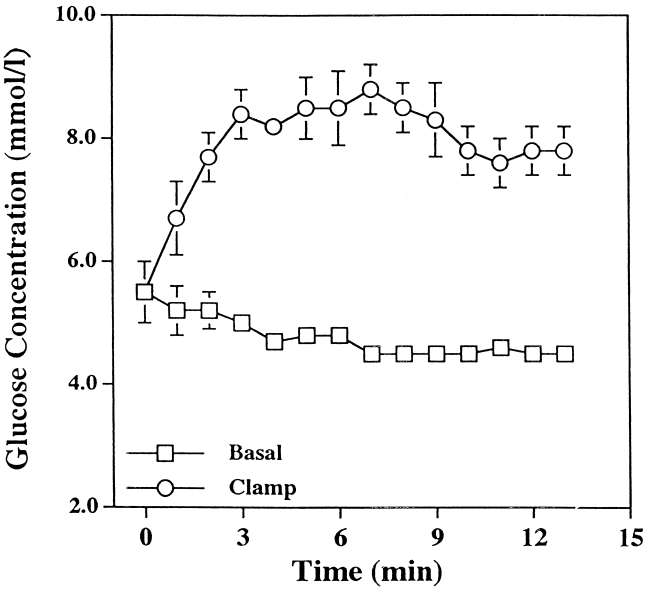

Figure 1 Blood glucose concentration in an antecubital vein in the basal state and during hyperglycemia–hyperinsulinemia. Values are means ± SEM for five volunteers and derive from measurements performed overnight, prior to the placement of the femoral arterial, femoral venous, and hepatic venous catheters.

$$\text{ExGspl} = (\text{CGA} - \text{CGHV})/\text{CGA} \quad (5)$$

$$\text{ExGleg} = (\text{CGA} - \text{CGFV})/\text{CGA} \quad (6)$$

The percentage of infused glucose taken up by the splanchnic bed (% to spl) and by the leg (% to leg) was determined by dividing the net glucose uptake by the glucose infusion rate:

$$\%\ \text{to spl} = \text{NBspl}/\text{I} \quad (7)$$

$$\%\ \text{to leg} = \text{NBleg}/\text{I} \quad (8)$$

where I is the infusion rate of glucose.

Statistical analysis

Results are reported as means ± SEM. The effects of the glucose infusion on the various parameters were evaluated using a two-tailed paired Student's *t*-test. A *P*-value of less than 0.05 was considered significant.

Results

Substrate and hormone concentrations

Overnight (i.e., 0 to 13 hours) substrate concentrations were determined for samples from an antecubital vein (*Figures 1 through 3*). Data during the last 2 hours of the study were obtained from samples drawn from the femoral artery, the hepatic vein, and the femoral vein (*Figures 4 through 6*).

Glucose. Plasma glucose concentration decreased overnight but it remained constant during the final 8 hours of the study in the basal state (*Figures 1 and 4A*). As expected, glucose concentration was higher in the hepatic vein than in the femoral artery and femoral vein, reflecting glucose release by the liver (*Figure 4A*). During the clamp, glucose concentration increased shortly after the start of dextrose

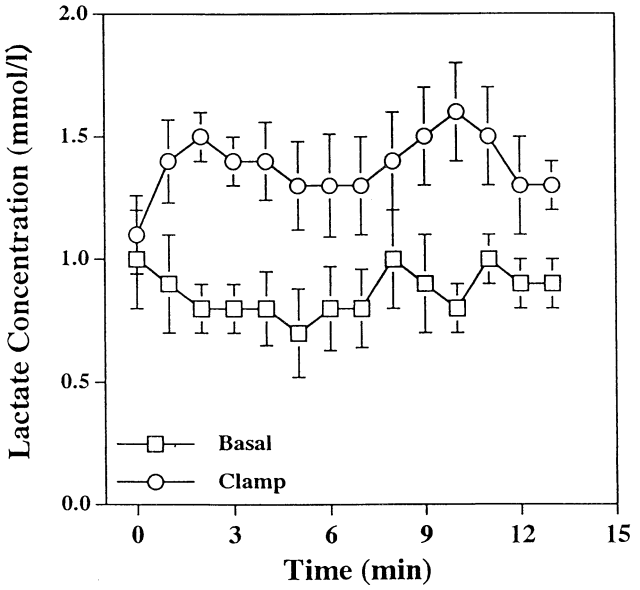

Figure 2 Blood lactate concentration in an antecubital vein in the basal state and during hyperglycemia–hyperinsulinemia. Values are means ± SEM for five volunteers and derive from measurements performed overnight, prior to the placement of the femoral arterial, femoral venous, and hepatic venous catheters.

infusion and it remained relatively constant during the last 6 hours of the study (*Figures 1 and 4B*). Glucose concentration was highest in the femoral artery, followed by the femoral and the hepatic veins, indicating glucose uptake across the leg and the splanchnic region, respectively (*Figure 4B*). To achieve the desired blood glucose levels,

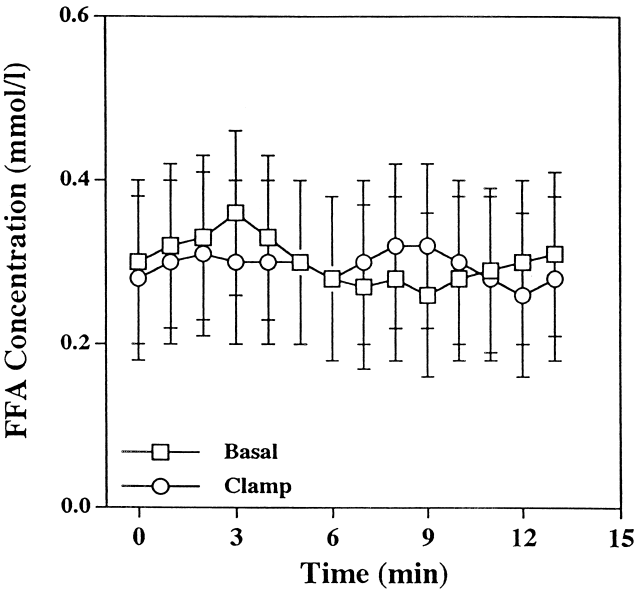

Figure 3 Plasma free fatty acid (FFA) concentration in an antecubital vein in the basal state and during hyperglycemia–hyperinsulinemia. Values are means ± SEM for five volunteers and derive from measurements performed overnight, prior to the placement of the femoral arterial, femoral venous, and hepatic venous catheters.

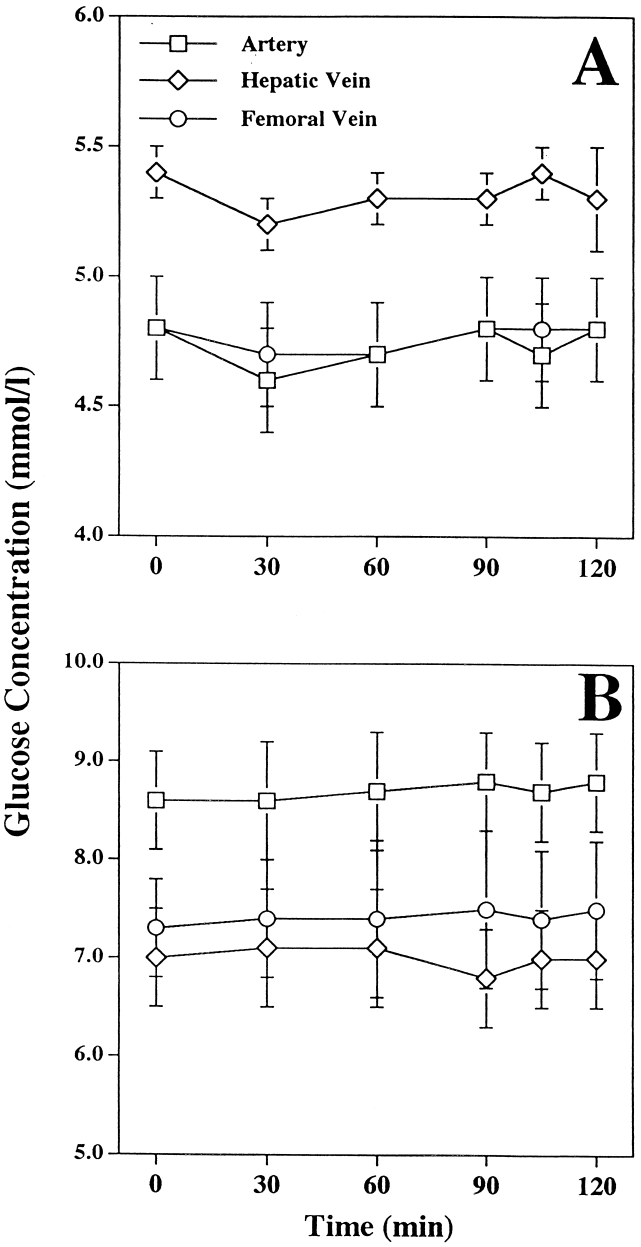

Figure 4 Blood glucose concentration in a femoral artery, a hepatic vein, and a femoral vein during the final 2 hours of the studies in the basal state *(A)* and during hyperglycemia–hyperinsulinemia *(B)*. Values are means ± SEM for five volunteers.

dextrose was infused during the clamp experiments at an average rate of 49 ± 4 μmol/kg/min.

Lactate. Lactate concentration increased significantly during the clamp compared with the basal state (*Figure 2*). The concentration of lactate during the final 2 hours in the basal state was highest in the femoral vein, indicating release of lactate across the leg, and lowest in the hepatic vein, indicating uptake of lactate across the splanchnic region (*Figure 5A*). During the final 2 hours of the clamp, lactate concentration was similar in the artery femoral vein and hepatic vein (*Figure 5B*).

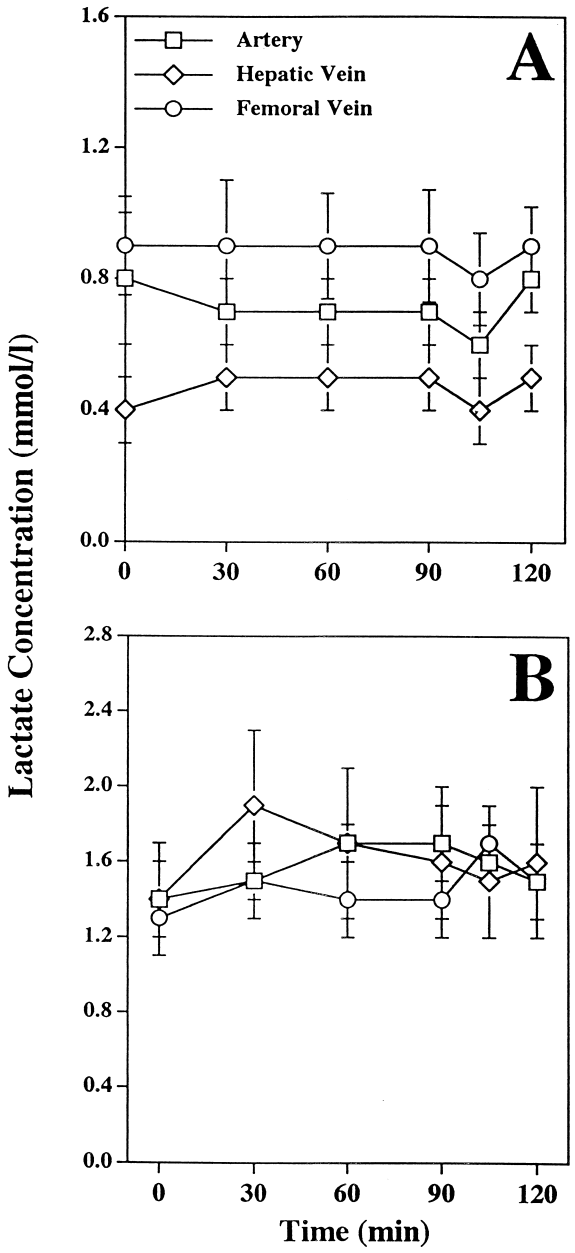

Figure 5 Blood lactate concentration in a femoral artery, a hepatic vein, and a femoral vein during the final 2 hours of the studies in the basal state *(A)* and during hyperglycemia–hyperinsulinemia *(B)*. Values are means ± SEM for five volunteers.

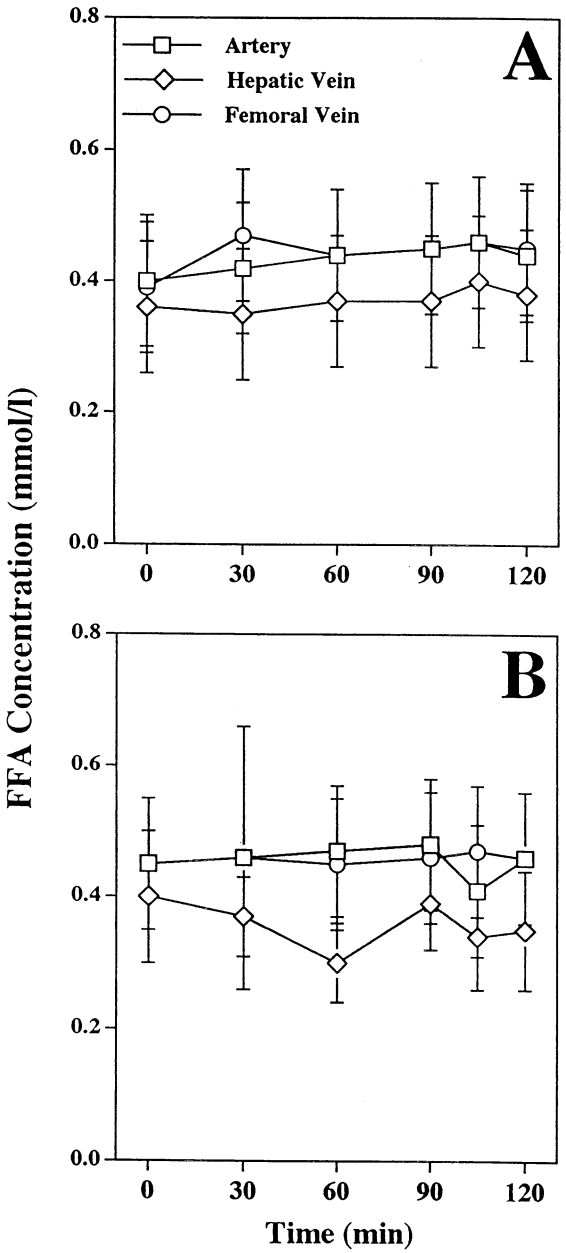

Figure 6 Plasma free fatty acid (FFA) concentration in a femoral artery, a hepatic vein, and a femoral vein during the final 2 hours of the studies in the basal state *(A)* and during hyperglycemia–hyperinsulinemia *(B)*. Values are means ± SEM for five volunteers.

Free fatty acids. Infusion of lipids and heparin prevented the expected decrease in plasma FFA concentration during the clamp and maintained the concentration of FFA similar to that observed in the basal state (*Figures 3 and 6*). FFA concentration was similar in the artery and femoral vein and higher in the artery than in the hepatic vein, both in the basal state and during the clamp (*Figure 6*).

Insulin. Insulin concentration increased from 5.5 ± 1.1 μU/mL in the basal state to 31.3 ± 12.7 μU/mL during the clamp ($P < 0.05$).

Blood flow

Splanchnic (hepatic) blood flow increased from 1.12 ± 0.06 L/min in the basal state to 1.23 ± 0.07 L/min during hyperglycemia ($P < 0.05$). Leg blood flow was 0.49 ± 0.04 L/min and 0.44 ± 0.04 L/min in the basal and hyperglycemic states, respectively (P = NS).

Regional substrate kinetics

Splanchnic region. In the basal state the splanchnic region released glucose and took up lactate (*Tables 1 and 2*).

Table 1 Plasma glucose balance across the splanchnic region and the leg in the basal state and during hyperglycemia

	Splanchnic region	Leg
Basal	−5.8 ± 0.7	0.7 ± 0.2
Hyperglycemia	19.8 ± 3.7*	5.5 ± 2.2*

Values are means ± SE for five volunteers expressed in μmol/kg/min. Negative sign denotes glucose release whereas positive sign denotes glucose uptake. *$P < 0.05$ vs. basal.

Hyperglycemia–hyperinsulinemia reversed this. During the final 30 minutes of the clamp, the splanchnic region took up glucose at a rate of 19.8 ± 3.7 μmol/kg/min ($P < 0.05$ versus basal) and released lactate at a rate of 2.1 ± 0.9 μmol/kg/min ($P < 0.05$ versus basal; *Tables 1 and 2*). The fractional extraction of glucose delivered to the splanchnic region was 15.8 ± 2.9% (*Figure 7*). Clearance of glucose by the splanchnic region accounted for 41 ± 8% of all the infused glucose (*Figure 8*).

Leg. Hyperglycemia significantly increased the rate of glucose uptake across the leg (*Table 1*). The increase in glucose uptake was due in part to an increase in the fractional extraction of glucose delivered to the leg from 2.5 ± 0.8% in the basal state to 13.7 ± 5.4% during the clamp ($P < 0.05$; *Figure 7*). Glucose uptake across the leg accounted for 10.4 ± 3.7% of all the infused glucose (*Figure 8*). In the basal state the leg released lactate, whereas during hyperglycemia we observed uptake of lactate across the leg (*Table 2*).

Discussion

We utilized the splanchnic and leg balance technique to determine regional uptake of intravenously infused glucose during prolonged, moderate hyperglycemia–hyperinsulinemia while maintaining normal systemic fatty acid concentration in healthy human volunteers. Glucose uptake across the splanchnic region accounted for approximately 40% of the infused glucose, with the remainder taken up by other extrahepatic tissues, mainly muscle. These findings demonstrate the importance of the liver in disposing of intravenously infused glucose during hyperglycemia–hyperinsulinemia in insulin resistant states.

The calculated rates of splanchnic glucose disposal in the present study are significantly higher than previously reported during hyperglycemia–hyperinsulinemia.[2–5] There

Table 2 Plasma lactate balance across the splanchnic region and the leg in the basal state and during hyperglycemia

	Splanchnic region	Leg
Basal	1.5 ± 0.8	−0.7 ± 0.2
Hyperglycemia	−2.1 ± 0.9*	0.5 ± 0.3*

Values are means ± SE for five volunteers expressed in μmol/kg/min. Negative sign denotes lactate release whereas positive sign denotes lactate uptake. *$P < 0.05$ vs. basal.

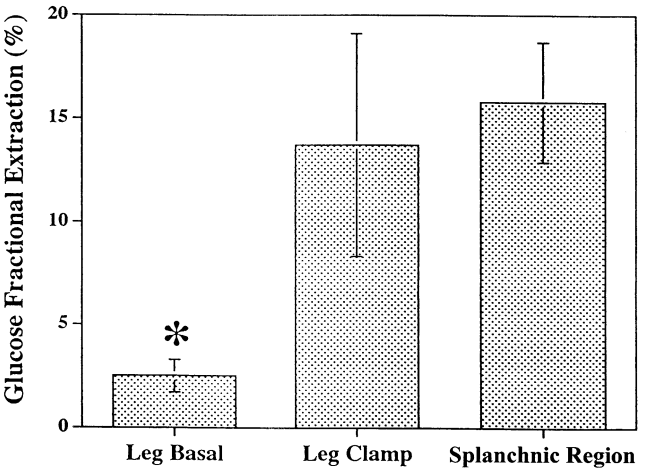

Figure 7 Glucose fractional extraction across the leg in the basal state and during the clamp and across the splanchnic region during the clamp. Values are means ± SEM for five volunteers. *$P < 0.05$ vs. clamp.

are two possibilities to explain an overestimation of splanchnic glucose disposal in the present study: We could have overestimated splanchnic blood flow and/or we could have overestimated the blood glucose arteriovenous difference. Splanchnic blood flow during the clamp in the present study was 1.2 L/min, which is similar to a value previously reported in the literature.[10] Regarding the measurement of the arterio-hepatic venous glucose balance, back-flow contamination of blood from the vena cava into the hepatic vein, which would have resulted from improper positioning of the hepatic catheter and/or from rapid blood draw from the hepatic catheter, is the most likely source of error. However, such an error would be expected to increase the concentration of glucose in the hepatic vein. This is because in the setting of hyperglycemia–hyperinsulinemia the concentration of glucose in the caval blood is higher than that

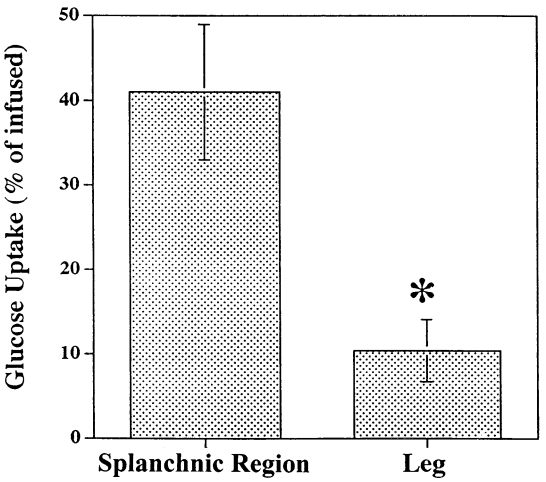

Figure 8 Percent of glucose infused that was taken up (cleared) by the splanchnic region and the leg during the clamp. Values are means ± SEM for five volunteers. *$P < 0.05$ vs. splanchnic region.

in the hepatic venous blood. Therefore, contamination of hepatic vein blood with caval blood would decrease the glucose arterio-hepatic venous difference and, consequently, decrease the calculated rate of splanchnic glucose uptake. Thus, this potential error could only underestimate, not overestimate, our estimates of splanchnic glucose uptake during the clamp. The potential of back-flow from the vena cava into the hepatic vein is well recognized from clinical experience in interventional radiology.[13] In the present study great care was taken to assure correct positioning of the hepatic vein catheter and prevent contamination of hepatic vein blood from caval blood.

In our calculations we assumed complete suppression of hepatic glucose production during hyperglycemia–hyperinsulinemia. However, it has been suggested that even during high rates of glucose infusion there is residual glucose production that amounts to less than 25% of the fasting rate.[14] The rate of glucose uptake during hyperglycemia in the present study was 20 μmol/kg/min, which corresponds to approximately 40% of infused glucose. If there was residual glucose production of 25% of the fasting level (i.e., 5.8 μmol/kg/min), estimates of hepatic glucose uptake would increase to 21.5 μmol/kg/min and would account for an even greater percent of glucose uptake, approximately 45% of infused glucose.

Studies utilizing the hyperinsulinemic–euglycemic clamp technique have suggested that approximately 5% of infused glucose is taken up and metabolized by the liver.[3,5] However, during hyperglycemia splanchnic glucose uptake has been reported to be significantly higher than in hyperinsulinemic–euglycemic clamp studies and accounts for approximately 14[3,5] to approximately 27%[9] of infused glucose. There are at least two potential explanations for the differences in hepatic glucose clearance in the present study versus previous observations.[3,5,9] First, in the above mentioned studies[3,5,9] glucose was infused for 2 to 4 hours, whereas in the present study calculations of glucose uptake across the splanchnic region and the leg were performed in the last 30 minutes of 15 hours of hyperglycemia–hyperinsulinemia. Because we did not make any measurements over the first 2 to 4 hours of glucose infusion in the present study, it is possible that the liver cleared less glucose at that time than it did 10 to 12 hours later. Second, the concentration of glucose, fatty acids, and insulin were different in our study than in the above mentioned studies.[3,5,9] There is evidence to suggest that the clearance of infused glucose by the liver is regulated not only by the systemic glucose concentration but also by the concentration of other substrates and hormones.[15,16] Indeed, the fact that in the present study plasma fatty acid concentration was maintained at basal levels may have played a role in the pattern of glucose disposal.

Our finding that during prolonged (i.e., 15 hours) hyperglycemia–hyperinsulinemia approximately 40% of the infused glucose is taken up by the splanchnic region is similar to results from studies on glucose intolerant patients in whom the liver glucose uptake reportedly accounts for 47% of the infused glucose in the setting of hyperglycemia.[9] The explanation for the similarity of our results with results from glucose intolerant patients might be that in the present study we created a metabolic profile in healthy volunteers that was similar to glucose intolerance by inducing hyperglycemia, allowing insulin to increase, and maintaining fatty acid concentration at fasting levels. In this model peripheral glucose uptake is not stimulated, as it is in the hyperinsulinemia–euglycemia model, because insulin is only modestly elevated and fatty acids are maintained at fasting levels. If fatty acid concentration had been allowed to decrease in response to insulin elevation, peripheral glucose uptake would likely have increased,[12] thereby changing the pattern of regional glucose disposal. The effect of fatty acid concentration on peripheral glucose disposal is exerted on the rate of glucose uptake and not oxidation.[17]

The fate of intravenously infused glucose is of particular importance because of the potential implications that accelerated hepatic glucose uptake and oxidation may have on liver function. Increased systemic glucose concentration as a result of high rates of glucose infusion and/or glucose intolerance will result in accelerated glucose uptake by the liver, which in turn is expected to stimulate hepatic glucose and inhibit hepatic fatty acid oxidation.[18] We recently showed that hyperglycemia–hyperinsulinemia-induced inhibition of fatty acid oxidation in the liver stimulates triacylglycerol synthesis, because a significant portion of newly synthesized triacylglycerols remain in the liver.[18] Accumulation of triacylglycerols in the liver may induce hepatic steatosis, which is an unfavorable condition for the liver.[19,20] Keeping the glucose concentration near normal or administering insulin to enhance peripheral glucose disposal may be beneficial for the liver, because it has been shown that the addition of insulin enhances peripheral but not hepatic glucose uptake.[15]

In summary, the findings of the present study suggest a more important role for the liver in disposing of intravenously infused glucose than previously thought. Accelerated hepatic glucose uptake may disrupt normal liver metabolism, with potentially dangerous consequences for the patient. Measures to control systemic glucose concentration may be necessary to prevent excessive glucose disposal in the liver during glucose administration.

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