# Comparison of Arterialized Venous Sampling From the Hand and Foot in the Assessment of In Vivo Glucose Metabolism

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**To determine whether arterialized venous blood obtained from a foot vein could be substituted for arterialized venous blood obtained from a hand vein during studies using the glucose clamp technique, we simultaneously measured glucose concentrations and $po_2$ in blood samples obtained from the heated hands and feet of five normal volunteers during the euglycemic and hyperglycemic steps of a hyperinsulinemic clamp. Plasma glucose concentrations were found to be virtually identical in arterialized venous blood drawn from the hand and the foot under both euglycemic and hyperglycemic conditions. The correlation between these values was significant ($R^2 = .99$, $P < .001$). $po_2$ measurements in blood drawn from the heated hand or foot were not statistically different. We conclude that the glucose concentration measured in arterialized venous blood drawn from the foot is equivalent to the concentration in arterialized venous blood drawn from the hand. These observations will allow investigators to study in vivo glucose metabolism in individuals with poor venous access in the upper extremities and to use protocols that make the arms of the subject inaccessible for blood sampling during the study.**
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DURING THE PAST THREE DECADES, the glucose clamp technique has been widely applied to the study of in vivo glucose turnover and insulin action in humans. Using this method, the investigator holds the serum insulin concentration at a fixed level while maintaining glycemia at a desired concentration by adjusting the rate at which exogenous glucose is infused.[1]

Traditionally, the investigator relies on the glucose concentration in arterialized venous plasma obtained from the hand every few minutes to determine the appropriate rate at which to deliver exogenous glucose, and the quantity of glucose required to maintain the target level of glycemia is used as a measure of glucose utilization. While this approach has been successful in defining the regulation of total-body glucose turnover, it has been difficult to use in settings in which the patient has poor venous access in the arms because of the presence of a shunt or an amputation. In addition, experimental situations in which the subject is largely inaccessible to the investigator present problems with obtaining blood samples from the upper extremities. One such investigative paradigm is magnetic resonance spectroscopy, a noninvasive method that allows quantification of tissue metabolites in individual organs and often requires placement of the entire subject into the magnet.

A solution to these venous access problems would be to cannulate a foot vein and use the plasma glucose concentration measured in blood obtained from the foot in the adjustment of the glucose infusion. However, whether blood from a foot can be arterialized as well as blood from a hand and whether glucose concentrations are the same in arterialized venous blood from the upper and lower extremities have not been determined. Consequently, we sought to learn whether glucose concentrations in plasma obtained from an arterialized foot vein are equal to the concentrations in plasma obtained from an arterialized hand vein in the basal state and during hyperglycemia.

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## SUBJECTS AND METHODS

Healthy control subjects were studied in the General Clinical Research Center at the University of Minnesota in the morning after a 10-hour fast. All subjects recruited for participation were employees of the University of Minnesota, and the protocol was approved by the Institutional Review Board of the University. After obtaining informed consent, three intravenous catheters were placed in each subject. The catheter placed anterograde in the antecubital fossa was used for infusion of glucose and insulin. Catheters placed retrograde in the hand and retrograde into the most distal vein accessible for cannulation in the leg were used to obtain blood samples from which glucose and insulin concentrations were subsequently determined. All foot veins used for the study were at or distal to the ankle. Arterialization of venous blood in the catheterized hand was achieved by placement into a warming chamber set at 45 to 50°C. Arterialization of venous blood in the catheterized foot was accomplished by wrapping the leg with an electric heating pad that maintained a temperature of 50°C. Retrograde catheters and the veins in which they were placed were kept patent by infusion of 0.9% saline.

After the subject was prepared as just described, baseline samples for glucose, insulin, and $po_2$ were obtained simultaneously from the hand and foot at −30, −20, −10, and −5 minutes. Insulin infusion at a rate of 1 mU/kg/min was begun at minute 0 and continued for the duration of the study. Between minutes 0 and 60, plasma glucose concentrations were clamped at 100 mg/dL by infusion of dextrose (10% in water). Between minutes 60 and 120, plasma glucose concentrations were clamped at 200 mg/dL. Potassium phosphate (120 mEq/L) was infused at a rate of 30 mL/h throughout the study. Blood samples were simultaneously obtained from the hand and foot every 5 minutes for the immediate determination of plasma glucose concentration, and every 20 minutes for the measurement of serum insulin concentration and $po_2$.

Plasma glucose concentrations were determined using an autoanalyzer (Beckman, Fullerton, CA). Serum insulin concentrations were measured using a double-antibody radioimmunoassay.[2] The $po_2$ was assessed by an oxygen-specific electrode (Radiometer, Copenhagen, Denmark).

All values presented are the mean ± SEM. Differences between groups were evaluated using ANOVA. Statistical significance was set at $P$ less than .05.

## RESULTS

Five subjects participated in this investigation. Three were women and two were men. The mean body mass index was 25.2 ± 1.5 kg/m$^2$ and the mean age was 30 ± 8 years. None of the subjects were taking medication at the time of the study.

During the study, plasma glucose concentrations obtained from arterialized venous blood in the hand and in the foot were virtually identical (Fig 1). The mean plasma glucose concentrations achieved during the final 30 minutes of the euglycemic clamp were 5.3 ± 0.1 mmol/L in samples drawn from the hand and 5.2 ± 0.1 mmol/L in samples drawn from the foot. During the final 30 minutes of the hyperglycemic phase of the study, plasma glucose concentrations were 11.4 ± 0.2 mmol/L and 11.0 ± 0.2 mmol/L in samples drawn from the hand and foot, respectively. Serum insulin concentrations were maintained at 416 ± 3.6 pmol/L from minute 20 to 120.

A significant correlation was found between the plasma glucose concentrations in samples drawn simultaneously from the hand and foot ($R^2$ = .99, $P$ < .001; Fig 2). The differences between the simultaneously obtained plasma glucose concentrations were smallest during euglycemia and increased during the hyperglycemic phase of the study, but these differences were not statistically significant (Table 1). The differences between $po_2$ measurements made on blood drawn from the hand and the foot also were greatest during hyperglycemia, but these differences also failed to reach statistical significance.

## DISCUSSION

In this investigation, we found that a significant correlation exists between plasma glucose concentrations measured in arterialized venous blood obtained simultaneously from the hand and the foot. This relationship is present both at euglycemia and at hyperglycemia. Our data demonstrate that blood drawn from a foot heated to 50°C provides glucose concentration data equivalent to data obtained from blood drawn from a similarly heated hand. In addition, these results support the use of arterialized blood drawn from the foot in performing glucose clamps in patients with poor venous access in the upper extremities, or under conditions in which the foot is the only portion of the body accessible for blood sampling, such as experiments using magnetic resonance spectroscopy.

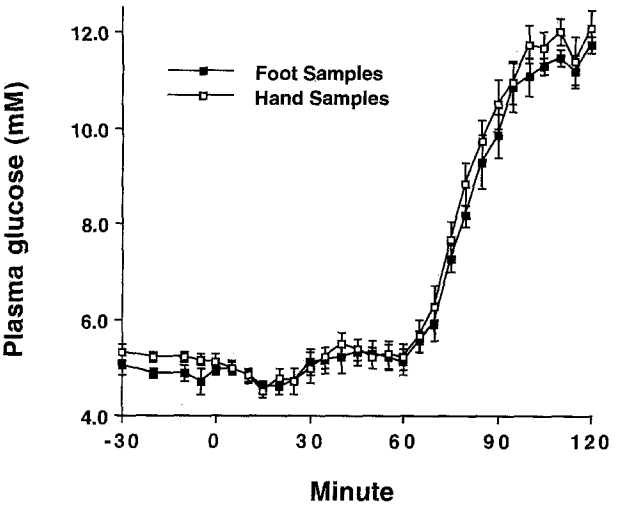


**Fig 1. Glucose concentrations in plasma drawn simultaneously from the hand and the foot. Plasma glucose concentrations were measured in samples obtained simultaneously from the hand and foot during a 120-minute hyperinsulinemic clamp study performed at euglycemia and hyperglycemia in 5 subjects. No statistical differences were found between concentrations measured in plasma obtained from the hand *v* the foot.**

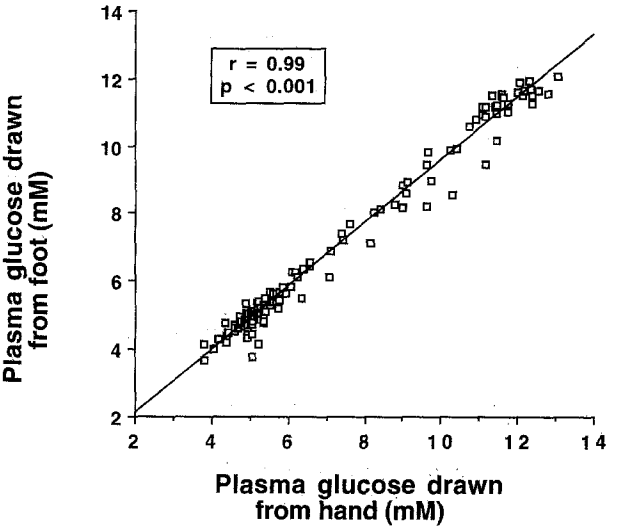


**Fig 2. Correlation between glucose concentrations in plasma drawn simultaneously from the hand and the foot. Plasma glucose concentrations were measured in 29 pairs of samples obtained simultaneously from the hands and feet of each of 5 subjects during a hyperinsulinemic clamp study performed at euglycemia and hyperglycemia. A statistically significant correlation was found between plasma glucose concentrations measured simultaneously from hands and feet ($r$ = .99, $P$ < .001, $N$ = 145).**

In metabolic studies, arterialized venous blood has been used as a surrogate for arterial blood to avoid the significant risks associated with frequent arterial punctures. Validation of this approach for the study of in vivo glucose metabolism has been provided by studies in which glucose concentrations measured in arterialized venous blood drawn from a hand have been shown to be equivalent to glucose concentrations measured in arterial blood, an observation made by most[3-6] but not all[7] investigators. Additional support for this approach comes from studies in which glucose concentrations measured in venous blood were shown to be more different from arterial values than were the concentrations measured in arterialized venous blood.[3,8] As a result of these observations, most investigators have used arterialized venous blood drawn from the hand to obtain the

**Table 1. Differences Between Glucose and $po_2$ Values Measured in Samples Drawn From the Hand and the Foot**

| State | $Glucose_{hand}$ − $Glucose_{foot}$ (mmol/L) | $po_{2\,hand}$ − $po_{2\,foot}$ (mm Hg) |
|---|---|---|
| Baseline | 0.1 ± 0.1 | 2 ± 7 |
| Euglycemia | 0.1 ± 0.1 | 7 ± 4 |
| Hyperglycemia | 0.4 ± 0.1 | 12 ± 5 |

NOTE. No statistically significant differences were found between measurements made at baseline, euglycemia, or hyperglycemia.

plasma glucose concentrations necessary to appropriately adjust the glucose infusion rate during a glucose clamp. Arterialization has been accomplished either by placing the cannulated hand into a warming chamber set at approximately 50°C[6,7,9] or by wrapping the hand in heating pads.[10] Our study, in which the hand was arterialized by placement in a warming chamber and the foot was arterialized by wrapping with a heating pad, demonstrates the equivalence of these two methods of heating.

Despite the widespread use of this method, some have questioned whether arterialization is necessary to obtain glucose values from venous blood that are equivalent to arterial glucose concentrations.[11] Green et al[12] suggest that arterialization is unnecessary based on their demonstration that no statistical difference exists between glucose concentrations measured in arterial blood versus venous blood drawn from a cool or heated hand. Others have made similar observations, but propose that heating one hand to 50°C causes sufficient vasodilation to arterialize the venous blood in the contralateral arm.[6] These investigators believe that heating a hand is necessary to obtain venous blood with glucose concentrations that are equivalent to those measured in arterial blood, but that it may not matter if the venous blood is obtained from the hand inside the warming chamber or from its cooler mate.

In our investigation, we found that glucose concentrations measured in venous blood drawn from a foot surrounded by a heating pad set at 50°C are not different from the concentrations measured in arterialized venous blood drawn from a hand. Since previous investigators have demonstrated that glucose concentrations measured in venous blood drawn from a hand heated in a warming chamber set at 50°C are equivalent to those measured in arterial blood, we can conclude that the glucose concentrations measured in venous blood drawn from the heated feet in our study are equivalent to the glucose concentrations present in arterial blood. It is interesting that the greatest differences found between glucose concentrations measured in blood drawn from the hand and the foot occurred when the differences in $po_2$ in blood drawn from these locations were at a maximum. This suggests that the degree of arterialization of venous blood may be important in determining the similarity between glucose concentrations in arterial and venous blood. A similar observation was made by Liu et al,[6] providing additional evidence of the importance of adequate arterialization in experiments where venous glucose concentrations are used as a surrogate for arterial glucose levels.

In summary, we have observed that the glucose concentration measured in arterialized venous blood drawn from the foot is equivalent to the concentration in arterialized venous blood drawn from the hand. This information gives investigators greater flexibility in selecting patients and settings with which to study in vivo glucose metabolism.

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