Blood extraction from lancet wounds using vacuum combined with skin stretching

DAVID D. CUNNINGHAM, TIMOTHY P. HENNING, ERIC B. SHAIN, DOUGLAS F. YOUNG, JURGEN HANNIG, ERIC BARUA, AND RAPHAEL C. LEE. Blood extraction from lancet wounds using vacuum combined with skin stretching. J Appl Physiol 92: 1089–1096, 2002; 10.1152/japplphysiol.00798.2001.—Key factors and practical limits of blood extraction from lancet wounds on body sites other than the finger were determined by testing a large number of conditions. During these tests, the pain associated with lancing alternate body sites was rated as less painful than a fingerstick 98% of the time. Vacuum combined with skin stretching was effective in extracting an adequate volume of blood from the forearm for glucose testing, up to an average of 16 μl in 30 s. The amount of blood extracted increases with the application of heat or vacuum before lancing, the level of vacuum, the depth of lancing, the time of collection, and the amount of skin stretching. Vacuum and skin stretching led to significant increases, up to fivefold in the perfusion of blood in the skin as measured by laser Doppler. Our observations suggest that vacuum combined with skin stretching increases blood extraction at alternate sites by increasing the lancet wound opening, increasing the blood available for extraction by vasodilatation, and reducing the venous return of blood through capillaries.

succion; diabetes; diagnostcs; alternate site; glucose measurement

THE MOST COMMON METHOD of obtaining small amounts of blood from humans for diagnostic testing is by lancing the finger. The finger is typically lanced because it can be squeezed to expel more blood. People with diabetes lancer their fingers several times a day. Whereas the finger can readily supply the volume of blood needed for conventional test strips, 3–10 μl (16), the process is painful and results in soreness that can last for several days. Thus the development of painless and convenient methods to access blood for measurement, particularly glucose, has been an active area of research.

Interstitial fluid has been accessed by suction effusion (19), transcutaneous microdialysis (12), intradermal pressure harvesting with a cannula (31), iontophoresis (35), and low-frequency ultrasound (20, 26); however, analysis of samples collected using these techniques is difficult because of the small amount of glucose extracted and dilution of the sample. Several mechanical lancet devices have been developed to harvest capillary blood from lancet wounds on sites other than the finger by applying pressure or vacuum around the lanced site (2, 13, 40). Lancet sticks at alternate sites are virtually pain free, with 60% of the sticks being rated as painless and 90–97% being rated as less painful than a fingerstick (9, 13, 14, 40). Unfortunately, these mechanical devices require multiple manual manipulation steps that may be poorly controlled by the user. We are unaware of studies reporting the amount of blood extracted or factors that may be associated with the successful extraction of blood with the mechanical devices. In a published study, our laboratory reported the distribution of blood volumes obtained from diabetic subjects by vacuum-assisted lancing of the forearm; however, a limited number of extraction conditions were evaluated (9).

The aim of the present study was to understand the key factors and practical limits of blood extraction from lancet wounds on alternate sites using vacuum. A large number of extraction conditions were screened by testing several conditions on a group of volunteers and comparing the results for each extraction condition. The vacuum level, lancing depth, lancet size, and collection time were investigated. Treatment of the site with heat or vacuum before lancing was performed to increase the amount of blood extracted. Stretching of the skin with vacuum was studied with the goal of developing an integrated system that supplied vacuum, lanced the skin, and positioned the test strip over the wound to collect the blood. The success of these efforts resulted in the commercial introduction of an automated device for alternate site blood glucose monitoring that is less painful (14).

MATERIALS AND METHODS

Lancing and blood collection. Four or more individuals participated in each of 16 blood collection trials after informed consent was obtained, as approved by an Institutional

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Table 1. Summary of blood collection trials and conditions

<table>
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<th>Conditions, no.</th>
<th>Reps., no.</th>
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<th>Prevacuum Time, s</th>
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<th>Height, mm</th>
<th>Lancing Depth, mm</th>
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<td>8</td>
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<td>pulsed vacuum</td>
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</tr>
<tr>
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<td>4</td>
<td>2</td>
<td>4</td>
<td>30</td>
<td>5</td>
<td>15</td>
<td>0</td>
<td>1.6</td>
<td>net to prevent stretching</td>
<td></td>
</tr>
<tr>
<td>3</td>
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<td>4</td>
<td>30</td>
<td>7.5</td>
<td>30</td>
<td>8</td>
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<td>30</td>
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<td>8</td>
<td>1.6</td>
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<td>4</td>
<td>30</td>
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<td>8</td>
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<td>preheat site</td>
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<td>40</td>
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<td>6</td>
<td>40</td>
<td>7.5</td>
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<td>10</td>
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<td>23-gauge lancet</td>
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<td>4</td>
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<td>4</td>
<td>30</td>
<td>7.5</td>
<td>15</td>
<td>10</td>
<td>3</td>
<td>1, 1.6</td>
<td>various body sites</td>
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</tbody>
</table>

Conditions, no. of extraction conditions tested. Reps., no. of repetitions of each condition on each subject. Collection diameter is the nosepiece diameter. Collection height is the nosepiece height; when no value is listed, the height of skin stretching into the nosepiece was not limited. In all trials, the dorsal forearm was lanced with a tribeveled 28-gauge Becton-Dickinson Ultra-Fine lancet. psig, lbs./in.² gauge.

Review Board. Subjects with a history of excessive bleeding were excluded. Blood was collected from a minimum of 16 lancet wounds for each of the 105 different conditions, as summarized in Table 1.

In each trial, the dorsal forearm was lanced with a Becton-Dickinson (BD) Ultra-Fine lancet and retrotracted, regulated vacuum was applied over the wound with a collection nosepiece for a fixed time, the vacuum was vented to the atmosphere, the nosepiece was removed, and the amount of blood was collected and measured using a microcapillary tube (Drumond Scientific, Broomall, PA). Automated lancing and vacuum systems were constructed to keep the time between steps to a minimum. Pulsed vacuum was produced by regulating the vacuum with a vent line and solenoid valve. The depth of lancing was controlled by constructing custom caps for a standard spring-loaded lancing device and by placing a metal collar around the lancet. In cases where vacuum was applied to the forearm before lancing, the vacuum level and nosepiece geometry were the same as in the blood collection step. The 8-mm-diameter collection nosepiece consisted of a pipette tip (Rainin Institute, Woburn, MA) with the narrow end connected to the vacuum source. In trial 9, glass tubes of known diameter were used for collection. In trial 10, the prevacuum, lancing, and collection steps were all completed without releasing the vacuum (see Fig. 1). In trial 15, all steps were completed under vacuum using a 10-mm-diameter, 3-mm-high nosepiece, as previously described (9). For trials 6, 7, and 14, one nosepiece was used for prevacuum and lancing, and a nosepiece of the same geometry without the lancet was used for blood collection. To prevent the skin from stretching inside the nosepiece in trials 2 and 3, a checkerboard pattern of four thin nylon strings was glued across a plastic cylinder with an inside diameter of 15 mm.

For heat treatment in trials 11–13, feedback-controlled heaters were constructed using a Kapton film heating element (Minco Products, Fridley, MN), temperature sensor, and aluminum block (25 × 25 × 0.6 mm) attached to a square, circular, or donut-shaped copper skin contact block. The feedback control was set to heat the skin to either 40 or 45°C.

Immediately after each lancet stick, the subject rated the sensation into one of the following categories: 1) didn’t feel anything or not sure they felt anything; 2) definite prick, although not as painful as a fingerstick; or 3) definite pain, approximately equal to a fingernail.

Skin stretching: Four trials including from 9 to 80 subjects were performed to determine the height that skin stretches into a cylinder with different levels of vacuum. Glass tubes of different diameters were fitted with scales and a regulated vacuum supply. The subject’s forearm was drawn into the tube, and a video camera was used to magnify the image and
reduce the parallax error. Both blood collection and skin stretching were measured on subjects enrolled in trial 10. Subjects with diabetes were recruited for trial 18.

RESULTS

Vacuum and time. Prevacuum and increasing levels of vacuum increased the volume of blood collected (Fig. 2). The mean volume increased linearly with collection time over the range of 10–40 s (trial 6) when both the BD lancet (μL = 0.092 × s + 1.8; r = 0.92, P = 0.08) and the MediSense TLC lancet (μL = 0.16 × s + 0.4; r = 0.99, P = 0.01) were used. When the total pre- and postvacuum time was held constant at 45 s (trial 7), the mean blood volume increased linearly with collection time (μL = 0.068 × s + 1.2; r = 1.00, P = 0.005).

Nosepiece geometry. Increasing the diameter of the nosepiece in the range of 4–10 mm increased the height that the skin stretched up into the nosepiece (Table 3) and increased the volume of blood collected (Fig. 3). For larger diameters, the mean height of skin stretching increased linearly with the diameter (Table 3, trial 10) and with the level of vacuum (trial 18). At constant, applied vacuum, the mean blood volume increased as the step height of the nosepiece increased (Fig. 2). The mean volume increased linearly with collection time (μL = 0.068 × s + 1.2; r = 1.00, P = 0.005).

Lancing depth and heat. Lancing depths in the range of 0.7–1.6 mm gave linearly increasing volumes of

Table 2. Effect of vacuum level and skin stretching on blood extraction

<table>
<thead>
<tr>
<th>Trial</th>
<th>Variable Conditions</th>
<th>Blood Volume, μL</th>
<th>Average SD, μL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No vacuum</td>
<td>0.8 ± 0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>2</td>
<td>−2.5 psig</td>
<td>1.6 ± 0.2</td>
<td>0.7</td>
</tr>
<tr>
<td>3</td>
<td>−5.0 psig</td>
<td>3.1 ± 0.3</td>
<td>1.1</td>
</tr>
<tr>
<td>4</td>
<td>Net</td>
<td>0.7 ± 0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>5</td>
<td>No net</td>
<td>5.1 ± 1.4</td>
<td>5.6</td>
</tr>
<tr>
<td>6</td>
<td>No prevacuum</td>
<td>1.8 ± 0.3</td>
<td>1.0</td>
</tr>
<tr>
<td>7</td>
<td>Net with prevacuum</td>
<td>2.8 ± 0.3</td>
<td>1.2</td>
</tr>
<tr>
<td>8</td>
<td>No net with prevacuum</td>
<td>4.7 ± 0.6</td>
<td>1.9</td>
</tr>
</tbody>
</table>

Results of blood volume extracted from lancing each of 4 volunteers, 4 times, for a total of 16 lances per condition. Means ± SE were calculated for 16 lances. Average SDs were calculated from the SDs of each individual’s 4 sites. (Note: 1 atm = 760 Torr = 760 mmHg = 1.01 bar = 14.7 lbs/In.² area = 0 psig = 1.01325 10⁵ Pa.)
blood with depth, but results in the range of 1.7–2.3 mm were more variable and showed no statistically significant increase with depth (Fig. 6). Mean blood volumes as large as 17 μl were collected after the skin was heated to 45°C for 45 s before lancing and extraction (Table 4). Increasing the heating time from 15 to 45 s resulted in 1.4- to 1.9-fold increases at 40°C and 2.6- to 4-fold increases at 45°C. Although blood collection without preheating of the skin was not determined in trials 11–13, identical conditions except without skin preheating were used in trials 4 and 8, resulting in volumes of 3.9 ± 0.4 and 3.1 ± 0.5 μl, respectively.

Pulsed vacuum. Skin was observed to stretch up and fall back when the vacuum was pulsed. Volumes showed no trend with pulse frequency (0, 0.2, 0.8, 3.2, 13, 25, and 100 Hz; trial 1) at 2.5 or 5 psig. No difference was found in the overall average volumes with pulsed vacuum and continuous vacuum (1.8 μl pulsed vs. 1.6 μl continuous at –2.5 psig, P = 0.75; and 3.1 μl pulsed vs. 3.1 μl continuous at –5 psig, P = 0.39; trial 1). In the follow-up trial at higher levels of vacuum (–5, –7.5, and –10 psig; trial 8), larger blood volumes were obtained with continuous vacuum than with 3.2- or 100-Hz pulsed vacuum.

Body sites. The study of various body sites (dorsal forearm, palmar forearm, upper arm, stomach, and thigh) with lancing depths of 1.0 and 1.6 mm gave

Table 3. Height skin stretched into different diameter cylinders with various levels of vacuum

<table>
<thead>
<tr>
<th>Trial</th>
<th>Subjects, no.</th>
<th>Diameter, mm</th>
<th>–2 psig</th>
<th>–4 psig</th>
<th>–6 psig</th>
<th>–8 psig</th>
</tr>
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<tr>
<td>17</td>
<td>9</td>
<td>4</td>
<td>0.8 ± 0.0</td>
<td>1.0 ± 0.3</td>
<td>1.3 ± 0.0</td>
<td>1.5 ± 0.3</td>
</tr>
<tr>
<td>18</td>
<td>10</td>
<td>9.5</td>
<td>1.2 ± 0.3</td>
<td>1.7 ± 0.4</td>
<td>2.0 ± 0.4</td>
<td>2.2 ± 0.3</td>
</tr>
<tr>
<td>10</td>
<td>21</td>
<td>9.5</td>
<td>1.9 ± 0.3</td>
<td>2.5 ± 0.4</td>
<td>3.1 ± 0.3</td>
<td>3.1 ± 0.3</td>
</tr>
<tr>
<td>19</td>
<td>80</td>
<td>10</td>
<td>3.1 ± 0.3</td>
<td>4.0 ± 0.4</td>
<td>4.4 ± 0.4</td>
<td>4.8 ± 0.5</td>
</tr>
</tbody>
</table>

Values are means ± SD. Subjects in trial 18 had diabetes. *Range was 3.0–7.5 mm.

Fig. 3. Blood volume extracted with different diameter glass tubes in 30 s at –7.5 psig (●) and –5 psig (■) in trial 9. Values are means ± SE.

Fig. 4. Blood volume extracted with nosepieces of different inner diameters (A) and inside step heights (B) in trial 10. Values are means ± SE in A. B: diameters are 9.5 mm (●), 12.7 mm (■), 15.9 mm (▲), and 19.1 mm (●).
trials 6

deep lancing depths, and various body sites tested in approximately equal to a specific condition were rated as less painful than a full as a thing, 15% felt a 83%

study, the sensation after lancing was rated as follows:

/H11006


flangerstick.

ifferent amount of blood (3.5

on the upper arm and stomach gave statistically dif-

ther) to 8.0

/H11006

sites studied. Lancing alternative sites minimized pain,
in skin stretching (24) and blood perfusion (38) at the

which is in accord with the relatively small variations

cluded the vacuum level, lancing depth, and collection

the amount extracted. Other important factors included

the vacuum nosepiece lead to a dramatic increase in

amounts of blood. Allowing the skin to stretch up into

cause replicate tests on an individual gave different

vacuum. The exact site of lancing was important be-

extraction from lancet wounds on alternate sites using

stand the key factors and practical limits of blood
ingestion, of blood in the skin. Five volunteers were measured in duplicate before and during a 1-min application of −7.5 psig vacuum using a 12.7-mm-inner-diameter nosepiece. For each perfusion data point, 10 s of continuous measurement (40 ± 5 s into the vacuum period) were averaged to smooth temporal fluctuations due to the heart. Values are means ± SE.

blood volumes in the range of 2.4 ± 0.4 μl (1.0 mm, thigh) to 8.0 ± 1.0 μl (1.6 mm, stomach). Compared with the dorsal forearm, only the 1.6-mm-deep lances on the upper arm and stomach gave statistically different amount of blood (3.5 ± 0.5 vs. 5.5 ± 0.8 μl, P = 0.04; and 8.0 ± 1.5 μl, P = 0.006, respectively).

Pain. From the total of 2,614 lancet sticks in the study, the sensation after lancing was rated as follows: 83% “didn’t feel anything or not sure they felt anything,” 15% felt a “definite prick, although not as painful as a fingerstick,” and 2% felt “definite pain, approximately equal to a fingerstick.” For the larger lancets, deeper lancing depths, and various body sites tested in trials 6 and 14–16, a minimum of 94% under any specific condition were rated as less painful than a fingerstick.

DISCUSSION

A large number of conditions were tested to understand the key factors and practical limits of blood extraction from lancet wounds on alternate sites using vacuum. The exact site of lancing was important because replicate tests on an individual gave different amounts of blood. Allowing the skin to stretch up into the vacuum nosepiece lead to a dramatic increase in the amount extracted. Other important factors included the vacuum level, lancing depth, and collection time. Both heat and vacuum treatment of the site before lancing were effective in increasing the amount of blood extracted. Pulsing the vacuum to knead the skin around the lancet wound was ineffective in obtaining more blood. Microliter volumes of blood were relatively rapidly extracted from various anatomic sites, which is in accord with the relatively small variations in skin stretching (24) and blood perfusion (38) at the sites studied. Lancing alternative sites minimized pain, in agreement with previous studies (9, 13, 14, 40). Informal feedback from the subjects revealed that the soreness and tenderness associated with lancing the finger were eliminated, presumably because of the facts that a normal lancing depth penetrates a portion of the underlying muscle on the finger but is limited to the dermis and subcutaneous fat layer at alternate body sites (21) and that normal use of the fingers involves frequent high-pressure contact.

Site of lancing. Blood volumes collected using standard fingerstick sampling methods are characterized by large coefficients of variation, in the range of 62–103% (11, 15). Presumably, the heterogeneity of the microcirculation of the skin is important. Laser Doppler and biopsy and histology studies have shown regions of relatively rich and poor perfusion of the forearm on a scale of 1 mm, which is larger than the diameter of a lancet (5–7, 22). The density of small capillaries has been reported as 60–70 mm−2 (28), whereas the density of larger arteriolar and venular branches is 19 mm−2 (23) or 8–10 mm−3 (4). Thus the 1.6-mm-deep penetration of a BD Ultra-Fine lancet, which results in a wound of an approximate area of 0.09 mm2 and volume of 0.08 mm3, generally penetrates several small capillaries and may penetrate a larger vessel. Indeed, large superficial veins may be only 1 mm below the surface, and we confirmed that lancing over a visible vein results in a small hematoma. At the other extreme, several lancet wounds where little or no blood was collected (data not shown) were viewed under magnification, and the lancet had clearly penetrated the skin. From a practical standpoint, a small percentage of the lancet sticks may hit a relatively avascular region, where insufficient blood is collected for testing. In an earlier report (9), slightly more blood was obtained from vacuum lancet sticks that were more painful (8.7 vs. 7.1 μl; P = 0.07), which concurs with the view that cutaneous nerve trunks follow the course of blood vessels in the skin. Considerable site-to-site variability was also found in the healing of lancet wounds on the forearm (10).
detailed understanding is lacking. The pooling of blood under the area that is stretched, but a nosepiece height (Fig. 4) may be explained by the radius of vacuum, but lower values were available for use become more limited.

Vacuum skin stretching. The most surprising result was the large influence that stretching the skin up into the nosepiece had on blood extraction, as most clearly demonstrated when a net is used to prevent stretching (Table 2, trial 2). When the skin was not allowed to stretch into the nosepiece, the amount of blood collected was minimal, <1 µl. Stretching may open the lancet wound, overcoming the natural tendency for the wound to close up and shut off the blood flow. Increasing the diameter of the nosepiece allows more skin to stretch up into the nosepiece (Table 3), and increasing amounts of blood were extracted with larger diameter nosepieces (Fig. 3).

In an integrated device, if the skin did not stretch up to the top of the nosepiece, the lancet stick would be shallow, and the blood would not directly wick into the suction device (8, 18, 27). Both the diameter of the nosepiece and the level of vacuum affected the height of skin stretching, with the diameter having the greater effect over the range of conditions studied (Table 3). Previous studies also showed that the skin elevation is related to the diameter and level of vacuum, but lower values were observed in the earlier studies because the skin was held in place by double-sided tape and was not allowed to slide up into the suction device (8, 18, 27).

The general pattern of increasing blood extraction with nosepiece height (Fig. 4) may be explained by the pooling of blood under the area that is stretched, but a detailed understanding is lacking. The fivefold increase in perfusion (Fig. 5) is strong evidence that vasodilatation is involved; however, stretching may also result in partial occlusion of the capillaries. Certainly, the skin is forced to form a relatively sharp angle at the inside rim of the nosepiece, and the area-to-height ratio determines the shape (spherical, ellipsoidal, parabolic, etc.) and thereby the mechanical stress distribution pattern of the produced skin “bubble.” Thus application of vacuum may reduce the venous return of the skin section involved by stretching it against the inside rim of the nosepiece and thereby (at least partially) occluding the venous capillaries. Arteries supplying the capillaries are larger and deeper in the skin and less likely to be occluded. A previous study found that prolonged application of vacuum increased blood perfusion, presumably because of the trauma of blistering (34); however, none of our conditions produced blistering.

The amount of blood extracted at each nosepiece height was roughly equal for three of the four diameters tested (Fig. 4B). The 12.7-mm-diameter nosepieces with step heights of 3–6 mm extracted 1.5- to 2-fold more blood than the others, suggesting that this nosepiece geometry might stretch the skin in the most favorable way to produce the (at least partial) occlusion of the venous blood return and stress-induced perfusion increase postulated above. The preferred geometry at a given vacuum pressure is also suggested by our laboratory’s previous work in which the 12.7-mm-diameter nosepiece gave twice the amount of blood as a 10-mm-diameter nosepiece with a similar height-to-diameter ratio (10.0 vs. 5.0 µl; P < 0.0001) (9). In the present studies, the differences between nosepieces with similar ratios did not reach statistical significance, perhaps because of the relatively small number of tests at each condition (n = 42) compared with that in our laboratory’s previous study (n = 240). Detailed investigation of larger diameter nosepieces with larger step heights was not undertaken because skin distension became less comfortable and the areas on the body available for use become more limited.

Skin blood flow rates and the vacuum collection rates can be used to estimate the volume of tissue extracted. Assuming that blood is extracted from a hemisphere that is perfused at the maximum skin blood flow rate, 50 ml·min⁻¹·100 g⁻¹ (17, 30), the maximum extraction rate of 34 µl/min (Fig. 4, 30-s collection time) corresponds to a hemisphere with a radius of 3.1 mm. This value is smaller than the hemisphere produced by the nosepiece. On one hand, insertion of a needle or small probe is known to increase skin blood flow at least five to sevenfold (1, 28, 33) over an area of 9 cm² (32). On the other hand, it is unclear whether maximum perfusion is achieved. Thus, if the combined effects of vacuum, lancing, and skin stretching did not maximize the skin perfusion, a radius larger than our calculated radius of 3.1 mm would be expected. The calculated radius of extraction is about one-half the size of the nosepiece but twice the depth of lancing. Most importantly, a maximum skin perfusion is able to supply the amounts of blood extracted to the skin section within the nosepiece to justify the volumes extracted. For nosepieces >8 mm in diameter, elevation of the skin into the nosepiece also includes subcutaneous tissue (8); however, further investigation is required to deter-

Table 4. Blood collection after heating the site before lancing

<table>
<thead>
<tr>
<th></th>
<th>Blood Volumes, µl</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trial 11</td>
<td>Trial 12</td>
<td>Trial 13</td>
</tr>
<tr>
<td></td>
<td>25 mm²</td>
<td>9 mm diam.</td>
<td>16 mm/3 mm†</td>
</tr>
<tr>
<td></td>
<td>45°C</td>
<td>45°C</td>
<td>40°C</td>
</tr>
<tr>
<td>Time, s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>6.9 ± 1.5</td>
<td>6.6 ± 1.5*</td>
<td>6.1 ± 1.2</td>
</tr>
<tr>
<td>30</td>
<td>11.6 ± 2.6</td>
<td>17.3 ± 3.1*</td>
<td>12.4 ± 2.4</td>
</tr>
<tr>
<td>45</td>
<td>12.4 ± 2.4</td>
<td>12.2 ± 2.3*</td>
<td>7.5 ± 1.4</td>
</tr>
</tbody>
</table>

Values are means ± SE. Skin was preheated for 15, 30, or 45 s before lancing and blood collection for 30 s. *Significant difference at P < 0.05 between shorter and longer preheating time. †Outer and inner diameter, respectively, of the heating element in contact with the skin.
mine whether there is any special interaction of the subcutaneous tissue with the 12.7-mm-diameter nosepiece.

Other factors affecting blood extraction. Blood collection was linearly related to the level of vacuum (Fig. 2). A linear relationship is also described by the Poiseuille equation (Eq. 1), which has been used to predict the amount of blood collected from a vein with a cannula (25)

\[
V = \pi \Delta P r^4 t / 8L \eta
\]

where \(V\) is volume, \(\Delta P\) is the level of vacuum applied, \(r\) is the radius of the cannula, \(t\) is the time, \(L\) is the length of the cannula, and \(\eta\) is the viscosity of blood. By assuming various lengths, diameters, and numbers of arterioles, the equation can be used to predict blood volumes from vacuum extraction conditions; however, adequate justification of the required assumptions is beyond the scope of this report.

Blood extraction might be expected to increase linearly with time, and we confirmed this dependency for times up to 45 s. Clotting may begin to inhibit blood flow at longer times, especially when the flow is confined in a small space. Application of a prevacuum for 30 s increased the amount of blood collected by approximately twofold (Fig. 2), but ~1.5-fold more blood can be collected in a fixed total time by devoting the time to collection rather than to prevacuum.

The size of the lancet wound can be varied by using a larger diameter lancet or by increasing the depth of lancing. In several trials with 23- and 28-gauge lancets, where the volume of the lancet tip entering the skin is about twofold different, the blood volumes were either larger with the smaller diameter lancet or not statistically different (trials 6 and 15 and Ref. 9). These unexpected results may be due to a difference in the sharpness of the cutting edge of the lancets or some other unrecognized factor. The systematic increase in blood volumes with puncture depths up to 1.6 mm indicates that more capillaries are cut. The greater variability found at puncture depths >1.6 mm may be due to the increasing involvement of subcutaneous tissue, because the thickness of the dermis on the dorsal forearm is 1–1.5 mm (21). Also, the nosepiece geometry in combination with the applied vacuum may become less effective in stretching open a deeper wound.

Heating the skin produced more blood than in trials without heating, and the size of the heater was relatively unimportant (Table 4). Previously, heating the skin before lancing proved effective in reducing the time required for blood collection (3). Increasing the heating time increased the blood extracted (Table 4), indicating that some time is required for maximal effect. Local heating to 44°C results in a threefold increase in blood flow after 40 s and maximum vasodilation in 2 min (39). Maximum vasodilation is reached by local heating to 45°C (17). After local heating for 45 s, an average of 1.6-fold more blood was extracted at 45°C than at 40°C, whereas the perfusion of the forearm is known to be ~1.3-fold larger (37). Thus heating the skin increases the amount of blood extracted but at the expense of time and complexity of the apparatus.

Limitations of the studies. Because the average relative standard deviation was 70%, testing a blood extraction condition with 16 sticks gave the protocol a statistical power to detect an ~50% increase in blood volume. Smaller differences might be detected with a larger study; however, in a study of 215 diabetic subjects, the average relative standard deviation increased to 88% (9), presumably because of increased person-to-person variability. Over the course of multiple trials, larger or smaller than average blood volumes were often extracted from certain individuals, making comparison among trials difficult. Obviously, further work is needed to identify the underlying factors for person-to-person differences. Collection of blood directly into a glucose test strip was accomplished in a number of trials (data not shown); however, an understanding of the key interactions between the lancet wound and the test strip also requires further study. Alternate methods for increasing perfusion, such as mechanical trauma, topical drug treatment, iontophoresis, or transcutaneous electrical nerve stimulation, were not explored.

In summary, blood can be effectively extracted from lancet wounds using vacuum combined with skin stretching. This technology has been incorporated into a commercially available glucose monitoring system (14).

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REFERENCES