Drop-to-Drop Variation in the Cellular Components of Fingerprick Blood

Implications for Point-of-Care Diagnostic Development

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ABSTRACT

Objectives: *Blood obtained via fingerprick is commonly used in point-of-care assays, but few studies have assessed variability in parameters obtained from successive drops of fingerprick blood, which may cause problems for clinical decision making and for assessing accuracy of point-of-care tests.*

Methods: *We used a hematology analyzer to analyze the hemoglobin concentration, total WBC count, three-part WBC differential, and platelet count in six successive drops of blood collected from one fingerprick from each of 11 donors, and we used a hemoglobinometer to measure the hemoglobin concentration of 10 drops of fingerprick blood from each of 7 donors.*

Results: *The average percent coefficient of variation (CV) for successive drops of fingerprick blood was higher by up to 3.4 times for hemoglobin, 5.7 times for WBC count, 3 times for lymphocyte count, 7.7 times for granulocyte count, and 4 times for platelets than in venous controls measured using a hematology analyzer. The average percent CV for fingerprick blood was up to 5 times higher for hemoglobin than venous blood measured using a point-of-care hemoglobinometer. Fluctuations in blood parameters with increasing volume of fingerprick blood are within instrument variability for volumes equal to or greater than 60 to 100 μL.*

Conclusions: *These data suggest caution when using measurements from a single drop of fingerprick blood.*

Blood obtained via fingerprick is commonly used in point-of-care assays because fingerpricks are less invasive than venipuncture, they require less clinical training than venipuncture, and their small blood volume is sufficient for point-of-care tests. Accuracy in these tests is important for diagnosing anemia or infection and managing human immunodeficiency virus, sickle-cell anemia, malaria, and other diseases, especially in low-resource settings where performing venipuncture and using a hematology analyzer is not feasible. Many researchers have examined differences in blood parameters for fingerprick (or fingerstick) and venous blood.[1-5] A few researchers have examined variations in blood parameters for different fingerprick protocols by comparing results for fingerpricks performed on both hands, on different days, using different devices, or by comparing several drops of blood from a fingerprick.[6-10] However, few studies have analyzed the variation in blood parameters between the successive drops of blood obtained from one fingerprick. Because of the growing number of clinically important tests performed using fingerprick blood, especially in low-resource settings, it is important to understand how variations in fingerprick blood collection protocols can affect point-of-care test accuracy and the potential variability introduced when two point-of-care blood tests are performed using fingerprick blood from the same patient.

The goal of this pilot study was to determine the drop-to-drop variability in blood parameters obtained from fingerprick blood. We also aimed to determine the minimum volume of blood needed to reduce variability to acceptable levels for clinical decision making, such as determining if a patient is anemic. To answer these questions, we analyzed the hemoglobin concentration, total WBC count, three-part WBC

differential (lymphocytes, monocytes, and granulocytes), and platelet count in six successive drops (20 µL each) of blood collected from one fingerprick using a hematology analyzer. Venous blood was drawn for comparison. This study also assessed the variability of the hemoglobin concentration of 10 successive drops (10 µL each) of fingerprick blood when measured using a point-of-care hemoglobinometer.

Materials and Methods

We assessed drop-to-drop variation of blood parameters using a laboratory-grade hematology analyzer (Ac·T diff2; Beckman Coulter, Brea, CA). The hematology analyzer reported hemoglobin concentration, total WBC count, three-part WBC differential, and platelet count. To validate the use of small sample volumes on this device, we first measured successive drops of venous blood from a volunteer donor. Then, we measured successive drops of blood from fingerpricks of volunteer donors. In both cases, blood samples were collected with separate 20-µL MicroSafe capillary tubes (SafeTec, Ivyland, PA), dispensed into tubes with premeasured diluent, and analyzed in predilute mode.

We also assessed drop-to-drop variation in hemoglobin concentration on a device designed to be used at the point of care (HemoCue 201+; HemoCue AB, Ängelholm, Sweden). We first measured drops of venous blood to validate the repeatability of the device itself; then, we measured successive drops of blood from fingerpricks of donors. For measurement on this device, 10-µL blood samples were collected directly into a HemoCue disposable cuvette.

Small Volumes of Venous Blood Measured Using a Hematology Analyzer

To validate the method of measuring small volumes of blood using the hematology analyzer, we analyzed venous blood by using the same procedure as fingerprick blood. Normal volunteer blood was used undiluted and diluted with human plasma to simulate various levels of anemia and leukopenia. Blood was obtained from volunteers (healthy, nonpregnant adults weighing at least 110 pounds) who gave written informed consent. Plasma for diluting blood was purchased from the Gulf Coast Regional Blood Bank (Houston, TX). Both protocols were reviewed and approved by the institutional review board at Rice University.

Venous blood samples were well mixed, and six drops of approximately 25 µL were pipetted onto Parafilm (Bemis, Oshkosh, WI). Each drop was drawn into a 20-µL MicroSafe capillary tube. An air vent in the wall of the plastic tube regulated the amount of blood collected (within 0% to +10% of the stated volume), and the integrated bulb facilitated dispensing of the blood. To measure a complete blood count using such a small volume of blood accurately on the Ac·T diff2 hematology analyzer, we used the predilute function. (In this mode, the Ac·T diff2 predispenses 1,580 µL of diluent into a tube. The user adds 20 µL of blood, mixes the sample well, and presents it to the analyzer, which performs the necessary calculations to account for the dilution. This procedure is specified in the operator's manual.) The drops of venous blood collected in the MicroSafe tubes were dispensed using the integrated bulb into the tubes with premeasured diluent, and the solution was mixed well. These tubes were analyzed on the Ac·T diff2 for hemoglobin concentration, WBC count, three-part WBC differential, and platelet count.

Drop-to-Drop Variation in Fingerprick Blood Parameters Measured Using a Hematology Analyzer

Healthy volunteers had 3 to 9 mL of blood drawn into appropriately sized K2 EDTA Vacutainer tubes (BD, Franklin Lakes, NJ) by venipuncture. Then, the side of the third or fourth finger was warmed, cleansed with an alcohol wipe, and pricked with a BD Contact-Activated Lancet (High Flow, 1.5-mm blade, 2.0-mm depth, product number 366594; BD), except for donor A, who was pricked with a Unistik 3 Dual lancet (18-gauge needle, 1.8-mm depth; product number AT 1062; Owen Mumford, Oxford, England). The initial drop of blood to form at the puncture site was wiped away with sterile gauze in accordance with standard procedures.[11] This drop was wiped away because of the possible contamination of the drop of blood with alcohol, cell debris, and tissue fluids. The next six successive drops to form at the site were collected with separate 20-µL MicroSafe capillary tubes. If blood flow began to slow, the puncture site was wiped firmly with sterile gauze to remove the platelet plug and encourage further blood flow. The puncture sites were not "milked" to encourage blood flow since this action can lead to erroneous results, such as a falsely low hemoglobin concentration.[11] Fourteen donors were recruited; data from three donors were rejected from analysis because the fingerpricks required milking to reach six drops or had clots in the first six drops.

Using the integrated bulb, the drops of blood collected in the MicroSafe tubes were dispensed into the tubes with premeasured diluent, and the tubes were mixed well. Each drop was analyzed on the Ac·T diff2 analyzer, followed by analysis of the donor's venous blood in whole-blood mode. A single investigator (M.M.B.) trained and certified in performing fingerpricks collected all blood and performed all experiments, and all blood from a single donor was measured on the same day as soon as possible after collection.

Drop-to-Drop Variation in Fingerprick Blood Parameters Measuring Using a Point-of-Care Device

We also assessed the variation of hemoglobin concentration in successive drops of fingerprick blood using

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a HemoCue 201+. To establish the degree of variability caused by the device itself, venous blood samples were well mixed, and 10 drops of approximately 15 µL were pipetted onto Parafilm, drawn into the HemoCue 201+ cuvettes (10 µL volume) by capillary action, and analyzed for hemoglobin concentration. One blood sample was used undiluted and diluted with varying amounts of human plasma to simulate degrees of anemia.

To assess drop-to-drop variability in fingerprick blood, volunteers were recruited, and their third or fourth fingers were pricked using the same procedure as above but with a Unistik 3 Dual lancet (18-gauge needle, 1.8-mm depth; product number AT 1062; Owen Mumford). The first drop was wiped away, and 10 successive drops (approximately 10 µL each) were collected directly into the HemoCue 201+ cuvettes. Samples were analyzed in order of collection as soon as the last drop was collected (within the recommended 10 minutes after collection). None of the seven donors recruited required milking to reach 10 drops or had clots in the first 10 drops. Venous blood was not drawn from these donors. A single investigator (M.M.B.) trained and certified in performing fingerpricks collected all blood and performed all experiments.

Results

Drop-to-Drop Variation Measured Using a Hematology Analyzer

We first used a hematology analyzer to assess the drop-to-drop variation in measuring small volumes (20 µL) of venous blood. Theoretically, the drop-to-drop variation of drops taken from a well-mixed sample is zero. The variation of hemoglobin concentration in six drops of venous blood is shown graphically in **Figure 1A** and numerically in **Table 1**. The variation was slightly higher in samples with a higher concentration of hemoglobin but in all cases compared favorably with the reported accuracy of the hematology analyzer (<2% coefficient of variation [CV] for 31 samples, according to the instrument manual).

We then measured the variability in successive drops (20 µL) of fingerprick blood. The hemoglobin concentration of six successive drops of fingerprick blood from 11 donors is shown in **Figure 1B**. The hemoglobin concentration of the last drop of blood has been subtracted from that of each drop to better visualize drop-to-drop changes independent of the baseline hemoglobin concentrations of the donors. Table 1 summarizes these data numerically; the standard deviation, percent CV, and range (maximum – minimum value) were determined for each donor and then averaged for all donors. (Data are broken down by donor in Supplemental Table 1. Supplemental material can be found at http://bit.ly/BondDec15.) The average percent CV for successive drops of fingerprick blood was between 2.3 and 3.4 times greater than that measured for small volumes of venous blood. Indeed, taking multiple drops of blood from one fingerprick can result in hemoglobin concentrations that differ by more than 1.6 g/dL. Note that there was no generalizable trend of the change in hemoglobin concentration as more drops were collected. For example, in Figure 1B, donor B shows a decrease of more than 2 g/dL from baseline in drop 3 but returns to baseline in drop 5. Not all donors showed large changes across multiple drops: donor F deviated less than 0.5 g/dL from baseline across all six drops. Data from donors whose blood was not freely flowing for six drops were rejected from analysis, so these variations from drop to drop are not due to milking the finger.

Figure 1C shows the running average of the hemoglobin concentration of all previous drops of blood, shown individually in Figure 1B. The average of all six drops for each donor has been subtracted from each point to remove the effects of the donor's baseline hemoglobin concentration. For all 11 donors, fluctuations in hemoglobin concentration with increasing sample volume of fingerprick blood are within instrument variability (0.5 g/dL, calculated by averaging the ranges of the three venous samples measured using the hematology analyzer) for volumes equal to or greater than 60 µL (three drops).

Figure 1D shows the difference between the running average of fingerprick hemoglobin concentration and the venous hemoglobin concentration for the same donor. For nine of the 11 donors, the running average of fingerprick hemoglobin concentration was within ±1.1 g/dL of their venous hemoglobin concentration for all cumulative volumes. Donors B and C showed a greater deviation between fingerprick and venous hemoglobin concentration despite careful attention to proper blood collection procedures, including not leaving the tourniquet on for too long during venipuncture and not milking the finger during the fingerprick.

Figure 2 and **Table 2** show the results of the same analyses performed on WBC measures (WBC count and absolute number of lymphocytes, granulocytes, and monocytes). (Data are broken down by donor in Supplemental Table 1.) Figure 2A shows the WBC concentration of multiple drops of venous blood at three levels of WBC concentration, with the concentration of the final drop subtracted from each drop to normalize each sample. Figure 2B shows the WBC concentration of successive drops of fingerprick blood from 11 donors with the concentration of the final drop subtracted from each drop. Figure 2C shows the running average of WBC concentration for the drops in Figure 2B with the average of all six drops subtracted from each point to normalize each sample. For all 11 donors, fluctuations

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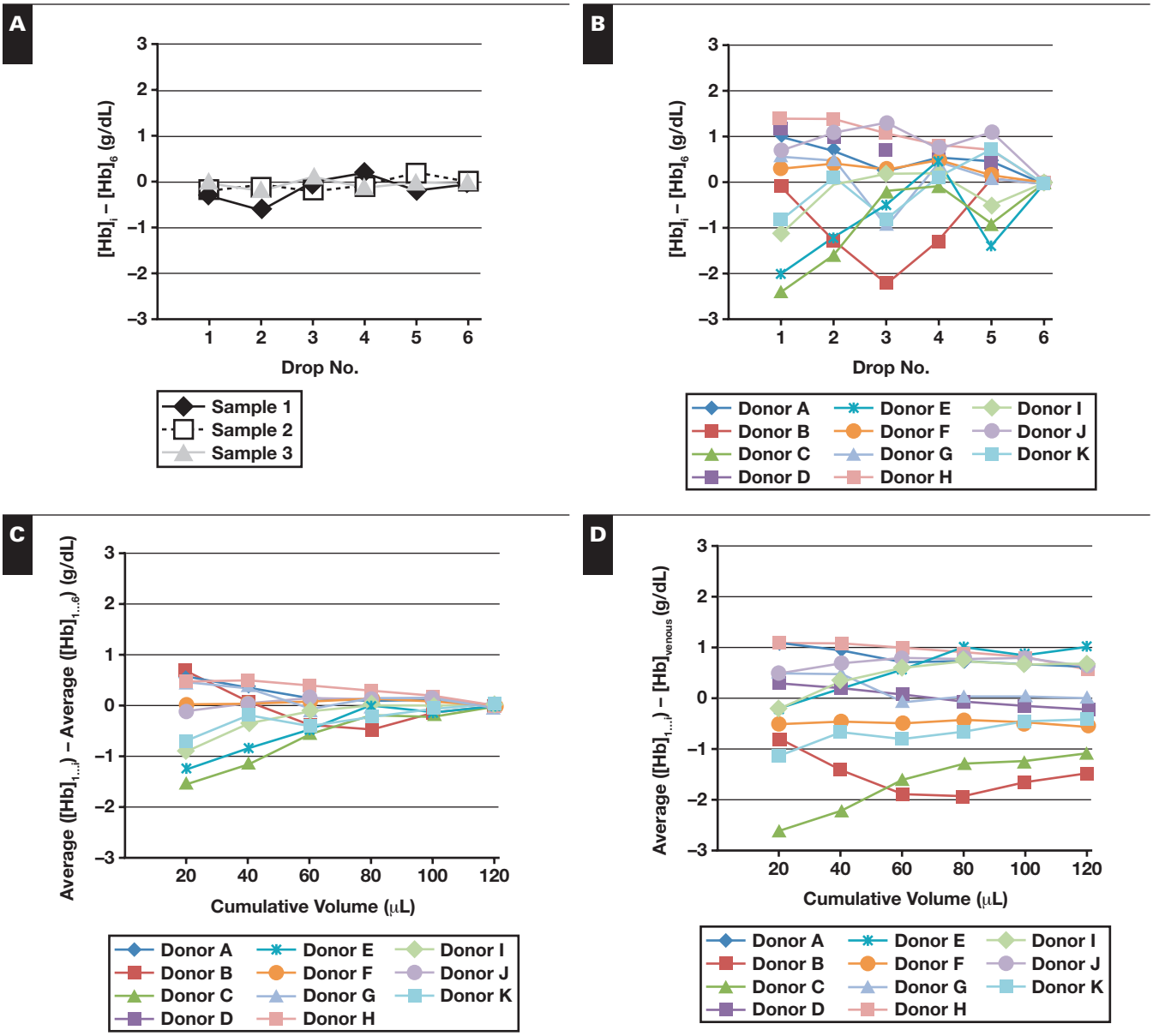

Figure 1 Hemoglobin (Hb) concentration measured using a hematology analyzer. **A**, Low variability for venous blood measured using a hematology analyzer. Normalized hemoglobin concentration of six drops (20 μL each) of venous samples at three hemoglobin levels. i = drop number. **B**, High variability for drops of fingerprick blood measured using a hematology analyzer. Normalized hemoglobin concentration of six successive drops (20 μL each) of fingerprick blood from 11 donors. **C**, Variability for fingerpricks decreases when averaging multiple drops. Normalized running average of hemoglobin concentration of the drops in **B**. **D**, Comparison of fingerprick hemoglobin concentration to venous hemoglobin concentration. Difference between running average of hemoglobin concentration of the drops in **B** and the venous hemoglobin concentration of the same donor.

Table 1
Hemoglobin Concentration Measured Using Hematology Analyzer[a]

Characteristic	Successive 20-μL Drops of Venous Blood			Successive 20-μL Drops of Fingerprick Blood, Average
	Sample 1	Sample 2	Sample 3	
Mean (SD)	14.8 (0.28)	9.5 (0.15)	7.1 (0.10)	0.59
%CV	1.9	1.6	1.3	4.4
Range	0.8	0.4	0.3	1.6

CV, coefficient of variation.
[a] The left side of the table shows the mean (SD), percent CV, and range (maximum – minimum hemoglobin value) of the hemoglobin concentration of samples depicted in Figure 1A (venous blood) in g/dL. The right side of the table shows statistics for the hemoglobin concentration of samples depicted in Figure 1B (fingerprick blood). For the fingerpricks, measures were calculated for six drops collected from one fingerprick of each donor, then averaged for all donors.

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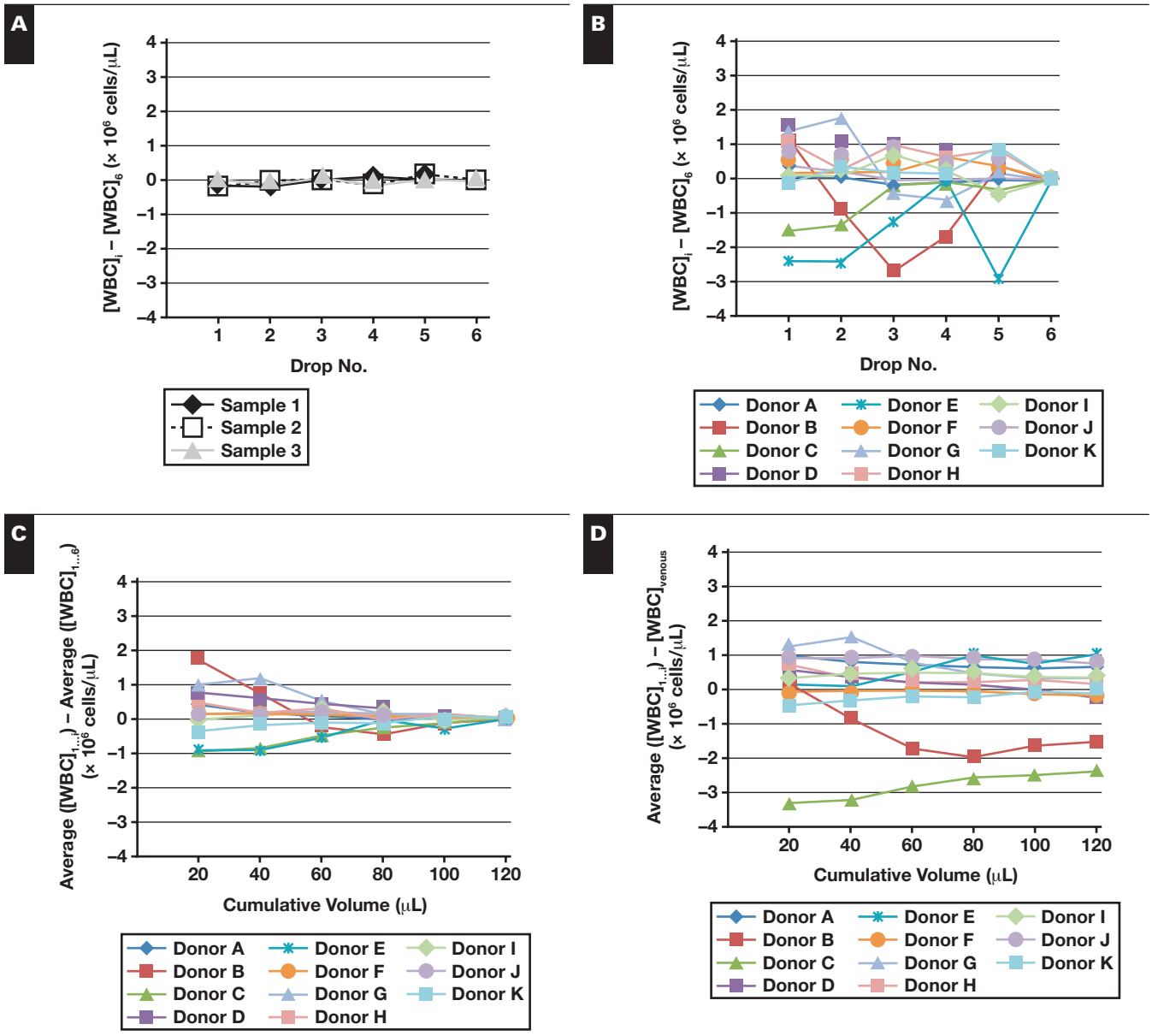

Figure 2 WBC concentration measured using a hematology analyzer. **A**, Low variability for venous blood measured using a hematology analyzer. Normalized WBC concentration of six drops (20 μL each) of venous samples at three WBC levels. i = drop number. **B**, High variability for drops of fingerprick blood measured using a hematology analyzer. Normalized WBC concentration of six successive drops (20 μL each) of fingerprick blood from 11 donors. **C**, Variability for fingerpricks decreases when averaging multiple drops. Normalized running average of WBC concentration of the drops in **B**. **D**, Comparison of fingerprick WBC concentration to venous WBC concentration. Difference between running average of WBC concentration of the drops in **B** and the venous WBC concentration of the same donor.

in WBC concentration with increasing sample volume of fingerprick blood are within instrument variability (0.3 × 10^6 cells/μL, calculated by averaging the ranges of the three venous samples measured using the hematology analyzer) for volumes equal to or greater than 100 μL (five drops). For 10 of the 11 donors, fluctuations are within instrument variability for volumes equal to or greater than 80 μL (four drops). Figure 2D shows the running average of fingerprick drops with the venous WBC concentration subtracted from each point.

The standard deviation, percent CV, and range of data taken from six drops of venous blood were low; the percent CV for WBC count was within the reported accuracy of the device, and the standard deviations for monocytes and granulocytes were within the reported accuracy of the device. Our results showed a slightly higher standard deviation for

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Table 2
WBC Concentration and Three-Part Differential Measured Using a Hematology Analyzer[a]

Characteristic	Successive 20-µL Drops of Venous Blood			Successive 20-µL Drops of Fingerprick Blood, Average
	Sample 1	Sample 2	Sample 3	
WBC concentration, $\times 10^6$ cells/µL				
Mean (SD)	6.8 (0.10)	6.5 (0.13)	4.8 (0.11)	0.60
%CV	1.5	2.1	2.2	8.6
Range	0.3	0.4	0.3	1.6
Lymphocyte count, $\times 10^6$ cells/µL				
Mean (SD)	1.7 (0.04)	1.5 (0.08)	1.2 (0.05)	0.18
%CV	2.4	5.1	4.3	7.2
Range	0.1	0.2	0.1	0.5
Granulocyte count, $\times 10^6$ cells/µL				
Mean (SD)	4.8 (0.06)	4.8 (0.15)	3.4 (0.08)	0.42
%CV	1.3	3.1	2.2	10
Range	0.2	0.4	0.2	1.1
Monocyte count, $\times 10^6$ cells/µL				
Mean (SD)	0.3 (0.05)	0.2 (0.05)	0.1 (0.05)	0.08
%CV	21.9	36.5	37.4	30
Range	0.1	0.1	0.1	0.2

CV, coefficient of variation.
[a] The left side of the table shows the mean (SD), percent CV, and range (maximum – minimum value) of the samples depicted in Figure 2A (venous blood). The right side of the table shows statistics for samples shown in Figure 2B (fingerprick blood). For the fingerpricks, measures were calculated for six drops from one fingerprick of each donor, then averaged for all donors.

lymphocytes than the reported accuracy of the device; this deviation may have been due to our method of dilution. Monocytes had a high percent CV compared with the other WBC types due to their low absolute count in these samples from healthy volunteers.

In contrast to the results for venous blood, all measures of WBC variability were higher for successive drops of fingerprick blood, except for the monocyte percent CV, which was high and comparable to that measured in venous controls. The average percent CV for successive drops of fingerprick blood was 3.9 to 5.7 times higher for WBC count, 1.4 to 3.0 times higher for lymphocyte count, and 3.2 to 7.7 times higher for granulocyte count than in venous controls.

Figure 3 and **Table 3** summarize the results of the same analyses performed on platelet count. (Data are broken down by donor in Supplemental Table 1.) The variation of venous samples was within the reported accuracy of the hematology analyzer (<7% CV for 31 samples, according to the instrument manual). The average percent CV for successive drops of fingerprick blood was four times greater than that measured for small volumes of venous blood. Figure 3A shows the platelet count of multiple drops of venous blood at three levels of platelet count with the concentration of the final drop subtracted from each drop to normalize each sample. Figure 3B shows the platelet count of successive drops of fingerprick blood from 11 donors with the concentration of the final drop subtracted from each drop. Figure 3C shows the running average of platelet count for the drops in Figure 3B with the average of all six drops subtracted from each point to normalize each sample.

Only five of the 11 donors had fluctuations in platelet count with increasing sample volume of fingerprick blood within instrument variability (33 platelets/µL, calculated by averaging the ranges of the three venous samples measured using the hematology analyzer) for volumes of 120 µL (six drops). Figure 3D shows the running average of fingerprick drops with the venous platelet count subtracted from each point.

In general, platelet counts decreased in each successive drop from the fingerpricks. In addition, venous platelet counts were generally higher than platelet counts in fingerprick blood. These findings may reflect the consumption of platelets during the clotting process observed after a fingerprick.

Drop-to-Drop Variation on a Point-of-Care Device

We also assessed the drop-to-drop variation of blood measured using a point-of-care hemoglobinometer, the HemoCue 201+. We first assessed the drop-to-drop variation in drops (10 µL) of venous blood. Theoretically, the drop-to-drop variation of drops taken from a well-mixed sample is zero. The variation of hemoglobin concentration in 10 drops of venous blood is shown numerically in **Table 4**. (Data are broken down by donor in Supplemental Table 2.) The range of variability for venous blood was within the manufacturer's reported accuracy for the HemoCue 201+. The average percent CV was 2.2 to 5 times higher when measuring fingerprick blood than venous blood.

Figure 4A shows the hemoglobin concentration of multiple drops of venous blood at three hemoglobin concentrations, with the concentration of the final drop subtracted

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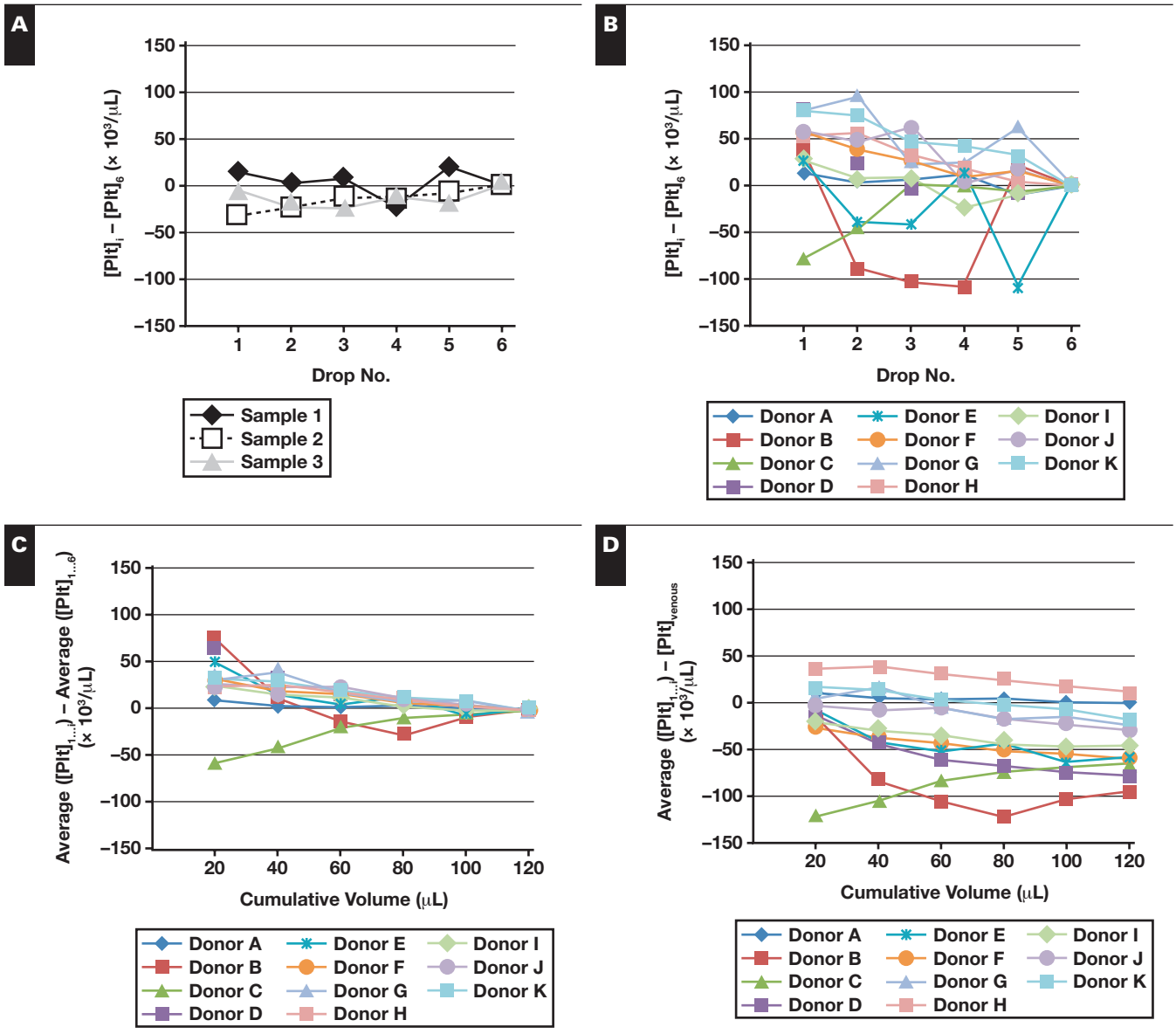

Figure 3 Platelet (Plt) concentration measured using a hematology analyzer. **A**, Low variability for venous blood measured using a hematology analyzer. Normalized platelet count of six drops (20 μL each) of venous samples at three platelet counts. i = drop number. **B**, High variability for drops of fingerprick blood measured using a hematology analyzer. Normalized platelet count of six successive drops (20 μL each) of fingerprick blood from 11 donors. **C**, Variability for fingerpricks decreases when averaging multiple drops. Normalized running average of platelet count of the drops in **B**. **D**, Comparison of fingerprick platelet count to venous platelet count. Difference between running average of platelet count of the drops in **B** and the venous platelet count of the same donor.

Table 3
Platelet Count Measured Using a Hematology Analyzer[a]

Characteristic	Successive 20-μL Drops of Venous Blood			Successive 20-μL Drops of Fingerprick Blood, Average
	Sample 1	Sample 2	Sample 3	
Mean (SD)	316 (14.6)	238 (11.4)	199 (9.5)	31.9
%CV	4.6	4.8	4.8	19
Range	42	32	25	80

CV, coefficient of variation.
[a] The left side of the table shows the mean (SD), percent CV, and range (maximum – minimum platelet value) of the platelet count (× 10^3/μL) of samples depicted in Figure 3A (venous blood). The right side of the table shows statistics for the platelet count of samples depicted in Figure 3B (fingerprick blood). For the fingerpricks, measures were calculated for six drops collected from one fingerprick of each donor, then averaged for all donors.

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from each point. **Figure 4B** shows the hemoglobin concentration of 10 successive drops of fingerprick blood from seven donors with the concentration of the final drop subtracted from each drop to better visualize the drop-to-drop changes regardless of baseline hemoglobin concentration.

Figure 4C shows the running average of hemoglobin concentration of the drops shown in Figure 4B with the average of all 10 drops subtracted from each point. For all donors, fluctuations in hemoglobin concentration with increasing sample volume of fingerprick blood are within instrument variability (0.3 g/dL, calculated by averaging the ranges of the three venous samples measured using the point-of-care device) for volumes greater than 90 µL (nine drops). When using the same target instrument variability as the hematology analyzer (0.5 g/dL), we find that for all donors, fluctuations in hemoglobin concentration with increasing sample volume of fingerprick blood are within 0.5 g/dL for volumes greater than 60 µL (six drops).

Discussion

Using both a hematology analyzer and point-of-care hemoglobinometer, we found the variability of blood component measures to be greater for successive drops of fingerprick blood than for multiple drops of venous blood. Our measurements of average percent CV for hemoglobin concentration from fingerprick blood (4.4% for hematology analyzer and 3.5% for the point-of-care device) were comparable to literature reports of similar experiments. Yang et al[6] measured the hemoglobin concentration of three drops (20 µL each) from a fingerprick and found an average percent CV of 2.45% ± 1.32%. Morris et al[7] found a CV of 6.3% when comparing hemoglobin concentration from fingerpricks on the right hand with those collected simultaneously on the left hand. Chen et al[9] found a CV of 8.0% when comparing hemoglobin concentration of the second drop with the third drop of a fingerprick.

Our measurements of venous platelet variation (4.6%-4.8% CV) are similar to those measured by Yang et al[6] (4.50% ± 3.02% CV). However, our measurement of platelet variation in fingerprick blood is markedly greater: 19% CV compared with 6.47% ± 6.57% CV. Our measurements are more comparable with those of Brecher et al,[12] who found 11% CV in venous blood and 24% CV in fingerprick blood.

Here, similar degrees of variability were seen in the hemoglobin concentration of venous blood on both the hematology analyzer and point-of-care hemoglobinometer. The measurements taken on the Ac·T diff2 may have been slightly more variable due to the number of steps involved in measuring small amounts of blood on the analyzer. The HemoCue method is designed to measure small volumes of blood, so the workflow is simpler, which may contribute to reduced variability on well-mixed samples. We do not believe that the MicroSafe capillary tubes were the source of the variability, since they were only used when measuring blood using the hematology analyzer, and the measures of hemoglobin variability were similar on both devices.

Similar degrees of variability were also seen in the hemoglobin concentration of successive drops of fingerprick blood on both the hematology analyzer and point-of-care hemoglobinometer. The literature reports conflicting results concerning the accuracy of the HemoCue 201+ and its predecessors. Studies that assess the device's accuracy using venous blood tend to show excellent agreement with laboratory hemoglobinometers[3,12-14]; studies that assess the device's accuracy in the field, using fingerprick blood, tend to report much poorer accuracy,[3,7,8] and some of these studies recommend against using the HemoCue 201+ entirely due to its poor accuracy.[9,15] The results presented in Figure 4 suggest that the cause of this discrepancy in reported results is the sample itself: when venous blood is used, the HemoCue gives accurate results; when fingerprick blood is used, the HemoCue is affected by the inherent variability of drops of fingerprick blood.

The fact that similar trends were observed for both hemoglobin concentration and WBC concentration measured using the hematology analyzer (eg, donor B showed a decrease in drop 3 in both hemoglobin concentration [Figure 1B] and WBC concentration [Figure 2B]) suggests that the changes from drop to drop are due to a different ratio of cellular components to plasma. Because donors were only included in the analysis if all drops could be obtained without milking the finger, we do not believe this effect was induced by the person collecting the blood. Morris et al[7] believe the higher variability of capillary blood compared with venous blood is due to the presence of extracellular fluid in capillary samples. In clinical practice, milking of the finger by insufficiently trained health care workers may result in even greater drop-to-drop variability than shown here.

Our data also suggest that collecting and analyzing more fingerprick blood does not necessarily bring the measured value closer to those of the donor's venous blood (Figures 1D and 2D). For example, donor B's hemoglobin and WBC concentration were similar for venous blood and fingerprick in drop 1 but became less concordant with additional drops, while donor C's fingerprick measures came closer to the venous measures with additional drops. These data may represent true differences between fingerprick and venous blood, or they may be the result of errors in collection (such as leaving the tourniquet on for too long during a venous draw). Further research is needed to determine how common these patterns are.

For testing the accuracy of new devices using fingerprick blood, we recommend collecting multiple drops of

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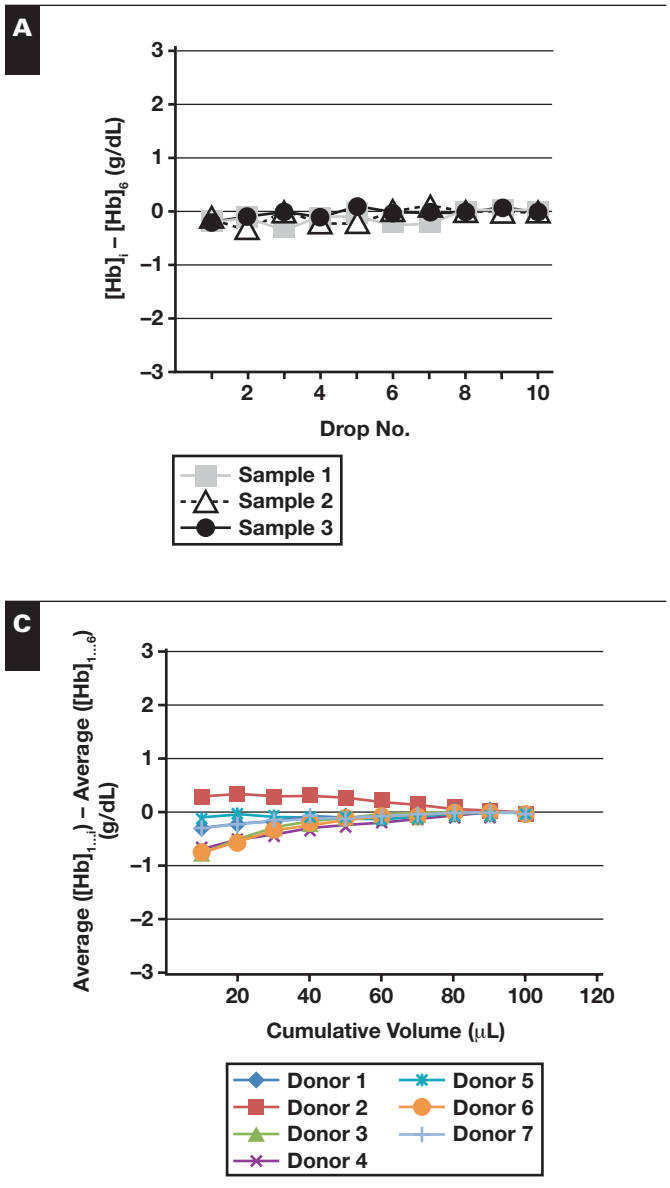

Figure 4 Hemoglobin (Hb) concentration measured using a point-of-care hemoglobinometer. **A**, Low variability for venous blood measured using a point-of-care device. Normalized hemoglobin concentration of 10 drops (10 µL each) of venous samples at three hemoglobin levels. **B**, High variability for drops of fingerprick blood measured using a point-of-care device. Normalized hemoglobin concentration of 10 successive drops (10 µL each) of fingerprick blood from seven donors. **C**, Variability for fingerpricks decreases when averaging multiple drops. Normalized running average of hemoglobin concentration of the drops in **B**.

Table 4
Hemoglobin Concentration Measured Using a Point-of-Care Device[a]

Characteristic	Successive 10-µL Drops of Venous Blood			Successive 10-µL Drops of Fingerprick Blood, Average
	Sample 1	Sample 2	Sample 3	
Mean (SD)	14.2 (0.10)	9.8 (0.13)	5.9 (0.09)	0.49
%CV	0.7	1.3	1.6	3.5
Range	0.3	0.4	0.3	1.6

CV, coefficient of variation.
[a] The left side of the table shows the mean (SD), percent CV, and range (maximum – minimum hemoglobin value) of the samples depicted in Figure 4A (venous blood) in g/dL. The right side of the table shows statistics for the samples depicted in Figure 4B (fingerprick blood). For the fingerpricks, measures were calculated for the collection of drops from one fingerprick of each donor, then averaged for all donors.

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fingerprick blood in an anticoagulant-coated tube (such as BD's Microtainer Tubes), mixing the blood thoroughly with a pipette, and then apportioning the blood to each device under investigation.[16] This method ensures that a test device and reference standard measure blood with the same concentration of components.

For clinical decision making, we recommend using fingerprick blood to assess hemoglobin or WBC concentration only when the degree of variability is acceptable (the degree of acceptable variability will depend on the clinical condition being assessed—for example, a clinician may desire higher accuracy when assessing the need for a blood transfusion than when assessing iron-deficiency anemia). Other studies[1,4,5] have examined more closely the bias of capillary blood compared with venous blood, and Neufeld et al[2] even suggest a conversion factor. However, these averages do not account for the large variability of hemoglobin and WBC concentration from drop to drop of fingerprick blood. Our data suggest that the running average of hemoglobin and WBC concentration stops changing after averaging 80 μL of fingerprick blood. That is, collecting more than 80 μL provides little additional information. This volume is similar to the four to nine drops (40-90 μL) recommended by Morris et al.[7] It should be noted that this volume was derived by mathematically combining individual, separately tested drops of blood; further studies should verify that combining drops before analysis reduces variability to acceptable levels.

In recent years, a large number of devices using tiny volumes of blood have been developed. Our data suggest caution in using the results of these hemoglobin and WBC tests for clinical decision making, such as determining anemia status. (Other studies need to be conducted to assess the drop-to-drop variability for other analytes.) The options for clinicians seem to be to (1) accept the inaccuracy of fingerprick blood on these devices as a trade-off for easy blood collection; (2) collect, read, and average multiple fingerprick samples, gaining accuracy but sacrificing cost and time; or (3) collect and analyze venous blood.

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