# Effects of Drugs on Glucose Measurements With Handheld Glucose Meters and a Portable Glucose Analyzer

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## Abstract

*Thirty drugs used primarily in critical care and hospital settings were tested in vitro to observe interference on glucose measurements with 6 handheld glucose meters and a portable glucose analyzer. Paired differences of glucose measurements between drug-spiked samples and unspiked control samples were calculated to determine bias. A criterion of ± 6 mg/dL was used as the cutoff for interference. Ascorbic acid interfered with the measurements on all glucose devices evaluated. Acetaminophen, dopamine, and mannitol interfered with glucose measurements on some devices. Dose-response relationships help assessment of drug interference in clinical use. High dosages of these drugs may be given to critically ill patients or self-administered by patients without medical supervision. Package inserts for the glucose devices may not provide adequate warning information. Hence, we recommend that clinicians choose glucose devices carefully and interpret results cautiously when glucose measurements are performed during or after drug interventions.*

Handheld glucose meters are used widely for point-of-care testing and for self-monitoring of blood glucose at home. The use of glucose meters in the care of critically ill patients is controversial.[1-3] Surveys[4,5] show that some hospitals do not allow handheld glucose meters in critical care units. Kost et al,[6] evaluated a new oxygen-insensitive, glucose dehydrogenase–based electrochemical biosensor and studied the clinical performance of the new handheld glucose meter system in critical care, hospitalized, and ambulatory patients.[6] Little research is available describing drug interference errors with the newest generations of point-of-care glucose devices. The objectives of this study were as follows: (1) to study how drugs commonly used to treat critically ill patients affect glucose measurements obtained with new glucose devices, (2) to introduce a quantitative error criterion for drug interference, and (3) to determine the clinical relevance of drug interferences for point-of-care glucose testing.

## Materials and Methods

### Drugs and Drug Levels Tested

■**Table 1**■ lists the 30 drugs tested. Drugs administered commonly at the University of California Davis Medical Center were selected for relevance to critical care based on a review of drug dispensary statistics during a 6-month period. Drug information was obtained from a clinical pharmacology book,[8] a drug handbook,[9] and the National Committee for Clinical Laboratory Standards (NCCLS).[10] The tested concentrations in test level 1 were as follows: (1) the level recommended by NCCLS, (2) the toxic level or 10 times the therapeutic level published in the clinical pharmacology

**❙Table 1❙**
**Drugs and Concentrations***

| Generic Name | Therapeutic Level | Toxic Level | Test Level | | | |
|---|---|---|---|---|---|---|
| | | | NCCLS | 1 | 2 | 3 |
| Acetaminophen | 10-20 | 150 | 200 | 200[†] | 300 | 1,000 |
| Acetylsalicylic acid | 20-100 | 150-300 | 500 | 500[†] | 450 | 3,000 |
| Aminophylline | 10-20 | 30-40 | 250 | 250[†] | 240 | 40 |
| Ampicillin | 5 | NA | 50 | 50[†] | 2,500 | 3,750 |
| Ascorbic acid | 8-12 | NA | 30 | 30[†] | 240 | 300 |
| Cefazolin | 400 | NA | 4,000 | 4,000[†] | 3,200 | 8,000 |
| Cimetidine | 1-10 | NA | 100 | 100[†] | 7 | 14 |
| Dexamethasone | NA | NA | NA | 4[‡] | 20 | 60 |
| Digoxin | >0.0008 | 0.0017-0.0033 | NA | 0.0033[§] | 0.003 | 0.08 |
| Dobutamine | 35-50 | NA | NA | 0.5 | 0.05 | NA |
| Dopamine | NA | NA | 130 | 130[†] | 60 | NA |
| Epinephrine | NA | NA | NA | 0.2[‡] | 0.7 | 1.4 |
| Erythromycin | 2-20 | NA | 200 | 200[†] | NA | NA |
| Furosemide | 1-3 | NA | 20 | 20[†] | 30 | 60 |
| Gentamicin | 8-12 | 10-30 | 120 | 120[†] | 30 | NA |
| Glipizide | NA | NA | NA | 4[‡] | 18 | 24 |
| Heparin sodium | NA | NA | 8 | 8[†] | 94 | 105 |
| Hydralazine | 0.1 | NA | NA | 1[§] | NA | NA |
| Lidocaine | 1.5-6 | 9-14 | 60 | 60[†] | 120 | NA |
| Mannitol | NA | NA | NA | 20,000[‖] | 24,000 | NA |
| Nitroglycerin | 0.0012-0.011 | NA | NA | 0.11[§] | 0.1 | 0.3 |
| Nitroprusside | NA | NA | NA | 7.5[‡] | 12 | NA |
| Norepinephrine | NA | NA | NA | 10[‖] | 15 | NA |
| Penicillin G potassium | NA | NA | NA | 2,400[‖] | 7,000 | NA |
| Phentolamine | NA | NA | NA | 5[‖] | 10 | 15 |
| Phenytoin | 10-20 | 20-40+ | 100 | 100[†] | NA | NA |
| Procainamide | 4-10 | 10-12+ | 100 | 100[†] | 40 | 20 |
| Quinidine | 0.3-6 | 10 | 50 | 50[†] | 60 | 76 |
| Regular insulin | 100 or less | NA | NA | 1,000[§] | 200 | 50 |
| Warfarin | 1-10 | NA | 100 | 100[†] | 180 | NA |

NA, not available; NCCLS, National Committee for Clinical Laboratory Standards.
* Drug concentrations are expressed as micrograms per milliliter, except heparin sodium (units per milliliter) and regular insulin (microunits per milliliter). Dobutamine
 therapeutic levels were incorrect in *Goodman & Gilman's The Pharmacological Basis of Therapeutics*[8] and were taken from Steinberg and Notterman.[7]
† Test level recommended by the National Committee for Clinical Laboratory Standards (NCCLS).[10]
‡ Estimated by distributing the highest dose published in *Goodman & Gilman's The Pharmacological Basis of Therapeutics*[8] in 5 L of blood volume. See
 "Methods and Materials."
§ Toxic level or 10 times the therapeutic level published in *Goodman & Gilman's The Pharmacological Basis of Therapeutics*.[8]
‖ Estimated by distributing the highest dose published in *The Critical Care Drug Handbook*[9] in 5 L of blood volume.

book,[8] or (3) if both the drug therapeutic and toxic levels were unknown, calculated according to the NCCLS guideline,[10] by distributing the highest therapeutic dosage published in the clinical pharmacology book[8] or the drug handbook[9] in 5 L of blood volume. The tested concentrations in test levels 2 and 3 were chosen higher or lower than test level 1 to cover the concentration spectrum. Each drug concentration listed in test levels 1, 2, and 3 was used to screen for drug interference.

**Glucose Devices Evaluated**

❙**Table 2**❙ lists device characteristics. Four electrochemical-based and 3 photometric-based systems were used in the study: Accu-Chek Advantage H and Accu-Chek Advantage (Roche Diagnostics, Indianapolis, IN), Precision G and Precision QID (Abbott Laboratories, Bedford, MA), SureStepPro and One Touch (LifeScan, Milpitas, CA), and HemoCue B-Glucose (HemoCue,

Mission Viejo, CA). Test strips for the handheld photometric and electrochemical systems are constructed with 1 or more membranes. Usually, a hydrophilic mesh membrane is on the top, and a reagent layer is on the bottom. The hydrophilic mesh membrane absorbs and disperses the specimen quickly and uniformly to the reagent layer. The reagent layer contains glucose catalytic enzymes and chromogen in photometric-based systems. Glucose reacts with the enzymes to produce intermediate products, which then can oxidize the chromogen to produce color. The handheld photometric systems measure the color and convert it to a glucose level. The dye intensity is proportional to glucose concentration in the sample tested. The HemoCue B-Glucose portable analyzer uses 2 wavelengths, 660 and 840 nm, to measure absorbance. The electrochemical-based systems have glucose catalytic enzymes, electron mediators, and electrodes in the reagent layer. During glucose oxidation, the electrochemical

■Table 2■
**Characteristics of Glucose Measurement Devices**

| Glucose System | Method | Electron Mediator or Indicator Dye | Enzyme | Linearity (mg/dL) | Manufacturer |
|---|---|---|---|---|---|
| **Test strip systems** | | | | | |
| Accu-Chek Advantage H | Electrochemical | Ferricyanide/ ferrocyanide | GD | 20-600 | Roche, Indianapolis, IN |
| Accu-Chek Advantage | Electrochemical | Ferricyanide/ ferrocyanide | GO | 10-600 | Roche |
| Precision G | Electrochemical ferrocene | Ferricinium/ | GO | 20-600 Laboratory, Bedford, MA | Abbott |
| Precision QID | Electrochemical ferrocene | Ferricinium/ | GO | 20-600 Laboratory | Abbott |
| SureStepPro , | Reflectance photometric | Naphthalene sulfonic acid salt; 3-methy 2-benzothiazolinone hydrazone, solubilized | GO | 0-500 | LifeScan Milpitas, CA |
| One Touch | Reflectance photometric | 3-methy 2-benzothiazolinone hydrazone hydrochloride; 3-dimethylaminobenzoic acid | GO | 0-600 | LifeScan |
| **Cuvette system** | | | | | |
| HemoCue B-Glucose | Absorbance photometric | MTT | GD | 0-400 , | HemoCue, Mission Viejo CA |

GD, glucose dehydrogenase; GO, glucose oxidase; MTT, 3–(4,5–dimethylthiazol-2–yl)-2,5–diphenyl-2*H*-tetrazolium bromide.

systems measure the current formed, the magnitude of which is correlated with sample glucose concentration.

### Whole-Blood Bench Glucose Analyzer

A whole-blood glucose analyzer (ABL 625 GL, Radiometer America, Westlake, OH) was used to determine the initial glucose levels in the venous blood samples with no dextrose addition and in those to which dextrose was added. The ABL 625 analyzer also was evaluated for drug interference. These results will be reported separately.

### Parallel Control Testing

Parallel testing was used to compare glucose measurements in the presence and in the absence of drugs. Samples not spiked with drugs were measured by each glucose device. These control measurements served as the reference measurements for each glucose system.

### Study Design

A low glucose level (80-100 mg/dL) was used to screen for potential drug interference. Samples spiked with drugs were defined as the test samples. Samples serving as controls substituted isotonic sodium chloride (0.9%) for the drug solution. For each drug test level listed in Table 1, we used 1 control sample and 2 parallel test samples with same drug concentration.

Sample volume (2 mL) was composed of blood and an aliquot of drug solution or isotonic sodium chloride. The aliquot added was less than 10% of the total volume, according to recommendations by the International Federation of Clinical Chemistry in guidelines for the evaluation of drug effects in clinical chemistry.[11] Each sample was measured in duplicate. The 2 glucose measurements from the control samples were averaged. The 4 glucose measurements from the 2 parallel test samples were averaged. The mean difference between the control and test samples was calculated by subtracting the mean of control readings from the mean of test samples:

$$\text{Glucose Difference} = \text{Mean}_{\text{(Test Sample)}} - \text{Mean}_{\text{(Control)}}$$

### Dose-Response Relationships

If a mean difference of greater than ± 6 mg/dL was observed at any of the 3 test levels, an evaluation of the dose-response relationship using 5 drug concentrations from therapeutic to toxic was performed 3 times (n = 3) each at low (80-100 mg/dL) and at high (approximately 200 mg/dL) glucose levels. A plot of the glucose differences vs drug concentrations was made to show interference and to determine by interpolation the drug concentration at which a ± 6 mg/dL bias was observed, based on the trend. For the

Accu-Chek Advantage system, the dose-response relationships reported herein were checked for test strips with recent minor modifications.
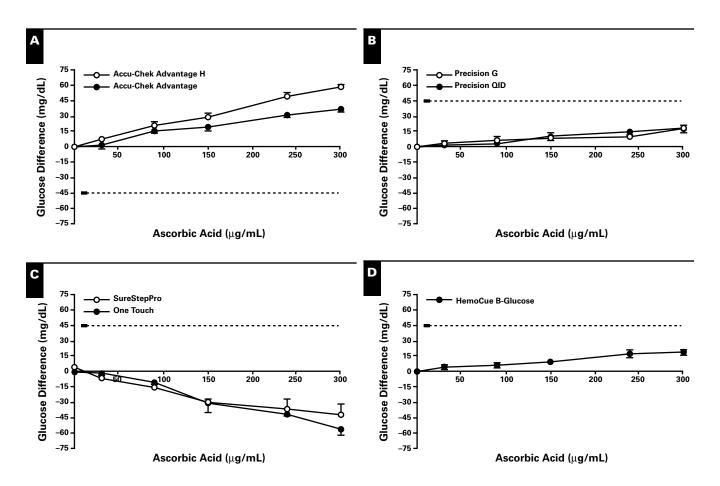
## Procedure

The study was performed in accordance with guidelines of the human subjects committee. Blood was obtained from the forearm of fasting healthy volunteers. This blood was collected in seven 5-mL lithium heparin Vacutainers (Becton Dickinson, Rutherford, NJ). After inverting the tube 20 times, the blood was pooled. The glucose concentration then was measured with the bench whole-blood analyzer (ABL 625 GL). Most of the drugs tested were injectable solutions. Noninjectable drugs in the form of tablets (glipizide and aspirin) were ground into a fine powder, then placed into preheated normal saline (37°C), and gently mixed until completely dissolved.

The target drug concentrations in the test samples were obtained by placing aliquots of blood into tubes containing predetermined amounts of drug or isotonic sodium chloride to achieve a total volume of 2 mL (drug plus blood). The high glucose level (200 mg/dL) was achieved by adding 10% dextrose solution to the blood pool. Testing was performed in parallel (control vs test samples) to minimize the effects of glucose metabolism. The hematocrit of each blood sample was measured on a microcentrifuge (Select-a-Fuge 24, Bio-Dynamics, Indianapolis, IN) by centrifuging the sample at 4,000 rpm for 5 minutes.

## Precision

Two or 3 levels of quality control solutions provided by the manufacturers were tested 20 consecutive times to assess within-day precision. Day-to-day precision of each glucose meter was obtained by collecting quality control solution measurements during the individual drug inter-



**Figure 1** Ascorbic acid interference evaluated at the low glucose level. Concentrations at which glucose differences were greater than ± 6 mg/dL were as follows: A, 90 μg/mL and 30 μg/mL for Accu-Chek Advantage H and Accu-Chek Advantage, respectively; B, 150 μg/mL and 240 μg/mL for Precision G and Precision QID, respectively; C, 90 μg/mL and 30 μg/mL for SureStepPro and One Touch, respectively; and D, 150 μg/mL for HemoCue B-Glucose. Mean difference ± SD is shown on all plots. The solid horizontal bar is the drug therapeutic level. The dashed line is the range of reported clinical drug concentrations that have been observed. For manufacturers of measurement devices, see Table 2.

ference runs. The precision was expressed as the coefficient of variation (CV).

### Criterion for Detection of Error, Statistics, and Units

The criterion for interference was a mean glucose difference between the test samples and the control samples of magnitude greater than ± 6 mg/dL. Plots of results show mean ± SD. The precision is expressed as CV = (SD/mean) × 100%.

Drug concentrations generally are expressed in conventional units, micrograms per milliliter, because these units are used commonly in pharmacy and critical care units. Glucose results are given in milligrams per deciliter, since these units are used most frequently in the hospital setting and by patients themselves in the United States. Glucose in milligrams per deciliter is converted to millimoles per liter (the Système International units) as follows: mmol/L = mg/dL × 0.05551.

## Results

### Glucose Levels

Initial venous glucose (n = 15) measured with the whole-blood bench analyzer averaged 81.9 ± 9.6 mg/dL. After the addition of dextrose, the glucose level (n = 15) averaged 201.2 ± 7.9 mg/dL. The hematocrit range was 35% to 46% (0.35-0.46), which was within the manufacturers' recommended ranges.

### Interference

Ascorbic acid, acetaminophen, dopamine, and mannitol interfered with glucose measurements. ❙**Figure 1**❙ shows that at the low glucose level, ascorbic acid increased the glucose readings of Accu-Chek Advantage H and Accu-Chek Advantage (Figure 1A), Precision G and Precision QID glucose meters (Figure 1B), and the HemoCue B-Glucose portable analyzer (Figure 1D), but ascorbic acid decreased the SureStepPro and One Touch glucose readings (Figure 1C).

❙**Figure 2**❙ shows that ascorbic acid increased the glucose readings of Accu-Chek Advantage H, Accu-Chek Advantage (Figure 2A), and HemoCue B-Glucose (Figure 2D) at the high glucose concentration. Ascorbic acid decreased SureStepPro and One Touch glucose readings (Figure 2C). No significant interference was observed with Precision G and Precision QID glucose measurements (Figure 2B).

❙**Figure 3**❙ shows that acetaminophen increased glucose readings on the Accu-Chek Advantage H and Accu-Chek Advantage but decreased Precision G and Precision QID readings. No significant interference was observed on the SureStepPro, One Touch, or HemoCue B-Glucose.

Dopamine showed positive interference with glucose measurements performed on the Accu-Chek Advantage H and the Accu-Chek Advantage ❙**Figure 4**❙ at low (Figure 4A) and high (Figure 4B) glucose levels. This interference appeared primarily at high drug concentrations and was dose-dependent.

❙**Figure 5**❙ showed that mannitol increased SureStep-Pro readings at low (Figure 5A) and high (Figure 5B) glucose levels. This interference was more prominent at high glucose levels than at low glucose levels. Mannitol interference at high glucose levels showed an apparent linear relationship (Figure 5B).
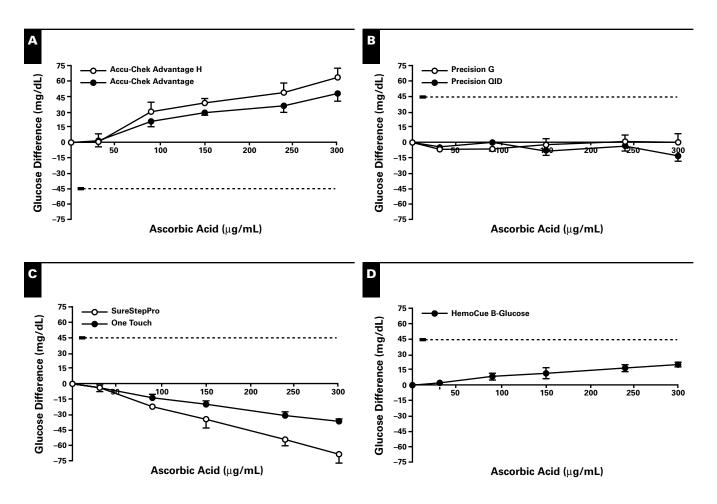
### Precision

❙**Table 3**❙ summarizes within-day and day-to-day precision results for the 7 glucose devices. The CVs for day-to-day precision ranged from 2.7% to 6.0%. The CVs for within-day precision ranged from 1.8% to 4.9%. Generally, the largest CVs resulted when testing the lowest glucose levels in quality control solutions.

## Discussion

### Glucose Levels, Error Tolerance, and Dose-Response Relationships

The 2 glucose levels chosen for the evaluation of drug interference were based on the fact that at the high level, 200 mg/dL, critical care physicians believe that critically ill patients have adequate glucose to reduce excess catabolism, preserve leukocyte function, improve strength and healing of wounded tissue, and avoid deleterious effects of hyperglycemia (eg, ketoacidosis and hyperosmolarity), while at the low level, 80 mg/dL, the glucose concentration is "high enough that hypoglycemia is not a major risk."[12] Thus, these 2 glucose levels are clinical decision brackets for the treatment of critically ill patients and other hospitalized critical care patients and, therefore, represent clinically meaningful test levels.

Accurate measurements of blood glucose are essential to diagnose critically ill patients and to guide algorithmic insulin regimens.[12,13] Kost et al[6] used an accuracy tolerance of ± 15 mg/dL for glucose levels of 100 mg/dL or less or ± 15% for glucose levels greater than 100 mg/dL to evaluate the clinical performance of glucose meters. We used ± 6 mg/dL as the error threshold for drug interference at glucose levels of 80 mg/dL and 200 mg/dL. This criterion is more stringent than the clinical performance criterion. System noise for handheld glucose meters may be as high as ± 3 mg/dL. Thus, dose-response relationships help show the clinical relevance of interference trends at low and high glucose levels.
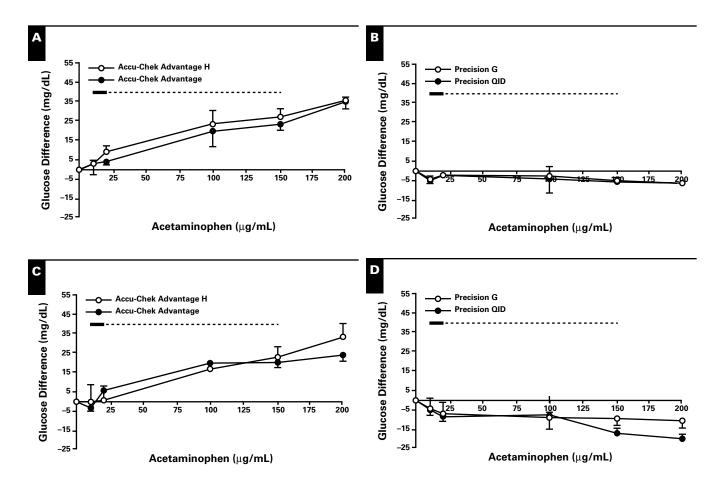
**Figure 2** Ascorbic acid interference evaluated at the high glucose level. Concentrations at which glucose differences were greater than ± 6 mg/dL were as follows: A, 90 μg/mL for Accu-Chek Advantage H and Accu-Chek Advantage; B, 300 μg/mL for Precision G; C, 90 μg/mL for SureStepPro and One Touch; and D, 90 μg/mL for HemoCue B-Glucose. Mean difference ± SD is shown on all plots. The solid horizontal bar is the drug therapeutic level. The dashed line is the range of reported clinical drug concentrations that have been observed. For manufacturers of measurement devices, see Table 2.

### Interference Trends and Their Mechanisms

Ascorbic acid affected the glucose devices in varying degrees (Figures 1 and 2). Ascorbic acid is used frequently in clinical practice.[14] The mechanism of ascorbic acid interference on glucose measurements with electrochemical strips is that ascorbic acid is oxidized at the electrode surface,[15] resulting in the production of more electrons and the generation of more current. There are 3 electrodes in the Precision G and Precision QID electrochemical strips (active, background compensation, and reference electrode). The background compensation electrode lacks glucose oxidase but measures the signal from potentially interfering substances. This nonspecific signal is used to modify the signal produced by the primary active electrode. The results show that the third electrode compensates for the ascorbic acid interference at the high glucose level but not completely at the low glucose level.

The influence of ascorbic acid on glucose oxidase–based photometric strips, such as SureStepPro and One Touch devices, may be competition with the redox indicator system. Ascorbic acid is a strong reducing substance that reacts with hydrogen peroxide. As hydrogen peroxide is consumed by ascorbic acid, less hydrogen peroxide is available to react with the dye on the test strips. Hence, dye color development is incomplete, resulting in falsely lower glucose readings.[16] With different indicator dyes, such as the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide) used in the HemoCue B-Glucose analyzer,[17] ascorbic acid increases the glucose reading instead of decreasing it. This suggests that the ascorbic acid interference may be indicator dye–dependent.[18]

Acetaminophen interference with glucose measurements has been studied previously.[15] Acetaminophen can

**Figure 3** Acetaminophen interference evaluated at the low (A, B) and high (C, D) glucose levels. Concentrations at which glucose differences were greater than ± 6 mg/dL were as follows: A, 100 µg/mL and 20 µg/mL for Accu-Chek Advantage H and Accu-Chek Advantage, respectively; B, 200 µg/mL for Precision G and Precision QID; C, 100 µg/mL for Accu-Chek Advantage H and Accu-Chek Advantage; and D, 20 µg/mL for Precision G and Precision QID. Mean difference ± SD is shown on all plots. The solid horizontal bar is the drug therapeutic level. The dashed line is the range of reported clinical drug concentrations that have been observed. For manufacturers of measurement devices, see Table 2.

diffuse across a porous membrane to the electrode surface where it is directly oxidized, producing an interfering current that increases the glucose reading.[19] The oxidation by acetaminophen is thought to be related to the free phenolic hydroxyl group present in acetaminophen.[20] Acetaminophen can cause positive interference with electrochemical glucose test strips and a whole blood analyzer.[15,20-22] In the present study, the devices that use 3 electrodes (ie, Precision G and Precision QID) seemed to overcompensate for the interfering current, especially at the high glucose level.
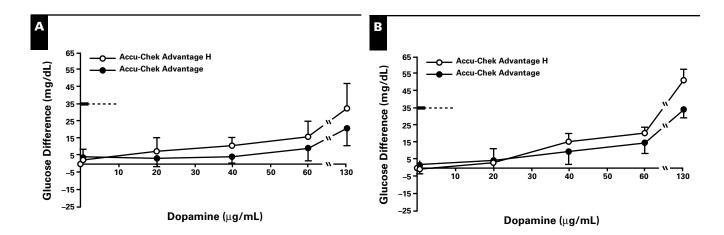
With photometry methods, the mechanism of dopamine [4-(2-aminoethyl) brenzcatechin-HCl] interference is assumed to be an inhibition of the chemical reaction on the test strips.[23] Whether this mechanism applies to electrochemical-based devices is unclear. An alternative explanation is that dopamine contains the same oxidizable

free phenolic hydroxyl group as acetaminophen; therefore, oxidation of this type of compound in the presence of reduced flavin enzymes will produce a catalytic redox cycle and chemical amplification of the oxidative signal.[24]
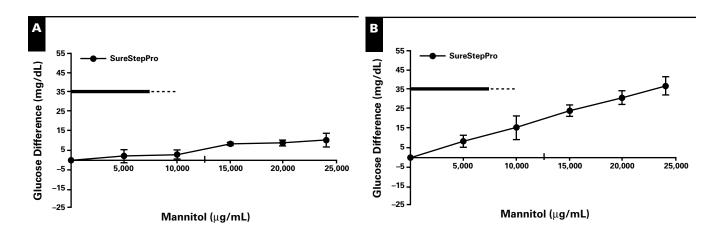
Mannitol introduced a positive bias on SureStepPro glucose measurements and a negative bias with glucose measurements performed on the ABL 625 whole-blood analyzer.[25] The mannitol effect may be a direct effect on the chemistry of the glucose test strip or an osmotic effect whereby water is repartitioned between erythrocytes and plasma. Additional study of the mechanisms involved is needed.

### Clinical Relevance

**Table 4** lists the drug concentrations at which interference with glucose measurements was greater than ± 6 mg/dL. Most of the drug concentrations are higher than the therapeutic levels, with the exception of acetaminophen,

**Figure 4** Dopamine interference with glucose measurements. Concentrations at which glucose differences were greater than ± 6 mg/dL were as follows: A, 60 µg/mL and 20 µg/mL for Accu-Chek Advantage H and Accu-Chek Advantage, respectively, tested at the low glucose level; B, 40 µg/mL for Accu-Chek Advantage H and Accu-Chek Advantage, tested at the high glucose level. For clinical significance, see the "Discussion" section. Mean difference ± SD is shown on all plots. The solid horizontal bar is the drug therapeutic level. The dashed line is the range of reported clinical drug concentrations that have been observed. For manufacturers of measurement devices, see Table 2.



**Figure 5** Mannitol interference with glucose measurements performed on the SureStepPro. A, Glucose paired differences were greater than 6 mg/dL at a mannitol level of 15,000 µg/mL, tested at the low glucose level. B, Glucose paired differences were greater than 6 mg/dL at a mannitol level of 5,000 µg/mL, tested at the high glucose level. Mean difference ± SD is shown on all plots. The solid horizontal bar is the drug therapeutic level. The dashed line is the range of reported clinical drug concentrations that have been observed. For manufacturers of measurement devices, see Table 2.

which in therapeutic concentrations increased Accu-Chek Advantage and decreased Precision G and Precision QID measurements at low and high glucose levels, respectively. The clinically toxic concentration of ascorbic acid is not established. High doses, ranging from 3 to 30 g/d,[26-28] may be recommended when treating patients with conditions such as the common cold,[29] diabetes,[30] critical illness,[31,32] and cancer.[26,33] Serum concentrations of ascorbate have been documented as high as 30 mmol/L (5,284 µg/mL).[28] We tested a spectrum of ascorbic acid levels up to 300

µg/mL, based on published observations,[33] to simulate most clinical scenarios. The results showed that at high concentrations, ascorbic acid can interfere with glucose measurements on all tested devices. Ascorbic acid is one of the most common interfering substances that affects the accuracy of glucose meters.[14,15,34,35]

Acetaminophen is taken extensively in the United States. Acetaminophen screening is warranted because of the frequency of occult presentation and the severity of toxic effects.[36] Drug overdose cases are reported often,

**|Table 3|**
**Precision Results for Glucose Measurement Devices***

| Glucose System | N | Low | | Middle | | High | |
|---|---|---|---|---|---|---|---|
| | | Mean ± SD | CV | Mean ± SD | CV | Mean ± SD | CV |
| Day-to-day precision | | | | | | | |
| Accu-Chek Advantage H | 30 | 65.5 ± 3.1 | 4.8 | 149.3 ± 6.6 | 4.4 | 342.0 ± 12.3 | 3.6 |
| Accu-Chek Advantage | 30 | 64.4 ± 2.8 | 4.3 | 163.2 ± 6.3 | 3.9 | 298.7 ± 8.2 | 2.7 |
| Precision G | 30 | 47.1 ± 2.8 | 6.0 | — | — | 283.5 ± 13.1 | 4.6 |
| Precision QID | 30 | 42.5 ± 2.3 | 5.5 | — | — | 275.6 ± 12.3 | 4.5 |
| SureStepPro | 30 | 41.4 ± 1.6 | 3.9 | 103.3 ± 4.0 | 3.9 | 325.5 ± 7.2 | 2.2 |
| One Touch | 30 | 51.5 ± 1.9 | 3.6 | 109.5 ± 3.7 | 3.3 | 333.0 ± 7.6 | 2.3 |
| HemoCue B-Glucose | 30 | 64.0 ± 1.9 | 2.9 | — | — | 332.4 ± 7.9 | 2.4 |
| Within-day precision | | | | | | | |
| Accu-Chek Advantage H | 20 | 67.0 ± 3.0 | 4.4 | 149.4 ± 5.3 | 3.6 | 342.5 ± 8.6 | 2.5 |
| Accu-Chek Advantage | 20 | 64.9 ± 1.7 | 2.6 | 169.7 ± 2.8 | 1.8 | 301.2 ± 6.2 | 2.0 |
| Precision G | 20 | 47.1 ± 2.2 | 4.6 | — | — | 279.4 ± 9.3 | 3.3 |
| Precision QID | 20 | 43.4 ± 2.1 | 4.9 | — | — | 273.6 ± 8.8 | 3.2 |
| SureStepPro | 20 | 41.2 ± 1.1 | 2.6 | 105.1 ± 2.6 | 2.5 | 327.9 ± 2.0 | 2.5 |
| One Touch | 20 | 53.8 ± 1.4 | 2.7 | 108.9 ± 2.4 | 2.2 | 337.8 ± 6.3 | 1.9 |
| HemoCue B-Glucose | 20 | 64.5 ± 1.7 | 2.6 | — | — | 337.3 ± 7.5 | 2.2 |

CV, coefficient of variation.
* Two quality control levels were evaluated for Precision G, Precision QID, and HemoCue B-Glucose. For manufacturers, see Table 2.

especially in children.[37,38] On the basis of reports of the Rocky Mountain Poison Control Center, at least 1 to 2 cases of acetaminophen poisoning occur daily in the United States.[39] Acetaminophen affects the results of not only handheld glucose meters,[16,21,22,36,40] but also whole-blood bench analyzers.[19,41] In the patients with an overdose, the acetaminophen blood concentrations were as high as 534 and 680 µg/mL (3,535 and 4,502 µmol/L).[42,43] Unnecessary insulin therapy has been given[42,43] because of inaccurate glucose measurements. This interference is a potential risk if a therapeutic decision depends on erroneous glucose meter results.

Dopamine increased Accu-Chek Advantage H and Accu-Chek Advantage glucose measurements at concentrations much higher than the therapeutic level, less than 0.2 µg/mL,[44] and higher than those typically found clinically, 0.07641 µg/mL for dopamine at the infusion rate of 3 µg/kg per minute.[45] However, the blood concentration of dopamine is titrated according to actual cardiovascular responses. Therefore, higher doses of dopamine (50 µg/kg per minute) used in critically ill patients may generate high drug levels in the blood.[46] Also, since patients with hepatic and renal dysfunction show a significantly reduced dopamine clearance resulting in a steady-state plasma dopamine concentration approximately 8 times that of patients without renal and hepatic dysfunction,[47,48] higher drug concentrations could be reached during multiple organ system failure in these patients.

Poor performance by glucose meters has been observed for patients who had inadequate tissue perfusion,

were hypotensive, or were in shock.[1-3] High failure rates have been reported in intensive care unit settings.[49] Possibly, drug interference contributed to errors. Lower glucose levels were found in capillary samples than in venous samples during adrenergic agonist interventions,[2,3] and "in the patients in shock, it is possible that peripheral vasoconstriction with shunting of blood from periphery and continued tissue glucose consumption can lead to the decreased peripheral glucose levels."[2] These additional clinical factors can increase glucose meter error rates in patients with shock and must be considered when interpreting glucose results.

Mannitol is an osmotic agent used for diuresis in cerebral edema, toxin excretion, and glaucoma.[9,50] Doses used can be as high as 6 g/kg per 24 hours.[9] The therapeutic concentration is 25 to 7,300 µg/mL,[51] and the recommended blood concentration of mannitol is below 10,000 µg/mL.[52] Clinically, massive mannitol infusion has been used and has caused renal failure.[53-57] Hence, high mannitol blood concentrations can appear in patients with inadequate renal function. Knowledge of mannitol interference with glucose measurements is helpful in point-of-care testing for patients with renal problems.

## Conclusions

Ascorbic acid, acetaminophen, dopamine, and mannitol interfered with glucose measurements performed with the latest generation of handheld glucose meter test

**■Table 4■**

**Drug Interference Concentrations Associated With Glucose Differences of Greater Than ± 6 mg/dL***

| Glucose System | Drug | Level | | Drug Interference Concentrations | |
|---|---|---|---|---|---|
| | | Therapeutic | Toxic | At Low Glucose Level | At High Glucose Level |
| Accu-Chek Advantage H | Ascorbic acid | 8-12 | — | 90 | 90 |
| | Acetaminophen | 10-20 | >150 | 100 | 100 |
| | Dopamine | <0.2 | — | 60 | 40 |
| Accu-Chek Advantage | Ascorbic acid | 8-12 | — | 30 | 90 |
| | Acetaminophen | 10-20 | >150 | 20 | 100 |
| | Dopamine | <0.2 | — | 20 | 40 |
| Precision G | Ascorbic acid | 8-12 | — | 150 | 300 |
| | Acetaminophen | 10-20 | >150 | 200 | 20 |
| Precision QID | Ascorbic acid | 8-12 | — | 240 | † |
| | Acetaminophen | 10-20 | >150 | 200 | 20 |
| SureStepPro | Ascorbic acid | 8-12 | — | 90 | 90 |
| | Mannitol | <10,000 | — | 15,000 | 5,000 |
| One Touch | Ascorbic acid | 8-12 | — | 30 | 90 |
| HemoCue B-Glucose | Ascorbic acid | 8-12 | — | 150 | 90 |

* All units are given as micrograms per milliliter. For manufacturers, see Table 2.

† No interference observed in the tested concentration.

strips and, to a lesser extent, with the portable analyzer. These drugs are used commonly for the treatment of critically ill patients and possibly in high doses. The package inserts of glucose meters may not provide adequate information for drugs used in critical care settings. Also, ascorbic acid and acetaminophen can be bought over the counter and may be ingested in relatively high doses without medical supervision.

Understanding of clinical relevance is facilitated by knowledge of the patient's drug regimen and concentration in the blood in relation to the dose-response relationship of the interfering substance. We recommend that dose-response relationships be determined by clinical investigators of these devices and be part of interference evaluations required by the US Food and Drug Administration.

Drug interferences potentially could mask the presence of hypoglycemia or hyperglycemia and could lead to inappropriate insulin therapy. Therefore, physicians and critical care staff should choose handheld glucose devices carefully for point-of-care testing and should interpret results with current knowledge of interfering substances and the patient's drug regimen before treating hypoglycemia or hyperglycemia.

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