the remaining two patients with increased cTnI, the reasons for their increases could not be determined from clinical review.

Our data therefore suggest that cTnI is more discriminating than cTnT for myocardial injury. cTnI was increased in only 8.9% of our patients, but cTnT was increased in 63.4%. It is not surprising that this nonspecific increase of cTnT was detected in such a proportion of uremic patients because these patients can have myopathy with muscle regeneration [4]. However, this can be clearly settled only by an outcomes study. Our findings of fewer increased concentrations of cTnT than of cTnT in renal failure is in agreement with that of Bhayan et al. [5] in a smaller group (n = 8). In a study of cTnT in patients with ESRD, Katus et al. [6] suggested that cTnT is more sensitive than cTnI but did not present data to support this claim. A persistent increase of cTnT lasting over 6 months, reported by Hafner et al. [7], argues against significant myocardial injury because the serial rise and fall of cardiac markers such as CK-MB and cTnT has been documented in acute myocardial injury in the clinical setting [8, 9]. With the higher cutoff value of 0.2 μg/L for the cTnT assay as proposed by Katus et al. [7], 15 of 51 (29%) of their patients on chronic maintenance hemodialysis had increased cTnT concentrations. In our patient population, selecting 0.2 μg/L as a discriminating value still left a substantial proportion (38 of 82; 46.3%) of patients with chronic renal failure who had increased cTnT. Conversely, none of the patients with normal values for both cTnT and cTnI had clinical evidence of myocardial injury in the time frame associated with our sampling.

Both cTnT and cTnI are useful in ruling out myocardial injury, but cTnI has not been shown to be expressed in skeletal muscle, either in embryonic development or in repair states. Evidence continues to accumulate supporting the true cardiосpecificity of the cTnI marker, and we consider it the preferred marker for myocardial injury in the setting of chronic renal disease.

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Precision and Accuracy of the Accu-Chek® Advantage® Blood Glucose Monitoring System at High Altitude

To the Editor:
Self-monitoring of blood glucose is an important tool for assessing glycemic conditions in people with diabetes mellitus. Recently, the Diabetes Control and Complications Trial (DCCT) [1], an unprecedented work by multiple institutions, showed that the progression of all major complications associated with this disease could be suppressed if patients were held in tighter glycemic control. One component of the DCCT was to accurately and precisely predict a patient's blood glucose concentration from monitoring devices used to assay finger-puncture whole blood. Monitoring device data allowed participants to readily modify their therapy so as to more closely approximate euglycemia.

Although much has been published on self-monitoring of blood glucose and the various instruments and procedures used for measurement, relatively few studies have provided information about the performance of these systems in high altitude or simulated high-altitude environments [2-6]. Some of these reports have indicated that environmental effects, including altitude, could change the apparent performance of the systems. A monitoring system response as low as ~34% from the reference method response has been reported [3]. Because of these reports, many healthcare professionals and patients in locations of high altitude have inquired about the performance of these systems in their environment. Further, the US Food and Drug Administration suggests that new devices be tested in real or simulated high-altitude environments as part of the application package that device manufacturers must use when applying for a 510(k) premarket notification of a new or enhanced system for monitoring blood glucose. Therefore, it is important to understand how these systems work at high elevations.

Here, we report the results of an investigation into the environmental altitude effects of the Accu-Chek® Advantage® blood glucose monitoring system (Boehringer Mannheim Corp., Indianapolis, IN). Our investigation included accuracy data collected for assays performed at 2668 m with capillary blood from 143 diabetic donors, and precision data collected for assays performed at 213, 2668, and 3665 m with blood, manufacturer's control solutions, and Sugar-Chek® whole-blood glucose product (Streck Labs., Omaha, NE). This evaluation typifies how the system will be used by patients and assessed by clinicians in high-altitude environments.

We had the opportunity to test a large patient population (n = 143) of children and young adults at an American Diabetes Association-sponsored camp in Colorado. The camp was located at an elevation of 2668 m above sea level. All participants and their parents or legal guardians signed consent forms approved by the Institutional Review Board of The Children's Hospital, Denver, CO. The accuracy of the system was assessed by comparison with a Somogyi-like [7-9] hexokinase-based assay of deproteinized whole blood. The whole blood to be assayed with the comparison method was...
collected from patients’ fingers immediately after dosing the monitoring system with blood. The precision of the system was assessed by using the same Advantage meters, vials containing test strips, control solutions, and Sugar-Chex solutions at 213 m (Indianapolis, IN), 2668 m (camp), and 3665 m (Rocky Mountain National Park, CO) above sea level.

After cleansing and drying of the donor’s finger, the site was lanced and blood was placed on two Advantage monitoring system test strip lots. A microhematocrit sample and the comparison method samples (which were collected in duplicate in 50-μL tubes and deproteinized in 500 μL of 0.33 mol/L perchloric acid) each were immediately collected from the same finger-puncture site. After digestion and centrifugation, the decantate of each of the duplicate reference samples was analyzed in triplicate with a Boehringer Mannheim–Hitachi 717 analyzer by the hexokinase/glucose-6-phosphate dehydrogenase methodology [7–9]; the mean value was used to assess the performance of the monitoring system response. Accuracy was determined by plotting the Advantage results vs the whole-blood comparison results by using the error grid analysis of Clarke et al. [10–12], which includes a least-squares linear regression analysis to calculate the slope, intercept, correlation coefficient (r), and bias from the comparison method mean [13].

The response of the Advantage system for two test strip lots at 2668 m showed a mean bias of −4.6% (95% confidence interval, −5.8% to −3.4%) and −3.8% (−5.0% to −2.5%) for strip lots 1 and 2, respectively, across the blood glucose reference range of 2.8–26.4 mmol/L. For samples with comparison method results ≤8.3 mmol/L [14], the mean bias was −3.1% (−4.9% to −1.2%) and −1.5% (−3.4% to 0.5%), respectively, for lots 1 and 2, and −6.5% (−7.8% to −5.2%) and −6.8% (−7.9% to −5.6%), respectively, for results >8.3 mmol/L. Linear regression statistics for strip lot 1 (n = 143) were: slope = 0.923 (95% confidence interval = 0.90–0.94), intercept = 0.21 mmol/L, r = 0.993, and S_{YX} = 0.59 mmol/L. Statistics for lot 2 (n = 143) were: slope = 0.925 (0.91–0.94), intercept = 0.23 mmol/L, r = 0.993, and S_{YX} = 0.58 mmol/L. For both strip lots combined (n = 286), the statistics were: slope = 0.924 (0.91–0.93), intercept = 0.22 mmol/L, r = 0.993, and S_{YX} = 0.59 mmol/L. Both lots of test strips performed almost identically, giving mean glucose values of 8.78 and 8.83 mmol/L and median values of 7.17 and 7.28 mmol/L for lots 1 and 2, respectively. Additionally, 80% of the results were within 10% of the comparison method results, 93% were within 15% of the comparison method results, and 98% were within 20%. No values >20% from the comparison method value (6 of 286, or 2% of the total results) provided a clinically significantly different patient’s result, as defined by Clarke et al. (Fig. 1) [10].

The precision of the whole-blood assay was assessed at 213 and 2668 m with venous blood that had been collected in heparin-containing Vacutainer Tubes (Becton Dickinson, Rutherford, NJ) and allowed to glycolize at ambient room temperature overnight. The next day, the blood was supplemented to contain different glucose concentrations (4.00 to 31.0 mmol/L) and placed in oxalate/fluoride-containing Vacutainer Tubes to quench the glycolysis. For logistical considerations, we were not able to test with blood at 3665 m or to use the same blood at 2668 and 213 m. However, we did try to supplement blood that had been collected from the same donor to comparable glucose concentrations at both 2668 and 213 m. Precision assessment for all three sample types (blood, control solutions, and Sugar-Chex) was analyzed by calculating the mean, SD, and CV for each concentration tested (Table 1).

Using the system data collected at 213 m as a baseline, we then compared the imprecision and difference in mean response attained at elevations of 2668 and 3665 m for the sample types tested. There was a slight increase in imprecision of ~1–3%; however, the differences were not as great as those published by others and are clinically insignificant [3, 4].

We conclude that the Accu-Chek Advantage blood glucose monitoring system shows clinically acceptable performance at high altitude.

### Table 1. Precision of the Accu-Chek Advantage system using three sample types at various altitudes.

<table>
<thead>
<tr>
<th>Altitude, m</th>
<th>Controls Low</th>
<th>High</th>
<th>Sugar-Chex Low</th>
<th>Mid</th>
<th>High</th>
<th>Blood Low</th>
<th>Mid</th>
<th>High</th>
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<tr>
<td>213</td>
<td>Mean*</td>
<td>3.55</td>
<td>17.2</td>
<td>4.44</td>
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<td>SD*</td>
<td>0.15</td>
<td>0.57</td>
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<td>0.59</td>
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<tr>
<td></td>
<td>CV, %</td>
<td>4.22</td>
<td>3.31</td>
<td>4.50</td>
<td>2.31</td>
<td>2.43</td>
<td>4.67</td>
<td>3.56</td>
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<td>2668</td>
<td>Mean*</td>
<td>3.61</td>
<td>16.9</td>
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<td>11.4</td>
<td>23.3</td>
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<td></td>
<td>SD*</td>
<td>0.21</td>
<td>0.53</td>
<td>0.25</td>
<td>0.49</td>
<td>0.92</td>
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<td>CV, %</td>
<td>5.82</td>
<td>3.14</td>
<td>5.84</td>
<td>4.30</td>
<td>3.95</td>
<td>5.51</td>
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<tr>
<td>3665</td>
<td>Mean*</td>
<td>3.56</td>
<td>16.4</td>
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<td>SD*</td>
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<td>7.01</td>
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* n = 20 per concentration per sample type (mmol/L).
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