Effect of Adverse Storage Conditions on Performance of Glucometer Test Strips

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NOTE: This is a student project paper as noted in the text.

OBJECTIVE: A study was conducted to assess the impact of adverse storage environments, i.e., not manufacturer recommended, on the performance of reagent test strips used with a point of care testing (POCT) glucometer to measure whole blood glucose levels.

DESIGN/SETTING: Glucose reagent test strips were placed in open, i.e., uncapped, and closed, i.e., capped vials. These vials were those used by the manufacturer to package and store the reagent test strips. One of each type of vial was placed in the manufacturer-recommended storage environment at room temperature and the adverse environments (incubator, direct light to mimic sunlight exposure, humidity, and refrigerated). The Accu-Chek Easy® glucometer and reagent test strips as well as Accu-Chek Easy high and low glucose control solutions, manufactured by Roche, were used for this study.

MAIN OUTCOME MEASURES: On day-3, day-7, and then once every 7 days, one strip from each vial in each environment was tested with the same glucometer using both a high and a low glucose control. The strip was considered failed for a type of vial and storage environment when either control was out of the reference range on a regular testing day and still out of range when tested the subsequent day. Testing continued up to 50 days.

RESULTS: For the tested environments it was found that, overall, test strip stability lasted longer for closed vials than open vials. For open vials in adverse storage conditions, the refrigerator environment offered the longest stability at 35 to 50 days and direct light and humidity offered the shortest periods of stability at 3 to 14 days.

CONCLUSIONS: The results of this study support the manufacturer's recommendations to store POCT glucose test strips in their original vial, capped, and at room temperature, though refrigeration may offer an alternative storage environment with acceptable stability. As compliance with testing, quality control, and storage instructions is often an issue with POCT, the manufacturers of these systems for blood glucose measurement should design storage systems that allow the patient to store the glucose meter and the reagent strips in the same location. Manufacturers may also need to consider designing storage systems that are more portable, knowing that patients must take the glucose meters and test strips with them when they travel. Roche's Accu-Chek Compact system is an example of such a design. The glucose test strips are incorporated into a drum that is stored in the Accu-Chek meter itself. When a patient performs a fingerstick blood glucose measurement, the drum advances to move a test strip outside the meter. When the test is complete, the test strip is ejected for disposal.[1]

Future studies to clarify the effect of adverse storage conditions, particularly refrigeration, on the integrity of POCT test systems and reagent strips is warranted with currently marketed brands.

ABBREVIATIONS: CLS = clinical laboratory science; CV = coefficient of variation; POCT = point of care testing; SD = standard deviation; µL = microliter.

INDEX TERMS: diabetes; glucometer, glucose meter: point-of-care-testing glucose levels.

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Diabetes affects approximately 6% of the U.S. population, with over 90% of these cases classified as Type 2, or adult onset, diabetes. In addition, it is estimated that there are at least as many persons with pre-diabetes, i.e., blood glucose levels higher than normal but not clinically meeting the criteria for a diagnosis of diabetes.[2] Complications of diabetes constitute a substantial cost in healthcare as well as debilitation to the patient.

FDA approval of POCT glucometers for home use has made it possible for diabetic patients to monitor their own blood glucose levels.[3] The quick turnaround time allows for more rapid intervention via diet or medication for blood glucose values that are above or below desired levels. This has shifted the responsibility for quality control from healthcare personnel to the diabetics themselves. This shift in responsibility to patients has increased the amount of variability present in blood glucose testing, and questions have arisen as to the reliability and accuracy of the values obtained by the patient at home. Inaccurate results can lead to inappropriate, and possibly harmful, adjustment of the patient's medication or diet.[4]

There are a number of factors that can negatively affect the accuracy and precision of glucometer results including user variability, instrument malfunction, and defective reagent strips. Some patients may not necessarily follow all of the manufacturer's instructions for using their glucometers and corresponding test strips. Erroneous results can occur if control solutions are not analyzed routinely to ensure that the instrument and strips are actually working properly, or by not storing the reagent strips according to the manufacturer's instructions. If the drop of blood does not cover the entire testing area, reflectance glucometers can give a falsely low glucose value. These errors may occur as a result of poor patient training provided by non-laboratory personnel or by the patient's negligence in adhering to the proper procedures for in-home testing and quality control.[2,3]

Most glucometer research to date has focused on the actual performance of the test procedure under varying conditions. Testing under conditions of increased humidity or atmospheric pressure has been found to adversely affect the precision and accuracy of glucose results measured by glucometers.[5-9] The reagent strips can be defective due to normal expiration, mishandling, or storing them in environments not recommended by the manufacturer, resulting in inaccurate results. Glucose test reagent strips are supplied by the manufacturer in tightly capped vials, and it is recommended that only one test strip at a time be removed. The cap must then be replaced on the vial immediately and the vial stored at room temperature in a location free of extreme temperature changes. Exposure to light causes discoloration of the test area on the strips, falsely elevating glucose results.[4]

The effect of improper storage of glucose reagent strips used for glucometers has not been well documented in the literature. One study found glucose values falsely elevated after storage of strips in a refrigerator for 24 hours.[10] A study by Gonzales and Kampa using the Accu-Check Easy Glucose Monitor test system, i.e., glucometer and test strips, measured performance of these strips for both capped and uncapped vials under adverse storage conditions which included refrigeration (4 °C to 7 °C), incubation at elevated temperatures (37 °C), exposure to direct sunlight (excessive variable heat), and increased humidity as in a laundry washroom. Deterioration of the test strips as indicated by high and low control results outside their expected ranges, was found to occur the earliest in refrigeration environments for both the uncapped and capped vials. Of the adverse environments tested by Gonzales and Kampa, glucose reagent test strips were most stable in a humid environment.[11]

To supplement the limited research on stability of glucometer test strips under various storage conditions, a replication of the Gonzales and Kampa study with slight modifications was conducted by the researchers. This study used the same POCT glucose monitoring system as in the Gonzales and Kampa study, and served as a senior research project for three clinical laboratory science (CLS) students at East Carolina University (ECU). Faculty served as supervisors and co-researchers for the study. This study, therefore, also offers an example of viable research by CLS undergraduate students.

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VOL 18, NO 4 FALL 2005 CLINICAL LABORATORY SCIENCE 204

METHODS

Instrument and reagents

The Accu-Chek Easy Glucometer and Accu-Chek Easy Test Strips by Roche were used in this study to measure glucose in control solutions with low and high glucose concentrations. The test strips contain all the reagents for the glucose oxidase reaction that is initiated when blood is placed on the strip. β-D-glucose in the patient's sample is oxidized and ferricyanide is reduced to ferrocyanide using glucose oxidase as a catalyst. The ferrocyanide reacts with ferric ion to produce a blue color via the Prussian blue indicator, with the intensity of the color being proportional to the glucose concentration in the sample. The color is measured by reflectance photometry.[11] All measurements in this study were carried out according to the manufacturer's instructions.

Specimens and testing

Accu-Chek Easy glucose high and low control solutions were used in this study as the test specimens. One lot number of Accu-Chek Easy Test Strips was used. Two vials of test strips, one open and one closed, were assigned to each storage condition. The storage conditions were room temperature (22 °C to 25 °C) as recommended by the manufacturer, incubator (37 °C), refrigerator (4 °C to 8 °C), light (direct, constant exposure to a 60-watt lamp two inches away), and increased humidity (in a laundry washroom). The adverse environments were chosen to be similar to possible storage environments in a patient's home or on the nursing floors in a hospital. The number of strips in each vial in each storage environment was determined based on the results of the Gonzales and Kampa study as well as to minimize the study costs for the CLS program (Table 1).[11] The temperature in each storage environment except the washroom, was measured for ten consecutive days prior to beginning the study to detect any fluctuations outside the required temperature range. Temperatures were monitored and recorded for each environment during the study.

Table 1. Number of strips stored in each vial in each environment

Storage environment	Closed vial	Open vial
Room temperature	39	26
Refrigerator	26	16
Incubator	28	18
Light	28	22
Humidity	28	26

Glucose concentrations were measured by using one test strip for each control level from each vial in each storage environment. The strips were not allowed to reach room temperature; instead, they were tested at the environment's temperature. Strips in all environments were tested at day-3, day-7, and then once a week on Monday thereafter, according to the manufacturer's procedure.

Methodology evaluation

Accuracy and precision studies were performed on two POCT glucometers owned by the CLS program using the Accu-Chek Easy glucose high and low control solutions. A single glucometer that had both precision and accuracy CVs of less than 5% was used for all testing of reagent strips. Precision studies using gravimetric analysis were performed on the droppers on all four bottles of control solutions (two high controls, two low controls) to verify consistent drop size. All four droppers were found to have CVs of less than 5% with delivery of a drop size of 30 µL.

The manufacturer's acceptable ranges for the high and low glucose control solutions were 202 to 274 mg/dL and 36 to 66 mg/dL, respectively. These ranges were used to determine whether the measured glucose value indicated continued stability of the strip. If the control result for a strip was out of range on a particular day, then another strip was tested on that same day. A third measurement was performed on the following day. The second and third glucose measurements were used to confirm strip failure in a storage environment. When the strips demonstrated failure for duplicate testing on two consecutive days for a vial in a storage environment, that particular environment was noted as having failed for that vial, and testing was discontinued. All testing was stopped at 50 days. The control results for the manufacturer's recommended storage environment, i.e., room temperature in capped vials away from extremes of temperature, were found to be within expected ranges for the duration of the study.

Data analysis

Using Microsoft Excel 2000 software, glucose values (y-axis) were plotted versus the day (x-axis) on which they were obtained for each vial and each environment. The glucose values obtained on the closed vial at room temperature were used as the reference (or comparison) variance value for F-test and mean value for student t-test analyses with alpha set at 0.05 for both statistical analyses.

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RESULTS

The day on which each vial in each storage environment failed with regard to a level of control solution is displayed in Table 2. Descriptive statistics by type of vial with significant F-tests and t-tests at p <0.05 noted, are displayed for glucose low control and high control in Tables 3 and 4, respectively. The glucose values obtained by individual testing days by type of vial and level of control solution are displayed in Figures 1 through 4.

Table 2. Reagent strip stability time in days per vial and environment for each control solution

Storage environment	Low control		High control	
	Closed	Open	Closed	Open
Room temperature	>50	14	>50	21
Refrigerator	>50	35	>50	>50
Incubator	28	21	28	14
Light	28	3	35	14
Humidity	>50	3	>50	14

DISCUSSION

With the exception of test strips stored in the refrigerator and tested with the high glucose control solution, Accu-Chek Easy Test Strips stored in open vials deteriorated more rapidly than those in closed vials for each environment and control solution. This result is similar to the findings from the Gonzales and Kampa glucometer reagent strip stability study.[11] The closed vials in the room temperature, refrigerator, and increased humidity environments all remained stable throughout 50 days of testing; whereas in the earlier study, the closed vials in the room

Table 3. Descriptive statistics of glucose values for low control by type of vial

Storage environment	Closed vial			Open vial		
	Mean	SD	Variance	Mean	SD	Variance
Room temperature	59.3	5.2	27.3	68.8*(p 0.023)	3.7	13.7
Refrigerator	54.4	7.9	62.3† (p 0.025)	58.6	11.2	126.6† (p 0.003)
Incubator	65.5* (p 0.001)	4.8	23.4	69.9* (p 0.006)	6.3	39.8
Light	64.4	9.8	95.1† (p 0.017)	81.2	10.6	113.2** (p 0.000)
Humidity	59.8	7.1	51.1	72.8	3.1	9.6† (p 0.004)

* Based on comparison to mean for closed vial at room temperature by student t-test at p <0.05.
† Based on comparison to variance for closed vial at room temperature by F-test at p <0.05.
Expected range of control values was 36 to 66 mg/dL.

Table 4. Descriptive statistics of glucose values for high control by type of vial

Storage environment	Closed vial			Open vial		
	Mean	SD	Variance	Mean	SD	Variance
Room Temperature	256.5	6.9	47.1	271.3	13.7	188.2* (p 0.012)
Refrigerator	247.5† (p 0.005)	7.7	59.1	245.9† (p 0.007)	6	36.1
Incubator	269† (p 0.000)	8.6	74.7	274.3† (p 0.007)	5.1	26.2
Light	231.8† (p 0.312)	38	1445.1	300.3	38.6	1487.1* (p 0.006)
Humidity	257.9	7.2	52.4	274.3	15.6	242.3

* Based on comparison to variance for closed vial at room temperature by F-test at p <0.05.
† Based on comparison to mean for closed vial at room temperature by student t-test at p <0.05.
Expected range of control results was 202 to 274 mg/dL.

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temperature, sunlight, and incubator environments remained stable throughout 56 days of testing.[11]

Test strips stored in open vials in the increased light and humidity environments showed the shortest period of stability, failing at 3 and 14 days with control results elevated above the expected range. For both light and humidity, the low control failed at day 3 and the high control at day 14. These results support the manufacturer's warnings about exposure to light and moisture resulting in increased glucose values due to discoloration of the strip's test area. An interesting difference from results obtained in the Gonzales and Kampa study was the stability of test strips stored in the refrigerator environment. While test strips in the Gonzales and Kampa study had the lowest stability period at eight days, refrigerated test strips in the ECU study demonstrated stability for at least 35 days.[11] This difference may have been due to the location of the open vials in the refrigerator in ECU's study. The test strip vials in this study were stored within the main compartment of the refrigerator where temperatures tend to be more constant, while the vials in the Gonzales and Kampa study may have been stored in the shelves of the refrigerator door that would be subject to more temperature fluctuations. The open vials in the incubator were stable until days 14 and 21 for the high and low control, respectively. The closed vials in the incubator and light both lost stability at 28 days.

According to the t-test analyses, the following environments showed a significant difference in mean values from the reference test strips, i.e., closed vial at room temperature, for the low and/or high control(s): open vial at room tem-

Figure 1. Glucose low control values for closed vials

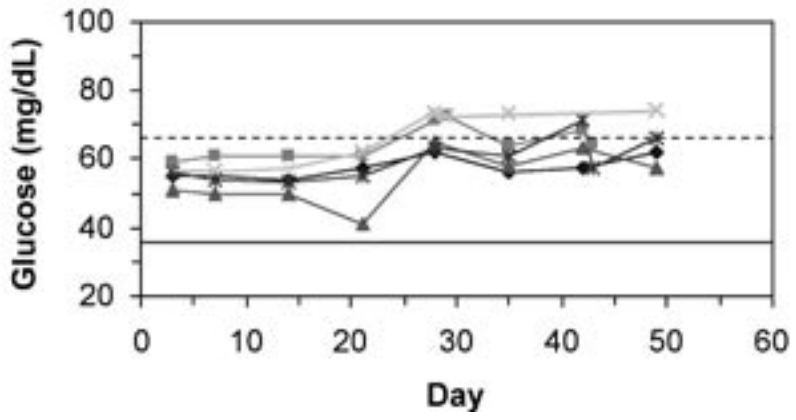
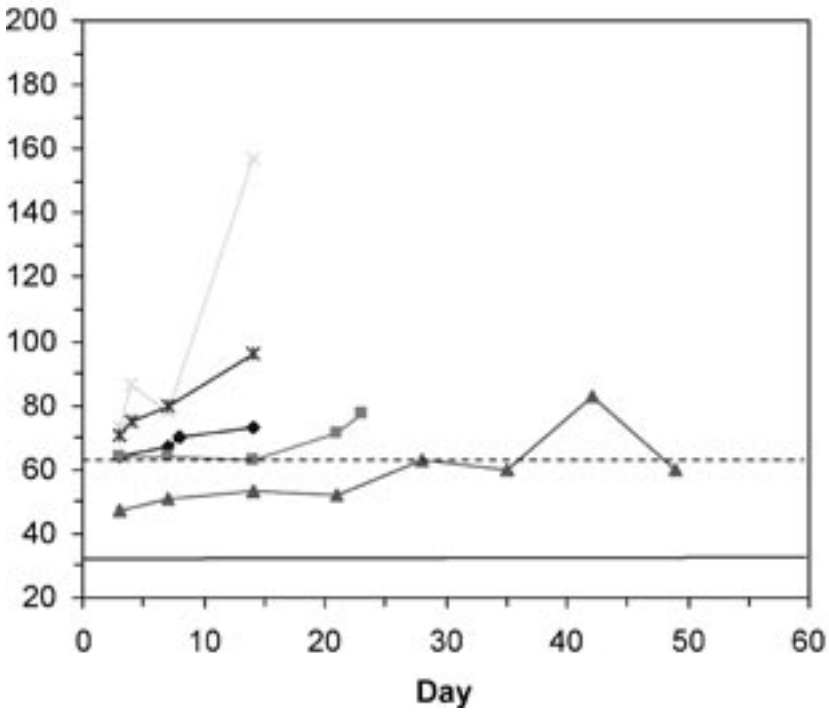
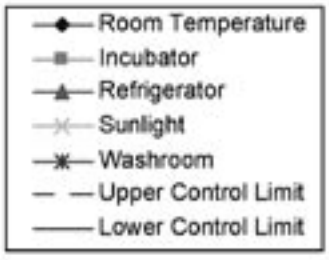


Figure 2. Glucose low control values for open vials



Figures 1 and 2 legend



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perature, closed vial in light, and open and closed vials in incubator and refrigerator. For comparison of variances to the values for the closed vial strips at room temperature, the significant differences were predominantly for the refrigerator and light environments.

CONCLUSIONS

The results of this study indicate that glucometer reagent test strips stored in open vials, regardless of storage environment, lose stability more quickly than those in closed vials do. The quickest deterioration in test strip stability was found with open vials exposed to direct light or to humidity. These results support the findings of the most recent similar study as well as the recommendations of the manufacturer to avoid light and moisture which can cause the strips to produce falsely elevated glucose results.[11] The results support the manufacturer's instructions, which state that the test strip vials should be stored tightly capped at room temperature. Other than the recommended storage environment, the study found the overall longest period of stability to be the refrigerator environment for both open and closed test strip vials. This is in contrast to the Gonzales and Kampa study, which found refrigeration of strips to provide the least stability.[11]

The results of this study are limited by several constraints inherent in the study design. Only a limited number of reagent test strips from the same lot number were available from the manufacturer due to discontinuation of the Accu-Check Easy POCT glucose testing system. This prevented the study from evaluating performance of the test strips over a longer period of time, and did not allow for 50 strips in all vials at the beginning of testing. The need to contain the costs of student research projects necessitated doing the study with a glucometer the program

Figure 3. Glucose high control values for closed vials

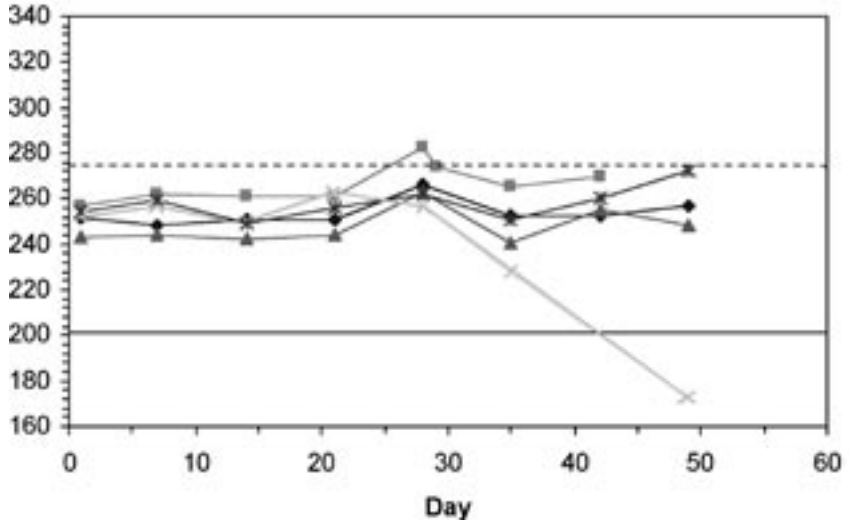
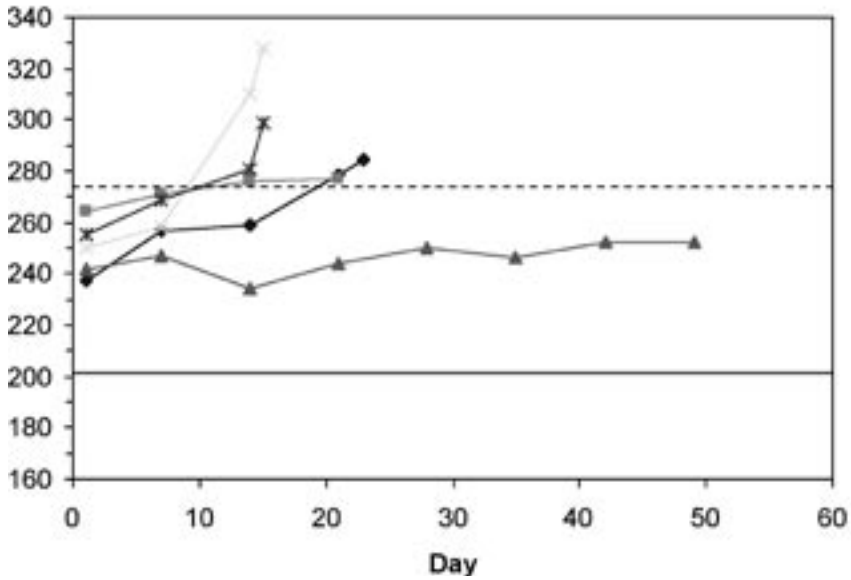
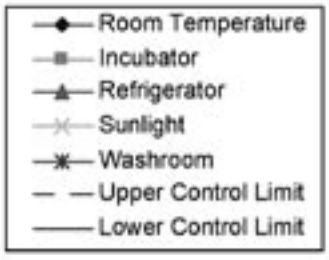


Figure 4. Glucose high control values for open vials



Figures 3 and 4 legend



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purchased several years previously, but which has since been discontinued by the manufacturer. Knowing the exact day at which stability was lost was not possible due to the clinical rotation schedule of the students that allowed testing strips only every seven days.

Some newer glucometer models have discontinued the reflectance photometry, i.e., colorimetric, method of glucose reaction detection, and instead use an electrochemical detection system. Some manufacturers have also begun storing test strips individually wrapped in foil for the newer systems.[2,3] Roche Diagnostics, the manufacturer of the Accu-Chek line of glucometers, has converted the glucose test system to an electrochemical measurement and continues to package the test strips in tightly capped vials.[12]

Future studies of the effects of varying storage conditions on the performance of glucometer reagent test strips are warranted on the newer glucometer models using the electrochemical principle of measurement and newer packaging systems. Future research may include longer testing periods that are closer to the expiration periods of the strips, daily testing of strips, multiple storage locations within a refrigerator environment, and financial support from manufacturers to allow a more comprehensive study and a better assessment of test strip viability in adverse storage conditions. As patients do not always precisely follow the manufacturer's instructions, better understanding of test strip stability in alternate storage environments should improve the use of glucose results generated through at-home testing.

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