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How Does the Age of a Blood Sample Affect It's Activated Clotting Time? Comparison of Eight Different Devices

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Abstract: Monitoring activated clotting time (ACT) during extracorporeal procedures is virtually universal. The ACT test is usually performed immediately following blood collection. However, certain situations may occur that delay rapid measurement. It is unknown how an aged blood sample affects the ACT measurement. It is hypothesized that the ACT will be affected as a blood sample ages. Multiple blood samples were taken from six patients undergoing cardiopulmonary bypass (CPB). Samples were divided into two groups, heparinized (H) and unheparinized (UH). ACT/HMT tests were performed with each sample on eight devices (Array Actalyke, Gem PCL, Hemochron Jr. Signature, Hemochron Response, Hemochron 801, Hemotec HMS, Rapidpoint Coag, and Sonoclot II) at three different sample ages [<60 s (fresh blood), 10 min, and 15 min after sample collection. ACT/HMT results of aged samples (10 min and 15 min after sample collection] were compared to ACT/HMT results for fresh blood using a repeated measures analyses of variance (ANOVA) with Student's–Newman-Keuls post hoc test. In the unheparinized group, no device produced an ACT significantly different from the fresh sample counterpart at the 10 min time point. At the 15 min time point, the Hemochron 801 produced a significantly lower average ACT when compared to the fresh sample. (120±25 vs. 135±15 s). In the heparinized group, the Actalyke device produced results with 10 and 15 min aged blood that were significantly longer than fresh blood sample results (ACT <60 s = 426±66, 10 min = 457±82, 15 min = 450±68 s, $p < .05$). No other device produced significant differences for either time period. Based on this limited sample population, it seems that accurate ACT may be performed on blood samples up to 15 min old in many devices. **Keywords:** activated clotting time, ACT, cardiopulmonary bypass, heparin, accuracy. *JECT. 2002;34:175–177*

The activated clotting time is a parameter that is universally monitored for assessment of anticoagulation during cardiopulmonary bypass (CPB)(1,2). Currently, more than 10 different point-of-care (POC) devices exist that can perform ACT tests. These devices provide quick, accurate results at the patient's bedside when used correctly.

To ensure accuracy, it is recommended that the ACT test be performed immediately following blood sample withdrawal (3–5). However, in the clinical setting, there are circumstances that may preclude immediate testing and lead to sample aging. Sample aging could occur because of device preparation, incorrect initiation of the test requiring the technician to restart the tests, and inability to run the test immediately following blood draw because of an overriding clinical priority.

The purpose of this investigation was to evaluate eight commonly available POC ACT devices and determine the effect of time delays on the ACT measurements. This investigation could aid the clinician to devise guidelines regarding the management of blood samples with respect to age of sample.

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MATERIALS AND METHODS

Patients

Following approval from the Institutional Review Board for the Protection of Human Subjects, informed consent was obtained from six adult patients undergoing elective cardiopulmonary bypass (CPB) for CABG or valve repair/replacement. Patient inclusion criteria were as follows: age ≥ 18 years, body surface area ≥ 1.2 m^2, and pre-CPB hematocrit of ≥ 35%. Patient exclusion criteria were as follows: redo sternotomy, abnormal laboratory coagulation profile, and pre-operative intravenous heparin.

Blood Collection

Before anesthetic administration, a radial artery catheter was placed in the left arm of each patient for hemo-

dynamic monitoring and blood sampling purposes. Multiple blood samples were drawn into 30-mL plastic syringes at two time periods during the case (before heparinization and post heparinization). Blood samples were left undisturbed between tests but were gently agitated before initiating tests with aged blood. Before heparin administration, 2–4 blood samples (UH group) were drawn from each patient's radial arterial line. Following full heparinization (300 U/kg), and initiation of CPB, 2–4 blood samples (H group) were taken from the manifold of the extracorporeal circuit (ECC).

ACT Devices

The following eight different ACT testing devices were utilized for blood analysis: Array Actalyke (Array Medical, Somerville, NJ), Gem PCL (Instrumentation Laboratories, Lexington, MA), Hemochron Jr. Signature, Hemochron Response, Hemochron 801 (International Technidyne Corporation, Edison, NJ), Hemotec HMS (Medtronic, Inc. Minneapolis, MN), Rapidpoint Coag (Bayer/Chiron, Medfield, MA), and Sonoclot II (Sienco, Inc. Wheat Ridge, CO). Before investigation on each testing day, quality control tests were performed on each machine in accordance with manufacturer's recommendations. Table 1 provides specific information regarding the devices and tests. The same operator drew all samples.

Protocol

ACT tests were initiated at three specific times for each blood sample. The three times corresponded with three different sample ages— <60 s (fresh blood), 10 min, and 15 min. Between test times, samples were left undisturbed. Immediately before test initiation, the syringe was gently agitated to ensure that the sample was uniform throughout.

Statistical Analysis

All data are expressed as mean ± standard deviation of the mean (SD). Comparative data were analyzed using repeated measures analyses of variance (ANOVA) with Student's–Newman-Keuls post hoc test. Statistical significance was accepted at a $p < .05$.

RESULTS

Patient Parameters

The average pre-CPB hematocrit (HCT) was 37.5 ± 4.7 % (range = 35–42.3%). During CPB, the average HCT was 27.3 ± 3.2% (range = 22.3–28.8%). In five of six patients, tempeatures were allowed to drift to 34°C during CPB. A single patient had blood cooled to 20°C.

UH Group

Comparisons of unheparinized blood sample average ACT results at the three time point are shown in Table 2. For all devices, there were no statistically significant differences in average ACT measurements between fresh unheparinized blood samples when compared to samples that had aged 10 min. At the 15 min sample age, one device, the Hemochron 801, showed a significant difference in the ACT when compared to fresh blood (120 ± 25 s vs. 135 ± 15 s; $p < .0001$). The remaining seven machines produced no statistically significant difference at the 15 min time point.

H-Group

With heparinized blood samples, no significant differences were seen in ACT measurements of fresh blood, 10 min aged samples, and 15 min aged samples for seven of eight devices tested (Table 3). The Actalyke was the single device that did show statistically significant differences between fresh, 10 min aged, and 15 min aged samples (426 ± 66, 457 ± 82, 451 ± 68 s, respectively; $p = .0004$).

DISCUSSION

In this study, differences in ACT measurements between fresh blood sample and aged sample time points occurred in only three cases: 1) Hemochron 801, UH-group at 15 min time point; 2) Actalyte, H-group, 10 min time point; and 3) Actalyte, H-group, 15 min time point. Closer evaluation of these three instances shows that for the Hemochron 801 the difference seen at the 15 min time point in the UH-group was a significant reduction in the ACT (120 ± 41 vs. 135 ± 13 s) In contrast, for H-group

Table 1. POC devices and ACT tests investigated.

Device	Test	Volume	Activator	Detection
Array Actalyke	MAX-ACT	0.5 mL	Celite, Kaolin, & glass particle "cocktail"	Mechanical
Gem PCL	ACT	1 Drop	Silica & kaolin	Photo-optical
Hemochron Jr. Signature	ACT+	1 Drop	Silica & kaolin	Photo-optical
Hemochron Response	FTCA 510	2 mL	Celite	Mechanical
Hemochron 801	FTCA 510	2 mL	Celite	Mechanical
Hemotec HMS	ACT	1 mL	Kaolin	Photomechanical
Rapidpoint Coag	HMT	1 Drop	Celite	Photo-optical
Sonoclot II	SonACT	360 μL	Celite	Electromechanical

POC = point-of-care devices, ACT = activated clotting time.

Table 2. Comparison of unheparinized fresh blood ACT results to aged blood ACT results.

Device	Sample Size (*N*)	Mean ACT (s) (t < 60 s)	Mean ACT (s) (t = 10 min)	Mean ACT (s) (t = 15 min)
Array Actalyke	14	141 ± 13	134 ± 15	131 ± 24
Gem PCL	11	112 ± 7	114 ± 16	111 ± 9
Hemochron Jr. Signature	14	109 ± 12	112 ± 9	116 ± 15
Hemochron Response	10	128 ± 17	124 ± 19	119 ± 26
Hemochron 801	17	135 ± 15	134 ± 16	120 ± 25‡
Hemotec HMS	12	138 ± 10	139 ± 16	131 ± 30
Rapidpoint Coag	9	117 ± 39	115 ± 31	117 ± 41
Sonoclot II	14	128 ± 23	128 ± 30	120 ± 41

UH = unheparinized, pre-bypass, ACT = activated clotting time, ‡ = $p < .05$.

Table 3. Comparison of heparinized fresh blood ACT results to aged blood ACT results.

Device	Sample Size (*N*)	Mean ACT (s) (t < 60 s)	Mean ACT (s) (t = 10 min)	Mean ACT (s) (t = 15 min)
Array Actalyke	19	426 ± 66	457 ± 82‡	451 ± 68‡
Gem PCL	14	460 ± 56	471 ± 55	472 ± 52
Hemochron Jr. Signature	17	490 ± 130	497 ± 97	485 ± 97
Hemochron Response	13	516 ± 103	524 ± 141	508 ± 126
Hemochron 801	20	513 ± 139	537 ± 124	542 ± 119
Hemotec HMS	16	497 ± 81	500 ± 82	495 ± 81
Rapidpoint Coag	18	449 ± 34	441 ± 41	451 ± 41
Sonoclot II	5	479 ± 110	444 ± 49	466 ± 89

H = heparinized, on-bypass, CPB = cardiopulmonary bypass, ‡ = $p < .05$.

samples performed on the Actalyte device, the significant difference seen in the 10 and 15 min time points was from an increase in ACT from fresh sample time point values (ACT < 60 s = 426 ± 66, 10 min = 457 ± 82, 15 min = 450 ± 68 s, $p < .05$). This observation has no clear interpretation. The Hemochron 801 showed no effect of sample age in the H-group and the Aktalyte device also showed no effect in the UH-group.

It has been suggested that such other factors as hemodilution and temperature can affect the accuracy of ACT measurements (6,7). In this study, no correlation or trends were identified when data were examined with respect to these variables.

Product literature suggests that it is good practice to initiate ACT measurements immediately after the blood sample is drawn. However, there are few, if any published studies that have examined the effects of time delays on the accuracy of the ACT. It was hypothesized that drawing a blood sample and the allowing a delay of 10 to 15 min before measurement would significantly alter the ACT results when compared to the fresh sample measurement. This hypothesis was not supported and, overall, based on this small study, it seems that both heparinized and unheparinized blood samples remain stable inside of a syringe and accurate ACTs can be performed for time periods up to 15 min in most devices.

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