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## Urban Myths and the ACT: What is Not True and What Really Matters When it Comes to Monitoring Anticoagulation

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### INTRODUCTION

The activated clotting time (ACT) was developed in 1966 by Hattersley (1). However, it was Bull et al. that first suggested that Hattersley's test should be applied to coagulation monitoring of the systemically heparinized CPB patient (2). In their cornerstone manuscript it was noted that visible clot formation rarely occurred below ACT times of 300 seconds. Consequently, a safety margin was added to this minimum time and the recommendation was made that regular monitoring and maintenance of ACT values of >480 seconds was appropriate for CPB. This recommendation quickly became the gold standard. Since that time nearly a dozen automated machines and tests have been developed to provide ACT results and ACT monitoring has become standard of care for the CPB patient. Despite the widespread acceptance of the ACT test, there is no shortage of references which mischaracterize the ACT test thereby promulgating a degree of misinformation which permeates our profession. Therefore, the purpose of this presentation is to dispel some of the most common myths associated with ACT test results. Original data from our laboratory will be used to compliment an extensive literature review on this topic.

### MYTH: AN ACT IS AN ACT IS AN ACT . . .

All too commonly the results of ACT tests have been generically referred to in scientific literature and conversation as if there were no more difference between the results of different ACT tests than there is between the flow rates of different roller pumps. In an effort to provide evidence of the similarity or disparity between results of different ACT tests we initiated a project to identify the comparability and reproducibility of all the major ACT tests available in the USA (3,4).

## METHODS

With IRB approval, blood samples from 17 CPB patients were collected at six time points during surgery. All tests were performed in duplicate on 8 different ACT devices (ACTalyke, Gem, HMS, Hemochron 801, Response, Jr. Signature, Rapidpoint, and Sonoclot). Duplicate samples from each machine were compared to determine reproducibility. The average of the duplicate samples was used for comparison between machines.

## RESULTS

Reproducibility for all devices produced a range from 3.7 ± 5.3–20.6 ± 27.3 seconds for unheparinized samples with the HMS and the Rapidpoint being the most and least reproducible respectively. For heparinized samples, the range was 16.0 ± 16.8–69.7 ± 81.2 seconds with the Rapidpoint and the Sonoclot being the most and least reproducible respectively. The Rapidpoint was the most consistently reproducible at all time points. Comparison between machines of unheparinized samples demonstrated a range of ACT values from 107.1 ± 34.4–136.4 ± 14.2 seconds with the Rapidpoint and the Response having the lowest and highest values respectively. Heparinized samples had a range from 451.1 ± 117.5–633.5 ± 158.3 seconds with the Rapidpoint and Hemochron 801 having the lowest and highest values respectively. The difference between the highest and lowest unheparinzed results were 29 seconds (27%) and for heparinized results, 182 seconds (40%).

## CONCLUSION

Overall, heparinized samples had the poorest reproducibility. The HMS was the most reproducible and the Sonoclot was the least reproducible. For unheparinized samples, the Rapidpoint and Sonoclot were significantly shorter than all other machines. For heparinized samples, the ACTalyke, Rapidpoint, and Sonoclot were significantly shorter while the Hemochron 801 and Response were significantly longer than most other machines.

## MYTH: APROTININ PROLONGS THE CELITE ACT TEST THROUGH AN IN VITRO MECHANISM

In the mid 1980s, reports of aprotinin's ability to decrease hemorrhage after cardiopulmonary bypass introduced the drug to the realm of cardiac surgery. Unfortunately, its introduction into this arena was followed by the publication of multiple studies and case reports that blamed aprotinin for poor outcomes in the form of early graft closure. Almost 20 years have passed since the initial manuscript describing the use of aprotinin during cardiopulmonary bypass, and with time there has been a significant increase in scientific knowledge and clinical experience. For a comprehensive review of the literature with regard to aprotinin's anticoagulant properties the reader is referred to the Swartz et al. article (5). Unfortunately, many clinicians still believe that aprotinin is procoagulant and that celite ACT tests are unreliable in the presence of aprotinin. Therefore, we set out to identify the exact influence that aprotinin does have on all the major ACT tests (6).

## METHODS

With IRB approval, blood samples were collected from patients undergoing CPB before and after full heparinization (300 u/kg). Each blood sample was divided into two aliquots and aprotinin was added to one sample to yield a final calculated concentration of 300 KIU/ml. Both aliquots were used simultaneously to perform the 12 ACT tests. A paired student T-test was performed on the data.

## RESULTS

Overall, test results from 9 of 12 devices were significantly increased by aprotinin. Of these, 4 were increased only when the sample was heparinized, 3 were elevated by both heparinized and unheparinized blood, and 2 were elevated only when the sample was unheparinized.

## CONCLUSION

Each affected test responded uniquely to aprotinin producing ACT test results ranging from 12–51% above nonaprotinized values. Several tests that were affected by aprotinin using heparinized blood samples were unaffected using unheparinized blood samples.

As we have reported, aprotinin administration does influence the results of various ACT tests, and consequently different methods of anticoagulation have been developed. It has been suggested that the mechanism behind the elevation of ACT test results by aprotinin is a result of aprotinin's anticoagulatory activity. Researchers have demonstrated that, in fact, the celite ACT is not "artificially" prolonged in the presence of heparin and aprotinin, rather the kaolin ACT is "artificially" shortened due to binding of the aprotinin by the activator (7).

## MYTH: ACTS ARE USED TO MONITOR HEPARIN

While the primary function of the pressure transducer on your arterial line may be to detect aortic dissection, we would all agree that there are many other causes for an elevated line pressure. The results of your ACT are very similar; the primary cause of elevated ACT during CPB is heparin concentration, however, because it is a nonspecific measurement of whole blood coagulation, anything that affects coagulation will ultimately affect the ACT. Unfortunately this detail is largely overlooked by many authors and clinicians and consequently there is a widespread acceptance that ACTs are used to monitor heparin during CPB. Curiously, most perfusionists will agree that the ACT is effected by other variables such as hemodilution, hypothermia and (as discussed above) aprotinin (8,9). Paradoxically, these two concepts manifest themselves into the belief that ACT test results are mistaken in the face of these non-heparin variables. Therefore we determined to identify the relationship between ACT results and heparin concentrations during CPB (4).

### METHODS

With IRB approval, blood samples from 17 CPB patients were collected at six time points during surgery. Test results were performed in duplicate on 8 different ACT devices (ACTalyke, Gem, HMS, Hemochron 801, Response, Jr. Signature, Rapidpoint, and Sonoclot) and compared to results of anti Xa activity (STA Rotochrom Heparin assay). The average of the duplicate samples was used for comparison to the anti Xa results.

### RESULTS

Correlation of results to anti Xa activity (1.1–5.75 IU/ml) for each device produced a range of r = .071 to .502. Conclusion: No device correlated with the laboratory anti Xa data.

### CONCLUSION

In summary, the ACT test is a whole blood coagulation test which is useful for monitoring anticoagulation during CPB. It is affected by anything that affects coagulation, especially heparin, but also non heparin variables such as hemodilution, hypothermia, aprotinin and others. There are many automated devices available to the clinician for ACT monitoring. Each machine responds to anticoagulant variables uniquely and therefore it should not be assumed that the results from different machines are interchangeable. Each institution should develop clinical parameters based on the device they are using and their clinical environment.

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## From Trash To Leucocytes: What Are We Filtering and Why?

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### INTRODUCTION

A filter processes non-homogeneous matter to allow the free passage of some elements, whilst preventing downstream passage of specific others. In the context of cardiac surgery, blood is the most commonly filtered "matter."

Filters can be classified as either "screen filters" or "depth filters" (1). Screen filters are typically comprised of material "woven" into a "screen" with a carefully calibrated pore size. Consistency of pore size is a characteristic of screen filters, and they are frequently named by this parameter, for example, a "40 micron filter." Clearly, they are designed to remove matter larger than the screen pores. Depth filters are typically comprised of material that is not precisely woven and through which the filtered matter must pass, typically over a longer distance and greater time when compared to screen filters. In these devices, the removal of matter occurs by several possible means that are discussed later.

Potential filtration sites in cardiopulmonary bypass (CPB) are itemized in Table 1 along with examples of the targets for removal. The majority of relevant research has been focused on filtration of arterial blood, and arterial line filtration will occupy most of this review.

**Table 1.** Filtration sites and targets in cardiopulmonary bypass

| Site or Substance | Target |
|---|---|
| 1. CPB circuit prime | Manufacture-related particulates, spallation material, bubbles |
| 2. Arterial blood | Potentially everything, but mainly aggregates, bubbles, leucocytes, spallation material |
| 3. Venous blood | Bubbles, leucocytes |
| 4. Cardioplegia | Leucocytes |
| 5. Pericardial suction blood | Aggregates, bubbles, bone, other tissue, surgical material, lipid, leucocytes |
| 6. Allogenic blood | Leucocytes, aggregates |
| 7. Autologous blood | Leucocytes, aggregates, bubbles |
| 8. Sweep gas | Bacteria, particulates |