

# Guidelines on the Use of Antithrombin III Concentrate in Cardiac Surgical Patients

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## Background

Heparin resistance is defined as the inability to reach a target ACT (usually 400 to 480 sec) after an adequate dose of heparin (usually 200-400 units/kg) or a slope of less than 80 seconds per unit/cc of heparin on the Hepcon® device heparin dose response assay. In the cardiac surgical patient population this is most often due to acquired antithrombin III (ATIII) deficiency resulting from preoperative heparin exposure. It can also be seen in the setting of increased binding of heparin at non-specific binding sites as can be seen with thrombophilia. The reported incidence of heparin resistance in the literature is as high as 20% but in the current era at BIDMC the incidence is in the 2 to 5% range. The concern with heparin resistance is that inadequate heparin anticoagulation on cardiopulmonary bypass can lead to, in the worst case, massive thrombosis and embolism. In situations where there is enough anticoagulation to prevent overt thrombosis, inadequate heparin effect can lead to depletion of coagulation factors and platelets, post-operative bleeding, and enhanced inflammatory response to cardiopulmonary bypass.

An effective treatment strategy for heparin resistance must consider the possible causes. Heparin resistance due to increased non-specific binding will not respond to administration of ATIII. In this situation, the appropriate treatment is the administration of more heparin. The more common issue of acquired ATIII deficiency may or may not always respond adequately to more heparin. This will depend on the patient's inherent level of ATIII activity and amount of available heparin.

FFP is a source of exogenous ATIII and had been the standard treatment for heparin resistance due to presumed ATIII deficiency. Concerns regarding transfusion related complications and time availability have been the major impetuses for the current strategy of using AT III concentrate in this setting. It is imperative to consider the cost of ATIII concentrate (\$2 per unit) when considering its use to prevent significant waste.

## Indication for Use

Antithrombin III concentrate is indicated for the intraoperative treatment of cardiac surgical patients with heparin resistance that is due to presumed antithrombin III deficiency and which prevents safe and adequate anticoagulation for the use of cardiopulmonary bypass or for the completion of off pump coronary bypass grafting. **It will be used only after the cardiac care team has established that reasonable heparin dosing has not resulted in or maintained adequate anticoagulation as measured by ACT.**

## Procurement and Dosing

When the indication for use has been established by the cardiac care team, the cardiac anesthesia team will notify the blood bank at x43300 to place a request for AT III concentrate.

***The initial dose of AT III concentrate will be 576 units (one vial). This dose will be specifically ordered by the cardiac anesthesia team.*** The dose will be “tubed” to the appropriate operating room station and a confirmatory phone call will be placed to the blood bank by operating room staff as to receipt of the product. The product will come in a lyophilized form and will be reconstituted by the cardiac anesthesia team using standard procedures. It will be immediately delivered to the patient and, after 3 to 5 minutes, another ACT will be run to test for a response. If there is not an adequate response, a second dose of 576 units can be requested and delivered to the patient. In the very unlikely event that this does not result in an adequate ACT, consideration to another cause for heparin resistance should occur and more heparin should be given. In addition, strong consideration should be given to consultation with an available hematologist.

The blood bank will make every attempt to ensure that AT III concentrate is available. In the rare event that it is unavailable, FFP will be requested and should be regarded as a reasonable alternative to AT III concentrate.