

## CORRESPONDENCE

study,<sup>9</sup> platelet function was altered intraoperatively in the control group, whereas (1) aprotinin preserved spontaneous platelet aggregation and ADP induced platelet aggregation and platelet adhesivity; and (2) postoperative platelet aggregates concentration decreased significantly with aprotinin when compared with placebo. We have not discussed liver transplantation because aprotinin has failed to significantly decrease blood loss in such cases.<sup>10</sup>

That aprotinin can achieve by different mechanisms an identical therapeutic goal in different surgical fields would be puzzling. Consequently, in regard to the mechanism of the blood-sparing effect of aprotinin, it is our opinion that this hypothesis should be revisited.

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Although the mechanisms underlying the beneficial effects of aprotinin on blood loss during surgery were not fully elucidated, reconsidering the hypotheses evoked in the literature involving platelet receptor protection may not be fully justified.

The complex action of aprotinin, a natural serine protease inhibitor, is situated at the cross-section of several reactions triggered during surgery: contact phase activation, tissue factor and tissue plasminogen activator (tpa) release from subendothelial sites, plasmin activation by kallikrein and activated factor XII, as well as the release of kinins and activated C3b fragments.<sup>2-4</sup> Furthermore, aprotinin activation depends on blood aprotinin levels, and as such the administered perioperative dose, whether or not cardiopulmonary bypass (CPB) is used.

Major surgery can activate the extrinsic coagulation pathway by the release of tissue factor from the endothelial cells.<sup>4,5</sup> Aprotinin can limit the onset of disseminated intravascular coagulopathy (DIC) *via* its anti-VIIa activity.<sup>6</sup>

Aprotinin's role in the inhibition of fibrinolysis, reported primar-

ily in works concerning liver surgery,<sup>7,8</sup> is based on the limitation of contact phase activation,<sup>9</sup> direct anti-plasmin activity by inhibition of tpa release,<sup>7,10</sup> and protein C activity.<sup>11</sup> Aprotinin also has been shown to have a local antifibrinolytic effect, limiting perioperative bleeding when injected directly into the pericardial cavity.<sup>12,13</sup> During surgery performed without CPB, this antifibrinolytic effect probably implies aprotinin activity. Both the limited postoperative d-dimer values seen in our patients treated with aprotinin<sup>1</sup> and the greater number of patients in Janssens *et al.*'s<sup>14</sup> control group presenting higher than normal d-dimer values seem to confirm the hypothesis.

It is not improbable that aprotinin's role in limiting bleeding is based on a multimodal mechanism. During surgery with CPB, aprotinin activity seems to primarily involve platelet receptor protection from plasmin activity and contact phase activation.<sup>15</sup> In contrast, a more global action on fibrinolysis and DIC seems to predominate during major surgery without CPB.

In consequence, aprotinin would achieve one therapeutic goal by several different mechanisms of action.



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## Perfuse or Precondition?

*To the Editor:*—We read with interest the case report about coronary revascularization without cardiopulmonary bypass. In the article, the authors discuss ischemic preconditioning to prepare the myocardium for a 5- to 15-min period of coronary occlusion. The authors cite, "brief periods of occlusion have been shown to paradoxically protect or precondition the heart and to reduce the infarct size caused by a subsequent period of coronary artery occlusion."<sup>1</sup> The key point is that in undertaking an operation to protect or save myocardium, this procedure already acknowledges that one is going to kill some off—but only a little.

Our question is why precondition? Why not perfuse? In a case report published in another journal, we described the use of a perfusion cannula connected from the side port of a femoral artery DLP cannula.<sup>2</sup> The perfusion cannula is inserted into the coronary artery under direct visualization. This allows oxygenated arterial blood to perfuse the myocardium during the period of anastomosis. This is similar in function to a shunt used during a carotid endarterectomy. It is not necessary to use a femoral perfusion cannula to make this system work; many innovative sites, catheters, and tubing can be used. The key here is the concept of maintaining perfusion to the myocardium during the period of anastomosis to prevent infarction. Minimally invasive cardiac

surgery that avoids the use of cardiopulmonary bypass is an important new procedure that will only increase in popularity as new technologies and techniques continue to make it safer and more effective.

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