Hematologic Complications
of extra-corporeal by-pass

PART III

Activated clotting factors can be destroyed by inhibitors in the normal blood and may also be removed by reticuloendothelial tissue (23). Both of these mechanisms require adequate rates of circulation to carry the activated factors to a site where they may be neutralized before they promote progressive coagulation.

Prevention of intravascular clotting thus requires adequate perfusion flow rates, maintenance of blood volume and sufficiently high levels of heparin. If intravascular clotting occurs, abnormal bleeding results from consumption of platelets and coagulation factors (Table 8).

Activation of fibrinolysis occurs to a degree detectable by sensitive technics in most by-passes (Table 9). Often, accelerated lysis may be apparent before surgery begins, presumably as a result of emotional stress (24). The degree of lysis tends to increase with the duration of bypass (25); but it is extremely rare, in our experience, for it to reach the point where lysis of whole blood clots will occur. Clinically significant fibrinolysis is generally associated with obvious lysis of whole blood clots.

FIBRINOLYSIN INHIBITORS

Fibrinolysin inhibitors such as epsilon amino caproic acid (EACA) and Trasylol have been used in a few reported instances to stop abnormal bleeding, and it has been demonstrated by some groups that routine EACA will decrease the total amount of blood lost during and following surgery (26). Nonetheless, increasing acceptance of the fact that fibrinolysis is almost always secondary to intravascular clotting (27) implies that one might be wiser to direct attention to preven-
tion of clotting rather than to secondary fibrinolysis, and EACA administration is associated with definite hazards (28).

If a fibrinolysin inhibitor is to be used, it should be administered along with adequate levels of heparin. If the patient is receiving a fibrinolysin inhibitor, it would seem particularly dangerous to neutralize heparin too soon after bypass, before the cannulae have been removed and all clotting intermediates cleared. This could result in major clot formation which the patient cannot clear spontaneously. Fibrinolysin inhibitors similarly increase the dangers associated with clot formation in the chest after surgery is over.

Transfusion therapy itself may be responsible for abnormal bleeding (Table 10). ACD blood stored more than one or two days is devoid of viable platelets. The presence of viable platelets in the blood used to prime the pump-oxygenator is not essential (see above), but unusually great degrees of blood loss replaced with blood devoid of viable platelets can drive the platelet count of the patient to a level which will result in abnormal bleeding. This can be avoided if replacement, in such instances, employs blood collected within the prior 24 hours. In extreme instances platelet concentrates may have to be transfused, but the requirement for these has been extremely rare in our experience.

A hemolytic transfusion reaction due to inadvertent administration of incompatible red cells will deplete the patient of platelets and coagulation factors, apparently via the mechanism of intravascular coagulation (29). A similar mechanism appears to explain bleeding following blood containing bacterial endotoxin (an extremely rare event, preventable usually by simple inspection of the blood and rejection of any units with an abnormal color or gross clots). As already stated, excessive amounts of dextran may also potentiate a hemostatic defect.

The use of sterile, pyrogen-free disposable bypass equipment eliminates a major hazard of this procedure. In heart-lung by-passes with dogs, in the early developmental days of open heart surgery, it was not always appreciated that sterile equipment is only part of the requirement. Materials were often inadequately cleaned or sterilized and bacterial endotoxin was delayed long enough for bacterial growth to occur. Bacterial endotoxin resists autoclaving and may result in intravascular coagulation (see above). Moreover, particulate matter of any sort will be trapped by platelets and result in thrombocytopenia.

A final mechanism postulated to explain abnormal bleeding involves protein denaturation. Denaturation of proteins in plasma may result from severe mechanical trauma and also from exposure to air-blood interphases (30). This is one reason for increasing interest in membrane oxygenators. There has been no definitive evidence yet presented that protein denaturation results in clinically significant destruction of hemostatic factors, however. (To be concluded)

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REFERENCES


