FIG 1 The Vivostat processor for the preparation of autologous fibrin sealant in 30 minutes.

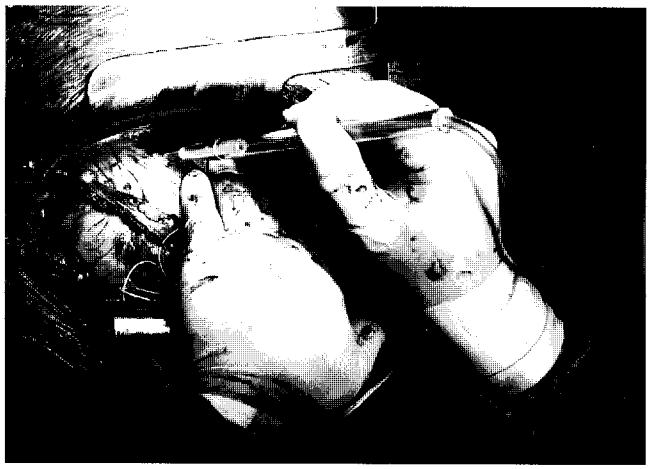

FIG 2 The spraypen applicator in use during cardiac surgery – dispensing autologous fibrin sealant.

60 ml of plasma, which is reacted with biotinylated batroxobin for 10 minutes at 37° C. The biotin-batroxobin catalyses the release of fibrinopeptide A only from fibrinogen and does not activate factor XIII. This results in the formation of a fibrin I polymer which is acid soluble. The fibrin I polymer is isolated by centrifugation and dissolved in 3.5 ml 0.2 M sodium acetate buffer (pH 4.0). After removal of the serum, avidin, covalently bound to agarose, is added to the solution, which complexes the biotin-batroxobin, and the biotin-batroxobin:avidin-agarose complex is then separated from the fibrin I solution by filtration. By this process more than 99% of the complexed biotin-batroxobin:avidin-agarose is removed.

The acidic fibrin I solution is drawn into a vial and transferred to the applicator unit. A syringe within the applicator unit contains 0.75 M carbonate/bicarbonate buffer (pH 10). The two solutions are administered simultaneously and intimately mixed during the application process in a 7:1 ratio (fibrin I:buffer) to initiate polymerization. At the resulting neutral pH, in the presence of calcium ions, endogenous prothrombin is converted to thrombin, causing fibrinopeptide B to be cleaved from fibrin I to form fibrin II. Thrombin also activates factor XIII which acts upon the fibrin II polymer to form a stable fibrin II polymer which is a fibrin sealant. The Spraypen™ applicator allows the solution to be evenly spread over the target tissue. Small amounts of sealant can thus be accurately delivered and, if indicated, the spray can be applied intermittently in small quantities. The fibrin polymerizes immediately upon application and crosslinks over several minutes.

Results

The preparation process was completed in 30 min. From 120 ml of a patients blood the yield was 4.5 +/- 0.3 ml (mean +/- standard deviation) of fibrin sealant.

Discussion

Fibrin sealant is used in cardiovascular and thoracic surgery as a hemostatic and adhesive agent and as a sealant of pulmonary air leak. The number of controlled clinical studies of fibrin sealants is currently increasing, with the majority of the patients realizing the benefits of fibrin sealant when it is used in cardiovascular and thoracic surgery (6).

Conventional fibrin sealants are highly concentrated preparations of human fibrinogen which, when co-administered with added thrombin, form a clot. The commercially available products are entirely non-autologous. The fibrinogen is derived from heat-treated pooled plasma lots and the thrombin is either human or bovine (6,7). Fibrin sealants were briefly available in the United States, but were removed from the market in 1978 by the Food and Drug Administration because of concerns about infection (8). Although the risk is small, there is a potential for transmission of infectious agents, especially viruses. The use of exogenous thrombin in high doses, especially of bovine origin, is also associated with a risk since some of the products may contain factor V or other impurities, and some patients have developed antibodies to both human and bovine factor V, which may result in a severe bleeding diathesis (6,7,9). An additional adverse reaction that has been observed when fibrin sealant (comprised of bovine thrombin and cryoprecipitate) is injected into the bleeding parenchymal tissue of trauma victims is immediate severe hypotension (10). This may be in part due to various impurities in some thrombin preparations and to the high concentrations that are administered to patients in the USA, where this type of fibrin sealant is widely used (7). In addition, cryoprecipitate is not virally inactivated and has a variable fibrinogen concentration. The concentration of fibrinogen preparations also varies widely due to the procedures employed and variable plasma fibrinogen levels in the donated blood, which can vary both physiologically and pathologically (a typical range is 2-6 mg/ml) (11). Such differences directly affect the prop-