PMN-E and IL-6 reached a peak a little later than C3a, at 1 hour after CPB termination. Although the intergroup difference of IL-6 was not significant, the peak value of PMN-E was significantly lower in group P. We believe that the suppressed complement activation in group P contributed to the lower peak PMN-E value. Although the influence of blood transfusion on the values of PMN-E or IL-6 was not eliminated completely, we thought the intergroup comparison was justified because the intergroup difference in the amount or incidence of blood transfusion was not significant.

As for the clinical outcomes, the intergroup difference of the duration of mechanical ventilation was not significant. We speculated that this finding was partly due to the relatively small sample size of this study.

Platelets were well preserved until 1 hour after CPB initiation in group P and acutely decreased to nearly the same level as in group U thereafter. This finding was somewhat different from that of Suhara and colleagues [9], ie, complete preservation of pre-bypass level of platelets until at least 2 hours after CPB initiation with the PMEA-coated circuits in a swine model. In actual operations, many factors such as blood loss and implantation of a prosthetic valve affect platelet consumption and may cause such a difference between clinical and experimental findings.

Heparin-coated CPB circuits, which have been reported to be superior to uncoated circuits in terms of postoperative systemic inflammation in numerous publications [10–12], were not tested in this study. Although comparing the advantages and disadvantages of the PMEA-coated circuits with the heparin-coated circuits requires more data, the relatively low price of the PMEA-coated circuits is worth mentioning. The price of the PMEA-coated circuits is the same as that of the uncoated circuits and is 33% lower than that of the heparin-coated circuits supplied by the same company (Terumo Corp). In addition, the PMEA-coated circuits are thought to be better for patients with heparin allergy.

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INVITED COMMENTARY

The clinical study of Ninomiya and colleagues is an encouraging addition to biomaterial research in cardiopulmonary bypass. The findings related to complement activation from this report are affirmative as they are consistent with the findings and predictions of in vitro studies with this surface, and they have been reproducible in several clinical trials. Inhibition of complement activation is also the most reproducible surrogate marker of the efficacy of heparin-coated surfaces; however, the molecular interactions by which the latter achieves this are not as well categorized as poly(2-methoxyethylacrylate) (PMEA).

Poly(2-methoxyethylacrylate) represents one of a novel group of coatings engineered to positively enhance protein adsorption from blood, such that the proteins appear to coat the surface in an unaltered form. For example, when fibrinogen undergoes a conformational change after adsorption to other biomaterials, it is more likely to result in platelet adhesion and activation than if its structure is identical to that the cells "see" in circulating blood. The weight of evidence from this and other research is directing us to abandon the concept of trying to design biomaterial surfaces that completely inhibit protein adsorption. These attempts have inexorably failed and often they result in unpredictable blood activation in vivo. Protein adsorption is inevitable; we have to design surfaces to preferentially adsorb the right proteins in the right configuration.

To complete the picture, future in vitro and in vivo studies with PMEA need to address whether this surface is also relatively thromboresistant, and if so, to characterize the mechanism. Regardless, it would appear that PMEA has intrinsic antiinflammatory properties, but it remains to be seen whether these biochemical changes are associated with improved clinical outcomes. How-

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ever, I suspect that it is entirely possible that the inhibition of inflammation with this surface has as much relevance as pharmacologic agents such as aprotinin, at a much lower incremental cost. These are the types of questions that demonstrate that we still have room to maneuver and avenues to explore to improve the biocompatibility of this device.

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