Concluding Remarks

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We have just completed a most informative and impressive review of the status of low-molecular-weight (LMW) heparin fractions. The spectrum of presentations has covered virtually all aspects of these interesting compounds.

As I see it, LMW heparin fractions were developed with the hope that they might be different from regular heparin preparations by basically three properties: (1) The frequency of subcutaneous injection might be reduced to once a day; (2) the incidence of bleedings might be decreased, and (3) the occurrence of thrombocytopenia might be less frequent.

The first premise that LMW heparin fractions administered subcutaneously once a day might be as effective as regular heparin preparations injected twice a day seems to be fulfilled.

Pharmacokinetic studies in animals and several clinical studies have now provided sufficient evidence to suggest that LMW heparin fractions are absorbed differently, and that one injection provides patients with an equally effective antithrombotic protection than two injections of regular heparin. The reduction in frequency of injections is by itself a major advantage for patients and health-care providers.

The second hope that LMW heparin fractions might be associated with less bleedings seems to be still somewhat controversial. While animal studies have unequivocally shown that less bleedings are encountered when LMW heparin is used, human studies have yielded discrepant results. Some studies, especially those reported at this Symposium, find a reduced bleeding incidence, while others reported in the literature revealed equally frequent if not increased bleeding tendencies. However, the bleeding complications reported seem to be dose related, and were seen in patients who received rather high doses of the LMW heparin preparations.

The LMW fractions seem not only to be absorbed differently, but also more completely. These findings suggest that more clinical studies are needed with different doses of LMW heparins to find the most effective antithrombotic dose, and then observe the incidence of bleedings. Two of the clinical studies reported today seem to underline the accuracy of this observation. Such studies may then indeed show that the use of LMW heparin is associated with less bleedings in humans, as has already been shown in animals. The second major problem related to

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the optimal dose of LMW heparin is related to the lack of uniform unitage and lack of regulation of such unitage. Unless regulatory agencies and manufacturers agree on a uniform way to express activity soon, one can foresee a bewildering confusion which will make the clinical use of these preparations by practicing physicians very difficult.

The third premise that LMW heparin fractions might be associated with less thrombocytopenia is still under investigation. Two forms of thrombocytopenia seem to be encountered with the use of heparin, an immediate drop in platelet counts that seems to be observed in almost all patients, and a second, apparently antibody-induced type. It is this latter form that represents a real complication since it may be associated with paradoxical thromboembolisms.

In several clinical trials of LMW heparin, no patients with thrombocytopenia were noted, and few investigators have success-

fully used LMW fractions in patients who had developed thrombocytopenia with regular heparin.

Yet, there are some reports where thrombocytopenia was associated with LMW heparins. It remains to be seen whether this is encountered with all available forms of LMW heparin or only with a specific type. Clearly, more studies will have to be conducted to address this issue. Initial impressions are favorable, however.

We also heard today that LMW heparin fractions can be used for systemic, therapeutic anticoagulation and this opens an entirely new area of clinical research.

I believe that the future of LMW heparin fractions is a bright one and will encourage further research and scholarly investigation.