Introductory Remarks

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Clinical studies on low-molecular-weight heparins have been recently started, mainly in Europe.

The aim of this Symposium is to raise important questions about the pharmacological properties of low-molecular-weight heparins in order to try to bring out clear answers. Our wish is also to gather some available information about the efficacy, in different groups of patients at risk for venous thromboembolism, of low-molecular-weight heparins, especially Enoxaparin PK 10169 from Rhône-Poulenc (France) (table I). How should the potency of low-molecular-weight heparins be assigned? No international standard is presently available. Could such a standard help to obtain a uniform cross-referencing of different low-molecular-weight fractions? In the mean time, dosage assignment could be expressed in gravimetric units and/or in anti-Xa units.

What is the duration of the biological effects and what is the bioavailability of Enoxaparin when given by subcutaneous route as compared to unfractionated heparin? Low-molecular-weight heparins contain molecules that have either a high or low anti-thrombin III affinity? What is the role of low-affinity components?

We have learned recently that anti-Xa is not the sole determinant of antithrombotic action. This raises the question at what additional factors determine the antithrombotic action? Moreover, is some anticoagulant activity released endogenously in plasma after low-molecular-weight heparin injection?

Low-molecular-weight heparin antithrombotic action has been evaluated with different animal models of thrombosis. Is the thrombogenic challenge used important for a better approach to the relevance of these different animal models to human pathophysiology?

Neutralization of anti-Xa and anti-IIa activities of unfractionated heparin is well achieved by protamine salts. Are these compounds as effective for a low-molecular-weight heparin such as Enoxaparin for instance? (Table I shows characteristics of this heparin fraction as compared to unfractionated heparin.)

Which dose of low-molecular-weight heparin should be used in clinical trials in order to prove the efficacy and safety of low-molec-

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Table I. Some characteristics of Enoxaparin and unfractionated heparin

Enoxaparin	Heparin
Mean molecular weight	5,000 16,000

Activity, U/mg

Anti-Xa 100-140 160-180

USP 50-60 160-180

Anti-IIa 30-50 160-180

APTT 30-40 160-180

Anti-XA/APTT ratio 3-5 about 1

ular-weight heparins in patients undergoing general surgery? Since unexpected bleeding complications in some patients receiving low-molecular-weight heparin have been reported, there is a tendency to reduce the doses administered by subcutaneous route among many investigators. Is the dosage/ bleeding relationship clearly established in order to minimize hemorrhagic complications in these clinical studies? – Do we have clear data on low-molecular-weight heparin-platelet interactions. Could a reduction in the incidence of heparin-induced thrombocytopenia observed with unfractionated heparin be expected with low-molecular-weight heparin? Which tests should be used in vitro in the diagnosis of this condition and in the assessment of different low-molecular-weight heparins if such compounds can be helpful in eliminating this condition?

Could the suggested efficacy of low-molecular-weight heparin in the prophylaxis of postoperative thrombosis in general surgery be extended to orthopedic surgery and in patients with a constituted thromboembolic episode?

What is the value of low-molecular-weight heparin in patients undergoing extracorporeal circulation?

What are the possible advantages of low-molecular-weight heparin in chronic hemodialysis?

We hope that this Symposium, organized with the generous help of Rhône-Poulenc Santé, will improve our understanding of the concept concerning low-molecular-weight heparins and bring some information about the efficacy and safety of a promising new drug.