

Preface

It will shortly be the 100th anniversary of the discovery of heparin by Jay McLean in 1916, so a volume dedicated to the enormous progress that has since been made in the understanding and clinical exploitation of this complex biomolecule is particularly timely. The present volume has the principal aim of recording the current state of affairs concerning the use and study of heparin; in addition, we have tried to record the progress made, particularly within the last 30 years, a period full of incident in this field. For this reason, we begin with a chapter on the history of heparin (Barrowcliffe), before going on to outline what is currently known about its biosynthesis (Carlsson and Kjellen) and the molecular basis for its anticoagulant and antithrombotic activity (Gray et al.)

The number and variety of heparin products in use rose dramatically with the development of the low-molecular-weight heparins. These are now among the most commonly used drugs and are commercially very important indeed, all of which has provided the impetus for development of the advanced techniques of standardisation (Gray) and characterisation (Mulloy) addressed in Part II of this volume. The commercial importance of heparin may also have its negative aspect, in motivating the extraordinary recent contamination incident described by Chess et al. The necessity to determine detailed structures of such complex molecules as low-molecular-weight heparins and heparan sulphate has led to recent progress in techniques for their analysis (Guerrini and Bisio; Shriver et al.)

The three chapters that make up Part III of this volume are concerned with the current clinical use of heparin in the treatment and prevention of thrombotic disease (Gresele et al.). Being a powerful drug with multiple biological activities, however, heparin has a number of undesirable side effects (Alban), sometimes necessitating the use of specific antidotes (Pai and Crowther).

We have been especially interested in looking to the future of heparin use. In Part IV of this volume an introduction to the biological activities of heparin other than those based on its anticoagulant and antithrombotic activity (Lever and Page) is followed by two chapters going into more detail on the subjects of chemokines and growth factors (Shute) and the growing field of research into the neuroprotective effects of heparin and other glycosaminoglycans (Dudas and Semeniken).

Finally, the wide range of heparin-like compounds and their biological activities is explored in Part V. Many of these had scarcely been described 30 years ago; some

are naturally occurring compounds (Allegra et al.; Collic-Jouault; Gallagher) and others are wholly or partially modified (Coombe and Kett; Oreste).

It seems arbitrary and still mysterious that a complex polysaccharide extracted from hogs' intestines should be a potent and useful anticoagulant and antithrombotic agent in human medicine. No possible application of "rational design" could have found heparin. Had it not been found and recognised so many years ago, it is hard to see how it could be discovered, much less accepted for human use, by the drug discovery paradigms of the present age. We should be grateful for the skill and acuity of the team which identified heparin so long ago, and look forward to an expanded range of applications of its use in the future.

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