HANDBOOK OF ANALYTICAL SEPARATIONS

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VOLUME 5

DRUG MONITORING AND CLINICAL CHEMISTRY

EDITED BY
GEORG HEMPEL

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Drug Monitoring and Clinical Chemistry

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Preface

Drug monitoring has been practised for about 30 years now. Initially, the concept was limited due to methodological problems in analysing low concentrations of drugs in biological fluids. In earlier times, only thin-layer chromatography and spectroscopic methods were available for analysing complex matrices. Now, as can be seen from the first chapters of this book, the methodology has clearly improved and a number of alternative methods are available for most analytical problems. Today, almost all drugs can be separated from complex matrices like human blood or other biological material and determined in very low concentrations. In the future, the availability of mass spectrometric detectors at a reasonable price will enable the analyst to solve more analytical problems in the clinic.

Selection of a suitable method for a given analytical problem is often not only made based on the question which method is scientifically most appropriate. The personal expertise of the analyst also plays an important role because some experience is still required for running chromatographic or electrophoretic methods when analysing drugs in biological fluids. Furthermore, the limited availability of capillary electrophoresis, which is one of the most suitable methods for drug analysis when not too low concentrations are present, means it is not used as often as chromatographic or immunochemical methods.

With most of the analytical problems solved, the question that arises is: are the measured concentrations of the drug in the biological fluid clinically relevant? Clinical relevance of the measured concentrations implies that there is a clear relationship between the concentration and the effect of the drug. If this is the case, the next step is to show that dose individualisation based on drug concentration measurements can standardise the individual's exposure to the drug. Even more important, one has to clarify if there is a clinical endpoint which can be positively influenced by individualising drug therapy.

For the therapeutic areas covered in this book, it has been shown that patients do benefit from therapeutic drug monitoring (TDM), although this is not the case in all therapeutic areas. However, with the limited financial resources in the clinic, even in the developed countries, one has to show that TDM is also cost-effective and the efforts in

the laboratory result in reductions in mortality, severe side-effects that would lead to longer hospitalisation and/or prolonged pharmacotherapy.

Another concept for dose individualisation, which was introduced in the late 1980s, is the area of pharmacogenetics. Pharmacogenetic methods have been shown to be an important tool for identifying patients at risk of experiencing severe toxicity or underdosing. However, there are still concerns if pharmacogenetics is effective from a pharmaco-economic point of view. In the future, methods for genotyping based on chip technology will become cheaper and easier to handle, so pharmacogenetics definitely has the potential to be a routine tool to optimise pharmacotherapy in the clinic. However, even when many more genes responsible for drug metabolism or distribution have been identified, this approach will not completely replace drug monitoring in the future.

Finally, I would like to thank all the contributors to this book for their efforts. Hopefully, the reader will find useful information for setting up or improving TDM in the clinic, for teaching purposes and to become up-to-date on recent developments in this field. I would like to thank Prof. Boos and all other colleagues from the department of Paediatric Oncology (University Children's Hospital Manchester) for the excellent collaboration and want to dedicate the book to my teacher Gottfried Blaschke, a great analyst, with many thanks for his support over the years.

Georg Hempel

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