Introduction

The fact that every patient is different is one of the reasons why the art and science of medical diagnosis is so interesting. However, when it comes to treatment, this diversity can be viewed either as an obstacle or a challenge.

Traditionally, the pharmaceutical industry have generally considered individual variability in drug response to be a nuisance, and have endeavoured to ignore it by pursuing a 'one drug - one dose a day for all' ideal. Unfortunately, many prescribers also adopt this attitude and fail to tailor dosage adequately to individual patient need. On the other hand, clinical pharmacologists have long been at the forefront of the challenge of understanding the many sources of variability in drug response. The need for this understanding has now come into much sharper focus with the advent of molecular biology and its increasing impact on our appreciation of the genetic contribution to disease and to enzyme and receptor variability. Indeed, the captains of the pharmaceutical industry now see variability not as a threat but as a major opportunity, in the new development paradigm of drugs to treat selected patients based upon the genetic diagnosis of disease and pharmacogenetics. However, until the 'gene for non-compliance' has been sequenced, and all the 'genes that affect genes' have been unravelled, it remains important to take a balanced view of variability in drug response, as the outcome of environmental and behavioural as well as genetic factors.

The Esteve Foundation's eight Symposium held in Sitges, Spain (October 7-10, 1998) provided a timely forum to take stock of our understanding of the many aspects of variability in human drug response. With respect to sources of variability, considerations were split into those relating to drug metabolism enzymes, transporters and receptors, and their modulation by age, sex, race, disease and exercise; subjective factors (perception of treatment, pain, compliance, placebo response); and behavioural influences (particularly in the context of drug abuse). Methods of measuring variability were considered with regard to the role of phenotyping and genotyping and the use of population PK-PD modelling, overlayed with discussion of statistical and pharmacometric issues. Finally, the participants addressed questions related to the management of variability in drug response. Should we try to design it out of new chemical entities? When and how might it be minimised by pharmaceutical manipulation of the dosage form? What are the regulatory expectations with regard to variability and choice of drug dosage?

This volume represents a comprehensive account of the information shared by the participants in the Symposium, including a record of the lively debate that followed each individual presentation. On behalf of the contributors and the organisers, I hope that you enjoy reading the book as much as we enjoyed taking part in the Symposium.

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