Introduction

Ethan Rubinstein, Symposium Chairperson

Department of Internal Medicine and Unit of Infectious Diseases,
Tel Aviv University School of Medicine, Tel Aviv, Israel

Fluoroquinolones now stand as one of the most significant classes of antimicrobials, being the most commonly prescribed oral antibiotics in the US. The earliest agents in this class were beneficial in many clinical situations and were very well tolerated. This led to a rapid rise in interest in these compounds, and a corresponding development of newer agents with greater efficacy. Over the past few years, there have been a number of new fluoroquinolones developed, and some now marketed globally. Interest in such development has led to the emphasis on research into structure–activity relationships to help develop increasingly effective compounds. This has resulted in newer agents having greater potency, a broader spectrum of activity, and greater activity against resistant organisms. They maintain long half-lives, which in turn has allowed for once-daily administration. These improved features have been associated with the rise of fluoroquinolones as a class, making them the first choice in many infectious diseases in place of cephalosporins, macrolides, and older agents.

Along with this increase in activity, changes in side-effect profiles have been reported. Previously, it was believed that the fluoroquinolones were relatively similar in terms of their incidence and spectrum of adverse events. However, recent reports have highlighted substantial differences among agents concerning side-effect profiles, and this has led to interest in clarifying their structure–side effect relationships. By gaining a greater understanding of the roles that specific substitutions attached to the quinolone nucleus have, the possibility is there for safer drugs to be developed and unsafe ones withdrawn before market exposure. Thus, no longer can the fluoroquinolones be considered interchangeable. The clinician is now able to choose agents that are both effective and well tolerated.

To bring together all the strands of data detailing the structure–activity and structure–side effect relationships, a special roundtable discussion was chaired by the author of this introduction, Professor Ethan Rubinstein, Tel Aviv University School of Medicine, Israel. The discussion participants were experts from

around the world, who were able to clarify the differences among the fluoroquinolones based upon safety and tolerability issues. The papers following this introduction report on each individual presentation, as well as the informative discussion that was held at the end of the session. The first paper, by the present author, will set the scene for the reader, with a clear summary of the structure–activity and structure–side effect profiles of individual fluoroquinolones. Professor Claude Carbon, Bichat-Claude Bernard Hospital, Paris, France, then clarifies differences among individual fluoroquinolones, describing the relative incidences of specific adverse events. Professor Jacques F. Acar, Fondation Hôpital Saint-Joseph, Paris, France, will compare fluoroquinolones to other commonly used agents, such as macrolides and β -lactams, before describing the ecological impact of different antimicrobials upon the normal human gastrointestinal flora. With the possibility that such changes in flora may relate to the propensity of different agents to cause resistance, this is one area that needs to be fully addressed. By gaining a greater understanding of which agents are likely to be associated with the development of future resistance, the clinician will be able to prescribe safer drugs. Adding to the pre-clinical data will be the presentation by Professor Hartmut Lode, City Hospital Berlin-H-Heckshorn, Berlin, Germany, who looks at the differences in pharmacological features among the fluoroquinolones. These features are responsible for different profiles of the fluoroquinolones in terms of their bioavailability, penetration, and drug–drug interactions. With many patients taking more than one drug, it is important for interactions to be

documented, and for the effect of individual agents to be analysed. This will allow for the use of agents that are less likely to interact with other commonly used medications, thereby ensuring greater safety and more effective drugs.

Clinical data following extensive use of levofloxacin will then be presented to assess the safety and efficacy of fluoroquinolones, with particular emphasis upon levofloxacin. This will be assessed first from a US perspective, with results presented by Dr. James B. Kahn, Ortho-McNeil Pharmaceutical, Inc., N.J., USA, reporting on the latest clinical trial data, surveillance studies, and spontaneous reports. These incidence rates will be compared to results from Japan, as reported by Dr. Katsuro Yagawa, Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan, who will provide a comprehensive analysis of levofloxacin safety using Japanese and world-wide data from over 130 million prescriptions.

This roundtable discussion was developed with the aim of helping the clinician decide which antimicrobial to use. It is now well recognised that efficacy cannot be the sole criterion, but must be balanced against other factors, including safety, tolerability, cost, and administration options. The question as to which is the best agent to use can be a difficult one to answer, and one that has engendered a great deal of debate in the past. The roundtable discussion brings together experts who have distinguished and long careers in the field of infectious disease. They will help to develop a consensus differentiating the individual fluoroquinolones based upon evidence gained throughout the world, using both pre-clinical and clinical data.