

# **The Future of Antibiotherapy and Antibiotic Research**

*Edited by*

**L. NINET**

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**J. FLORENT**

*Centre Nicolas Grillet  
Rhône - Poulenc  
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In memory of David Perlman  
1920-1980

*Edward Kremers Professor of Pharmaceutical Biochemistry  
University of Wisconsin Madison - Wisconsin*

His previously mourned death deprived all the participants in the Rhône-Poulenc Round Table Conference of his exceptional knowledge and his attentive friendship.

## Preface

This volume contains the Proceedings of the Second Rhône-Poulenc Round Table, held in Paris in February 1980. The aim of this meeting was to evaluate the needs for new antimicrobial agents in human and animal medicine and to analyse those parts of our present knowledge which could be used to improve the performance of existing drugs and guide the search for new ones, especially natural antibiotics. In this respect, several renowned scientists, coming from all parts of the world and from different disciplines, met for three days to present their work and exchange their knowledge and ideas.

The reader will not find in this book the infallible means of discovering the "miracle antibiotic" or of drawing its structure, nor a complete picture of all the possible methods of tackling the problem. Perhaps through theories expressed here, some well established and others just emerging, he will realise the paucity of our general knowledge and appreciate the huge gaps to be filled in order ultimately to win the battle against infectious diseases. Perhaps he will also become acquainted with the intensive efforts that have already been made and are still being made by universities and industry in this direction.

It is our real pleasure to thank warmly all the contributors and participants who agreed to attend the meeting and to work actively together, in a friendly atmosphere of free discussion. We are particularly indebted to Drs. J. Acar, Y. Chabbert, J. Davies, A. Demain, F. Le Goffic and M. Richmond for their generous advice and kind help, before and during the conference. It would take too long to name all our colleagues of the Rhône-Poulenc Group of Companies who assisted us so efficiently in the organisation of the meeting. We wish to extend our hearty thanks to all of them, and especially to Miss M. Eiglier and Mrs. N. Gérard and to Mr. J.C. Blondel. Finally, this conference would not have been held without the initiative, the confidence, and the constant moral and financial support of the Research Manager of the Health Division of the Rhône-Poulenc Group, Dr. G. Jollès, to whom we express our deep gratitude.

The transcription of several presentations and of all the discussions, has been efficiently carried out by Dr. Mary Firth, and the translation of all the French communications by Dr. Allan Salem, with the cooperation of Miss S. Copping, Mrs. J. Schock, Mrs. M. Tantet, Mrs. M. Dorizon, Mrs. R. Hollevoet and Miss L. Yaghdjian. Mr. J.-P. Labbé and Mr. M. Lomont have taken special care over the general presentation of the figures. The help of all these people, together with the expert and kind assistance of the staff of Academic Press Inc. (London) are gratefully acknowledged.

May, 1981

L.N., P.E.B., D.H.B. and J.F.

## Opening Remarks

Dr. G. JOLLES

It is a great privilege for me today to open the second Rhône-Poulenc Round Table Conference on the Antibiotics of the Future.

The present time is certainly very rich in scientific events of all kinds, from major congresses including several thousand participants such as the Chemotherapy Conference last Autumn in Boston, to very exclusive meetings to which only specialists with the highest credentials are admitted.

Our objective today is neither to compete with these two types of meeting nor to find a half-way point between these two extremes. In fact, our primary goal is to do something else, something more pragmatic: the objective of our Round Table Conference is to try to create, on a broad and particularly topical issue of Pharmaceutical Research, a contact between top fundamental scientists and researchers of the Industry who want to initiate important therapeutic advances for tomorrow.

Two years ago for our first Round Table, the topic we chose was the Pharmacology of Immunoregulation. Immunology is currently undergoing rapid evolution and if major fundamental progress has so far been achieved, the transfer of all that new knowledge to the level of practical medicine and drug design has certainly not yet been achieved; this was therefore a question, the clarification of which could prove particularly useful.

However, the topic we chose for today's meeting, antibiotic therapy, may seem somewhat surprising because it includes a great number of positive achievements. What progress has been made since Fleming's and Waksman's discoveries, and how many compounds have been discovered, from cephalosporins to macrolides, from aminoglycosides to synergists! Pharmacopoeias are full of antibiotics; excellent products have been discovered and have given rise



to numerous "me too" drugs. Next to the antibiotics, there are also the synthetic antimicrobials ranging from sulphonamides to nalidixic and pipemidic acids.

Now, what can we still expect from antibiotics? Don't we have everything we need against infective diseases until the end of this century? Those who frequently meet with clinicians know quite well that everything is not yet solved in this field and it is true also that in medicine and in chemotherapy, as everywhere else, there is a steady and stepwise evolution.

If one looks into the future, it is certain that microbial infections will remain an enemy of every day life, it is certain that we shall need antibiotics and antimicrobials to fight them, but is it just as certain that it will *always* be the same antibiotics, that it will *only* be the same antibiotics?

I would compare the Conference on Immunoregulation we organised two years ago with the thoughts a young person may have while contemplating passionately his future which seems most promising. But today's conference on antibiotics makes me think rather of a middle-aged woman who has beautiful years full of success behind her and who is wondering whether yesterday's success will be just as rewarding tomorrow.

In a way, such considerations are very close to today's meeting programme: we intend to make a broad survey of the present situation, then look into the future and prepare adequate action.

In the first part entitled "Analysis of the present situation: needs, constraints and objectives for the future", we would like, first of all, those whose activities are closer to clinical practice to make a general review of the present status of antibiotic therapy; this should eventually lead them to identify the strong and weak points of antibiotics currently available and to determine the future needs. We have also included Animal Health because we want this review to be exhaustive.

In the second and third parts, suggestions should essentially be directed towards a research programme adapted to these needs for the future. In the second part, "Methods of selection and assessment of drugs", the new research pathways opened up by scientific progress should be reviewed, with particular emphasis on the knowledge of those mechanisms of action which may give rise to substantial innovations. The last contributions will deal with new methods of extraction of antibiotics, their screening and early identification, and also genetics and bioconversions.

In order to cement the various lectures within the framework of our conference, it was agreed to conclude the meeting by a short

review of each of the main trends in order to summarise and emphasise the major principles of our debates.

We are going to have three days of hard work with a particularly heavy programme. I hope that we were not too ambitious in trying to organise such a large survey, but in order to get an adequate prospective view, we really had to cover all aspects of antibiotics: the clinical and biochemical, the fundamental and practical, the human and veterinary. Some of you will perhaps be somewhat disorientated by some of the lectures which do not relate to your everyday activities. But our objectives was precisely to create a contact on a very broad basis and we hope that the quality of the lectures will give everybody the opportunity to find some interest in the different approaches to this problem.

I wish now to thank all of you for having agreed to spend some of your precious time working with us, all those who helped and advised us in organising this meeting, and all those who have come from distant places to join us today. One of our most distinguished guests however is not here with us. Many of you already know that Professor Perlman died a few days ago in Madison after fighting for a long time with enormous courage against a cruel disease, and it is with a great sadness that we face his absence from our meeting.

I wish furthermore to thank Dr. Ninet who has taken charge of organising the meeting from a practical and scientific point of view and I can assure you that he did his best to make the conference instructive and rewarding for all of us.

Many of the lectures and communications will be in English, some will be in French but we have provided simultaneous translation to avoid linguistic problems.

I really hope, therefore, that everything has been provided for the meeting to be successful.

Rhône-Poulenc devoted considerable attention to antibiotics when they first appeared many years ago. It was in our own laboratories that, after the second World War, the first milligrams of penicillin were prepared on this continent. In our factories, antibiotics from almost all the families were fermented. The Group's R & D budget for Human and Animal Health amounted to almost \$100 Million in 1979 and antibiotics accounted for 10% of this budget.

Thus we feel very concerned about the new generation of antibiotics which is approaching and we trust that, with your help, our meeting will provide a substantial contribution to therapeutic progress by preparing in different ways the ground for developing the antibiotics of the future.

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