Antimicrobial Agents and Chemotherapy

Various aspects of antimicrobial agents, infectious diseases, and chemotherapy were discussed during October 26-28, 1966, in the 175 papers and 2 round tables presented at the Sixth Interscience Conference on Antimicrobial Agents and Chemotherapy. This meeting was held in Philadelphia, under the sponsorship of the American Society for Microbiology, and was organized with the co-operation of the Infectious Diseases Society of America. The Society for Industrial Microbiology collaborated in the sponsorship of the symposium on ‘Non-pharmaceutical Uses of Antibiotics’. 1336 interested scientists attended this meeting; 87, representing 14 countries came from outside the United States.

The three-day conference opened with an address ‘Drugs and the Four Cultures’ by Professor H.F. Dowling, M.D. (retiring president of the Infectious Diseases Society). The four cultures considered by Professor Dowling included the pharmaceutical company executive, the scientist working for the pharmaceutical company, the scientist working in the regulatory governmental agency, and the physician. Professor Dowling concluded that although the aims of these four groups are often related, it is the scientist who acts as the bridge for cooperation and collaboration between all four groups, and without him each might be much less effective, and the public much less satisfactorily served.

Among the features of the 1966 meeting were four symposia. Dr. W.K. Hausmann (Ayerst Laboratories) chaired the first, which dealt with ‘Identification Aspects of the Production and Metabolism of Antibiotics’. The participants included Prof. V. Betina (Slovak Polytechnical University, Bratislava) discussing the usefulness paper chromatographic systems (including pH chromatography) in the identification of antibiotics from fungi, Professor C.P. Schaffner (Rutgers University) who spoke on the problems of identifying the amino sugar containing antibiotics, Dr. W. Keller-Schierlein (Eidgenössische Techni-sche Hochschule, Zurich) who described the usefulness of mass spectrometry in identification of the members of the macrotetralide series, Dr. Samuel Wilkinson (The Wellcome Foundation, Beckenham, England) who summarized his observations on the identification of the members of the polymyxin group by gas chromatography, Dr. A.J. Glazko (Parke, Davis & Co.) who discussed procedures useful in identifying metabolites of chloramphenicol, and Dr. R. G. Kelly (American Cyanamid Co.) who mentioned the use of fluorescence analyses in identification of tetracycline metabolites found in animal tissues and fluids.

The second symposium ‘Chemical Modifications of Antibiotics’ (organized by Dr. D. Perlman) stressed the collaboration of the chemist and microbiologist in preparing new antibiotics with attributes not found in the microbial product. Dr. K.E. Price (Bristol Laboratories) summarized a survey on about 5,000 semi-synthetic penicillins showing the relationships of chemical structure to antibiotic activity. Among the accomplishments achieved were increased antibac-
terial spectrum, oral absorption, and resistance to bacterial enzymes hydrolyzing the naturally occurring penicillins. Prof. Dr. P. Sensi and Dr. S. Füresz (Lepetit, S.p.A., Milan, Italy) gave an exciting report of their success in broadening the antibacterial spectrum of rifamycin and preparing derivatives which are orally absorbed. Rifaldazine (N-amino-N'-methylpiperazine of 3-formylieramycin SV) has demonstrated excellent oral absorption and promising results have been obtained in clinical trials in patients suffering from pneumonia, osteomyelitis, urinary infections, and tuberculosis. Dr. E.H. Flynn (Eli Lilly and Company) in his survey of the more than 1000 semi-synthetic cephalosporins described the successes with cephalothin and cephalaridine, and with the new cephaloglycin (which is orally active). The symposium closed with a review of the biological activity-chemical structure relationships in lincomycin.

Introduction of halogens resulted in higher specific activity against Gram-positive bacteria and some activity against Gram-negative bacteria, according to Dr. B.J. Magerlein (The Upjohn Company).

‘The Epidemiology of Drug-resistant Infections’ was the topic of a symposium convened by Professor G.T. Stewart, M.D. (University of North Carolina). Among the participants were Dr. M.H. Richmond (Edinburgh University), Professor N.J. Ehrenkranz (University of Miami Medical School), Dr. M. Turck (University of Washington School of Medicine), Dr. D.H. Smith (Harvard Medical School), and Dr. J.M. Leedom (University of Southern California). The panel reviewed the main mechanisms responsible for drug-resistance including a) A mutation, probably affecting the structural gene governing a specific metabolic process; b) Production of enzymes, e.g. penicillinase, capable of destroying the antibiotic; and c) Decrease in permeability of the organism to one or more antibiotics. The role of the resistance factor was evaluated and the speakers concluded that the use of antibiotics is bound to aggravate the spread of drug-resistance among drug-sensitive as well as already-resistant bacteria, so that the term ‘infectious’ applies between species of bacteria as well as between bacteria and host. Among the practical examples of this spread of resistant organisms and of the ensuing clinical and epidemiological outcome were the reports on staphylococci, yeast-like fungi, pyogenic Gram-negative bacilli, and meningo-cocci.

‘Non-pharmaceutical uses of Antibiotics’ was the subject of a symposium organized by Professor David Pramer (Rutgers University) as a joint effort by the American Society for Microbiology and the Society for Industrial Microbiology. Dr. R.F. Elliott (American Cyanamid Co.) discussed the problems encountered in the use of antibiotics in increasing feed conversion to body weight in poultry and animals for food. Professor R. N. Goodman (University of Missouri) concluded that although antibiotics in plant disease control have not approximated the status of miracle drugs that they have vis-a-vis microbial pathogens of humans, they have had significant effects in controlling a number of pathogens affecting important food crops including the rice blast disease, and several of the bacterial and fungal pathogens of fruit crops. Dr. Claude Vezina (Ayerst Laboratories, Canada) summarized the marked success obtained with antimycin A as a teleocidal substance and predicted its use in removing unwanted fish from various ponds and lakes. The symposium closed with a paper by Professor Edward Katz (Georgetown University Schools of Medicine and Dentistry) on the usefulness of antibiotics in elucidating the mechanisms of biosynthesis of actinomycin D.
The two round table discussions included ‘Adverse Reactions to Drugs’ with Professor L.E. Cluff, M.D. (University of Florida) as chairman, and Professor W.M.M. Kirby, M.D. (University of Washington), Dr. J.E. Johnson, M.D. (Johns Hopkins University Hospital), and Dr. B.H. Minchew, M.D. (Bureau of Medicine, Food and Drug Administration, Washington) as participants. Special emphasis was placed on the cross-allergenicity between the penicillins and cephalosporins, and the treatment of suprainfections. Management of Infections Under Immunosuppressive Conditions’ was the topic reviewed by a panel including Professor Robert Austrian, M.D. (University of Pennsylvania) (chairman), Professor David Rifkind, M.D. (University of Colorado), and Professor J.P. Utz, M.D. (Medical College of Virginia). They were especially concerned with the incidence and treatment of infections caused by Gram-negative bacteria, Mycoplasma, and the yeast-like fungi.

Among the new antibiotics discussed at the Conference were:

Doxycycline (α-6-deoxy-5-oxotetracycline) a member of the tetracycline group giving higher blood levels and fewer side effects than other tetracyclines in clinical tests;

Minocycline (7-methylamino-6-demethyl-6-deoxytetracycline) a tetracycline with higher specific activity and broader antibiotic spectrum than other tetracyclines in animal studies;

Condensation products of rifamycin S with aromatic 1,2-diamines which have broader spectrum than the parent compound;

Leucomycin A3 a new antibiotic from Streptomyces kirasatoensis;

L-4-azaleucine, a leucine antagonist from Streptomyces neocaliberis;

Hedamycin, an antitumor substance from Streptomyces griseoruber active against Walker 256 intramuscular tumor;

Histidomycin, an antibiotic protecting mice against Salmonella schott-muelleri;

LL-A0341 A and B, (from Streptomyces candidus) chemically related to telomycin;

5-hydroxy-7-chlortetracycline, an antibiotic with the structural features of chlortetracycline and oxytetracycline;

10. A series of pyridinium and related derivatives of the semi-synthetic cephalosporins with therapeutic advantages over cephaloridine.

Among the papers on infectious diseases topics were reports of: a) An oral live tularemia vaccine in man; b) pneumonias caused by Escherichia coli and by Pseudomonas; c) Separation of thermoregulatory activities of endotoxin and endogenous pyrogen; d) Studies of the epidemiology of burn infections due to Pseudomonas aeruginosa using pyocine and bacteriophage taping; and e) studies on the bacteremia of streptococcal endocarditis.

The clinical and pre-clinical reports included discussions of synergism noted between ampicillin and other semi-synthetic penicillins, usefulness of hetacillin in a variety of infections, cephaloridine in laboratory and clinical studies, and penetration of acid-stable penicillin into bones.

Most of the papers presented at this conference will appear in Antimicrobial Agents and Chemotherapy–1966, which will be published in June, 1967, by the Varia.

American Society for Microbiology. The book will be distributed to all registrants at the meeting, and will be available from the headquarters of the Society, 115 Huron View Boulevard, Ann Arbor, Michigan.

Plans for the 1967 Interscience Conference on Antimicrobial Agents and Chemotherapy are already under way. This conference will be sponsored by the American Society for Microbiology.
and organized with the co-operation of the Infectious Diseases Society of America. The sessions
will be held during October 25-27, 1967, in the Edgewater Beach Hotel, Chicago, Illinois.
Among the topics that will probably be discussed in symposia and round tables are: mechanisms
of drug resistance; procedures for control of clinical evaluations of new drugs; synergism and
antagonisms in antibiotics; and chemistry and mechanisms of antitumor antibiotics. Further
information on the meeting and abstract forms can be obtained from Mr. R.W. Sarber, executive
secretary, American Society for Microbiology, 115 Huron View Boulevard, Ann Arbor,
Michigan. The deadline for submission of abstracts is July 1, 1967.
Erratum
Re: Paper by E. Krueger-Thiemer; P. Buenger; L. Dettli; P. Spring, and Ellen Wempe entitled
“Dosage Regimen Calculation of Chemotherapeutic Agents. Part III. Sulfasymazine”, published
in volume 10, No. 6 (1965/66). On page 336 it should read correctly: “Sulfasymazine reaches
sufficient concentrations in plasma water for a much shorter time than sulfamethoxypyridazine
because its antibacterial activity is lower and its protein binding is higher than that of
sulfamethoxypyridazine. The same is shown for two other test subjects in Figure 4 for these two
drugs and for sulfadiazine, which is equal in antibacterial activity to sulfamethoxypyridazine and
has an even lower protein binding than the latter drug (it should be noted that the dose of
sulfasymazine has been about half of that of the two other drugs in these experiments).”