Concluding Remarks

G.L.

George L.

Petrikkos

1st Department Propedeutic Medicine, Athens University School of Medicine, Laiko, General Hospital, Athens, Greece

George L. Petrikos, Associate Professor, 1st Department of Propedeutic Medicine, Athens University School of Medicine, Laiko, General Hospital, GR-115 27 Athens (Greece)

From the previous very interesting presentations the following main points can be outlined: Dr. Höffken noted that the isolation of the agent responsible for respiratory tract infections (RTIs) is desirable, but it is difficult to differentiate between pathogen and commensals. The decision to treat is based usually on epidemiological, clinical and radiological assessments. The difference in the etiological spectrum of community and hospital-acquired RTIs, the underlying disease and immunosuppression are crucial in the decision for treatment. Penicillins or macrolides are the drugs of choice, while the new oral cephalosporins exhibit excellent activity against many bacterial pathogens of typically community-acquired RTIs caused by resistant strains of *Haemophilus influenzae* and other β -lactamase-producing gram-negative bacteria.

Dr. Cullmann discussed the importance of β -lactamase stability in treating RTI, and noted that nowadays 70 to 90% of *Moraxella catarrhalis* are β -lactamase-producing (bla+) isolates. The enzymes BRO-1 and BRO-2 which are transposon mediated explain their rapid spread. Bla+ *H. influenzae* isolates make up 6% of the total in Northern Europe, up to 55% in Southern Europe and in many African countries more than 80%. Resistance is mainly due to the prevalence of the most widespread transposon-mediated TEM-1 β -lactamase. Recently, new extended spectrum enzymes (TEM-3 to TEM-21) inactivating even the oxyimino-cephalosporins have arisen by mutation from TEM-1 or TEM-2 enzymes. The compounds least affected by these enzymes are cefibuten and cefetamet.

Professor König explained the role of the immune system in recovery from infection. The efficacy of nonspecific as well as specific host defence mechanisms is obligatory to counterbalance microbial infection. He described the process of inflammation by the release of mediators, the regulation by cytokines of endothelial-granulocyte interaction and migration of granulocytes to the focus of inflammation, the triggering of the humoral or cell-mediated immune response, antibody formation and allergic reactions. Microorganisms can activate or deactivate the host response thus facilitating opportunistic microbial growth.

Dr. Scheffer presented data on the effect of several oral cephalosporins on inflammatory host reactions. Cefaclor, but not the oral cephalosporins cefetamet, Ro 40-6890 or cefpodoxime increased histamine release from human basophils. A significant increase in phagocytosis in the presence of various cephalosporins was demonstrated and the bactericidal activity of human granulocytes for several bacterial strains was also enhanced. Cefetamet, cefaclor, Ro 40-6890 and cefpodoxime increased the chemiluminescence response of human neutrophils

when stimulated by *Escherichia coli* but not by *Staphylococcus aureus*. The cephalosporins decrease the synthesis of leukotrienes from human neutrophils. Furthermore, the cephalosporins studied decreased the release of IL-6 and TNF.

Dr. Kneer discussed the relevance of antibiotic tissue penetration in treating RTI and noted that factors which influence the outcome of an infection are the intrinsic microbiological activity and concentration time profile of free drugs in the infected loci. The penetration of the antibiotic drug depends on its lipophilicity and protein binding. However, the diffusion rate depends on the structure and physicochemical properties of the drug molecule. For β -lactam antibiotics the bactericidal efficacy is predictable by maintaining the free drug concentration above the bacterial MIC. Tissue homogenate data can only be useful if correctly interpreted by correcting for the partitioning between the tissue components. Professor Dagan discussed the difficulties in diagnosing lower RTI in pediatric patients where most of the community-acquired RTIs are of viral origin. He also noted that no antibiotic agent exists that covers efficiently all possible pathogens, and in severe cases when the likelihood of the presence of bacterial pneumonia is high, a broad-spectrum antibiotic should be used.

Finally, Dr. Kissling presented an overall review of the clinical literature on cefetamet pivoxil, till March 1992. Published trial results included 4,112 patients. A total of 3,128 patients were treated with cefetamet pivoxil: 2,612 adults and 516 children; standard antibiotic therapy was given to 984 patients with genitourinary infections and RTIs as well as infections of the ear, nose and throat. At the end of treatment the clinical outcome was successful in 90.7% of the patients who received cefetamet and in 86% of those who were given a standard antibiotic. *Enterococci* and *Pseudomonas aeruginosa* did not respond to cefetamet. Mild to moderate adverse events were reported in 279 (8.9%) of the patients receiving cefetamet.

Premature treatment withdrawals occurred in 0.8%. All adverse reactions were mild to moderate and were mainly of gastrointestinal nature, rapidly subsiding after treatment. From the above interesting and excellent presentations it can be concluded that: (1) community-acquired RTIs are very common and pneumonia remains one of the most common potentially serious infections seen in general practice; (2) the variety of the involved pathogens and the difficulties of diagnosis complicate the selection of an antibiotic to treat community-acquired pneumonia; (3) the role of the immune system is very important in recovery from RTI; therefore, the increasing average life-span and the rising number of immunocompromised patients have increased the population susceptible to RTI; (4) the problem of resistance of several community-acquired respiratory pathogens (*Streptococcus pneumoniae*, *H. influenzae*, *M. catarrhalis*) has increased in some countries; (5) in RTIs where the percentage of resistance strains, particularly those producing β -lactamase, is high, newer oral cephalosporins like cefetamet pivoxil offer an alternative choice for empirical therapy.