Preface

A. Dalhoff

The fact that the bacterial population develops resistance against antibiotics has been and still is viewed as an inevitable consequence of the exposure of bacteria to any antibiotic used. Resistance to antibiotics is a problem that confronts all of us, the patient, the physician and the economy.

The patient, and especially the hospitalized patient at risk, has to be treated adequately and the physician has to make the appropriate decision to optimize efficacy and to minimize emergence of resistance. In order to treat the patient most effectively and to prevent emergence of resistance the latest and most broad-spectrum antibacterials are used. Especially the immunocompromised intensive-care patient is quite often treated with many antibacterials of different drug classes and of a bewildering complexity of drug actions and interactions. However, many of these patients acquire resistant bacteria – either by the action of antibacterials on their own bacterial flora or by acquisition from another patient, the personnel or the environment due to an inappropriate choice of antibiotics and/or faulty medical and nursing procedures.

The most highly resistant bacteria, such as e.g. methicillin-resistant *Staphylococcus aureus* or vancomycin-resistant enterococci, sometimes being resistant to other antibacterials as well, have been isolated from intensive-care patients, transplant recipients or victims of accidents. In individual cases there may be the risk of running out of effective therapeutic options. Thus, the hospital intensive-care units are at the forefront of the problems.

Resistance data which have been derived from hospitals, especially tertiary care hospitals, may not be easily transferred to rural areas. However, significant pockets of antibiotic resistance have already existed

for quite a while in the community and the resistance frequencies increase in some areas. Penicillin-resistant *Streptococcus pneumoniae* (PRSP) is the most prominent example. In South Africa, for example, PRSP was initially isolated from hospitalized children but became subsequently prominent in their playmates or siblings. High levels of prevalence of PRSP have been reported from clustered rural areas in Africa, Asia, America and several countries in Europe. The problems of penicillin-resistance in *S. pneumoniae* are exacerbated by the emergence of macrolide resistance and even ceftriaxone resistance in PRSPs. Other examples for resistance problems in the community are β -lactamase-producing or otherwise penicillin-resistant *Haemophilus influenzae*, approaching $\geq 40\%$ in some countries, or *Moraxella catarrhalis*, which was susceptible to penicillin G and aminopenicillins before the 1970s. Thereafter the susceptibility pattern began to change and nowadays between 70 and 90% of *M. catarrhalis* are reported to be β -lactamase producers; these strains do not seem to be restricted to local clusters.

Obviously, the problems in the community are on the one hand global, but may differ from place to place thus demanding local solutions. The problems in the community may put outpatients at risk if they are not treated adequately by the general practitioner (GP). The problem should not be minimized, the fact being that many of the rural clusters of PRSP are of clonal origin and/or that bacteriological assessment may be restricted to only those patients who failed their initial therapy. The precise definition and analysis of the local problem should help to come to local solutions.

Resistance problems putting the hospitalized as well as outpatients at risk have to be tackled by many;

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Fax + 41 61 306 12 34
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A. Dalhoff
Klinikum der Christian-Albrechts-Universität Kiel
Institut für Medizinische Mikrobiologie und Virologie
Brunswiker Strasse 4
D–24105 Kiel (Germany)

the physician treating the patient has a dual function: based on the knowledge of the focal epidemiology of resistance he has to select the appropriate antibacterial; he, too, has to contribute to strategies that resistance does not emerge or is not being spread. The resistance problems with which a clinician is confronted and the antibacterial armamentarium he can use to optimize treatment and to minimize the likelihood of resistance emerging are different from those of a GP. Not only because of different pathogens and different resistance patterns but also as the latest and most effective antibacterials are, at least in principle, available to the clinician whereas the GP tends to prescribe drugs which were developed at the beginnings of the antibiotic era. The GP should use antibacterials prudently, and in the main they do so. In the UK for example, approximately 80% of all antibacterials are prescribed for outpatients; the figures in other countries will not be very different. Therefore, GPs are expected to reduce treatment costs by for example prescribing cheap drugs, i.e. drugs having already been available for many years. However, by prescribing drugs developed in the early days of antibacterial therapy such as erythromycin or in some countries nitrofurantoin or even nalidixic acid, therapy may not be optimal – especially not in rural clusters of antibiotic resistance – and resistance development may be triggered or increased. Furthermore, GPs are encouraged to stop using antibiotics except when absolutely necessary, but they are also encouraged to keep patients out of hospital by treating many mild-to-moderate infections at home. Thus, the GP is confronted with conflicting advice and it may be questionable if the antibiotic policies are adequate. The antibiotic policy to reduce treatment costs by prescribing cheap old antibacterials inherently triggering resistance development should be revised; newer drugs covering the relevant spectrum of pathogens with a low propensity for resistance development should be the preferred choice for the treatment of community-acquired infection by the GP.

Bacterial resistance is not only a serious threat to human health but also a significant economic threat: the number of patients in whom resistance develops and the number of patients who die from diseases due to a resistant pathogen directly translate into increased costs of health care, longer stays in hospital, the need for more expensive treatment, an increased number of diagnostic tests, and the loss of productive work by individuals and/or their family members; furthermore, increasing numbers of people will be infected by carriers of resistant bacteria or by patients still harboring resistant bacteria remaining infectious because of an ineffective therapy.

Emergence of resistance can be directly attributed to economic factors: poverty may result in noncompliance. The full treatment course may not be completed as the patient cannot afford to buy as many tablets as needed. Inadequate treatment (i.e. too low a dose and/or too short a duration of dosing) may trigger the development of resistance.

Emergence of resistance in *Mycobacterium tuberculosis* may also be triggered by economic factors. Poverty results in noncompliance with the combination treatment regimen; a reduction in the number of combination components results in the emergence of drug and quite often multidrugresistance in *M. tuberculosis*.

The current volume of *Chemotherapy* addresses select topics of antibiotic resistance in *S. pneumoniae*, *S. aureus*, enterococci and *M. tuberculosis*. In particular the epidemiology of resistance is described. The epidemiology of antibiotic resistance illustrates that these are global problems; however, the problems differ from country to country or even from city to city and local problems need local solutions.

The more precise definition of resistance mechanisms should help to select the appropriate antibacterial to tackle the threat.