Resistant organisms: a dilemma for primary care?

ANTIBIOTICS are one of the most important therapeutic discoveries in medicine, but now their benefits are about to be lost through antibiotic resistance. Antibiotic resistance is not new, but what is new is that many more bacteria have developed resistance — and to a larger number of antibiotics. This rapidly developing problem is global and is related to the pattern of antibiotic use. There are significant implications for health and patient care.[1]

Up to now, the effect of resistance has been small. The pharmaceutical industry has either provided alternative antibiotics or developed new ones. The result has been a steady supply of new agents to keep ahead of the problem. But the development of new agents has slowed, with no new antibiotic groups foreseen in the next 10 years.[2] Until recently, bacterial resistance was uncommon, and any resistance was often to only one or two antibiotics. The problem was first seen in the 1950s, with the emergence of Staphylococcus aureus resistance to the penicillin group. Now the frequency of antibiotic-resistant bacteria has increased, and strains have emerged that are resistant to multiple drugs. The development of multiple resistance is worrying, as this broad spectrum can be transferred to non-resistant bacteria. Currently, some bacteria are resistant to 8–10 antibiotic agents.

Already, methicillin-resistant *Staphylococcus aureus* (MRSA) is well known both in hospitals and in the community, causing serious management problems. Patients who have MRSA require special management techniques, particularly in surgical and intensive care wards, and in residential and nursing homes. More recently, penicillin- or erythromycin-resistant pneumococcal strains have rapidly emerged. In addition, the penicillin-resistant pneumococcus has become multi-resistant. In the UK, the pneumococcus problem is still relatively uncommon, but in some countries, such as South Africa and Spain, the problem is so common that it is causing treatment failure on a significant scale. Another worrying trend is the emergence of Group A beta-haemolytic streptococcus resistance to erythromycin. In the past, the problem of amoxycillin-resistant haemophilus was overcome by combining amoxycillin with clavulinic acid (co-amoxiclav), but now resistance has developed. Tuberculosis is another disease for which single drug resistance is increasing, and now a form of tuberculosis (MDR-TB) has appeared in the UK that is resistant to many drugs. There are a number of other examples, including trimethoprim-resistant salmonella. The worst scenario is the development of a super-bug where the bacterium is resistant to all known antibiotics, thus resulting in untreatable infections. If the vancomycin-resistant enterococcus gene passed to the MRSA, the result would be a super-bug.

Increased antibiotic resistance has enormous cost implications for health care. These result from the use of more costly antibiotic agents, the need for additional drug testing and more prolonged hospital stays, and the difficulty in eradicating the antibiotic-resistant bacteria. Additional costs arise from the use of non-antibiotic management, such as isolation techniques. Other effects include the psychological consequences of isolation on the patient, and discrimination against people who are antibiotic-resistance carriers.

While the health systems of developed countries may be able to cover the additional costs associated with antibiotic resistance, those of developing countries are not. With the lack of cheap alternatives, developing countries are likely to continue to misuse antibiotics with known resistance problems. This will compound the problem further.

The resistance gene is normally present in a few bacteria, known as mutant forms. It is the use of antibiotics that causes the selection and propagation of these mutant forms, which can be transmitted from person to person through asymptomatic carriers. The rapid rise in antibiotic resistance is linked not only to the use of antibiotics in medicine, but also to the use of antibiotics for disease prevention and growth promotion in animal husbandry and crop propagation. This prodoces a reservoir of resistant bacteria that can cross animal species to humans. Furthermore, international travel has resulted in a rapid global spread, with travellers to developing countries acquiring resistant strains, e.g. *E. coli.*

In medicine, the size and pattern of antibiotic resistance relates to the use of antibiotics within a country. Even within countries there are wide variations which relate to the local antibiotic density. In the UK, general practice antibiotic prescriptions have increased by 60%, from 896 (1980) to 1453 (1991) per 1000 population, with little change in the prevalence of bacterial infections. The greatest increase has been with the newer antibiotics, which are often those heavily promoted by the pharmaceutical industry.[3] Market penetration of new drugs shows an increase in prescribing, greater than can be accounted for by an increase in patients with specific indications for these drugs. In 1994, the cephalosporins had increased to represent 6% of usage and 19% of antibiotic costs, with the 4-quinolones representing 3% of usage and 11% of costs (Prescription Pricing Authority (UK), personal communication, 1996.

Recently, the use of antibiotic prescribing has been linked to the incidence of meningococcal infections. Erythromycin prescribing was more frequent in towns with a high incidence of meningococcal infections.[4] In another study, antimicrobial use was strongly associated with penicillin-resistant pneumococci in children;[5] these worrying trends require further studies. Antibiotic prescribing often occurs when the bacterial infection doesn't require an antibiotic or when the infection is not bacterial. Even when used correctly the antibiotic selection, duration, and dose of treatment may be inappropriate. The outcome is that many patients are exposed to repeated courses of antibiotics, which subsequently results in a high local antibiotic density. Patients' attitudes and beliefs are important influences on the doctor's decision to prescribe antibiotics. Patients often use a medical model to approach illness, believing that medicine has the cure for illness. They expect antibiotics for all infections. In developing countries there are even fewer controls, owing to the open availability of antibiotics through pharmacies and the widespread use of combination drugs.

The Alliance for the Prudent Use of Antibiotics' (PO Box 1372, Boston, MA02117, USA) is a voluntary organization set up to advise on the preservation and protection of the use of antibiotics. However, action is required at an international level, with governments regulating the control of antibiotic use. A contentious issue is global travel. With increasing global travel rapidly spreading the resistant organisms, there may need to be immigration testing to identify carriers of the mutant forms.

Strategies are needed that involve both the rational use of antibiotics and the control of infection. This means antibiotic and infection control policies, strong educational initiatives, and sur-

veillance of bacterial infections. An effective surveillance system is essential to identify the threat from the changing bacterial resistance patterns, and to identify the geographical variations. Once the threat has been identified, intervention strategies can be planned to reduce the emergence and spread of antibiotic resistance.

General practice will need to control the use of antibiotics. This can be done by giving shorter courses at the right dose, restricting their use to specific indications, and rotating the antibiotic when resistance occurs. Practice antibiotic policies, consisting of a formulary and guidelines on treatment, will be necessary to achieve this. The development of diagnostic tests to rapidly identify bacterial infections will greatly help the sometimes difficult decision to prescribe and target the choice of antibiotic. Educational programmes have already shown that antibiotic misuse can be reduced and the changes in prescribing sustained. In addition, prescribing protocols, adapted to the locality pattern of bacterial resistance, and community-surveillance policies are needed, with adherence to them supported by education and training.

If antibiotic misuse continues, the problem of resistant bacterial infections will become increasingly common. Ethical prescribing is essential to prevent the loss of one of the most important therapeutic discoveries in medicine. How long will it be before a super-bug emerges that is resistant to all known antibiotics?

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