Lung & Asthma Information Agency

Antibiotic resistant organisms in respiratory disease

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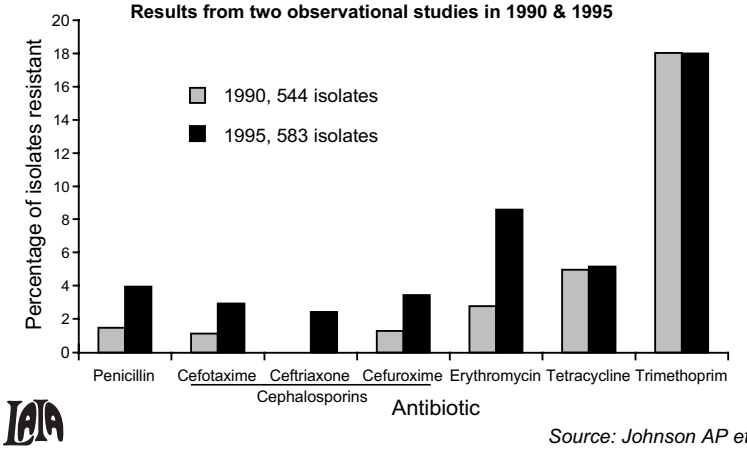
Introduction

Antibiotic resistance is an important consideration when treating bacterial infections and there is some evidence that resistance is becoming more widespread. Bacterial antibiotic resistance can either be intrinsic or acquired. For example, some bacterial species, such as Mycoplasmas, are intrinsically not sensitive to penicillin. The second phenomenon, where a normally sensitive organism acquires resistance for some reason, has long been recognised. However, the acquisition and rapid spread of resistance to commonly used antibiotics in common respiratory pathogens has become a widespread problem in recent years. There are three main settings where this phenomenon has been observed (figure 1).

Figure 1: The main types of antibiotic resistant bacteria.

Setting	Organism	Antibiotics
The community and especially in HIV infection	Mycobacterium tuberculosis	All first line agents
The community	Streptococcus pneumoniae	ß-lactams e.g. Penicillins Cephalosporins Macrolides e.g. Erythromycin
	Haemophilus influenzae	Aminopenicillins
Hospitals, especially intensive care units	Staphylococcus aureus Enterococci	Methicillin Vancomycin

Figure 2: Trends in the prevalence of antibiotic resistance of pneumococci in England and Wales.



Source: Johnson AP et al

Epidemiology

Streptococcus pneumoniae and *Haemophilus influenzae* are the two most important bacterial causes of respiratory infection. Penicillins and macrolides are the antibiotics most commonly used to treat such infections.

S. pneumoniae

Penicillin resistance in *S. pneumoniae* was first observed in New Guinea in 1967 and was subsequently found to be common in South Africa and Spain. It is now a global phenomenon and all countries which have been monitoring *S. pneumoniae* resistance have found a steady rise in its frequency. In the UK, levels of such resistance have generally been lower than in most other countries, but even here this is increasing (figure 2). Penicillin resistant pneumococci (PRP) are found more commonly in children and in hospital-acquired infections. Macrolide resistance in *S. pneumoniae* has received less attention than penicillin resistance but also appears to be increasing and in the UK is over twice as common as penicillin resistance.

H. influenzae

Aminopenicillin resistance in *H. influenzae* is also rising and shows wide geographic variation. One study showed resistance rates of 6.3% in Germany, 9.7% in the UK, 19.3% in France and 32.2% in Spain.

Causation

The root cause of acquired resistance is exposure to antibiotics and figures three and four show how use of most antibiotics is steadily rising. About half of all antibiotic use is in veterinary work. By suppressing the growth of sensitive strains, antibiotic use favours the development of a resistant strain which may then

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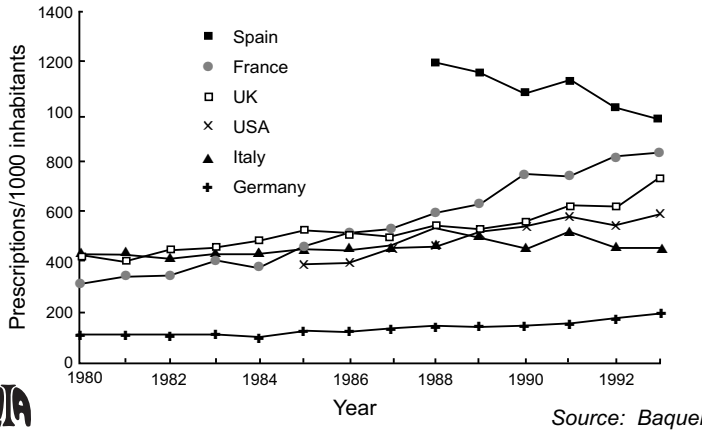
spread between individuals, from country to country and continent to continent by commensal organisms, as has been clearly documented for penicillin resistant pneumococci.

The actual mechanism of resistance varies from antibiotic to antibiotic and organism to organism. For example, penicillin resistance in pneumococci occurs through changes in the penicillin binding proteins in the cell wall. In contrast, aminopenicillin resistance in *H. influenzae* is predominantly caused by ß-lactamase production.

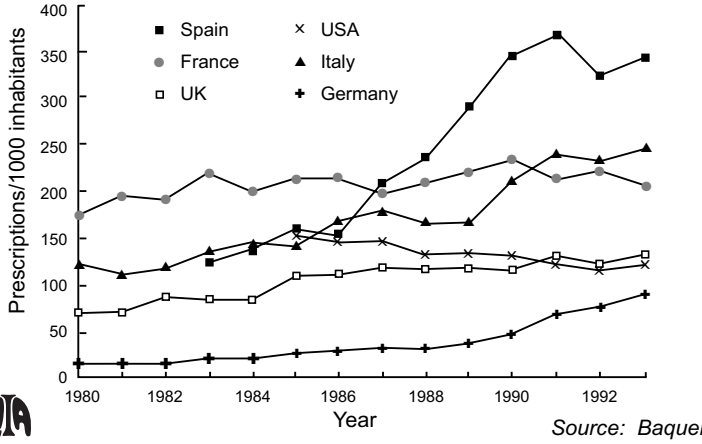
Figure 3: Annual ß-lactam prescriptions per 1000 inhabitants in six countries.



Clinical relevance

Penicillin resistance is a graded phenomenon and the effectiveness of an antibiotic depends on the concentration at the site of the bacteria being above the level which inhibits bacterial growth. This means that an alternative antibiotic will be required for organisms with borderline resistance isolated from a site where penicillins penetrate poorly, such as the central nervous system. For the same organism at a site where penicillins penetrate well, such as the lung, penicillins can still be effective.

Figure 4: Annual macrolide prescriptions per 1000 inhabitants in six countries.



Most PRP isolates are of only intermediate resistance, and so penicillins in high dose are still effective treatment in most pneumococcal respiratory infections. Little clinical experience has been gained with highly resistant PRP, but it is likely that alternative antibiotics should be used in these cases.

Macrolide resistant pneumococci should not be treated with erythromycin. It is not known whether the newer macrolides, which have better tissue penetration, remain effective. Aminopenicillin resistant *H. influenzae* should be treated with alternative antibiotics.

Since most patients are treated without knowledge of the causative pathogen, let alone its antibiotic sensitivities, information on the prevalence of resistance in the local population is important for guiding empirical therapy. While it is not clear at what level changes should be made, continued surveillance is an important tool in the management of the problem and the patient.

We are grateful to Dr Mark Woodhead for preparing this factsheet.

The data presented in figure two are taken from Johnson AP, Speller DCE et al, *Br Med J* 1996;**312**:1454-6.
Figures three and four are taken from Baquero F, *J Antimicrob Chemother* 1996;**38**,Suppl A:117-32
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