balanced microbiology of the pre-antibiotic era—that is, one populated by a predominantly susceptible flora.

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Control of antimicrobial resistance: time for action

The essentials of control are already well known

Until recently the medical community world wide has seemed incapable of reacting to the imminent crisis of antibiotic resistance. Several explanations exist for this lack of action, including the complex interaction between doctors, patients, and parents over antibiotic use[1 2] and the fact that the pharmaceutical industry has so far succeeded in developing new antibiotics when resistance to existing ones has emerged. Although we still need a better understanding of the factors involved in the emergence and spread of antibiotic resistance, action cannot wait until all the answers are available. The essentials of better control of antibiotic resistance are already well known.

Surveillance of bacterial resistance is a key element in understanding the size of the problem. The large number of existing networks for resistance surveillance need to be coordinated and the results made available.[3] To help doctors choose appropriate antibiotics and to detect local epidemics of resistant bacteria surveillance at local level is necessary. Good quality local data provide a basis for national and international surveillance.

There are two ways of fighting the development and spread of resistant bacteria. The first is to reduce the use of antimicrobial agents to decrease selection of resistant bacteria. About 85-90% of antibacterial drugs are used in the community, and up to 80% of these are used to treat respiratory tract infections. Thus, major efforts have to be targeted on diagnosis and treatment of respiratory tract infections in the community.[4 5] Sales of antibiotics over the counter should be stopped. Statistics on the use of antimicrobial agents (including sales over the counter) are of key importance for changing prescription patterns but at present are available only in some countries. We also need to know the patterns of prescription of antibacterial agents in different infections to identify where clinical practice needs to be improved.[4]

To reduce antibiotic consumption we need a multifaceted approach that includes education of doctors; widely accepted recommendations for good clinical diagnosis and treatment; and follow up of compliance with such guidelines. Evidence exists that changing the way general practitioners are paid can change their prescribing behaviour.[6] Measures to improve the public's knowledge about the risks and benefits of antimicrobial therapy are also important. A free return visit for patients not prescribed antibiotics at the first consultation for a respiratory tract infection has been used as one way of changing patients' expectations.[7] Restriction policies such as the requirement for written justification or automatic stop orders may be useful in hospital settings. Integrated strategies have reduced antibiotic use or curtailed antimicrobial resistance.[7–10]

The second major way to tackle resistance is by improving hygienic measures to prevent the spread of resistant bacteria. Only 40-50 years ago hygienic measures were the most important means of preventing the spread of transmissible diseases. Indeed, during this century Western societies have been transformed by major investments in preventing the spread of pathogenic bacteria: tap water and sewerage, as well as our kitchens with all their equipment. The question is simple: how much are we ready to pay to prevent the spread of resistant bacteria?

In hospitals effective prevention of cross infection and the development of strict antibiotic policies should be in the hands of experts.[11] Each hospital thus needs an infection control team with infectious disease specialists, clinical microbiologists, and infection control nurses and sufficient resources and a mandate to run the programme. One urgent practical question is how to raise the standard of hand hygiene in hospitals: at best hand disinfection is achieved on fewer than half the occasions it is required.[12]

Research is also a cornerstone in the fight against bacterial resistance. We have to improve our understanding of bacterial flora, the evolution of resistance, and the mechanisms of transmissibility of resistant bacteria. New diagnostic technologies to enable rapid identification of viral and bacterial infections are also necessary: for too long it has been easier for clinicians to prescribe an antibiotic than to make a specific diagnosis.

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Surveillance of antimicrobial resistance

Centralised surveys to validate routine data offer a practical approach

Antibiotic resistance is increasing and significant public health problems are feared. Actions to mitigate the problem include development of new antimicrobials, better infection control, and greater conservation of existing agents. One pressing problem is the paucity of data to measure the impact of resistance on public health or the effect of interventions to prevent its emergence and spread. Moreover, other factors besides clinical prescribing may drive resistance—failure of infection control; institutionalisation of care for the very young and elderly; changing population age structures; agricultural use of antibiotics; and the spread of strains that are effective colonists and which, coincidentally, are resistant.[1] Better surveillance of resistance is needed to understand this interplay as well as to advise on empirical therapy.[2 3] Once relations between use and resistance have been established surveillance data then can serve as "information for action" for initiatives to decrease unnecessary prescribing and prolong the usefulness of existing antibiotics.

Establishing such surveillance presents several problems.[2 3] It is easiest to count resistance rates of bacteria received at laboratories, but these organisms form a biased sample because *(a)* laboratory requesting varies greatly among clinicians; *(b)* some diseases (such as chronic obstructive airways disease) are more likely to generate laboratory specimens than others (such as pneumonia); *(c)* some age groups, particularly the elderly, are more likely to have specimens taken than others; and *(d)* primary care specimens are usually sent only from patients who have failed to respond to empirical treatment or who have comorbidities. Ideally resistance should have a clinical denominator (number of infected patients) not a laboratory one (number of isolates), but this is not easy except in uncommon diseases such as tuberculosis in the United Kingdom.[4]

If surveillance is based on isolates submitted to laboratories either routine susceptibility results can be collected or the isolates can be sent to a central laboratory for testing. Using routine results exploits data that exist already in sufficient quantities for relation to prescribing and population denominators.[3] However, the quality of these data is patchy if, as in Britain, laboratories use different methods and do not routinely speciate many fermentative Gram negative bacilli. Few antibiotics are tested against all isolates, and "second line" antibiotics are tested only against those with an index resistance, giving a very biased sample. Finally, unless the data are analysed with respect to antibiogram phenotypes, anomalies and new mechanisms cannot reliably be recognised.

Centralised testing, or testing to an agreed protocol by sentinel laboratories, allows standardised methods and measurement of levels of resistance. It also allows early detection of those resistances that accrue and can be linked to molecular studies to identify resistance mechanisms and monitor the spread of their encoding genes. However, centralised testing is limited by throughput and the sentinels may form a biased sample.

Both routine data gathering and centralised surveys are undertaken. Programmes using routine data include MicobeBase in Britain[5]; monitoring of blood and cerebrospinal fluid isolates in England and Wales by the Public Health Laboratory Service (PHLS)[6]; and a commercial system, the Surveillance Network.[7] The European antimicrobial resistance surveillance system (see box) aims to follow a similar strategy, collecting high quality routine data for subsets of isolates. International surveys with centralised testing include the Alexander project for respiratory pathogens[8] and SENTRY,[9] which examines blood culture isolates—chosen because they are of clear clinical importance. Many smaller centralised surveys are undertaken on particular pathogen groups or countries, mostly sponsored by the pharmaceutical industry.

What has been lacking is cross testing of the data gathered by different approaches and relating it to prescribing data. Such cross validation is an attractive strategy for comprehensive surveillance: if centralised surveys with high quality microbiology confirm the trends in routine data then greater confidence can be placed in these routine datasets, which are sufficiently large for relating to prescribing data.

A surveillance programme for Britain and Ireland is being established on this rationale by the PHLS, Scottish and Irish colleagues, and the British Society for Antimicrobial Chemotherapy. The PHLS antimicrobial susceptibility surveillance unit will analyse routine susceptibility data from as many hospitals as possible to relate to population and prescribing denominators. The quality of these data should improve as Britain adopts standardised susceptibility testing,

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