

11 AREAS OF CLINICAL PRACTICE WHERE ANTIMICROBIAL RESISTANCE HAS, OR IS LIKELY TO HAVE, THE GREATEST IMPACT

KEY POINTS

- Resistance is greatest where antimicrobial use is heaviest
- Major problem areas in hospitals include ICUs, transplant units
- Key patient groups include the immunocompromised
- Resistance is also rising in common community pathogens

Resistance is most frequent where there are large numbers of susceptible patients. These are also the situations where antimicrobial chemotherapy is most essential. Nevertheless, the consequences of resistance are not restricted to specialised units but are also seen in general in-patients and in the community.

INTENSIVE CARE UNITS

Resistance is most common in patients receiving mechanical ventilation and in university or teaching hospitals. Intensive care and similar units present special problems. Ventilator-associated pneumonia due to antimicrobial-resistant bacteria often follows prior antimicrobial exposure and is a particularly important problem.

Heavy antimicrobial use probably lies behind the high rates of antimicrobial resistance in ICUs. Furthermore, ICU patients often require invasive support activities which increase the risk of infection, demanding more antimicrobial treatment and exacerbating the risk of selecting resistance.

ADMISSIONS WARDS

Over the last decade there has been a 50% increase in emergency admissions to general hospitals in the UK. General hospitals increasingly accept emergency patients on an admissions ward, where a pre-registration house physician makes a diagnosis, orders investigations, and prescribes treatment. Most of these patients have 'medical' rather than surgical problems and so are admitted under physicians.

Infection is often considered, but may be difficult to diagnose. The diagnosis of infection relies on microbiological investigation. Meanwhile the junior doctor has to decide whether to prescribe empirically. This provides many opportunities for inappropriate or unnecessary antimicrobial prescribing.

IMMUNOCOMPROMISE

Immunocompromised patients may present with difficult-to-diagnose or occult infections. They are vulnerable to a wide range of opportunist infections and often require urgent empirical treatment, without the opportunity to take appropriate microbiological samples. Broad-spectrum antibiotics are used, selecting for broad resistance.

12 WHAT PRACTICES BY CLINICIANS AND THE PUBLIC PREDISPOSE TO THE DEVELOPMENT OF ANTIMICROBIAL RESISTANCE?

KEY POINTS

- Some antimicrobials are more selective than others for resistance
- Selection varies with the dosage and duration of therapy
- Unnecessary antimicrobial use selects resistance without any gain
- Unnecessary use includes over-long prophylaxis and therapy of infections that are trivial, self-limiting, or viral
- Public expectations of 'A pill for every ill' encourage over-prescribing

Spread of resistant bacteria is aided by:

- i) crowding of children and the elderly
- ii) increased travel
- iii) increased 'bed-efficiency' in hospitals
- iv) increased hospital throughput
- v) antimicrobial use

Health care practitioners and the public both carry a responsibility. Claims that the *entire* responsibility lies elsewhere – with veterinary antimicrobial use – do not withstand scrutiny, since resistance is widespread to antimicrobials used only in man.

This is not to absolve veterinary use – it is a major driver of resistance among enteric pathogens and, maybe, enterococci – but it is important to stress that the *whole* responsibility cannot be passed to another group.

Ultimately, resistance is an inevitable consequence of use, as micro-organisms are selected in an environment of antimicrobials. Nevertheless the practices of prescribers and consumers affect the rate of this evolution. Key factors are:

ANTIMICROBIAL USED

Some antimicrobials are more prone to select resistance than others, either by encouraging overgrowth of an undesirable flora (eg yeasts or *Clostridium difficile*) or by favouring resistant mutants within the original infection.

Oral cephalosporins and clindamycin are both associated with selection of *Clostridium difficile*; fusidic acid and rifampicin notoriously select resistant mutants in their target species, as do cephalosporins with *Enterobacter* and *Citrobacter* spp.

REGIMEN

Dosage and duration of therapy are key factors in modulating selection pressure. Regimens vary greatly from hospital to hospital and practice to practice, often with no underlying rationale. A review of prescribing guidelines showed that simple information such as dose, frequency and total length of course was often missing.

BOX 9. ANTIMICROBIAL GUIDELINES SHOULD:

- be evidence-based
- be dated
- contain information on the antimicrobial, dose, frequency and length of course
- indicate the strength of the evidence for the recommendation
- show local variation from national recommendations

Necessary antimicrobial use – whether prophylactic, empirical or therapeutic – exerts selection for resistance. The question is always whether the gain outweighs the risk; whether the choice of antimicrobial maximises the benefit and minimises the risk. Unnecessary use exerts selection pressure with no gain.

PRESCRIBING UNNECESSARILY OR INAPPROPRIATELY

Antimicrobials are prescribed unnecessarily and empirically for trivial complaints where no treatment is necessary, or where culture and sensitivity

results could safely be awaited. The use of empirical antimicrobials in community upper respiratory tract infections is a key concern, since 50% of clinical antimicrobial usage is for infections at this site and 70% of infections are viral.

A survey of 21,400 patient encounters revealed that over 80% of patients were prescribed an antimicrobial for upper RTI, including 70–80% not actually seen by the doctor. Even where the diagnosis was coryza (common cold), 42% of patients were prescribed an antimicrobial.

PROPHYLAXIS

Prophylactic antimicrobial use, ie use to prevent infection, carries a selection risk, whether the use is warranted or not. This risk is increased where the prophylaxis is prolonged. In most cases effective surgical prophylaxis can be achieved with one or two doses at operation, yet prophylaxis is sometimes continued for several days, without any evidence of need.

EMPIRICAL THERAPY

Empirical antibacterial therapy should be given when bacterial infection is suspected, *and poses a sufficient health risk to demand immediate treatment*. Clear examples include fever of unknown origin in neutropenic patients, pneumonia, meningitis and tuberculosis.

In reality, empirical therapy is used far more widely. In community practice, microbiological examination of specimens is rarely undertaken before initiating therapy and, in hospitals, therapy that begins empirically remains so owing to difficulty in obtaining a specimen or disinclination to do so.

The specific problems with empirical therapy are:

- it is often given to patients who do not have bacterial infections;
- inappropriate antimicrobials may be selected;
- it is common to use broad-spectrum agents or combinations.

Where warranted, empirical regimens should be based on knowledge of the likely pathogens and their antimicrobial susceptibilities. This depends on access to good LOCAL surveillance data.

PUBLIC BEHAVIOUR AND SOCIAL CHANGE

Public behaviour and changing lifestyles impact on the resistance problem. Excessive prescribing of antimicrobials for trivial and non-bacterial infections in primary care partly reflects 'consumer' pressure. Patients should be encouraged to take control of their own health care but, without appropriate advice, this may lead to increased demand for inappropriate treatment such as antimicrobials for 'colds', 'flu' or sore throats. Failure to prescribe may lead to dissatisfaction, yet this usage augments the overall selection for resistance.

GPs can over-estimate patients' expectations. In one study, a quarter of patients received antimicrobials when they stated that, before the consultation, they had not wanted antimicrobials.

TRAVEL

Many countries have greater rates of antimicrobial resistance than the UK. These may reflect greater prescribing, poorer control of infection and over-the-counter availability of antimicrobials. Laws on patents and pharmaceutical quality are absent or not enforced in some developing countries, where antimicrobial agents are often sold by the single tablet, leading to frequent underdosage.

The UK is not isolated from these problems. Resistant bacteria may enter with visitors or returning travellers, or be imported by those who come for medical treatment.

LONG-TERM CARE FACILITIES

Increasing numbers of elderly people – often in poor health – live in nursing homes and other long-term care facilities (LTCFs). The role of these as reservoirs for resistant bacteria is an increasing concern, with MRSA the main problem organism.

Elderly patients increasingly are shuttled between LTCFs and hospitals, with the risk of MRSA being transferred and of its spreading within LTCFs, where control-of-infection measures are mostly minimal.

DAY-CARE FACILITIES

Crowded day-care facilities for children facilitate the spread of colonisation and infection. The role of modern child-care systems, combined with international travel, is illustrated by the spread of multidrug-resistant pneumococci in Iceland. From 1989 to 1993, the incidence of penicillin-resistant

pneumococci rose swiftly, from being virtually unknown to 20% of all pneumococci isolated. This reflected the spread of a resistant strain previously prevalent in Spain. It seems that children were colonised by the strain whilst on holiday and that it then spread among them in child-care facilities, which most attend.

VETERINARY ANTIMICROBIAL USE AND THE EMERGENCE OF RESISTANCE

Disease is inevitable in farm and companion animals. Moreover, healthy animals can be carriers and asymptomatic excretors of pathogens. Antimicrobial resistance rates vary with the animal species, the type of husbandry, environmental pressure, the standard of stockmanship and the patterns in trade. Antimicrobial use in animals has been proposed as a factor in the emergence of resistance in human pathogens.

Resistant bacteria selected in animals may be transferred to man via the food chain, or may transfer their resistance genes to human pathogens.

TYPES OF ANTIMICROBIAL USAGE IN ANIMALS

The main reasons for antimicrobial use in animals are therapy, prophylaxis and, in farm animals only, performance enhancement (growth promotion).

Therapy involves individual animals or defined groups with identified disease. Its justification is not difficult; disease can cause death or morbidity.

Prophylaxis aims to contain the spread of infection in herds or flocks. Following diagnosis of illness in one or more of the members of a herd or flock, the whole herd may be treated to prevent spread.

Performance enhancement (growth promoting) is the most contentious usage. Antimicrobials improve the productivity of healthy animals by increasing growth rate, feed conversion or yield. They are given continuously at sub-therapeutic doses, usually as feed additives or, occasionally, by addition to the drinking water.

Antimicrobials that are used in man cannot be used as growth promoters in the UK. Nevertheless there is concern that:

- growth promoters may select cross-resistance to antibiotics used in man
- antibiotics for human use are now being sought among classes previously used only as growth promoters; it is feared that the prior use of the agents as growth promoters may have undermined their activity even before they become available for human use.

These concerns are echoed world-wide: in 1994 the WHO Scientific Working Group on the Monitoring and Management of Bacterial Resistance to Antimicrobial Agents recommended that the unnecessary antimicrobial use for prophylaxis in food animals should be discouraged, and that antimicrobials should not be used as a substitute for adequate hygiene in animal husbandry.

To this we would add the desirability of phasing out use as growth promoters.

KEY POINTS

- Without a guarantee of new antimicrobials, conservation of present agents is desirable
- Careful antimicrobial use should slow the emergence of new resistance
- Reduced use may – but cannot be guaranteed to – reduce present resistance
- Prevention of spread of resistant strains is also critical, especially for MRSA

SHOULD RESISTANCE DECLINE IF ANTIMICROBIAL USE IS RESTRICTED?

Whilst the relationship between antimicrobial use and the emergence of resistance is clear, if circumstantial, its corollary – that resistance should decline if use is restricted – is much less certain. Studies of disused antimicrobials are useful since they examine agents where direct selection is no longer significant and where no active steps are being taken to reduce resistance. Neither streptomycin nor chloramphenicol has been used against Enterobacteriaceae for over 25 years. Yet, a recent survey in London found that 20% of *Escherichia coli* isolates remained resistant to streptomycin and chloramphenicol resistance occurred in 5–10% of isolates. These studies show how difficult it is to displace accumulated resistance.

DO GOOD PRESCRIBING PRACTICES PREVENT OR SLOW DEVELOPMENT OF RESISTANCE?

Intensive control or monitoring of prescribing has been accompanied by an increase in susceptibility in a few institutions. Co-operative multicentre studies are needed to assess fully the value of control measures.

One investigation from Finland has caused much comment. An increase

was noted in resistance to macrolides amongst *Streptococcus pyogenes* isolates in Finland through the late 1980s and early 1990s. Nationwide recommendations calling for a reduction in macrolide use were introduced. Macrolide prescriptions and the incidence of erythromycin resistance among *Streptococcus pyogenes* isolates halved over the next 3 years. A causal relationship was assumed, but this is arguable, not least because the incidence of macrolide resistance increased in pneumococci in the same period.

Although reducing antimicrobial use may not reduce rates of resistance, it should limit the rate at which new resistance accumulates, and this may be critical.

14 DEVELOPMENT OF NEW ANTIMICROBIAL AGENTS

KEY POINTS

- Antimicrobial research is more efficient than previously
- New antimicrobials are under development, but success cannot be guaranteed
- Development cost is high (£350 m) and patent life brief (17 years)
- Anti-infectives are not amongst the most profitable pharmaceuticals
- Vaccines may be an answer to pneumococci, but little advance against other key pathogens
- Little progress achieved in developing non-antimicrobial treatments of infection

NEW STRATEGIES IN ANTIMICROBIAL DEVELOPMENT

Despite the recent dearth of new antimicrobials there are several promising factors for antimicrobial development, on a 10-year view:

- the new science of 'genomics' may yield new families of antimicrobials
- methods of synthesising new candidate drugs have become vastly more efficient
- methods of screening antimicrobial activity have been improved

These strategies may (although this is not certain) yield whole new families of antimicrobials towards the end of the next decade.

However, even if this optimism is warranted, there will be a window with resistance accumulating and a dearth of new antimicrobials. Furthermore, it is virtually certain that resistance will develop to any new compounds, therefore good prescribing habits will help preserve their value when they appear.

15 PROMOTING GOOD PRACTICE

KEY POINTS

We need:

- **Faster diagnosis to allow identification of those patients needing antimicrobial therapy**
- **Faster susceptibility testing to allow better-tailored therapy**
- **Guidelines for therapy of common infections**
- **Computer-assisted antimicrobial prescribing**
- **Better surveillance as background to empirical therapy and to monitor effects of interventions to alter antimicrobial usage patterns**
- **Better communication of resistance surveillance data to GPs and in hospitals**
- **Better control of infection to stop spread of resistant bacteria**
- **Education of prescribers, health care staff and consumers**
- **Greater public awareness of antimicrobial resistance**
- **A higher profile for research on the epidemiology and bases of resistance**

From the preceding sections of this synopsis, it is clear that:

- Resistance is increasing to many antimicrobials and in many species
- We face the prospect of having no useful antimicrobials for some infections
- Development of new antimicrobials is in progress, but will take time and success cannot be guaranteed
- Careful antimicrobial use, and prevention of cross-infection, can minimise the emergence and accumulation of resistance
- Once resistance has accumulated, it cannot readily be displaced

The recommendations that we make are based on these premises.

KEY POINTS

Improved prescribing can be encouraged by:

- evidence-based guidelines for prescribing (or not prescribing)
- computer-assisted systems to aid antimicrobial choice and to help the physician and patient avoid an antimicrobial when it is not needed
- swifter microbiological diagnosis to minimise inappropriate therapy

BOX 10. BETTER PRESCRIBING

- Stop unnecessary antimicrobial use
eg viral upper respiratory tract infection
- Shorten unnecessarily long courses
eg cystitis; surgical prophylaxis
- Avoid inappropriate broad-spectrum antibiotics
eg ciprofloxacin for URTI
- Avoid inappropriate repeat prescriptions without microbiological confirmation
eg repeat courses
- Further research into inappropriate prescribing

GUIDELINES FOR ANTIMICROBIAL USE

The huge variation and incompleteness of current prescribing guidelines in many centres has already been noted. Evidence-based guidelines are urgently needed for antimicrobial use, particularly for the treatment of common conditions in the community. Local guidelines should take their cue from these national guidelines to avoid re-invention of the wheel.

Guidelines should be sufficiently flexible to accommodate regional and local differences in the prevalence of antimicrobial resistance, especially in hospitals. Such differences would be informed by an antimicrobial resistance surveillance programme.

It is not suggested that there should, say, be a 'national standard regimen for UTI'; rather, *that there should be a series of potential regimens, designed to optimise success and minimise the emergence of resistance, with the choice between these based on local circumstances.*

COMPUTER-ASSISTED PRESCRIBING (or non-prescribing!)

Improved prescribing can potentially be encouraged by computer-based advisory systems.

Systems are being developed, piloted and used. They are designed to enable clinicians to augment their clinical decision-making skills rather than to replace or control them and to use locally derived data (with respect to the epidemiology of resistance) to guide the selection of drugs.

Potential for the use of such systems exists in primary care, where there is likely to be less local variation in pathogen prevalence and resistance, as well as in hospitals. Use of these systems deserves urgent investigation.

Prescribing guidelines should be incorporated into the computer-aided decision-support systems, improving their availability and implementation. If the computer systems can be made relevant to both the prescriber and the patient this will assist in their interaction and help the prescriber to explain why a prescription may not be necessary.

IMPROVING EMPIRICAL THERAPY THROUGH SWIFTER DIAGNOSIS

Empirical therapy is often given when only a few patients – the minority with bacterial infections – are likely to benefit.

Simple pathogen detection tests can be introduced into GPs' surgeries and are valuable if they give an instant result, identifying those who may benefit from antimicrobial therapy. Examples include dipsticks and leucocyte esterase tests to identify UTI. A rapid antigen-detection test for *Streptococcus pyogenes* led to a reduction in the proportion of culture-negative patients with sore throats who were given antimicrobials from 53% to 32%. The savings on antimicrobial costs offset the costs of the tests, irrespective of any long-term gain achieved by reducing antimicrobial usage.

ROLE OF THE MEDICAL MICROBIOLOGIST

All major acute hospitals in the UK are served by departments of medical microbiology, under the direction of a medically qualified consultant microbiologist. Most medical microbiologists have close links with their hospital and GP colleagues and collect information on the susceptibility patterns of their local bacterial isolates. Many departments provide prescribing information for use in hospitals and general practice, based upon these local patterns.

The local medical microbiology department also can offer advice on infection control matters. As GPs undertake increasing numbers of procedures in their surgeries, it is especially important to ensure that responsible and thorough infection control advice is provided.

The diagnostic facilities of the local laboratory can assist in the rational choice of antimicrobials by advising on the submission of specimens. Some laboratories have guidelines as to whether, for example, sputum should be examined from all patients who have a respiratory tract infection, or only those patients in whom previous therapy has failed.

It is vital that hospital doctors and GPs form strong links with their medical microbiology colleagues in the battle against antimicrobial resistance, with the aim of optimising prescribing patterns.

IMPROVING MEDICAL EDUCATION

Education on antimicrobials and resistance often takes place in the early pre-clinical years of medical and dental training and is divorced from clinical situations where students are exposed to prescribing decisions. There is a paucity of experts available to teach antimicrobial prescribing in the context of clinical medicine and microbiology and this is less than ideal. Greater exposure of medical and dental students, house staff and postgraduates in all specialities to the issues of antimicrobial prescribing, and the threat posed by antimicrobial resistance, is desirable.

COMMUNICATION

Data on local rates of pathogen prevalence and resistance are often poorly disseminated from the laboratory to physicians, both within hospitals and in the community. This information should be the key to the choice of therapy and better communication is essential.

ROLE OF HEALTH CARE PROFESSIONALS, OTHER THAN MEDICAL PRESCRIBERS

Although doctors are responsible for most antimicrobial prescribing, other professionals also have a role. The roles of dentists, nurses and pharmacists are described below. In hospitals and community care facilities ALL staff have a role in controlling cleanliness and hygiene, which impact hugely on the transmission of infection and on the need for antimicrobial chemotherapy.

DENTISTS

Dentists are prescribers, albeit for only a small fraction of total antimicrobial usage. Dental practice is significant for certain antimicrobials which dentists prescribe frequently, eg metronidazole.

NURSES

Nurses should be familiar with prescribing protocols so that they can alert doctors, when for example, antimicrobials are being prescribed for excessively long periods. Nurses help patients to understand the nature of their illness and the actions and side-effects of medications. They are in an excellent position to maximise concordance and to educate patients. They may be able to identify those individuals and families in whom concordance is likely to be a problem and where single-dose therapy is desirable if available.

Most of all, nurses have a key role in the prevention and control of infection, especially in hospitals.

PHARMACISTS

The pharmacist is frequently the point of contact for the patient when a prescription is collected and thus can help educate the public about concordance. Within the community, the role of the pharmacist in providing services to nursing homes is developing, and is one where pharmacists could

have an important role in influencing change in the prescribing of antimicrobials.

Hospital pharmacists are involved in a number of key areas. They are well qualified to advise prescribers on choice and change of agent as well as suitable routes and durations of therapy. Pharmacists commonly have an input into the education of junior hospital doctors about prescribing. They may also be able to help in the enforcement of prescribing policies.

VETERINARY SURGEONS

Veterinary surgeons have a responsibility to use antimicrobials prudently. We recommend that the use of antimicrobials in veterinary practice should be guided by the same principles as in human prescribing – viz antimicrobials should be used only where their use is likely to yield a specific health benefit.

PUBLIC EXPECTATIONS AND ATTITUDES TO ANTIMICROBIALS

Over-prescribing of antimicrobials partly reflects public expectation. If campaigns to reduce prescribing are aimed only at health care professionals, then these professionals will be left facing dissatisfied patients or carers, not all of whom take refusal to prescribe kindly.

We therefore propose a **National Advice to the Public (NAP)** campaign, to run concurrently with the efforts to reduce and rationalise prescribing. Since most inappropriate community use of antimicrobials is for upper RTI, this usage should be targeted, with key messages that:

Patients should not expect antimicrobials for trivial infections

GPs may give post-dated prescriptions when the need for an antimicrobial is doubtful

Antimicrobials are magic bullets – invaluable – but not to be taken lightly

Taking antimicrobials unnecessarily does you no good and damages them for everyone else

For serious infections – eg meningitis – swift antimicrobial therapy is essential

Various ways of communicating these messages could be envisaged, from simple slogan-based advertising:

**‘Antimicrobials cure serious diseases
– not colds, coughs and wheezes...
Save them for when it’s important’**

through billboard advertising, and on to patient information leaflets such as those produced in America by the Alliance for the Prudent Use of Antibiotics.

These messages should also be communicated in schools, with information on antimicrobials included in health education, maybe as part of the National Curriculum. It is highly desirable that children are taught the difference between bacteria, which antibiotics kill, and viruses, which they do not kill. The failure of many adults, and of the national press, to make this distinction is an obstacle to understanding the problem of resistance.

Those who design school curricula should consider including antimicrobial resistance as an eloquent demonstration of evolution in action – and of evolution with very direct consequences for mankind.

CHERISHING YOUR FLORA – THE BENEFICIAL NATURE OF BACTERIA

The normal human microflora comprises more bacteria than there have ever been people upon the planet. The microflora has a role in the metabolism of nutrients, vitamins, drugs, endogenous hormones and carcinogens. This role is poorly understood, but probably largely beneficial. Furthermore, the microflora is probably protective against invasion by pathogens.

Unnecessary insults to the normal microflora through the injudicious use of antibiotics can lead to adverse health outcomes. These may be transient and self-limiting, such as the diarrhoea that may accompany a course of antibiotics, but more serious problems may also arise (eg pseudomembranous colitis).

The role of our normal resident microflora is now beginning to be understood, and with understanding comes a realisation that we should be ‘cherishing our normal bacterial flora’.

To measure the public health impact of antimicrobial resistance and of interventions to minimise antimicrobial usage, requires close surveillance. The PHLS, in liaison with the British Society for Antimicrobial Chemotherapy and other interested parties, is developing a multi-faceted national surveillance scheme.

It is critical that this receives support, both financially and in terms of encouragement to laboratories to participate.

Alert organism reporting and reference laboratory activities will identify unusual resistances deserving priority work, but will provide minimal denominator data. Sentinel laboratory surveys and those where isolates are collected centrally will provide high quality microbiology and quantitative measurement of levels of resistance, but with small sample sizes. Collection of routine data will provide mass information, suitable for relation to prescribing and population denominators, but will be based on routine susceptibility tests, which are poorly standardised in the UK.

Collectively, however, these activities will validate each other to give a comprehensive picture. The sentinel laboratory and *ad hoc* studies will test the quality of the routine data, whilst the appearance of trends (or unexpected results) in the routine data will advise the choice of organisms demanding enhanced surveillance.

18 RESEARCH ON RESISTANCE AND ON NEW ANTIMICROBIALS

KEY POINTS

- Research on resistance has been unfashionable and underfunded
- Research is key to the development of new antimicrobials
- Research is key to understanding how to preserve the value of current antimicrobials

Whilst the problem of resistance is clear, there are many aspects on which our understanding is limited. Consequently, there is much scope for useful research.

BOX 11. ASPECTS MERITING FURTHER RESEARCH

- Factors driving resistance
- Mathematical modelling of resistance
- Geographical information systems
- Basic research on mechanisms of resistance
- Links between prescribing and resistance at individual and population levels
- Beliefs concerning antimicrobial use, their influence on demand and concordance
- Factors leading to inappropriate prescribing
- The role of social change, particularly day-care of the elderly and children
- Computerised decision-support systems
- Investment versus restriction in antimicrobial use

ANTIMICROBIAL DEVELOPMENT

The thrust of this Report is upon the conservation of present antimicrobials. Past resistance problems have been overcome (if only temporarily) by the development of new antimicrobials. In recent years, the pharmaceutical

industry has developed vastly more efficient systems for seeking new antimicrobials. These strategies will, hopefully, yield new generations of antimicrobials by the end of the next decade. It is vital that research on new antimicrobials is encouraged and not made uneconomic.

If the recommendations of this Report are followed, they should reduce overall antimicrobial usage. As a result there may be financial implications for the pharmaceutical industry, upon whose profitability the development of new antimicrobials depends. Consideration may, therefore, need to be given to finding ways, through pricing and other mechanisms (eg, extended patents), of making investment in the development of new antimicrobials commercially attractive.

19 CHANGING PRACTICE

KEY POINTS

- A national strategy aimed at the professional and the public is required
- This should be supported by the development of surveillance, education and decision – support systems

Although the Terms of Reference of the Sub-Group were to concentrate on changing professional activities in order to reduce antimicrobial resistance (Box 1), ‘change management’ cannot be undertaken in isolation. The overall culture and organisation in which professionals work has to be addressed at local and national levels. This includes modifying patient expectations.

There have been many attempts to identify strategies for changing professional behaviour and some general lessons have emerged. Change needs to be carefully planned and all essential protagonists need to be identified, as well as the associated barriers. Specific interventions need to be implemented for each obstacle. The whole process must be co-ordinated and progress evaluated.

CREATING A SUPPORTIVE ENVIRONMENT FOR CHANGE

In making recommendations aimed at influencing doctors’ prescribing in primary care, through a national **Campaign on Antibiotic Treatment (CAT)**, we acknowledge the importance of patients’ expectations in the decision-making process. Therefore there must be a concurrent and co-ordinated programme to modify patients’ expectations through a **National Advice to the Public (NAP)** campaign of public education. This will help GPs to adhere to the recommendations, all of which relate to unnecessary prescribing. This approach will need to be co-ordinated at a national level, hence the recommendation for a Steering Group, charged with ensuring the implementation and monitoring of the strategy, of which **CATNAP** is a central feature.

Change will also be supported by the production of high quality, evidence-based guidelines. Computer systems will improve access to guidelines and aid their implementation, particularly if the systems can be made relevant to both the prescriber and the patient, assisting in their interaction and helping the

prescriber to explain why a prescription may not be necessary.

All guidelines will need to be up-to-date and locally relevant; otherwise they risk losing credibility. They need underpinning with information on local antimicrobial sensitivity profiles. These local profiles, in turn, should feed into regional and national surveillance databases.

National, regional and local surveillance will provide:

- i) *closure of the audit feedback loop*
- ii) *data for the adaptation and revision of guidelines*
- iii) *outcome data for studies to identify the drivers of resistance and the effectiveness of interventions to improve antimicrobial prescribing*

The national strategy for resistance surveillance currently under development between the Public Health Laboratory Service, the British Society for Antimicrobial Chemotherapy, the Scottish Centre for Infection and Environmental Health and the Northern Ireland Department of Health and Social Services, is a key element in the strategy for improving antimicrobial prescribing practices.

As part of the process of preparing our Report the Sub-Group on Antimicrobial Resistance commissioned an independent review of the literature to determine the nature and quality of the evidence that changing prescribing patterns could result in reduction or limitation of the spread of antimicrobial resistance.

This literature review aimed:

- To assess the evidence that inappropriate use of antibiotics leads to increased levels of antimicrobial resistance
- To assess the quality of evidence that antimicrobial resistance levels can effectively be reduced or reversed
- To examine the evidence that effective implementation of changes in prescribing practices will result in reduction of antimicrobial resistance levels
- To provide independent confirmation, or otherwise, that the conclusions reached in the main report were justified

Key conclusions are incorporated into the body of this Synopsis. The full results are available in the Report.

IN CONCLUSION

Antimicrobial prescribing is an activity with roots in many cultures, clinical and lay. It is only through addressing all of those involved that we are likely to find

‘ the path of least resistance’

22 LIST OF RECOMMENDATIONS

PRESCRIBING IN THE COMMUNITY

Patients with minor infections mostly present to GPs; consequently, 80% of UK human prescribing is in the community. This Report therefore concentrates on community prescribing of antimicrobial agents.

There should be a national Campaign on Antibiotic Treatment (CAT) in primary care on the theme of: 'Four things you can do to make a difference' (see Box 2).

The CAT must be matched by a National Advice to the Public (NAP) campaign aimed specifically at supporting the initiative in primary care. A key feature of the NAP campaign should be to highlight the benefits of 'cherishing and conserving your normal bacterial flora'. Further support for appropriate prescribing in primary care should be provided by developing and promulgating evidence-based national guidelines for the management of certain infections, under the aegis of the National Institute for Clinical Excellence. Such national guidelines should be adapted for local use during the development of Health Improvement Plans.

To make the incorporation of the guidelines into everyday practice as effort-free as possible they should be integrated within computerised decision-support systems.

FOUR THINGS YOU CAN DO: ·

- no prescribing of antibiotics for simple coughs and colds ·
- no prescribing of antibiotics for viral sore throats ·
- limit prescribing for uncomplicated cystitis to 3 days in otherwise fit women
- limit prescribing of antibiotics agents over the telephone to exceptional cases

PRESCRIBING IN HOSPITALS

Hospital prescribing accounts for c. 20% of human prescribing of antimicrobial agents in the UK; nevertheless, resistance problems are greatest in hospitals and infections may be life-threatening. Although prescribing in hospitals poses some different issues from those in primary care, hospital clinicians would benefit as much as GPs from the availability of computer-aided decision-support systems.

Studies should be undertaken in selected hospitals to develop and test one or more prototype decision-support systems.

Systems should include information from local antimicrobial sensitivity profiles; these, in turn, should feed into regional and national surveillance databases.

PRESCRIBING GUIDELINES

Prescribing guidelines should be quality, evidence-based documents. They are often the first source of information for inexperienced prescribers. National guidelines, suitably adapted in response to local resistance patterns, could be integrated into decision-support systems.

Local prescribing information should, wherever possible, be harmonised with prescribing information in the British National Formulary (BNF) and other formularies. Guidelines and formularies should also take account of the proposed national evidence-based guidelines to be produced under the aegis of the National Institute for Clinical Excellence. Local prescribing guidelines should take their cue from these national guidelines. All such local guidelines should include, as a minimum, advice on drug dose, frequency and duration.

INTERNATIONAL CO-OPERATION

Resistant bacteria spread between countries, the UK is not isolated from the greater resistance problems that exist in other parts of the world, for example, Southern Europe.

Every effort should be made by the Government, in international fora, particularly in the European Union, to raise the profile of antimicrobial resistance as a major public health issue meriting priority action.

SURVEILLANCE OF RESISTANCE

Effective surveillance is critical to understanding and controlling the spread of resistance. Not only is surveillance essential for monitoring the existing situation, it allows the effects of interventions to be evaluated.

A national strategy for resistance surveillance should be developed and implemented as swiftly as possible, covering the whole of the UK.

RESEARCH

Antimicrobial resistance has been of low priority for Research Councils and scored poorly in the recent Research Assessment Exercise.

Research into antimicrobial resistance should become a high priority for all funding bodies concerned with health care and biomedical research.

EDUCATION

The development of guidelines and their widescale introduction into clinical practice will have important and beneficial spin-offs for the education of health care professionals involved in antimicrobial prescribing. The whole population would benefit from enhanced education about the benefits and disadvantages of antimicrobials.

Greater emphasis should be placed on teaching about antimicrobial prescribing in medical and dental schools as well as in the undergraduate curricula for pharmacists and nurses. Teaching about antimicrobials should be better integrated with teaching about the infections for which they are used. This enhanced emphasis on education in antimicrobial use should be carried over into continuing medical, dental and professional education and development. Similar concepts apply in the field of veterinary medicine.

In addition to health education material aimed at adults, teaching about antibiotics should be included as part of health education in the National Curriculum.

HYGIENE, INFECTION CONTROL AND CROSS-INFECTION

Infection control, although intimately bound up with problems of antimicrobial resistance – particularly in health care environments – was outside the Terms of Reference of the Sub-Group. Nevertheless, it is fundamental to preventing the spread of resistant organisms, not only in hospitals but also in the community.

Consideration should be given to producing guidance on infection control in the community, especially in nursing and residential homes, similar to that which exists for hospitals.

VETERINARY AND AGRICULTURAL USE

Antimicrobials are used in therapy and prophylaxis, and as growth promoters/enhancers in animals.

The use of antibiotics in veterinary practice should be guided by the same principles as for human prescribing – namely, they should be used only for clinical conditions where their use is likely to provide a genuine health benefit. Alternative means of animal husbandry should be developed so that the use of antibiotics as growth promoters can be discontinued.

IMPLICATIONS FOR INDUSTRY

If our recommendations are followed, they should have the effect, *inter alia*, of reducing antibiotic usage. There may be financial implications for the pharmaceutical industry, upon whose profitability the development of new antibiotics depends.

Consideration should be given by the appropriate bodies to finding ways – through pricing and other mechanisms – of ensuring that investment in the development of new antibiotics remains commercially viable. Industry should be encouraged to undertake studies of optimum prescribing regimens for new antimicrobial agents, for each indication and in adults and children as appropriate. Licensing authorities should have due regard to an antimicrobial agent's potential to select for resistance as well as to its safety and efficacy.

IMPLEMENTATION OF RECOMMENDATIONS

The aim of this Report has been to produce recommendations that can constitute the first phase of a national strategy for minimising the development of antimicrobial resistance.

- As part of this phase a small National Steering Group (NSG) should be established, charged with ensuring that these recommendations are implemented and that their effects on prescribing practice and on the development of resistance are monitored.
- The NSG, which might need to establish a small number of expert groups to take forward specific aspects of the recommendations, should report to the Chief Medical Officer within a year on progress.
- Thereafter the CMO may wish to consider asking SMAC to reconvene this Sub-Group, to provide a suitable inter-disciplinary forum for the development of the next phase of the strategy.

MEMBERS

Dr Diana Walford	Chairman of Sub-Group: Director of PHLS and SMAC member
Mrs A Close	Nursing Director, Dudley Group of Hospitals and SNMAC member
Dr A Dearmun	Principal Lecturer Practitioner, Senior Nurse Oxford Brookes University and SNMAC member
Professor T Duckworth	Professor of Orthopaedic Surgery, Sheffield University and SMAC member
Miss A Ewing	Director of Pharmacy, Countess of Chester Hospital and SPAC member
Dr J Gilley	General Practitioner, London and SMAC member
Dr R Horne	General Practitioner, Stockton on Tees and SMAC member
Professor A Johnson	Professor of Surgery, Sheffield University and SMAC Chairman
Professor C Peckham	Professor of Epidemiology and Public Health, Institute of Child Health and SMAC member
Dr S Willatts	Consultant Anaesthetist, Bristol Royal Infirmary and SMAC member
Dr G Youngs	Consultant Physician, Countess of Chester Hospital and SMAC member

CO-OPTED MEMBERS

Dr A M Johnston	Senior Lecturer, Royal Veterinary College
Professor P Littlejohns	Professor of Public Health, St George's Hospital Medical School
Miss C Murphy	BMA Junior Doctors Committee
Dr G Patou	Vice President, Anti-infectives Development, SmithKline Beecham Pharmaceuticals
Dr M Powell	Medicines Control Agency



Standing Medical Advisory Committee
Sub-Group on Antimicrobial Resistance