Resistance is futile—a conference to promote the rational use of antimicrobials in acute hospitals

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This article reports on the proceedings of a meeting held in London in July 2005 organized by the Specialist Advisory Committee on Antimicrobial Resistance in conjunction with the UK National Prescribing Centre and UK Department of Health. The focus of the meeting was the developing role of the antibiotic pharmacist. The main presentations tackled four aspects of hospital antimicrobial prescribing: the development, maintenance and presentation of guidelines; the role of prescriber education; the importance of team working in multidisciplinary prescribing networks; and preliminary findings on hospital antibiotic consumption in England. The speakers highlighted the progress that has been made and gave examples of good practice, in addition they drew attention to deficiencies and hence the challenges that lie ahead. These include the need for accurate hospital antibiotic usage data in the UK and more integration of clinical outcome data in studies on the control of antimicrobial consumption through the implementation of prescribing guidelines.

Keywords: prescribing guidelines, outcomes, interventions, education

Introduction

As a result of ongoing concern regarding rates of resistance to antimicrobials and inappropriate prescribing, in 2003 the UK Department of Health (DH) allocated £12 million to be spent over 3 years on developing the role of pharmacists to take a lead in the promotion of rational antibiotic prescribing. This 1 day meeting organized by the Specialist Advisory Committee on Antimicrobial Resistance (SACAR) in conjunction with the National Prescribing Centre (NPC) and the UK DH took place on 12 July 2005 at the London headquarters of the Royal Society of Pharmacists of Great Britain. This was the second 1 day meeting organized by SACAR, UK DH and NPC in support of these objectives. The meeting consisted of four main presentations considering guidelines, education, prescribing teams and hospital antibiotic usage in the UK. These presentations were interspersed with Table discussions and there were also a number of poster presentations. The poster presentations and summaries of Table discussions are beyond the scope of this article.

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The meeting was opened by Prof. Richard Wise (Chairman of SACAR). In his introduction Prof. Wise welcomed the ~120 delegates and acknowledged the remaining transport difficulties in the UK’s capital city after the bombings that had taken place only a matter of days earlier on 7 July. This was the second similar SACAR-sponsored meeting, the previous meeting entitled ‘Resistance is useless’ took place a year earlier. What has been achieved in the intervening year? Prof. Wise noted that SACAR continues with the approach envisaged by the UK DH in 2003 for antibiotic pharmacists. This role is being consolidated within Trusts with increased interdisciplinary cooperation. Antibiotic pharmacists have demonstrated savings on pharmacy budgets, but he emphasized that this was about more than saving money, it is more importantly a quality-of-care exercise.

The tools at hand to combat the problem of resistant organisms are limited: new drugs are an option, but it is widely recognized that there are fewer new drugs emerging and the new drug pipeline does not look particularly encouraging for a host of reasons that have been discussed elsewhere; vaccines, infection control in hospitals and in the community, and prudent prescribing are the other main options.

Over the last year methicillin-resistant *Staphylococcus aureus* (MRSA) has continued to be a headache, despite some evidence from the number of infections that we might be turning a corner in the fight. The British Society for Antimicrobial Chemotherapy (BSAC), Hospital Infection Society and Infection Control Nurses Association will shortly publish three joint Working Party Reports on MRSA. Community MRSA is proving to be a problem worldwide and has hit the headlines in the media. Extended spectrum β-lactamases (ESBLs) have rapidly emerged as a problem in the UK over the last few years and it is probable that we will have to come to terms with their presence. They are a problem in both...
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Dr T. Mayon-White, Department of Primary Healthcare, University of Oxford, UK

Dr Mayon-White began by considering a number of definitions for what constitute ‘guidelines’. Perhaps the simplest and most succinct of these was from the UK National Audit Office (NAO), which in 2000 defined antibiotic policies as ‘written guidance on treating and preventing specific infections’. He expanded on this by referring to the Scottish Intercollegiate Guidelines Network which defines guidelines as ‘recommendations for effective practice where variations in practice are known to occur’ and makes clear the crucial difference between guidelines that are either based on expert opinion or non-systematic reviews of the literature, and evidence-based guidelines that are derived from systematic review of the literature and are hence less susceptible to bias.

Adherence to guidelines has the potential to bring a number of desirable outcomes for patients, among these are: a better chance of effective treatment; less inequality (eliminating unnecessary variations in practice and so-called ‘postcode’ prescribing); clarity as to how and why treatment decisions have been reached; and improved safety. From the healthcare provider viewpoint they can also facilitate audit and result in a decrease in costs. However, guidelines can have negative effects if: it later proves that the evidence base was incorrect or inadequate; they are misapplied; they are applied too inflexibly; they are not frequently reviewed and updated; and they inhibit further research.

Dr Mayon-White then turned to the question of whether guidelines actually make a difference. In general, 55 out of 59 rigorous evaluations found improvements of between 10 and 40% in adherence to treatment or prophylaxis regimens, and 2 out of 11 studies recorded better outcomes. For antibiotics specifically, one study identified 11 articles that showed a reduction in resistance levels. In addition the UK NAO identified three cases where variations in practice are known to vary between hospitals and the community and there will need to be changes in practice in both areas. In terms of emerging problems, Prof. Wise identified carbapenemases, Clostridium difficile and Acinetobacter.

Looking to the challenges of the year ahead, Prof. Wise noted that DH funding of the antibiotic pharmacists will cease, and ways to support their continuing role will need to be found. At a different level, it is both astounding and embarrassing that the UK is the only remaining country in Europe that has no system for recording and measuring the extent of antibiotic usage in hospitals. It is impossible to track the extent of problems or measure the effectiveness of interventions without the availability of these data.

Looking towards new agents, it seems probable that daptoforny will receive a licence early in 2006; however, its indications will be fairly limited. Other newer drugs include new glycopeptides, streptogramins (quinupristin/dalfopristin) and oxazolidinones (linezolid). Notably these are all anti-Gram-positive drugs.

Above all we can be sure that new and unexpected difficulties will emerge, Prof. Wise concluded.

Guidelines: structure, content and evidence base

R. T. Mayon-White, Department of Primary Healthcare, University of Oxford, UK

A recent survey has shown that hospitals have adopted a wide variety of formats for the presentation of their guidelines, ranging from a majority employing A4 documents, some with pocket-sized summaries, to a number employing smaller-format documents and laminated notices. Interestingly, three hospitals were using their intranet to host the guidance. The longer documents were subdivided with headings and chapters, but it was noted that these headings and chapters were non-standard and therefore swapping from one set of guidelines to another in a different hospital would not be straightforward. Dr Mayon-White noted that it was pleasing that nearly every hospital now has guidelines and that clearly a great deal of often innovative thought had been given to their dissemination. It appears that the majority of guidelines are revised and updated every 2 years. This is a very complex and time-consuming undertaking.

In the study of policies in the UK South East Region it was clear that there was increasing use of electronic and internet versions, respiratory and urinary tract infections were particularly well-covered and there had been significant collaboration with community healthcare providers and with neighbouring hospitals, which is especially important for specialist hospitals.

Some of the weaknesses identified were: a few of the guidelines were out of date; some were thin on supporting evidence; Latin abbreviations still in use; some documents were too long and lacked summaries; there was variable detail on cautionary information and paediatric doses; and variable content on prophylaxis, MRSA and infectious diarrhoea.

Dr Mayon-White then introduced a ‘template’ for guidelines containing a suggested standard layout for the information consisting broadly of: a standard front page including information on the date of issue and the review date, and the authors; an Introduction indicating the intended use of the guidance, contact details for more advice, etc.; a list of antimicrobials (with or without costs); a list of common infections with specific guidance; and a section on prophylaxis and audit. A copy of this template can be found on the BSAC website http://www.bsac.org.uk/_db/_documents/Template_for_hospital_antimicrobial_guidelines_May_2005.doc

At the level of specific infections it is essential that information is included on the strength of the evidence used to back up the recommendations. Dr Mayon-White outlined the familiar A+ (systematic review of randomized controlled trials) to D (expert opinion) system for grading evidence but cautioned that there are several interpretations of some of the definitions of individual grades and different grading systems; the system being used should be made absolutely clear by guideline authors.

Using the specific example of prophylactic antibiotics for caesarian section, Dr Mayon-White illustrated how the systematic consideration of the evidence makes it clear that the evidence supporting the conclusion that prophylactic antibiotics prevent 2 out of 3 cases of endometritis and wound infections is very strong, and additionally highlights the fact that research is needed to determine whether prophylaxis is best given pre-operatively or at cord clamping. Thus also setting a research agenda.

For community-acquired pneumonia there are a variety of national guidelines including those of the British Thoracic
Optimizing antimicrobial use: the knowledge and skills required

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Prof. Finch began by emphasizing that antibiotics are different from other drugs in a number of respects: their activity is not directed at human metabolic processes; their microbiological activity may be required at many body sites; they are used in large numbers of patients for short periods, both prophylactically and therapeutically; their activity is rarely single-organism-specific and varies against different organisms; and drug resistance may emerge and disseminate clonally or by gene transfer.

There are quality and safety concerns regarding current prescribing practice, and Prof. Finch went on by outlining some of them. Approximately 1 in 10 inpatients suffers an adverse drug reaction (ADR) to a drug they do not actually need to be receiving. In up to 10% there are potentially harmful drug interactions, and ADRs increase substantially with multiple drug prescribing.

There have been several initiatives recently in the UK including the establishment of antibiotic sub-committees to Drug and Therapeutics Committees (DTCs), audit of policies and practice, and appointment of ward-based pharmacists and special pharmacist (e.g. for HIV/ID, haematology/oncology and infection control). However, action without education is at worst dangerous, or at best useless.

Prof. Finch explained how, at the University of Nottingham, the medical curriculum is organized under three interwoven strands: what the doctor should know (knowledge and understanding including, for example, the scientific basis of practice); what the doctor should be able to do (e.g. clinical and practical skills); and how the doctor should behave (attitudes e.g. to medicolegal and ethical issues). This structure exposes graduates to relevant parts of educational support and that there is adequate information readily available for the prescriber regarding a wide variety of subjects. Perhaps most important is the preparation of students for a process of lifelong learning, recognizing that everyone will need to keep their knowledge and skills updated.

The spectrum of prescribers is changing; today and tomorrow’s prescribers will include medical practitioners, dentists, optometrists, nurses, pharmacists and perhaps paramedics. It is essential that the necessary educational components be in place in the curriculum for all of these roles in order to achieve the goals of rational prescribing.

Prof. Finch then posed the question, ‘Why do current educational strategies require updating?’ It is clear that there are inconsistencies in current curricula, there will be a rapid increase in the range of prescribing professionals in the UK and we need to ensure that new knowledge and best practice rapidly influence prescribing in the field. This is of paramount importance if we are to address both public and political concerns about safe and effective prescribing.

Innovative approaches that adopt modern learning theory are under development and include the use of case-based prescribing scenarios. These permit independent and support distance learning with the opportunity for tutor support and assessment as well. The BSAC and a consortium from the Scottish Medical Schools have recently developed a prototype of this approach. (http://www.dundee.ac.uk/facmedden/APT/index.htm).

In conclusion, Prof. Finch stated that rational use of antibiotics requires rational prescribing and evidence-based recommendations. Rational prescribing is a lifelong process that requires core knowledge, skills and behaviour within a culture of continuous learning. Good prescribing is both an individual and a corporate responsibility. NHS Trusts need to support good prescribing practice by ensuring that their staff are adequately trained through educational support and that there is adequate information readily available to hand at the point of consultation.

Addressing antimicrobial resistance: the benefits of team working

P. G. Davey, Health Informatics Centre, University of Dundee, UK

Prof. Davey opened his presentation by stressing that there is a reawakening of emphasis on team working in medicine. Medical care often involves a complex and overlapping group of teams, which are multidisciplinary. This requires a team approach if initiatives in antimicrobial prescribing and resistance are to be successful. Owing to the complex nature of treatment in a modern healthcare system, Prof. Davey suggested that perhaps the most important initial problem is to identify all the team members!
Prof. Davey then explained that in the UK the last 12 years has seen a developing role for ‘non-medical’ prescribers, starting in 1994 with the granting of limited rights for District Nurses and Health Visitors. Since then, roles have been defined for Supplementary (currently nurses, pharmacists, chiropodists/podiatrists, physiotherapists and radiographers) and Independent nurse prescribers (doctors and dentists have been able to prescribe independently for many years). There has recently been a public consultation and further policy work undertaken that may result in pharmacists joining the list of Independent prescribers by 2006.

Although these groups of healthcare professionals may regard themselves as widely different, it soon becomes apparent that the prescribing competencies they require are actually rather similar. As referred to by Prof. Finch earlier, behaviours and attitudes, rather than just competencies are a relatively new focus in medical education. Prof. Davey emphasized that it is essential all prescribers are not only competent (have the necessary knowledge) but also possess the correct attitudes and behaviours to execute their role.

For example, in the multidisciplinary team context it is necessary for a Supplementary prescriber to display the following behaviours: negotiation with the Independent prescriber to develop a clinical management plan; define their relation to the Independent prescriber as an equal partner and agree the necessary level of support for their role. Medical students are not currently taught how to develop these interactions, it is another area where it is assumed that they will either naturally ‘know’ this or pick it up as they go along.

Prof. Davey then considered team working. It is increasingly recognized that in order to execute technical skills effectively, it is necessary to be in possession of a range of non-technical skills (especially relating to team working) that have generally been ignored in education. This was perhaps first recognized seriously during research into aviation accidents in the 1980s and 1990s, where it became apparent that in 70–80% of accidents there was no fault in the aircraft that would have made an accident inevitable. While these types of incidents may have been ascribed previously to ‘pilot error’ it became clear that in many instances a wider team had opportunities to intervene and prevent an accident, but that failures in team working were evident. Prof. Davey described a notable example during which an airliner had been essentially ‘flown into the ground’ in the Florida swamps: the air-traffic controller had repeatedly advised the pilot to ‘do something about his altitude’ without stating his/her concerns in more plain language! A lack of effective team working had prevented the situation being remedied when the opportunity presented itself. The necessary non-technical skills typically include leadership, communication, situation awareness, decision making and workload/stress and fatigue management. Importantly, flight simulators used to train aircrew have now been modified and incorporate development of team working skills in addition to their previous emphasis on the purely technical aspects of flying.

A similar approach can be applied to teams in acute medical situations, identifying individuals’ skills and characteristics and developing these into group processes (team skills) and outcomes. An example of this approach are the non-technical skills for surgeons (NOTSS), which build on the categories of situation awareness, decision making, task management, communication and leadership and can be used to identify and analyse good and bad behaviours. An example would be keeping the anaesthetist informed about the procedure (e.g. to expect changes in cardiovascular status because of excessive bleeding) versus waiting for the problem to actually arise before responding.

Prof. Davey then returned to the current antimicrobial scene. A Cochrane Review of Hospital Antibiotic Use has been undertaken by the BSAC and Hospital Infection Society. The primary aim was to systematically review the literature in order to identify interventions that alone, or in combination, are effective in promoting prudent antibiotic prescribing to hospital inpatients. This appeared in the Cochrane Library in October 2005.6 Twenty-six articles were included in the review that primarily aimed to reduce antibiotic prescribing to hospital inpatients. It was clear from this review that not enough studies focus on the clinical outcomes from the intervention, with currently too much emphasis on drug and microbial outcomes in isolation; more balance is required. Of the 60 articles only 5 looked at the clinical outcome of reduced antibiotic prescribing.

Prof. Davey stressed the importance of measuring outcomes if we are to ensure that gaining control of antibiotic prescribing levels does not actually result in poorer clinical outcomes than are enjoyed at present.

In conclusion, Prof. Davey reminded the audience that prescribing is a ‘team game’, competencies should be defined for all team members and non-technical (team working) skills are vital. All interventions to change prescribing must be multidisciplinary. Increased prescribing may improve clinical outcomes and decreased prescribing may improve microbial outcomes (resistance), it is therefore essential that intervention studies on antimicrobial prescribing address both aspects of the treatment equation.

Antimicrobial use in hospitals: how are we doing?

H. Wickens, Pharmacy Department, St Mary’s Hospital, London, UK

Dr Wickens began by explaining the background to the current situation in the UK. The Hospital Pharmacy Initiative (HPI) was launched in a letter from the UK Chief Medical Officer/Chief Pharmaceutical Officer in June 2003. This involved the allocation of £12 million over 3 years to hospital pharmacists in England to monitor and control more carefully the use of antibiotics. The money was allocated via Primary Care Trusts, with the Strategic Health Authority to monitor the use of funds (although the mechanism for this was not defined). Outcome measures were not rigidly defined. Rough calculations suggest that this amounts to approximately £15K per hospital per year.

Dr Wickens then described the specific activities undertaken to measure the effects of these changes. In order to assess the outcomes of the SACAR HPI, a questionnaire study was undertaken in April 2005. One hundred and eighty-three questionnaires were sent to acute hospitals in England. The questions addressed statistics regarding the individual hospital (bed numbers, staffing and the like), how the money has been spent and the outcome measures used. The full report on all the data should be published in late 2005.

The preliminary results show that most Trusts have a specialist member of staff employed under the HPI and that the majority of these persons are pharmacists. Reasons given for not having a specialist member of staff included insufficient funds or a failure to recruit. Perhaps worryingly, for a sizeable proportion of posts it

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was unclear that any measures had been put in place to continue the position after the HPI funding runs out in 2006.

Dr Wickens then addressed how the antibiotic pharmacists are applying themselves. This splits roughly into four aspects: monitoring antibiotic use (financial control); writing evidence-based guidelines, audit and feedback; clinical roles as a member of the infectious disease, microbiology or infection control teams; and education of other healthcare professionals and patients.

Applying measures of antibiotic consumption is a key area and Dr Wickens described the range of measures available and their merits. There are a number of established methods for monitoring antibiotic consumption; these differ in their ease of calculation and reliability. For example, gross expenditure is relatively easy to measure but may be confounded by pricing changes; quantity is more reliable still, but subject to vagaries of variable units; defined daily doses (DDDs) are better with WHO-defined standard dosing units, and these can be further normalized with DDDs/1000 bed days.

The results of the survey do, however, indicate that the vast majority of DDD reporting may only have become possible as a result of the HPI funding. Again it was noted by Dr Wickens that unified UK hospital prescribing data are lacking, although there may be steps underway in this direction.

Regarding the production of guidelines it was apparent that the HPI funding had contributed to this, but to a lesser extent, perhaps because initiatives were already in hand. HPI funding would appear to have contributed substantially to supporting the role of antibiotic pharmacists as educators of other health professionals, with a substantial increase in activity in this area being attributed to the new funding. There has also been an increase in specialist input as part of the clinical team through a range of activities including specialist unit ward rounds and pharmacy/microbiology ward rounds.

Dr Wickens then cited St Mary’s Hospital and Southampton University Healthcare Trust (UHT) as examples where Pharmacy/Microbiology ward rounds have been instituted. Southampton UHT reported drug cost savings probably related to stopping inappropriate prescriptions and initiating intravenous to oral switches, whilst St Mary’s reported up to 90% of interventions by the antibiotic pharmacist were accepted by teams.

Again Dr Wickens acknowledged that as the final step in the process, monitoring of clinical outcomes, which is arguably the most important measure, is under-monitored in comparison with antimicrobial resistance or adherence to the actual prescribing guidelines.

Dr Wickens concluded by stating that the preliminary findings show that the majority of HPI funding has been spent on staffing. Funding has allowed an increase in monitoring of antibiotic use, guideline development and clinical input. Challenges remain, however, in building the evidence base (particularly on clinical outcomes) and identifying sources of funding to maintain the initiatives that the HPI funding has made possible.

The future

Efforts to hone prescribing and hence curb the spread and impact of resistant organisms face a number of challenges on a broad front. The presentations that formed the core of this meeting focused on these challenges and what needs to be done in order to tackle and overcome them. First is the development of evidence-based guidelines for therapy, which sharpen our focus on exactly what we do and don’t know, and help in framing new and productive questions. Second is the knowledge, training and attitudes required by the expanding range of prescribers in order that any guidelines are applied effectively. Third is the increased teamwork that is required in modern, highly complex, healthcare-delivery organizations that incorporate these expanded prescribing teams. Finally comes the requirement to measure accurately the prescribing that is actually going on so that the effectiveness of interventions can be gauged, not only at the ‘compliance with the guidelines’ level but also at the patient outcome level.

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Transparency declarations

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References