

Minimum Antibiotic Stewardship Measures

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INTRODUCTION

Despite many years of concern about the ways in which antibiotics are prescribed, much still needs to be done to prolong the life of these valuable agents. As far back as the 1960s experts were expressing doubt about many aspects of use in humans and animal use came under similar scrutiny. The sceptic may say nothing much has changed with a recent report suggesting almost three quarters of the total antibiotic use in the USA is for commercial purposes, namely growth promotion (1).

The European Union, however, banned antibiotic use for growth promotion in 1999, according to the Swann report principles (2). So far there are no apparent deleterious effects. Prescribing in primary care throughout many European countries seems to have been falling throughout the 1990s with no obvious harmful effects (3). Neither of these findings is surprising as the scientific evidence for use of antibiotics as growth promoters was always lacking and audits have repeatedly shown excessive use of antibiotics in primary care, especially for the treatment of viral infections (4). While viral infections undoubtedly predispose to secondary bacterial infections in the respiratory tract, there is no evidence of protective effects of antibiotics in lower respiratory tract infection and there is evidence of no benefit in upper respiratory tract infection (5).

Antibiotics are unusual as a drug class in several respects, being used by all veterinary and medical practitioners, pharmacists, farmers and the general public who can frequently (legally or illegally) purchase them over the counter, often in generic or even counterfeit form of dubious quality. This aspect of use needs urgently addressed but will not be easy as it is a huge business worldwide with many entrenched interests. In many of the world's major cities, it is associated with poor access to medical care, sub-optimal treatment and insanitary, over crowded conditions, which promote the development, maintenance and spread of

antibiotic resistance. The role of the pharmaceutical industry in unethical promotion such as discounting products to pharmacists needs to be examined in this context.

The role of medical societies in battling antibiotic resistance is crucial and ESCMID has formed several working and study groups for this purpose.

ESGAP – the European Study Group on Antibiotic Policies of ESCMID is one of these groups and it, in its turn has formed several sub-groups (Table 1).

Subgroup 3 has developed a draft document by E mail discussion, which has been posted on the ESGAP section of ESCMID's website. The final version is reproduced here with a commentary, highlighting those aspects of particular relevance to the prescriber, the regulator and the pharmaceutical industry. The areas addressed are shown in Table 2. Members of sub-group III are:

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Clinical Practice

- Appropriate antibiotic prescribing should potentially benefit the patient. There should be clinical evidence supported, where possible by laboratory tests. Sepsis parameters should be documented and support the need for antibiotic treatment. Critical patients should receive appropriate treatment as quickly as possible.
- Treatment should be limited to bacterial infections, using antibiotics directed against the causative agent, given in optimal dosage, interval and length of treatment, with steps taken to ensure maximum patient compliance with the treatment regimen and only when the benefit of treatment outweighs the individual and global risks.

- Treatment Guidelines should cover both hospital and community, should be readily accessible, drawn up with multidisciplinary prescriber involvement, subject to peer review, evidence based where possible and compatible with national guidelines, where these have been adopted.
- Antibiotic therapy should be streamlined at the earliest opportunity, where possible using the results of laboratory tests.

There is a great need to improve the clinical diagnostic rigour prior to treating infection where, for too long, broad-spectrum antibiotics have been used as a substitute for accurate diagnosis because of their perceived safety (6). Sepsis parameters such as temperature, respiratory rate, pulse, blood pressure, white blood cell count and C-reactive protein are easily measured. Results should be documented for audit purposes and easy chart review to enable streamlined, rationalization of therapy at the earliest opportunity (7). While treatment (intravenous if necessary) must not be delayed even for half an hour in critically ill patients, there should usually be enough time to send off appropriate cultures to the laboratory. Our increased ability to optimise dosing schedules according to the latest pharmacodynamic evidence, both to optimise patient outcome and to reduce the emergence of resistance should be utilized (8).

Healthcare Administration

- An Antibiotic Policy and Formulary (limited list) should be created locally after widespread consultation and its implementation ensured by audit cycles. It should be regularly updated in the light of local resistance problems and availability of new drugs.
- Measurement of antibiotic consumption should be performed with regular benchmarking of figures and discussion between prescribers, pharmacists and infection specialists.
- Evidence based guidelines to be introduced should be incorporated into the Antibiotic Policy.
- Process and Outcome measures of antibiotic policies should be audited. Facilities for auditing doses, duration and route of administration of antibiotics should be provided.

- Restricted lists of key agents should be implemented.
- Single dose surgical prophylaxis should be encouraged.
- A drugs and therapeutic committee (or an antibiotic committee) should consider timely introduction of new agents and review of the old agents. The proceedings of this committee should be transparent and conflicts of interest declared.

The existence of antibiotic policies and formularies are probably the norm in hospitals, if not other health care institutions and primary care groups and evidence for their efficacy is increasing (9). It is essential that they are regularly updated and that pharmaceutical companies are allowed to present the case for inclusion of their product(s) as this gives credibility to the product.

A new European Commission, Belgium Government and ESGAP joint funded project on measuring consumption – ESAC (European Surveillance of Antibiotic Consumption) has recently started. Collection of antibiotic consumption data, which until now has been sporadic, is likely to become an important obligation of Member states. As electronic systems for Pharmacy stock-taking and prescribing become more widespread, auditing amount and quality of antibiotic prescribing should become easier (10).

The evidence base for the benefits of restricted lists is probably greater than for any other control (11). Similarly, there is some evidence that the Industry can circumvent their impact by social and educational means (12)

The first evidence based guideline in surgical prophylaxis with a full description of methodology used is available on www-sign.ac.uk or direct from the Royal College of Physicians in Edinburgh (13). It advocates single dose prophylaxis for the vast majority of

infections and gives advice on how to make local decisions on the need for prophylaxis in areas of debate such as the vast majority of clean, non-implant surgery. Using data on the baseline risk of infection and the efficacy of prophylaxis (odds ratio) one can calculate the numbers to be given prophylaxis to prevent a case of post operative infection. The criteria of whether prophylaxis will increase or decrease a Units antibiotic consumption may be helpful in reaching a policy decision, based on a Units total antibiotic exposure being a key factor in likely resistance problems (14).

Pharmacies and Laboratories

- Laboratories should regularly make local sensitivity patterns widely known and routinely should only report on those agents which appear in their formulary and policy.
- Susceptibility and culture results should be reported to clinicians with the minimum of delay to allow them to streamline or stop antibiotic therapy as appropriate.
- Microbiology and Pharmacy departments should have adequate facilities to ensure that education programmes can be carried out. They should have computer facilities for audit. The two departments should communicate freely and cooperate to ensure the best use of antibiotics. Ward pharmacists, in conjunction with medical microbiologists or infectious disease physicians, are well placed to monitor adherence to policies and formularies.
- Programmes for assessment and appropriate adoption of automatic stop dates, centralised intravenous administration service, antibiotic prescription forms and utilisation co-ordinators should be introduced. This will require appropriate finance.

Reporting of sensitivities is often perceived not only as a recommendation to treat but a sanction for a particular antibiotic so it is important that only those agents on the formulary are reported in a routine manner (although, of course, this does not prohibit testing of non-formulary agents on a research basis or where the request gives details of non-formulary treatment). While there is a case for diversity in antibiotic use, which argues against the restriction of formularies in terms of selecting resistance (14), cost savings in bulk purchase and the ability to limit use of inappropriate antibiotics argue for their extended use (11, 15).

Speed of reporting at all levels of the laboratory results process from initial microscopy to susceptibilities is important. Even using conventional techniques, the vast majority of results, including many sensitivities can be reported quickly enough to influence patients treatment (16). The biggest delays are often in transport of specimens and delivery of final paper results. Electronic delivery of results can make a big impact although the importance of ward visits and eyeball contact with prescribers by laboratory personnel cannot be over-emphasised (17).

The role of multi-disciplinary antibiotic teams and infectious disease pharmacists need to be explored further. Clearly, involvement of prescribers is paramount if antibiotic stewardship is to move forward in any meaningful way (18).

Hospital and Primary Care Executives

- Quality antibiotic prescribing should be a Strategic Goal of Executives and an objective of Clinical Governance.
- Infection Control and facilities for education and audit of antibiotic prescribing should be adequately resourced.
- A multi-disciplinary Antibiotic Team should be created and empowered to act to control injudicious use of antibiotics.
- Minimum Clinical Standards in Infection Control and Antibiotic Prescribing should be set and audited. Failure to achieve these standards should result in appropriate measures being taken to improve practice.

The public health aspects of antibiotic resistance necessitate that executive responsibility be taken for antibiotic prescribing in future (18). For the doctor making the prescribing decision on any individual patient, it is often difficult to balance the various aspects of the decision making progress. It is essential that the burden of some of the responsibilities be borne by the institution such that spiraling therapeutic empiricism does not dominate in the decision

making progress, resulting in unnecessary broad spectrum treatment in order to cover 100% of possible pathogens (6).

Formularies, policies and guidelines can, of course, address most of these issues so executive representatives need to be involved in drawing these up and the legal issues regarding compliance with them clarified (19)

Education

- Each country and region should have an educational programme for patients, health care professionals and students to reduce patient pressure on doctors to prescribe antibiotics and educate medical students and all health care professionals on good quality antibiotic prescribing and responsible use of antibiotics

Education at all levels, from the public and medical students to senior doctors, is essential but has often been neglected (20). This has implications for resource allocation but the evidence from the last few years is that this can be very successful (21). The Industry has had a major role in the education of prescribers although various aspects of this have been called into question. The challenge for the future is to harness the undoubted resources of the Industry to improve the quality of prescribing.

Continuous Professional Development/Clinical Governance

- As all doctors prescribe antibiotics, good quality antibiotic prescribing should be part of all doctors continuous professional development, accreditation and clinical governance programmes.

The concepts of clinical standards and clinical governance are gaining ground and as they are linked to continuous professional development, they can be linked into educational programmes (22). Clearly, quality of antibiotic prescribing can and should be an issue for

assessment of performance. Professional regulations and quality indicators should be set as part of the Strategic Goals of Healthcare Institutions.

National/European Measures

- Facilities should exist for regular expert review of new and old agents to ensure appropriate licensing of antibiotics.
- Facilities should be provided for national surveillance of antibiotic resistance, research into its clinical significance and support for production of evidence based guidelines on treatment of infections.
- Fast-track development of key agents and prolonged patent life of narrow-spectrum, limited use antibiotics should be facilitated.
- Financial aspects as they pertain to availability of key agents and their appropriate restriction should be considered.
- OTC availability of antibiotics should be banned and quality control of generic antibiotics ensured. Better access to medical advice should be ensured.
- Academic Bodies and National Organisations should be encouraged to take a lead in education of the public and prescribers.
- Harmonisation of certain practices, at all levels, should be encouraged to ensure adherence to policies.

There is a lot of work that can be done at a National and European level. The continued place of old antibiotics and the place of new agents need better means of assessment regarding promotion, areas of use and assurance regarding availability where it may not be economically viable for a manufacturer to make it available. Registration issues are currently being addressed by the European Medicines Evaluation Agency. Strategies for improving the usefulness of clinical trials and designing dosing schedules according to pharmacodynamic principles need to be expanded.

Medical Societies need to take on board issues of antibiotic prescribing, particularly as they pertain to clinical governance, standards for audit and education of the profession and public. Harmonization at a European level should ensure minimum standards.

Pharmaceutical Companies

- Ethical promotion of all antibiotics should be encouraged.
- Discounting to pharmacists should be discouraged.
- Promotional activities should be notified to Health Authorities and Health Care institutions in advance for prior agreement.

Promotional activities should be agreed in advance so that they do not contravene local policies. They should comply with agreed National Guidelines (obligatory or voluntary) and there should be satisfactory policing. Unethical practices such as discounting to pharmacists should be discouraged.

Table 1

<u>ESGAP subgroups</u>		
Subgroup	Topic	Chairperson
1. The Role of National/ European policies	Regulation, sale, supply, distribution	V Krcmery The Faculty of Nursing and Public Health Trnava University Hornoptocna 23 91843 Trnava Slovakia
2. Prescribing guidelines/	Hospital Community Inappropriate/ good prescribing Physician motivation	J van der Meer University Hospital Nijmegen Sint Radboud Dept. General Internal Medicine P.O. Box 9101 6500 HB NIJMEGEN
3. Minimum Standards In Antibiotic Stewardship	European Hospitals Implementation/Audit	I M Gould Dept. of Medical Microbiology Aberdeen Royal Infirmary Foresterhill Aberdeen Scotland AB25 2ZN
4. Use of laboratories	New diagnostic methods / rapid methods	H Verbrugh Academisch Ziekenhuis Rotterdam Dept. of Microbiologie 3000 DR Rotterdam The Netherlands
5. Education/information	Diffusion/ promotion of guidelines Public perception Community action	D Monnet Dept. of Microbiological R &D Statens Serum Institut Artillerie 5 (46/102) DK 2300 Copenhagen The Netherlands
6. Data centre, Research, Publications, Website	To keep up with literature/internet Communicate with expert groups	B Schlemmer Critical Medicine Hôpital St Louis 1, rue Claude vellefaux Paris Cedex 10 France 75475
7. New antibiotics/ pharmacoeconomics/ pharmacokinetic/ pharmacodynamics	Dosing/Indications	H Giamerellou National & Kapodistrian University of Athens Athens Medical School 4th Department of Internal Medicine Sismanoglio General Hospital 151 26 Attikis Greece

8. Consumption

Benchmarking

H Goossens
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9. Outcome

Antibiotic resistance

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Table 2

Minimum Standards for Antibiotic Stewardship

- Clinical Practice
- Health Care Administration
- Pharmacies & Laboratories
- Hospital and Primary Care Executives
- Education
- CPD/Clinical Governance
- National/European Measures
- Pharmaceutical Companies

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