



Title	Optimising antimicrobial prescription in hospitals by introducing an antimicrobial stewardship programme in Hong Kong: Consensus statement
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Optimising antimicrobial prescription in hospitals by introducing an antimicrobial stewardship programme in Hong Kong: consensus statement

改善醫院內處方抗生素而在香港設立抗生素導向計劃的結論綜述

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Objective. To discuss the implementation of an ‘antimicrobial stewardship programme’ as a means to improve the quality of antimicrobial use in a hospital setting in Hong Kong.

Participants. Consensus working group on ‘antimicrobial stewardship programme’, The Scientific Committee on Infection Control, Centre for Health Protection, Department of Health, comprised 11 experts. The remit of the working group was to discuss the rationale and requirement for optimising antimicrobial prescriptions in hospitals by the introduction of an ‘antimicrobial stewardship programme’.

Evidence. PubMed articles, national and international guidelines, and abstracts of international meetings published between January 2000 and December 2004 on programmes for improving the use of antimicrobials in hospitals. Only English medical literature was reviewed.

Consensus process. Data search was performed independently by three members of the working group. They met on three occasions before the meeting to discuss all collected articles. A final draft was circulated to the working group before a meeting on 3 January 2005. Five commonly asked questions about an ‘antimicrobial stewardship programme’ were selected for discussion by the participants. Published information on the rationale, components, outcome measures, advantages, and disadvantages of the programme was reviewed. Recent unpublished data from local studies of an ‘antimicrobial stewardship programme’ were also discussed. The timing, potential problems, and practical issues involved in the implementation of an ‘antimicrobial stewardship programme’ in Hong Kong were then considered. The consensus statement was circulated to and approved by all participants.

Conclusion. The continuous indiscriminate and excessive use of antimicrobial agents promotes the emergence of antibiotic-resistant organisms. Antimicrobial resistance substantially raises already-rising health care costs and increases patient morbidity and mortality. Pattern of prescriptions in hospitals can be improved through the implementation of an ‘antimicrobial stewardship programme’. A ‘universal’ and ‘continuous’ ‘antimicrobial stewardship programme’ should now be established in Hong Kong hospitals.

目的: 討論藉着「抗生素導向計劃」改善香港醫院內抗生素的使用質素。

參與者: 衛生署衛生防護中心轄下感染控制科學委員會內的「抗生素導向計劃」協議工作小組, 由十一名專家組成。工作小組討論成立此計劃以改善醫院內處方抗生素的理據和要求。

證據: 透過PubMed搜尋系統, 搜尋2000年1月至2004年12月期間, 關於改善醫院內處方抗生素計劃的文章、全國性或國際指引, 以及國際會議的論文撮要(只參考英文文獻)。

綜述過程: 工作小組其中三人負責獨立搜尋資料和數據。三人在會議前會面了三次, 討論搜尋到的所有相關文章, 並將宣言草稿在2005年1月3日會議前給予工作小組成員傳閱。參與者討論了五個關於「抗生素導向計劃」的常見問題, 並參考

了一些討論計劃理據、組成內容、結果測量、優點和缺點的已出版資料。工作小組亦討論了一些本地未曾出版的「抗生素導向計劃」的數據。然後考慮在香港實施「抗生素導向計劃」的時間、潛在問題和實施問題。結論綜述在傳閱後獲得所有參與者贊成。

結論：不斷無限制地濫用抗生素，會促使抗藥性生物的出現。微生物抗藥性會嚴重加重已節節上升的醫療成本和加劇病人發病率和死亡率。透過實施「抗生素導向計劃」，醫院處方抗生素的習慣會得到改善。現在香港的醫院應要實施一個包涵整體和持續的「抗生素導向計劃」。

Introduction

The discovery of penicillin by Alexander Fleming was a major breakthrough in the battle against infectious diseases. Today, antibiotics are the most widely prescribed drugs, yet their value is being threatened by an alarming increase in antibiotic-resistant bacteria. Multidrug-resistant strains of many commonly encountered bacteria such as *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella spp*, *Neisseria gonorrhoeae*, and *Pseudomonas aeruginosa* have already emerged. In Hong Kong, there is evidence that the drug-resistant pneumococci, methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum β -lactamases (ESBLs)-producing Enterobacteriaceae, and carbapenemase-producing *Acinetobacter* are more prevalent than in many other countries.¹ The indiscriminate and excessive use of antimicrobial agents within hospitals promotes the emergence of such antibiotic-resistant organisms. Strategies that optimise antimicrobial use are thus essential if this microbial threat is to be minimised.

The World Health Organization (WHO) defines optimal prescribing (prudent prescribing) as “the cost-effective use of antimicrobials which maximizes their clinical therapeutic effect, while minimizing both drug-related toxicity and the development of antimicrobial resistance.”^{2,3} In the United Kingdom, the Clinical Prescribing Subgroup (established in September 1999 as part of the response to the House of Lords report on ‘Resistance to Antibiotics and Other Antimicrobial Agents’⁴) uses a more comprehensive definition: “The use of antimicrobials in the most appropriate way for the treatment or prevention of human infectious diseases, having regard to the diagnosis, evidence of clinical effectiveness, likely benefits, safety, cost, and propensity for the emergence of resistance. The most appropriate way implies that the choice, route, dose, frequency and duration of administration have been rigorously determined.” In line with the above concepts, optimal antibiotic use should mean both ‘less’ use (ie less unnecessary use), and ‘appropriate’ use (ie not only the right antibiotic but also the right dosage, route, and duration to effect a cure while minimising side-effects and the development of resistance according to current knowledge). In hospitals, the concept of an ‘antimicrobial stewardship programme’ (ASP) as a means to achieve optimal prescribing is being increasingly discussed and adopted. This consensus group was formed to discuss the implementation of an ASP in Hong Kong.

Consensus process

Data in this review were identified by searches of PubMed,

references from relevant articles, national and international guidelines, and abstracts of recent international meetings on programmes to improve the use of antimicrobials and reduce bacterial resistance in hospitals. Search terms were “antibiotics”, “antimicrobials”, “antimicrobial agents”, “steward”, “stewardship”, “antimicrobial resistance”, and “program”. Recent reviews on related topics were also checked for additional references. Only papers in English language were reviewed. The review focused primarily on data published during the 5-year period from January 2000 to December 2004. The search was performed independently by three clinicians who met on three occasions to discuss all collected manuscripts and presented a final draft to all members of the consensus group. The group comprised local and overseas experts in the fields of clinical microbiology, clinical virology, dentistry, epidemiology, infection control, infectious diseases, and safety and environmental protection. The consensus meeting on “Optimizing antimicrobial prescriptions in hospitals by antimicrobial stewardship program in Hong Kong: rationale and requirement”, organised by the Scientific Committee on Infection Control, Centre for Health Protection, Department of Health, Hong Kong, was held on 3 January 2005. The document was discussed and subsequently revised before being re-circulated and finalised.

Questions and discussion

What is the rationale for optimising antimicrobial use?

The impetus behind the promotion of optimal antimicrobial use lies in the growing concern about antimicrobial resistance. As antimicrobial resistance increases, many previously time-honoured, first-line therapies (eg ampicillin for *E coli*, erythromycin for *Streptococcus pneumoniae*, fluoroquinolone for *N gonorrhoeae*) are rapidly losing their efficacy and are becoming obsolete.³ Antimicrobial resistance substantially raises already-rising health care costs: more expensive second- and third-line drugs must be prescribed; the infectious period for individuals is prolonged; morbidity, length of hospital stay, and mortality are increased. Infection with MRSA is a prime example. Nosocomial bloodstream infection prolongs hospitalisation by a mean of 8 days, longer than similar infections caused by methicillin-susceptible *S aureus*. This results in a trebling of direct cost.⁵ Treatment of MRSA may increase the cost per case by as much as US\$2500 to \$3700.⁶ In the United States, infection caused by nosocomial antibiotic-resistant organisms is estimated to result in an additional expenditure of US\$1.3 to \$4 billion yearly.⁷

There is an increasing amount of data linking antibiotic use with the development of bacterial resistance.³ In-vitro studies reveal that drug exposure selects for resistance, ecological studies correlate drug exposure with resistance, and clinical studies reveal that patients prescribed antimicrobial drugs are more likely to be colonised or infected with resistant bacteria. In the last two decades, bacterial resistance has evolved and spread rapidly in the health care setting. The treatment of several multidrug-resistant pathogens that have become widespread, including MRSA, vancomycin-resistant enterococci (VRE), ESBLs-producing Enterobacteriaceae, and multidrug-resistant *Pseudomonas aeruginosa* (MRPA) is difficult. This is largely due to the overuse and misuse of antimicrobial drugs.⁸

As many as 30% to 40% of hospital in-patients in developed countries are prescribed antimicrobial agents. Reasons for prescription vary widely and prescriptions are often suboptimal, indicating a need to standardise antimicrobial use.^{9,10} An attempt was made as early as the 1970s to assess the quality of antimicrobial drug prescription using specifically designed flowchart and quality indicators.¹¹ When such quality indicators were applied as tools for clinical audit of antimicrobial prescription, 49% to 55% of prescriptions for hospitalised patients were reported to be suboptimal.¹² This adversely affects patient outcome and increases the risk of antimicrobial resistance.¹³⁻¹⁶ For example, the selection of antimicrobial resistance in nosocomial pneumonia has been linked to suboptimal antimicrobial exposure.¹⁵ In Hong Kong, suboptimal antibiotic prescription has been reported to contribute strongly to the emergence of levofloxacin-resistant *S pneumoniae*.¹⁶

The problem of antimicrobial resistance may be further complicated by an uncertain supply of new agents¹⁷⁻¹⁹ and a dwindling number of companies investing in antimicrobial agents.²⁰ In the 1930s and 1940s, four new classes of antibiotics were approved: sulphonamides, β -lactamase, aminoglycosides, and chloramphenicol. In the 1950s and 1960s, a further six antibiotic classes were added: tetracycline, macrolides, glycopeptides, rifamycins, quinolones, and trimethoprim. From the 1970s to 1990s, no novel classes were licensed and all new drugs were derivatives of existing agents. Between 2000 and 2004, only two new classes of antibiotics have been approved: oxazolidinones (linezolid) and the cyclic lipopeptides (daptomycin). Additional novel antibacterial agents may be a future possibility but improvements by clinicians in their use of existing antibiotics is imperative.

What is an 'antimicrobial stewardship programme'? Who are the advocates?

The dangerous repercussions of antibiotic abuse have been recognised by institutions and hospitals for over half a century.²¹⁻²⁵ Professional societies and public health guardians including the WHO, Infectious Diseases Society

Methods to implement antimicrobial control

1. Provision of written hospital guidelines
2. Educational efforts aimed at changing prescribing practices of physicians
3. Providing consultation from clinical microbiologist/infectious diseases specialist
4. Restriction of hospital formulary through the Drug and Therapeutics Committee
5. Utilisation review with guidelines for rational and appropriate usage
6. Ongoing monitoring and analysis of antimicrobial usage
7. Ongoing surveillance of antimicrobial susceptibility
8. Monitoring adherence to advice on choice of antimicrobial agents
9. Feedback to physicians

of America (IDSA), Alliance for the Prudent Use of Antibiotics, Food and Drug Administration, Centers for Disease Control and Prevention, and National Institutes of Health all support programmes that promote optimal antimicrobial use,^{26,27} and some have proposed an action plan.^{2,28}

'Antimicrobial stewardship' involves the optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance.²⁹ In practice, this involves prescribing antimicrobial therapy only when it is beneficial to the patient, targeting therapy to the desired pathogens, and using the appropriate drug, dosage, and duration. It should not be viewed simply as reduced use or a strategy for cost containment. Instead, minimising exposure to drugs, performing dosage adjustments, reducing redundant therapy, and targeting therapy to the likely pathogens, can be viewed as a strategy to enhance patient safety.

The programme involves a multidisciplinary, programmatic, prospective, interventional approach to optimising the use of antimicrobial agents. The multidisciplinary team typically includes the clinical microbiologist, infectious diseases specialist, infection-control practitioner, and clinical pharmacist. Recruitment of members from other medical specialties, such as surgery and paediatrics, is also recommended. Multiple approaches have been employed to enforce hospital policies that limit or control antimicrobial use (Box). Under the auspices of an ASP, several behavioural methods have been used successfully to effect changes, including problem-based education, consensus guidelines, peer review, concurrent review, data feedback, computer-based reminders, financial incentives, and the use of opinion leaders.^{30,31}

The importance of a committed hospital administration is well recognised. The Society for Healthcare Epidemiology of America (SHEA) consensus statement, titled "Strategies to prevent and control the emergence and

Table 1. Methods and outcomes measured in recently published antimicrobial stewardship programmes³⁷⁻⁴²

Hospital size, primary strategy	Place	Length of study period	Patient outcomes	Bacterial resistance and infection outcomes	Impact on antibiotic use and costs
575-Bed, prior authorisation ⁴⁰	US	6 months	No difference in survival in patients with gram-negative bacteraemia; no difference in the time from positive blood culture to receipt of appropriate antibiotics; no difference in infection (bacteraemia)-related length of stay	Significant reduction in resistance rates	Significant reduction in the use of the following restricted agents: aztreonam, ceftazidime, imipenem, ticarcillin-clavulanate; first-year reduction in total antimicrobial expenditure was US\$803 910
2500-Bed, prior authorisation ⁴²	Italy	1 year	Not determined	Not determined	Usage and expenditure in the restricted group of antibiotics decreased by 78.5% and 53.5%, respectively; usage in the unrestricted antibiotics increased by 32.6%
250-Bed, concurrent review ³⁷	Argentina	2 years	No difference in crude mortality; the mean hospitalisation for infected patients decreased	Decreasing resistance to ceftriaxone by <i>Proteus mirabilis</i> and <i>Enterobacter cloacae</i> ; decreasing rate of methicillin-resistant <i>Staphylococcus aureus</i> ; decreasing resistance to carbapenem by <i>Pseudomonas aeruginosa</i>	Total cost saving was US\$913 236
Medium size, concurrent reviews ⁴¹	US	7 years	Not determined	Significant decrease in nosocomial infections caused by <i>Clostridium difficile</i> ; significant decrease in nosocomial infections caused by resistant Enterobacteriaceae (P=0.02)	22% Decrease in the use of intravenous broad-spectrum antibiotics (P<0.0001); use of third-generation cephalosporins and aztreonam decreased rapidly during the study period (from 24.7 DDD*/1000 patient-days to 6.2 DDD/1000 patient-days; P<0.0001); cost savings of US\$200 000 to \$250 000 per year
731-Bed, concurrent review ³⁸	US	3 years	No difference in the mortality and length of stay	No significant change in resistance rates of common nosocomial gram-negative organisms	28% Reduction of broad-spectrum antimicrobial use
80-Bed, concurrent review and prior authorisation ³⁹	US	4 years	No difference in overall and infectious disease-specific mortalities; no difference in relapse rate; no difference in hospitalisation for all patients and antibiotic-treated patients; no difference in re-hospitalisation rate	No significant change in susceptibility patterns of bacteria	Antibiotic expenditure decreased by 53%; intravenous drugs accounted for >90% of cost savings; significant decrease in usage of broad-spectrum antibiotics; using DDD data: reduction in overall antimicrobial use: 36%; reduction in intravenous antimicrobial use: 46%

* DDD denotes defined daily dose

spread of antimicrobial-resistant microorganisms in hospitals,”³² is the first document to state that without clear commitment from the hospital leadership, programmes to improve and optimise antibiotic use will never be successful. The willingness and interest of infectious disease specialists or infection-control practitioners will never be sufficient if the hospital administration does not emphasise antibiotic control as a priority. These sentiments

are echoed in the SHEA/IDSA guidelines³³ and by several opinion leaders.^{34,35}

The development of programmes to control and promote the rational use of antimicrobial drugs has become more prevalent in the United States, United Kingdom, and European countries, in the past few decades in an attempt to curb the development of multidrug-resistant bacteria

in hospitals.³⁶ Likewise in Hong Kong, there is considerable public, political, and professional awareness of the increasing burden of antimicrobial resistance.

Is an ‘antimicrobial stewardship programme’ beneficial? How can benefits be documented? Does an ‘antimicrobial stewardship programme’ result in better and more optimal antibiotic use in the hospital setting?

An ASP has several benefits (Table 1³⁷⁻⁴²). It reduces the use of targeted antibiotics and antimicrobial expenditure. Nonetheless crude or infection-related mortality rates, time to receipt of appropriate antibiotics, and length of hospitalisation are not affected by the implementation of ASPs.³⁷⁻⁴⁰ These findings are important because they indicate that patient safety is not compromised. The impact on antimicrobial resistance varies because the factors that promote resistance are complex.^{43,44} A strong relationship exists between certain antibiotic classes and multidrug-resistant pathogens: vancomycin and VRE; third-generation cephalosporins and ESBLs; as well as fluoroquinolones and MRSA and MRPA. At an institutional level, programmes designed to limit utilisation of agents that exert greater effect on the above have reduced specific resistance rates.

Measurement and monitoring is an essential part of the programme. After an initial implementation of a restricted formulary and antimicrobial approval system, the team should meet regularly to review and update the formulary, assess its effectiveness, provide and coordinate ongoing physician education, and analyse antimicrobial utilisation data within the hospital. The programme should be dynamic and continually reassessed, with new components added and unsuccessful components deleted.

To allow for accurate intra- and inter-institutional comparisons, confounding differences in expenditure related to acquisition costs and variations in the amount of individual antibiotic used for individual patients should be standardised. Each antimicrobial agent should be assigned a fixed or defined daily dose (DDD) in the manner recently supported by the WHO.⁴⁵ Defined daily dose is an assumed average maintenance dose per day of a drug used for its main indication in adults. It does not necessarily reflect the recommended or prescribed daily dose. Thus, it can give a rough estimation of consumption of the drugs being monitored but is independent of price or formulation. The following measures can be calculated as standardised rates (in terms of DDDs per denominators): (1) per patient admitted, (2) per patient treated, (3) per 1000 hospital-days, and (4) per 1000 treatment-days.

Is this the right time for Hong Kong to introduce an ‘antimicrobial stewardship programme’? Are we too early or are we too late, and why?

In Hong Kong, few would dispute the threat from antimicrobial resistance and the needless expenditure associated

with excessive antimicrobial use.⁴⁶ Recent surveys show that suboptimal antimicrobial prescriptions may be commonplace in our hospitals,⁴⁷ and such practice can be improved. In the two university hospitals, a recent prospective study found that 76% of antibiotic prescriptions for patients hospitalised with exacerbated chronic obstructive pulmonary disease were unjustified according to the prevailing Global Initiative for Chronic Obstructive Lung Disease guidelines.⁴⁷ A year later in 2004, real-time audit of “big gun” antibiotics in two hospitals revealed that 20% to 25% of the prescriptions were not justified or suboptimal. The most common errors included treatment of colonisation, omitting to use a more specific and equally effective alternative antimicrobial or less toxic antimicrobial, and inappropriate duration (personal communication). In another prospective study of antibiotic combinations prescribed over a 6-month period, one of the agents was redundant in 80% of 200 prescriptions.⁴⁷

In response to an increasing demand for a local antibiotic reference, a multidisciplinary group produced the IMPACT (Interhospital Multi-disciplinary Programme on Antimicrobial ChemoTherapy) document in 1999 with the vision of introducing antimicrobial stewardship into the Hospital Authority (HA) hospitals.⁴⁶ Despite some encouraging progress in the past 5 years, there are problems related to implementation, process evaluation, and programme sustainability. In order to properly address the complex issues in antibiotic prescription, specific mechanisms and designated manpower are required to identify the institutional pattern of use, areas of misuse, and all the suboptimal indications, dosages, formulations, routes, and duration. The issue of sustainability should be dealt with at managerial and professional levels. Without institutional priority, and clearly defined responsibilities and accountability, real improvement is unlikely.⁴⁸ Ongoing activities conducted by properly trained personnel such as infection-control doctors and nurses are essential for the implementation of infection-control policies. Infection-control staff and staff promoting an ASP have overlapping roles. Thus it may be prudent to expand the role of existing infection-control teams and introduce ‘antimicrobial and infection-control officers’ and ‘antimicrobial and infection-control nurses’.

More action is required in areas where antimicrobial resistance is most serious. In Hong Kong, there is evidence that antibiotic resistance of some important nosocomial pathogens is worse than that in many other parts of the world.¹ Methicillin-resistant *Staphylococcus aureus* is endemic among local hospitals with 30% to 50% of all *S aureus* resistant to methicillin. In intensive care units, 70% to 80% of *S aureus* is MRSA. Most MRSA are also resistant to a number of other drugs. The incidence of VRE in Hong Kong is low at present: the first isolate was imported in 1997. Since then sporadic cases have been identified in at least five public and one private hospitals. In two public hospitals, clustering and nosocomial trans-

Table 2. Potential barriers to reaching the strategic goals³²

Barrier	Countermeasures and improvement strategies
Ownership and accountability Lack of ownership and accountability for recognising and reporting trends Failure to integrate work of laboratory, infection-control, medical, nursing, and care-unit staff	Designate responsibility and accountability for the process Set up a multidisciplinary team to develop a collaborative system and monitor results
Staff knowledge and practice Lack of time for the laboratory and/or infection-control staff to generate and analyse data Lack of time for health care providers to examine and discuss data, and inconsistent or erroneous interpretation of data by staff	Ensure adequacy of laboratory and infection-control staffing and prioritise activities of staff so that data can be generated and analysed Report data in an easy-to-read/interpret format and, when appropriate, include data interpretation in the report
Physician attitudes Lack of trust in the hospital administration	Use a data-driven approach to cultivate trust, eg communicate regularly with physicians about trends in antimicrobial usage, cost, and resistance, feedback to individual physicians about their performance results
Expertise Lack of expertise in biostatistics (eg presenting trends and analysing data)	Ensure availability of consultants, especially when designing analytical strategy and interpreting trend data

mission has been reported. The ESBLs are bacterial enzymes that are capable of inactivating third-generation cephalosporins. A survey of four Hong Kong hospitals in 1997/1998 revealed rates of 6% to 23% for *Klebsiella pneumoniae* and 9% to 14% for *E coli*.¹

In the United States, a “Public health action plan to combat antimicrobial resistance (action plan)” was developed in 1999. In the United Kingdom, significant progress has been made in optimising the clinical use of antimicrobials since 2000 in terms of governmental directives, strategy, and action plan.^{28,49} Similar initiatives have also been launched in Taiwan and South Korea. Many studies have found that optimisation of antibiotics in hospitals is feasible, safe, and effective. A diversity of approaches have been reported and the experience accumulated so far indicates that a multi-faceted ‘stewardship’ approach has clear advantages.^{29,34-37,39,41,50,51} A systematic review of the quality of interventions to improve hospital antibiotic prescription reveals that the existing approaches are not ideal and further refinement will be required.⁵²

A ‘universal’ and ‘continuous’ ASP should now be established in Hong Kong hospitals. With the establishment of the Centre for Health Protection, this is a timely initiative. A closer collaboration between partners in different sectors including the HA, Department of Health, Hong Kong Medical Association, the private hospitals, the two medical schools, patient’s groups, and pharmaceutical companies is essential. During the process of introduction, the Centre for Health Protection could take the lead and work out the directions and strategies for public and private hospitals. Implementation of an ASP should not be hasty. Instead, definite targets should be set in order to monitor the uptake, progress, effectiveness, and safety of such a programme. The assistance of local experts who have the experience of ASP should also be sought.

What are the disadvantages of an ‘antimicrobial stewardship programme’? What problems have been reported? Are there any arguments against having the programme? Is there a role for an alternative mechanism?

The stewardship programme involves proactive monitoring and feedback. An alternative approach is ‘no control’ (ie only by passive means). Such an approach relies heavily on the distribution of national guidelines and has been shown not to work.⁵³ Guidelines are seldom studied thoroughly by clinicians, and even if read, are unlikely to be incorporated into everyday practice. There are concerns about ASP that should also be addressed (Table 2³²). The perception of ‘threatened physician autonomy’ can be a significant hindrance. Previous studies and local experience have indicated that this is often an ‘emotional’ response that can be resolved by immediate concurrent feedback, consensus building, involvement of institutional opinion leaders, and attention to process measures.⁵⁴⁻⁵⁶ Similar programmes have been launched successfully in some HA hospitals for other drugs, including the statins, calcium channel blockers, and acid-suppressive agents.

Another barrier to implementation is the perception that an ASP is solely cost-driven and patient safety may be compromised. For this reason, recent reports have emphasised the inclusion of quality indicators such as time to reception of appropriate empirical antibiotics. Other suggested indicators include: (1) clinical outcomes of bacteraemia due to gram-negative organisms,⁴⁰ (2) mortality for all patients, for those treated with antimicrobials, and for those with an infection, (3) duration of hospital stay for all patients and for those treated with antimicrobial drugs, and (4) re-hospitalisation rate within 30 days after discharge for all patients and those treated with antimicrobial drugs.³⁹ As in any quality improvement programme, a financial incentive is important to secure support by

the hospital management. The ASP is no exception. Good leadership and effective communication are essential to keep members, prescribers, and patients focused on the problem. This may be enhanced by the establishment of a multidisciplinary steering committee, and by regular use of data feedback on the patterns of use, patient outcomes, and antimicrobial resistance data. In principle, committee members should have a strong sense of commitment and cooperation. The composition of the multidisciplinary steering committee may be unique to each institute.

Strategic directions

In the face of rising rates of drug resistance among microorganisms and no promise of novel antibiotics, strategies are needed to minimise the development and spread of antimicrobial resistance. These strategies have in common three key and inter-related components: surveillance, prudent antimicrobial use, and infection control. With regard to promoting prudent antimicrobial use through implementation of ASP in the hospital setting, the present meeting group proposed the following strategic directions.

Focus on antimicrobial resistance containment

Containment of antimicrobial resistance is the main rationale for promoting optimal antimicrobial use. Since antimicrobial resistance may spread across health care boundaries, efforts directed at their containment by promoting better use of existing antimicrobial drugs should be on a territory-wide basis, and involve the public and private sectors. The hospital-based component should be part of a more comprehensive strategy for Hong Kong to be centrally coordinated by the Centre for Health Protection.

Focus on overcoming existing barriers to prudent prescribing by coordinated efforts

The concept of promoting prudent antimicrobial use by antimicrobial stewardship has clear merits. It is supported by a number of international and professional bodies, and should be given higher priority by hospitals in Hong Kong. In promoting the implementation of ASP, there should be coordinated efforts by professionals, administrative staff, regulatory agencies, pharmaceuticals, and the public directed at overcoming the existing barriers through a range of measures such as education, guidelines, prescribing support, organisational support, feedbacks, and data-driven communications. As an initial step, each institute or hospital will need to form a steering group to identify the institutional issues and priorities, and to devise a working plan.

Focus on health care quality improvement

The implementation of ASP to promote prudent antimicrobial use may be viewed as an example of quality improvement. Quality indicators and timely feedback of data are essential to safeguard health care quality. Before launching, specific programme targets should be set and process and outcome measures laid down. Subsequently, programme findings should be regularly monitored and feedback provided to parties concerned.

Conclusion

Antimicrobial drug resistance is an important public health threat because it endangers our ability to effectively treat infection. A multi-faceted approach that involves the continuous application of a package of interventions should be implemented at regional and international levels. In the health care setting, efforts should focus on infection prevention, effective diagnosis, early treatment, wise use of antimicrobials, and breaking the chain of transmission.⁵⁷ In Hong Kong, there is room for improvement in the use of antimicrobial drugs in hospitals. Recent research indicates that improvement in the pattern of prescriptions is feasible and can be implemented by means of ASP in a safe, scientific, and professional manner. As antibiotic-resistant bacteria become more widespread, such initiatives will become increasingly important. As the fight against antimicrobial resistance continues, a major challenge in future will be maintaining the viability of and sustaining an ASP in the long term.

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References

1. Wang TK, Ho PL. The challenge of antibiotic resistance in Asia: problems and solutions. *Medical Progress* 2003;30:41-8.
2. Simonsen GS, Tapsall JW, Allegranzi B, Talbot EA, Lazzari S. The antimicrobial resistance containment and surveillance approach—a public health tool. *Bull World Health Organ* 2004;82:928-34.
3. Smith RD, Coast J. Antimicrobial resistance: a global response. *Bull World Health Organ* 2002;80:126-33.
4. Clinical prescribing subgroup. Optimising the clinical use of antimicrobials: report and recommendations for further work. Hong Kong: Department of Health; 2001.
5. Abramson MA, Sexton DJ. Nosocomial methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* primary bacteremia: at what costs? *Infect Control Hosp Epidemiol* 1999;20:408-11.
6. Rubin RJ, Harrington CA, Poon A, Dietrich K, Greene JA, Moiduddin A. The economic impact of *Staphylococcus aureus* infection in New York City hospitals. *Emerg Infect Dis* 1999;5:9-17.
7. Cosgrove SE, Carmeli Y. The impact of antimicrobial resistance on health and economic outcomes. *Clin Infect Dis* 2003;36:1433-7.
8. Levy SB, Marshall B. Antibacterial resistance worldwide: causes, challenges and responses. *Nat Med* 2004;10(12 Suppl):122S-129S.
9. Carling PC, Fung T, Coldiron JS. Parenteral antibiotic use in acute-care hospitals: A standardized analysis of fourteen institutions. *Clin Infect Dis* 1999;29:1189-96.
10. Lesch CA, Itokazu GS, Danziger LH, Weinstein RA. Multi-hospital analysis of antimicrobial usage and resistance trends. *Diagn Microbiol Infect Dis* 2001;41:149-54.
11. Kunin CM, Tupasi T, Craig WA. Use of antibiotics. A brief exposition of the problem and some tentative solutions. *Ann Intern Med* 1973;79:555-60.
12. Kumarasamy Y, Cadwgan T, Gillanders IA, Jappy B, Laing R, Gould IM. Optimizing antibiotic therapy—the Aberdeen experience. *Clin*

- Microbiol Infect 2003;9:406-11.
13. Fowler RA, Flavin KE, Barr J, Weinacker AB, Parsonnet J, Gould MK. Variability in antibiotic prescribing patterns and outcomes in patients with clinically suspected ventilator-associated pneumonia. *Chest* 2003;123:835-44.
 14. Brown RB, Iannini P, Gross P, Kunkel M. Impact of initial antibiotic choice on clinical outcomes in community-acquired pneumonia: analysis of a hospital claims-made database. *Chest* 2003;123:1503-11.
 15. Thomas JK, Forrest A, Bhavnani SM, et al. Pharmacodynamic evaluation of factors associated with the development of bacterial resistance in acutely ill patients during therapy. *Antimicrob Agents Chemother* 1998;42:521-7.
 16. Ho PL, Tse WS, Tsang KW, et al. Risk factors for acquisition of levofloxacin-resistant *Streptococcus pneumoniae*: a case-control study. *Clin Infect Dis* 2001;32:701-7.
 17. James JS. Empty antibiotic pipeline critically endangers public: IDSA report. *AIDS Treat News* 2004;404:7.
 18. Nelson R. Antibiotic development pipeline runs dry. New drugs to fight resistant organisms are not being developed, experts say. *Lancet* 2003;362:1726-7.
 19. Wenzel RP. The antibiotic pipeline—challenges, costs, and values. *N Engl J Med* 2004;351:523-6.
 20. Projan SJ. Why is big Pharma getting out of antibacterial drug discovery? *Curr Opin Microbiol* 2003;6:427-30.
 21. Jawetz E. Infectious diseases: problems of antimicrobial therapy. *Annu Rev Med* 1954;5:1-26.
 22. Nolen WA, Dille DE. Use and abuse of antibiotics in a small community. *N Engl J Med* 1957;257:33-4.
 23. Kunin C. Antibiotic usage review needed to control resistant organisms. *Hosp Infect Control* 1981;8:131-2.
 24. Perry TL. Antibiotic abuse: the testimony of medical students. *Can Med Assoc J* 1975;112:1428-9.
 25. Hawley HB. Curbing antibiotic abuse: a tough pill to swallow. *Am Coll Physicians Obs* 1981;1:1.7.
 26. Bell DM. Promoting appropriate antimicrobial drug use: perspective from the Centers for Disease Control and Prevention. *Clin Infect Dis* 2001;33(Suppl 3):245S-250S.
 27. Bell DM. Development of the public health action plan to combat antimicrobial resistance and the CDC activities related to its implementation. In: Knobler SL, Lemon SM, Najafi M, Burroughs T, editors. *The resistance phenomenon in microbes and infectious diseases vectors: implications for human health and strategies for containment: workshop summary*. Washington, DC: National Academy Press; 2003:198-206.
 28. Department of Health. *Hospital pharmacy initiative for promoting prudent use of antibiotics in hospitals*. London: Department of Health; 2003.
 29. Gerding DN. The search for good antimicrobial stewardship. *Jt Comm J Qual Improv* 2001;27:403-4.
 30. Thomson O'Brien MA, Oxman AD, Davis DA, Haynes RB, Freemantle N, Harvey EL. Audit and feedback: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev* 2000; (2):CD000259.
 31. Cauffman JG, Forsyth RA, Clark VA, et al. Randomized controlled trials of continuing medical education: what makes them most effective? *J Contin Educ Health Prof* 2002;22:214-21.
 32. Goldmann DA, Weinstein RA, Wenzel RP, et al. Strategies to prevent and control the emergence and spread of antimicrobial-resistant microorganisms in hospitals. A challenge to hospital leadership. *JAMA* 1996;257:234-40.
 33. Shlaes DM, Gerding DN, John JF Jr, et al. Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: guidelines for the prevention of antimicrobial resistance in hospitals. *Clin Infect Dis* 1997;25:584-99.
 34. Owens RC Jr, Fraser GL, Stogsdill P; Society of Infectious Diseases Pharmacists. Antimicrobial stewardship programs as a means to optimize antimicrobial use. Insights from the Society of Infectious Diseases Pharmacists. *Pharmacotherapy* 2004;24:896-908.
 35. Masterson RG. Antibiotic policies and the role of strategic hospital leadership. *J Hosp Infect* 1999;43(Suppl):261S-264S.
 36. Gould IM. Stewardship of antibiotic use and resistance surveillance: the international scene. *J Hosp Infect* 1999;43(Suppl):253S-260S.
 37. Bantar C, Sartori B, Vesco E, et al. A hospitalwide intervention program to optimize the quality of antibiotic use: impact on prescribing practice, antibiotic consumption, cost savings, and bacterial resistance. *Clin Infect Dis* 2003;37:180-6.
 38. Cook PP, Catrou PG, Christie JD, Young PD, Polk RE. Reduction in broad-spectrum antimicrobial use associated with no improvement in hospital antibiogram. *J Antimicrob Chemother* 2004;53:853-9.
 39. Ruttimann S, Keck B, Hartmeier C, Maetzel A, Bucher HC. Long-term antibiotic cost savings from a comprehensive intervention program in a medical department of a university-affiliated teaching hospital. *Clin Infect Dis* 2004;38:348-56.
 40. White AC Jr, Atmar RL, Wilson J, Cate TR, Stager CE, Greenberg SB. Effects of requiring prior authorization for selected antimicrobials: expenditures, susceptibilities, and clinical outcomes. *Clin Infect Dis* 1997;25:230-9.
 41. Carling P, Fung T, Killion A, Terrin N, Barza M. Favorable impact of a multidisciplinary antibiotic management program conducted during 7 years. *Infect Control Hosp Epidemiol* 2003;24:699-706.
 42. Bassetti M, Di Biagio A, Rebesco B, Amalfitano ME, Topal J, Bassetti D. The effect of formulary restriction in the use of antibiotics in an Italian hospital. *Eur J Clin Pharmacol* 2001;57:529-34.
 43. Burke JP. Antibiotic resistance—squeezing the balloon? *JAMA* 1998; 280:1270-1.
 44. Livermore D. Can better prescribing turn the tide of resistance? *Nat Rev Microbiol* 2004;2:73-8.
 45. Maxwell M, Heaney D, Howie JG, Noble S. General practice fundholding: observations on prescribing patterns and costs using the defined daily dose method. *BMJ* 1993;307:1190-4.
 46. IMPACT working group. *Reducing bacterial resistance with IMPACT: Interhospital Multi-disciplinary Programme on Antimicrobial ChemoTherapy*. Hong Kong: Centre of Infection, The University of Hong Kong; 2003.
 47. Ho PL. Antibiotic guidelines and optimization programme. In: Yuen KY, Wong SY, editors. *Infectious diseases update: course 6*. Hong Kong: Centre of Infection, University of Hong Kong; 2004:1-110.
 48. Scheckler WE, Brimhall D, Buck AS, et al. Requirements for infrastructure and essential activities of infection control and epidemiology in hospitals: a consensus panel report. Society for Healthcare Epidemiology of America. *Infect Control Hosp Epidemiol* 1998;19: 114-24.
 49. Department of Health. *Winning ways: working together to reduce healthcare associated infection in England*. Report from the chief medical officer. London: Department of Health; 2003.
 50. Gross R, Morgan AS, Kinky DE, Weiner M, Gibson GA, Fishman NO. Impact of a hospital-based antimicrobial management program on clinical and economic outcomes. *Clin Infect Dis* 2001;33:289-95.
 51. Keuleyan E, Gould M. Key issues in developing antibiotic policies: from an institutional level to Europe-wide. European Study Group on Antibiotic Policy (ESGAP), Subgroup III. *Clin Microbiol Infect* 2001; 7(Suppl 6):16S-21S.
 52. Ramsay C, Brown E, Hartman G, Davey P. Room for improvement: a systematic review of the quality of evaluations of interventions to improve hospital antibiotic prescribing. *J Antimicrob Chemother* 2003;52:764-71.
 53. Goldmann DA. Resistance movement: the antibiotic crisis in hospitals. *Health Syst Rev* 1997;30:20-4.
 54. McGowan JE Jr. Minimizing antimicrobial resistance: the key role of the infectious diseases physician. *Clin Infect Dis* 2004;38:939-42.
 55. LaRocco A Jr. Concurrent antibiotic review programs—a role for infectious diseases specialists at small community hospitals. *Clin Infect Dis* 2003;37:742-3.
 56. Kumana CR, Ching TY, Kong Y, et al. Curtailing unnecessary vancomycin usage in a hospital with high rates of methicillin resistant *Staphylococcus aureus* infections. *Br J Clin Pharmacol* 2001;52:427-32.
 57. Campaign to prevent antimicrobial resistance in healthcare settings. 12-step fact sheets. Centers for Disease Control and Prevention website: <http://www.cdc.gov/drugresistance/healthcare/tools.htm#factsheets>. Accessed 14 Apr 2005.