EDITORIAL

Antimicrobial resistance [AMR] has been identified as a major threat by the WHO 1 and is the subject of much discussion. World Alliance Against Resistance to antibiotics (WAAR) 2 and REACT 3, amongst others, have highlighted the clinical, societal and economic impact of AMR. After saving countless lives, antibiotics are in danger of losing their effectiveness due to an alarming increase in bacterial resistance combined with a decline in the antibiotic pipeline flow. An increasing number of treatment failures already occur in patients with infections caused by multi-drug, and even pan-drug, resistant bacteria 4.

Antimicrobial stewardship is a key strategy in overcoming the resistance threat, alongside infection control and environmental decontamination. It promotes careful and responsible management of antimicrobial use to achieve the four key goals of stewardship programmes: 1/ improved patient safety, 2/ improved patient outcomes, 3/ reduced resistance, 4/ reduced costs 5. The evolution of such programmes has been significant in the last 5 years.

At the 2011 and 2013 World HAI Forums 6, a number of presentations from around the world summarised examples of good stewardship practice implemented in different healthcare settings with varying levels of resources. Sharing and learning from these experiences and communicating them to the global community is an important component of managing or influencing change. This newsletter provides examples of this good or innovative practice with the aim of informing, encouraging and motivating others to do the same, using what resources they have available to achieve the responsible management of antibiotic use.

For references, refer to page 8.
“WINNING OVER MINDS”

To succeed, the imperatives of AMS must be communicated effectively, its aims need to be embraced by the unconverted and outcomes have to be convincing and transparent.

The ‘battle for the minds’ requires collection of a cumulative evidence base to support AMS. This utilises surveillance data and quality improvement science to highlight the urgency of the crisis and show how selected interventions can achieve solutions linked to the four AMS aims (as defined in Dilip Nathwani’s editorial). Through infection prevention measures such as improved hand hygiene and hospital cleaning, MRSA bacteremia rates are declining. In contrast, in Europe, rates of ESBL E. coli bacteremia are rising on an exponential scale, with reports of a greater than two-fold excess mortality (Figure 1). Community and hospital studies measuring quinolone consumption reveal a close relationship between volume of use and resistance.

To be effective, stewardship in hospitals requires a team-based approach and the support of senior management, but there is also a need to convince prescribers that they can individually contribute and make a difference. Simplistically, AMS can be seen as a battle to win the hearts and minds of antibiotic stakeholders.

“WINNING OVER HEARTS”

The ‘battle for the hearts’ challenges decades of conditioned feelings and beliefs about prescribing. It engages prescribers in an understanding of the precarious place of antibiotics in health-care. It seeks to shift the balance from a prevailing risk-averse approach. Doctors prefer to remain within a comfort zone, to avoid risk and cover knowledge gaps. This results in ‘defensive’ prescribing of broad-spectrum antibiotics, which narrowly focuses on delivering patient care outcomes at any cost – and with only illusory credibility. Instead, AMS promotes the understanding that uncontrolled use results in long-term loss of efficacy and can worsen outcomes when collateral selection pressure results in increased rates of C. difficile, MRSA or ESBL-producing Enterobacteriaceae.

Unlike for other medical specialities, much of community and hospital antibiotic prescribing is made on a ‘just in case’ basis, in order to deal with diagnostic uncertainty. This often leads to poorly thought out antibiotic selection. But such broad-spectrum prescribing will not teach judicious antibiotic use to the young healthcare professionals of the future. Indeed, ‘just in case’ use of carbapenem in the intensive care unit or ceftriaxone in heart failure, as well as prolonged orthopedic prophylaxis or longer treatment durations (just in case) simply continues the spiral of unnecessary use. This is partly due to a problem with the reward system. Junior doctors in many specialities are rarely applauded by their senior doctors for using narrow spectrum antibiotics or questioning antibiotic use, but the result is that on review ~50% of physician prescriptions are inappropriate.
However, for sustainability, AMS cannot be just about restriction, it needs to change mindsets and behaviour. Educational interventions, utilising a questionnaire and/or biomarker testing (CRP or PCT) result in reduced community antibiotic prescribing without poorer outcomes.10

Much antibiotic overuse occurs in respiratory infections. In a prospective hospital study of community-acquired pneumonia, Charles et al. demonstrated equivalent efficacy of narrow-spectrum, penicillin based therapy compared with 3rd generation cephalosporin use (Table 1).11 A study of 8 versus 15 days duration of therapy for culture-proven VAP in French Intensive Care Units did not increase clinical failure rates, instead it was associated with reduced resistance.12 Reductions in 3rd generation cephalosporin prescribing have been repeatedly demonstrated to result in reductions in hospital C. difficile infection (Figure 3).13

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Penicillin-based treatment recipients</th>
<th>Ceftriaxone-based treatment recipients</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%) of episodes</td>
<td>494 (55.8)</td>
<td>326 (36.8)</td>
</tr>
<tr>
<td>30-days mortality, % of episodes</td>
<td>3.8</td>
<td>8.6</td>
</tr>
<tr>
<td>IRS requirement, % of episodes</td>
<td>3.4</td>
<td>19.3</td>
</tr>
<tr>
<td>Duration of hospitalization, days Mean ± SD</td>
<td>7.1 ± 6.8</td>
<td>10.0 ± 10.6</td>
</tr>
<tr>
<td>Median</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Time to clinical stability, days Mean ± SD</td>
<td>2.7 ± 2.6</td>
<td>2.8 ± 2.8</td>
</tr>
<tr>
<td>Median</td>
<td>2</td>
<td>2</td>
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Many other examples abound, including safe conversion from intravenous to oral therapy, recording of indications, adherence to guidelines, use of unit-specific antibiograms, reduced durations of surgical prophylaxis and rapid diagnostic methods such as mass spectrometry.2, 14, 15, 16

AMS utilises simple improvement strategies that can be adapted to optimise antimicrobial prescribing in daily practice.17 Educational campaigns and guideline provision are one part of this but work best when combined with simple and sustainable interventions - such as audit and feedback methods or prescribing interventions that address poor performance and improve understanding of the practical use of antibiotics. A publication by the Australian Commission for Safety and Quality in Health Care provides practical steps for implementation of AMS programmes that can be adapted to any number of national, regional or local settings worldwide.18

AMS WORKS!

A recent Cochrane publication19 and the CDC website “Get Smart for Healthcare”20 document the utility of AMS programmes to affect multiple end points including C. difficile incidence, decreased resistance, antibiotic use and guidance compliance. At national and local organisational levels, these confirm that AMS programmes are a cost-effective and positive investment in patient care. At the user level, they provide positive reinforcement for the time invested championing AMS activities.

Finally, slowing resistance evolution may be even more critical than enhancing drug development. A recent global stewardship survey identifies barriers to the initiation, development and implementation of stewardship programmes internationally.21 However, despite challenges and limited resources, the work of groups such as ReAct (http://www.reactgroup.org/) and the examples of good AMS practice from around the world included in this newsletter, illustrate the range of initiatives that can be successfully implemented. Resistance is too much of a looming threat to risk not succeeding.

One of the four core actions recommended in the CDC’s 2013 timely landmark report on the threat of antimicrobial resistance is to “use antibiotics responsibly”.2 Good AMS practice is no longer a choice we can put off until tomorrow, it is a responsibility for today!

TOP TEN TIPS FOR EFFECTIVE ANTIBIOTIC PRESCRIBING

- Institute antibiotic treatment immediately in patients with life-threatening infection.
- Prescribe in accordance with local policies and guidelines, avoiding broad-spectrum agents.
- Document the indication(s) for antibiotic prescription in the clinical notes.
- Send appropriate specimens to the microbiology lab.
- Use antimicrobial susceptibility data to de-escalate/replace/add agents and to switch from intravenous to oral therapy.
- Prescribe the shortest antibiotic course likely to be effective.
- Always select agents that minimise collateral damage (i.e. selection of multi-resistant bacteria/C. difficile).
- Monitor antibiotic levels when needed (e.g. vancomycin).
- Use single-dose antibiotic prophylaxis wherever possible.
- Consult your local infection experts.

Adapted from UK Chief Medical Officer’s report 2011 - Volume Two: Infections and the rise of antimicrobial resistance.

REFERENCES

20. CDC website Get Smart for Healthcare.
Impact of a National Antimicrobial Stewardship Programme

D Nathwani1, J Sneddon1, A Patton2, W Malcolm1 on behalf of the Scottish Antimicrobial Prescribing Group (SAPG)
1 NHS Tayside, 2 Scottish Medicine Consortium, 3 NHS National Services Scotland

Goal: Reduce CDI rates using prescribing indicators and restriction of high-risk antibiotics

As of 2009, the Scottish government set a target for all NHS boards to reduce their C. difficile infection (CDI) rates by 30% (later raised to 50%). Therefore, the Scottish Antimicrobial Prescribing Group (SAPG), set up in 2008, first focused on reducing the use of antibiotics associated with a high risk of CDI in both hospital and primary care settings.

The working group developed prescribing indicators based on compliance with local antibiotic policies to support reduction of CDI:

• **Empirical prescribing in hospitals:**
  - Indication for treatment recorded in patient medical record (Figure 1).
  - Antibiotic choice compliant with local Antimicrobial Prescribing Policy – target >95% (Figure 2).

• **Primary Care prescribing:**
  - Seasonal variation in quinolone use (consumption of quinolones in winter months <5% greater than in summer months).

Following implementation of these indicators:

• **CDI rates in Scotland fell nationally from 1.5 to 0.34 cases per 1000 acute occupied bed days.**

• **All NHS boards exceeded the original target of a 30% reduction in CDI rates.**

Improved antibiotic prescription in hospitals and primary care clearly contributed significantly to this reduction.

No significant change in 30-day mortality was observed following restriction of antibiotics associated with a high risk of CDI. Furthermore, the cost savings associated with this reduction in CDI is estimated at over £500,000/year (based on £4,000 per CDI episode)1.


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**Successful Infection Control through Persuasive Diplomacy**

A. Ghafur, V. Nagvekar, S. Thilakavathy, Chandra, R. Gopalakrishnan
Apollo Specialty Hospital, Chennai, India

Goal: Reduce carbapenem resistance in a high endemicity area

To tackle the rising prevalence of Carbapenem Resistant Enterobacteriaceae (CRE) currently observed in many countries, restricted use of higher-end antibiotics is of great importance.

In 2008, the Infection Control (IC) Team at the Apollo Specialty Hospital in Chennai, India, led by Dr Abdul Ghafur, therefore introduced a strict program to restrict access to carbapenems.

The program involved the following measures:

• Provision of a list of restricted antibiotics
• Regular feedback on resistance statistics and antibiotic usage
• Mandatory second opinion by ID Consultants within 48 hours, whenever a restricted antibiotic was used
• Daily list of restricted antibiotics collected from Pharmacy and compliance tracked by the IC Team
• Antibiotic stewardship policy of “save antibiotics, save lives” based on strict basic infection control measures

This program resulted in:

• a significant drop in carbapenem usage between 2009 and 2010 (Figure 1)
• an important reduction in carbapenem-resistant E. coli and Klebsiella rates (Figure 2).

This campaign shows that combination of strict infection control measures and a focused antimicrobial stewardship programme restricting access to carbapenems led to significant reduction in carbapenem use and resistance in a single Indian hospital.
Challenges of antimicrobial use control

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Goal: Restriction of antibiotics to reduce resistance

A national programme of antimicrobial use control in hospital settings reduced resistance amongst MRSA and resistance to anti-pseudomonal agents. However, an increase of carbapenem use was observed, due to the increase of infections caused by ESBL organisms. A much higher frequency carbapenem resistance was observed amongst Acinetobacter species.

In Malaysia, the government and Ministry of Health are committed to implementing an antibiotic stewardship program. Infection and antibiotic control committees established in hospitals help to monitor judicious antibiotic usage and antimicrobial resistance trends. Reports are submitted to the National Antibiotic Infection Control Committee (NAICC).

In the inpatient setting, various strategies have been put in place to improve the appropriateness of antimicrobial use:

• infection control policies,
• microbiology laboratory guidance,
• formulary development and antimicrobial restriction,
• use of antimicrobial order or automatic stop order forms,
• antimicrobial audits
• hand hygiene compliance.

This multi-faceted approach has led to:

• reductions in the use of cephalexins (80.04%), quinolones (10.27%) and vancomycin (11.35%) in 2009 compared to 2008
• downward trends of Pseudomonas aeruginosa resistant to anti-pseudomonal agents (Figure 1) and nosocomial MRSA rates (Figure 2).
• decreasing HCAI rates, based on bi-annual point prevalence studies (Figure 3).

However, an unintended consequence was the increased use of carbapenems (5.3%), possibly due to treatment of ESBL infections which show fluctuating rates (Figure 4). Consequently, increasing resistance to multiple antibiotics was noted among Acinetobacter sp from intensive care units with carbapenem-resistant Acinetobacter up to 67% in 2009.

A comprehensive, multidisciplinary approach to antimicrobial use can reduce inappropriate antimicrobial use and improve patient care.

In Malaysia, areas which require more effort to control antibiotic use include public antibiotic awareness campaigns, legislation to control antimicrobial prescribing and use in agriculture.

National guidelines for Medicine Policy, Antibiotic Guidance and Infection Control.

Six Steps to Antibiotic Control
Soie Chung, Taeksoo Kim, Sungkuk Hong, Eui-Chong Kim
Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul, Korea

Goal: Improve structure + processes to reduce antibiotic use and resistance
Faced with high antimicrobial resistance rates in Korean hospitals (60-70% MRSA, 24% VRE), Korean Governmental bodies have developed a strategy package to control antibiotic use in hospitals at a national level.

6 Steps to Antibiotic Control in Korea
1. Distribution of treatment guidelines for appropriate antibiotic use for Community-Acquired Pneumonia (CAP)

Figure 1: Treatment guidelines for CAP (Korean Society of Infectious Diseases, 2009)

2. Annual evaluation of an index for prophylactic antibiotic use in surgery
Appropriate use of prophylactic antibiotics is improving annually (Figure 2).

Figure 2: Antibiotic prophylaxis in surgery (2006 – 2009)

3. Public reporting of antibiotic prescription rates on HIRA* website (www.hira.or.kr)
Prescription rates for patients with upper respiratory tract infections (URI) fell dramatically after disclosure became mandatory (Figure 3).

Figure 3: Antibiotic prescription rates in URI (2002-2009)

4. Public education on antibiotic use through distribution of leaflets in primary care
General awareness of antimicrobial resistance and prudent antibiotic use in Korea is increasing. In 2009, over 55% of a study population correctly answered that a cold does not require antibiotic treatment as it is a viral infection.

Figure 4: Educational leaflet for patients

5. Pre-prescription approval for prescription of restricted antibiotics
Computerized protocols help reduce inappropriate use of list of restricted antibiotics in hospital setting.

Figure 5: Prescription approval protocol in Seoul National University Hospital

6. Setting up a national antibiotic stewardship committee (ASC)
The government works with the national ASC to set antibiotic management goals every 5 years. The multidisciplinary ASC team includes clinicians, pharmacists as well as food and environment experts.

Figure 6: National antibiotic management goals

Although the final goal of significantly reducing antibiotic consumption and its improper use has not yet been achieved, this strategy is already showing successful results.
Assessing the Need for Antimicrobial Use Guidelines

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\(^1\)Infection Prevention & Control, King Abdulaziz Medical City, National Guard Health Affairs; \(^2\)Emory Rollins School of Public Health

Goal: Evaluate medical education needs of staff for more effective guideline prioritization

Education is a key element for effective and safe prescribing. This recent initiative at the King Abdulaziz Medical City used clinical case vignettes to understand and enhance educational needs of medical advisers with a view to more targeted and relevant guideline development.

Initially, a survey was performed to better understand knowledge levels, attitudes and practices among the hospital’s medical staff. By email, 759 physicians and medical residents were requested to complete a 20-minute, web-based survey including five vignettes for three practice settings (primary care, intensive care, medical residents).

Among 134 (49%) of 285 primary care physicians who responded:
- > 90% correctly answered vignette one (oral amoxicillin for uncomplicated Group A streptococcal pharyngitis) and vignette two (oral TMP-SMX for seven days for uncomplicated E. coli UTI).
- Over 70% of participants correctly answered vignette three (oral moxifloxicin for uncomplicated acute maxillary sinusitis) and vignette five (oral ciprofloxacin for complicated S. pneumoniae in a smoker).
- Approximately 50% correctly identified TMP-SMX as a better choice than ampicillin for acute bacterial prostatitis (vignette four).

The most urgent gap in knowledge was for antibiotic use in acute bacterial prostatitis (vignette four). Vignettes one and two showed awareness levels were high, indicating that their inclusion within guidelines may not be necessary.

This survey demonstrates the value of vignettes as a guide to where education is required. Based on the vignette scores obtained, guideline creation and dissemination can be prioritized.

Impact of Intervention on Antimicrobial Consumption in Aquaculture

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Goal: Reduce antibiotic consumption in salmon fishing

The link between excessive use of antibiotics in agriculture and horticulture and resistance is well recognised. This study demonstrates the impact of national guidance from the Chilean Government and professional bodies on reducing quinolones use in aquaculture (salmon fishing).

Between 2000 and 2007, use of antibiotics in the Chilean salmon farming industry became excessive, compared to other countries, with potential risks for the environment and public health.

To combat this overuse, a task force was set up in August 2008 by the Chilean Government with the objective of developing a “National Plan for Regulation and Use of Antibiotics in Aquaculture”. The plan, launched in December 2008, proposed new regulations on the use of antibiotics in aquaculture, with special emphasis on the use of quinolones.

The plan proved to be highly effective, confirming a significant reduction in imports of quinolones by the salmon farming industry in Chile (Figure 1). The use of quinolones and fluoroquinolones in aquaculture decreased dramatically and the ratio comparison between use of these antimicrobials in human and veterinary medicine dropped from 1:11.3 (1998-2007) to 1:2.2 (2008-2009) (Figure 2). The impact on resistance to quinolones was not reported.
**HIGHLIGHT**

**ANTIMICROBIAL STEWARDSHIP – A PRACTICAL GUIDE FOR HOSPITALS**

This new booklet is a very practical, educational tool for any hospital facility wishing to set up an Antimicrobial Stewardship program (ASP).

It is authored by Professor Dilip Nathwani, and Doctor Jacqui Sneddon, two leading experts in Antimicrobial Stewardship, who are well-known advocates of the cause.

Eight steps are suggested for a very practical approach to implementing ASPs, with many useful diagrams, examples of good practice, as well as “solutions that work”, “key success factors”, and so on.

Contact your local bioMérieux representative, or christine.micolaud@biomerieux.com for your free copy.

Other Practical Guides on solutions to promote the responsible use of antibiotics are available at: www.biomerieux-besmart.com/Be-Smart-Practical-Guides.html

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