

# ARPAC Consensus Conference

## Day 1

12 noon	Registration and buffet lunch
<b>Introduction</b>	
1.30 pm	Welcome - <i>A. Lönnroth</i> Objectives - <i>I. M. Gould</i>
<b>Plenary Session:</b>	<b>Final Results from ARPAC European Hospitals</b>
<b>Chairpersons</b>	<i>H. Verbrugh, J. Vila</i>
2.00 pm	<b>Methods and participating hospital demographics</b> <i>J. Bruce</i>
2.30 pm	<b>Antibiotic Resistant ALERT micro-organisms</b> <i>H. Goossens</i>
3.00 pm	<b>Patterns of Antibiotic Consumption</b> <i>F.M. Mackenzie</i>
3.30 pm	Tea
4.00 pm	<b>Antibiotic Stewardship in ARPAC European Hospitals</b> <i>I.M. Gould</i>
4.30 pm	<b>Infection Control policies</b> <i>M.J. Struelens</i>
5.00 pm	<b>Role of molecular typing in controlling the spread of antibiotic-resistant bacteria</b> <i>K.J. Towner</i>
5.30 pm	<b>Organisation of attendance at workshops</b> <i>F.M. Mackenzie</i>
5.45 pm	Session end
7.00 pm	Conference dinner (optional)

## Day 2

Four simultaneous workshops will explore the ARPAC findings further and discuss these findings in the context of the worldwide literature.

Each session will finish with discussion and agreement on recommendations for good, minimum practice standards in Europe.

8 am	Workshop 1	Workshop 2	Workshop 3	Workshop 4	8 am
9 am	Session 1	Session 1	Session 1	Session 1	9 am
10 am	Coffee	Coffee	Coffee		10 am
11 am	Session 2	Session 2	Session 2	Coffee	11 am
12 noon	Lunch			Session 2 - part 1	12 noon
1 pm		Lunch	Lunch	Lunch	1 pm
2 pm	Session 3	Session 3	Session 3	Session 2 - part 2	2 pm
3 pm	Session 4			Session 3	3 pm
4 pm	Coffee	Coffee	Coffee	Coffee	4 pm
5 pm	Session 5	Session 4	Session 4	Session 4	5 pm
6 pm	<b>Break</b>				6 pm
7 pm	Workshop chairpersons, rapporteurs and ARPAC Steering Group meet to discuss draft workshop recommendations.				7 pm
Late					Late

## Day 3

Chairpersons - I.M. Gould, M.J. Struelens

9.00 - 10.30 am	<i>Final ARPAC Recommendations</i> <b>Workshops 1, 2, 3 and 4</b>
11.00 am	<b>Coffee</b>
11.30 am	<b>Lessons learned from ARPAC as a basis for future intervention studies</b> <i>J. van der Meer</i>
12.10 pm	<b>Looking to the future - roundtable discussion</b>
12.45 pm	<b>Closing remarks</b> <i>I.M. Gould / M.J. Struelens</i>
1.00 pm	<b>Lunch and depart</b>

## Workshop 1

## Surveillance of antimicrobial resistance

**Aim:**

*To review current methods for surveillance, choice of resistant ALERT organisms and resistance prevalence*

**Start time:**

**8.30am**

**Reporteur:**

**Georgia Duckworth**

Session 1 (08.30 - 10.00)

**Resistance determinants as targets for antibiotic selection**

*Chairperson and speaker: R. Canton*

Session 2 (10.30 - 12.00)

**Critical appraisal of antimicrobial surveillance studies**

*Chairperson and speaker: H. Goossens*

Session 3 (13.00 - 14.30)

**Methodological requirements of purpose-designed surveillance systems.**

*Chairperson and speaker: H. Grundmann*

Session 4 (14.30 - 16.00)

**Integrating local, regional, national and supranational surveillance.**

*Chairperson and speaker: V. Jarlier*

Session 5 (16.30 - 18.00)

**Future of antimicrobial resistance surveillance in Europe**

*Chairperson and speaker: G. Cornaglia*

## **Workshop 2: Antibiotic Policies in European Hospitals**

**Aim:** *The aim of this workshop is to address optimal antibiotic stewardship strategies*

**Start time:** 8.00am  
**Chairperson:** Jos van der Meer  
**Rapporteur:** Barry Cookson

Session 1 (08.00 - 10.00)

**How effective are antibiotic control measures?**

*D. Nathwani and I.M. Gould*

Session 2 (10.30 - 12.30)

**What's the formula for successful antibiotic guidelines?**

*D. Nathwani and B. Cookson*

Session 3 (13.30 - 15.30)

**Can the laboratory influence antibiotic use?**

*H. Kolmos and I.M. Gould*

Session 4 (16.00 - 18.00)

**Do education and audit optimise antibiotic prescribing?**

*I. Gyssens and J. van der Meer*

## **Workshop 3: Antibiotic Prescribing and Consumption in European Hospitals**

**Aim:** *The aims of this workshop are to explore the prospects for harmonisation of treatment guidelines and how/why antibiotic consumption should be measured*

**Start time:** 8.00am  
**Chairperson:** V. Krcmery  
**Rapporteur:** D. Monnet

Session 1 (08.00 - 10.00)

**How should antibiotic consumption be measured?**

*R. Polk and F.M. MacKenzie*

Session 2 (10.30 - 12.30)

**How does Consumption Relate to Resistance?**

*D. Monnet and C. Brandt for ARPAC*

Session 3 (13.30 - 15.30)

**Can the pharmacy influence antibiotic use?**

*R. Polk and V. Krcmery for ARPAC*

Session 4 (16.00 - 18.00)

**How can antibiotic prescribing be harmonised?**

*G. Zanetti and I.M. Gould for ARPAC*

## **Workshop 4: Containment of antimicrobial resistance: role of infection control policies and molecular typing**

**Aim:** *To address infection control policies, alert organism outbreak investigations and recommendations for their harmonisation in European hospitals.*

**Start time:** 08.00  
**Chairpersons:** P.J. van den Broek / J. Vila  
**Rapporteur:** M.Struelens

Session 1 ( 08.00 - 10.30)

**How to organize effective infection control programmes in healthcare facilities?**

*A.Voss and C.Suetens*

Session 2 (11.00 - 12.30 and 13.30 - 14.30)

**What is the role of targeted surveillance and control of "Alert" organisms?**

*M.Struelens and S.Harbarth*

Session 3 (14.30 - 16.00)

**What is the role of microbial typing in containing antibiotic resistance?**

*K. Towner and L. Dijkshoorn*

Session 4 (16.30 - 18.00)

**Construction and operation of typing databases & the ARPAC demonstration databases**

*J. Green, K. Levi and K. Towner*



# **Plenary Session**

## **Abstracts**

## Methods and participating hospital demographics

*Julie Bruce, Jill Mollison, University of Aberdeen, UK*

The overall aim of ARPAC was to identify antibiotic policies and infection control policies and practices associated with lower antibiotic resistance in European hospitals and to harmonise strategies for prevention and control of antibiotic resistance in European hospitals.

**Methods:** An observational, cross-sectional study design was adopted, with postal questionnaire surveys and consumption spreadsheets for retrospective collation of hospital data for 2001. Systematic reviews were also conducted and molecular typing databases developed. Hospitals were recruited via ESCMID membership and after contact with 53 European specialist societies. Data collected included: resistance data for 13 alert antibiotic-organism combinations; antibiotic consumption data collated using ABC calc spreadsheet; antibiotic stewardship and infection control policy data. Representativeness of the ARPAC sample of hospitals was compared to European hospital indicator data for 2001.

In 2002, a total of 263 hospitals from 34 countries were recruited via a screening questionnaire; 192 hospitals subsequently provided more than one dataset (i.e. resistance, consumption, infection control, antibiotic stewardship) thus were eligible for analysis. Geographical distribution of 192 participating hospitals from 32 countries: Western Europe (n=59, 31%); South (n=53, 28%); Central-East (n=48, 25%), North (n=20, 10%) and South-East Europe (n=12, 6%). Median (IQR) number of hospital beds in the ARPAC sample was 654 (407, 999 beds). Approximately two-thirds of hospitals were small (<500 beds; n=69) or moderate (500-1000 beds; n=70) in size, with 45 (23%) having more than 1000 beds. Hospital size differed across geographical region ( $p<0.01$ ). 93% of hospitals reported having ICU beds (median 26 ICU beds, IQR 12-45), no differences identified across geographical regions. A total of 192 hospitals provided antibiotic resistance data for one or more organisms; 153 provided antibiotic consumption data for whole hospital; 169 provided infection control policy data and 170 provided antibiotic stewardship data. Half of recruited hospitals (n=99) provided data for all measures. Characteristics of the ARPAC sample will be discussed in more detail.

### Interpretation of ARPAC findings

ARPAC is an extremely rich dataset and it will provide indication of associations that may exist between the different measures collected. However, the design of ARPAC does not allow these associations to be interpreted as causal. The generalisability of findings from ARPAC should be interpreted in consideration of the coverage and type of participating hospitals.

# Antibiotic Resistant ALERT micro-organisms

Herman Goossens, Marleen Van Looveren, University of Antwerp, Belgium

The collaborative study group, the European Study Group for Antimicrobial Resistance Surveillance (ESGARS) of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) was responsible for gathering data from recruited hospitals on antimicrobial susceptibility testing (AST) and on antibiotic resistance rates of ALERT organisms.

Responses on AST methods, interpretative criteria, participation in quality programmes, and on the detection of specific resistance types, were received from 192 (73%) of 263 acute care hospitals recruited to ARPAC, across 32 European countries. The highest response rate was from Belgium (n=21 hospitals), Spain (n=13), Turkey (n=12) and Germany (n=11). Three countries were only represented by one hospital, i.e. Macedonia, Malta, and Russia.

In 2001, 89.5% of the hospitals routinely used a disc diffusion method, 49.7% used Oxoid discs. MICs were routinely determined in 70.3% of the hospitals, 81.8% used Etest. In 90.6% of the hospitals, breakpoints were used to interpret AST results. The NCCLS guidelines were employed most widely (84.2%). 83.3% of the hospitals participated in an external quality assurance programme, and 88.9% carried out internal quality control. MRSA screening was carried out by 88.4% of the hospitals; 73.8% used disc diffusion and 56.5% screening plates. Screening for VREs was performed by 61.8% of the hospitals; 77.7% used disc diffusion and 37.4% screening plates. The double disk synergy test was most often used (54.7%) for ESBL detection. 53.8% of the hospitals performed screening for ESBL producing *Klebsiella pneumoniae*. Nineteen laboratories (9.9%) from 13 different countries further characterised the ESBL enzymes. The methods used were isoelectric focusing (68.4%), PCR detection (57.9%), and DNA sequencing (26.3%). Screening for quinolone resistant *Escherichia coli* and *Pseudomonas aeruginosa* was performed in 43.5% and 39.4% of the hospitals, respectively, with ciprofloxacin most often tested (91.7% and 96.4%, respectively). 39.6% performed screening for aminoglycoside resistance in *P. aeruginosa*, with gentamicin (91.0%) and amikacin (86.8%) most often tested. 81.2% of the hospitals tested for the presence of *Clostridium difficile*. Culture was the most frequently used method (39.8%) for the detection of *C. difficile*, followed by the *C. difficile* toxin A test (Oxoid) (32.5%). 78.8% was able to exclude duplicates. The majority (80.9%) excluded duplicates based on the criterium "only first isolate per patient for a given species". Other criteria used were episode-based (8.5%), patient-based (7.1%), or isolate-based (3.5%). Thus, AST testing in Europe is performed in great many ways, which may render comparison of susceptibility rates difficult.

The overall prevalence of MRSA, VRE, *K. pneumoniae* resistant to 3<sup>rd</sup> generation cephalosporins, *E. coli* resistant to quinolones, *Acinetobacter* resistant to carbapenems, *P. aeruginosa* resistant to imipenem, *P. aeruginosa* resistant to amikacin *P. aeruginosa* resistant to quinolones and *P. aeruginosa* resistant to ceftazidime was 20.8, 0.20, 8.3, 10.0, 2.3, 13.3, 13.7, 26.9, and 15.1. The resistance rates of these selected ALERT organisms will be discussed in more detail.

# Patterns of Antibiotic Consumption

*Fiona M. MacKenzie, Aberdeen Royal Infirmary, UK*

This presentation describes the aggregated hospital antibiotic use data from 2001, collected from 140 European ARPAC hospitals. This work was carried out under the auspices of the ESCMID Study Group on Antibiotic Policies.

Antibiotic use was measured in defined daily doses per 100 patient days (DDD/100PD), using DDDs described by the WHO (2004). Data are described for individual antibiotics as well as the ATC J01 classes. Data were analysed by various demographic characteristics. Relationships between antibiotic use and resistance were also explored.

For all hospitals, the antibiotic use range was 5 - 129 DDD/100PD (median = 55, IQR 40, 73). For all hospitals, J01C (penicillin B-lactams) were used most often, followed by J01D (non-penicillin B-lactams) and quinolones with median values of 22, 10 and 6 DDD/100 PD.

Total and class antibiotic use varied significantly by geographical region. It did not vary significantly by hospital size, teaching status or case mix.

Median total antibiotic use for the north, south-east, south, west and centre / east was 48, 45, 81, 63 and 37 DDD/100PD respectively. Median use of J01C for regions 1-5 was 25, 13, 24, 29 and 12 DDD/100 PD. The most used sub-class were the B-lactamase inhibitor combinations (J01CR) making up 1, 27, 79, 67 and 48% of J01C for regions 1-5 respectively.

The most frequently used individual antibiotics in the 140 European hospitals which contributed data were 1] amoxicillin + enzyme inhibitor (oral), 2] amoxicillin + enzyme inhibitor (IV), 3] ciprofloxacin (oral), 4] cefuroxime (IV) and amoxicillin (oral). The most frequently used individual antibiotic in the different regions were oral phenoxymethylpenicillin in the north, IV gentamicin in the south-east, oral amoxicillin + enzyme inhibitor in the south and IV amoxicillin + enzyme inhibitor in both the west and centre - east.

Relationships between the project's chosen ALERT organisms and specific classes of antibiotics were explored. The relationships were explored in most detail for MRSA and data relating to this organism were the subject of in depth statistical modelling.

Of 7 groups of antibiotics tested, total antibiotic use (both including and excluding glycopeptide use) as well as use of 3<sup>rd</sup> generation cephalosporins showed a significant, positive correlation with MRSA prevalence (unadjusted, unweighted tests). After removal of variation in MRSA due to demographic factors, a strong statistically significant partial correlation was found between MRSA prevalence and macrolide use. Relationships between antibiotic use and other ALERT organisms will be discussed.

Although collating antibiotic use data in hospitals is a routine task in some European countries, many hospitals collated their data for the first time in order to participate in ARPAC. This underlines the need for agreement and promotion of a common method of measuring and benchmarking antibiotic use.

# Antibiotic Stewardship in ARPAC European Hospitals

*Ian M. Gould, Aberdeen Royal Infirmary, UK*

The data on antibiotic stewardship was collected under the auspices of the ESCMID European Study Group on Antibiotic Policies (ESGAP).

A broad range of administrative, restrictive, structural and educational measures have been implemented in the 170 hospitals that provided this data.

86% of respondents had a Drugs and Therapeutics Committee (DTC), 80% had educational programmes, 77% had a written antibiotic formulary, 60% a restricted list, 57% an antibiotic policy and 52% an antibiotic committee. In 51%, control of antibiotic prescribing was a strategic goal of the hospital. 30% of respondent hospitals had multidisciplinary teams and computerised audit, 23% had antibiotic utilisation co-ordinators, 16% had computerised prescribing and 13% of respondents had voluntary or compulsory auto-stop procedures.

There were key geographic differences in the implementation of a written antibiotic policy ( $p = 0.003$ ) and a written antibiotic formulary ( $p = 0.001$ ) and some significant demographic differences related to implementation of restricted lists, written formularies and strategic goals where there was a high proportion of long stay beds (increases and decreases), written formularies, policies and computerised audit where there was a high proportion of paediatric beds (decrease) and frequently meeting DTCs where there was a high proportion of ICU beds (increase).

Utilisation co-ordinators, educational programmes and written formularies were consistently and / or significantly associated with lower antibiotic consumption figures for some or all of the following - total antibiotic use, glycopeptides, fluoroquinolones, carbapenems and 3<sup>rd</sup> and 4<sup>th</sup> generation cephalosporins, but differences in consumption as measured by DDD / 100 bed days were not large and  $p$  values were only marginal.

Antibiotic stewardship measures in ARPAC hospitals show room for significant expansion but much more needs to be done to establish the best measures to improve patient outcome, reduce consumption and decrease resistance. A programme of research to assess interventions by standard agreed criteria such as those proposed by EPOC ([www.epoc.uottawa.ca/](http://www.epoc.uottawa.ca/)) needs to be established in European hospitals.

# Infection Control Policies

Marc Struelens, Dominique Wagner, Université Libre de Bruxelles, Belgium.

The collaborative European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Study Group of on Nosocomial Infections (ESGNI) was responsible for collating data from ARPAC participating hospitals on infection control policies and practices including control of antibiotic resistant Alert organisms.

Responses on hospital infection control staff resources, organization, surveillance and control programmes, standard precautions and active screening, isolation and decontamination procedures for patients with Alert organisms were received from 169 (65 %) hospitals, of which 80% were teaching hospitals, in 35 European countries grouped in 5 geographical regions (N, W, S, CE, SE).

In 2001, an infection control (IC) committee was present in 90% of hospitals. ICN with a specific training in infection control were present in 80% centres (with regional differences from 54 % in SE and CE to 100% in N region) whereas 74% had specially trained ICD (with regional differences from 46 % in SE to 83% in W region). Median staffing level were 2.76 ICN/1000 bed and 1.54 ICD/1000 bed. Hand hygiene for healthcare workers (HCWs) was promoted by an educational programme in 85% centres and supported by written guidelines in 89%, audit and feedback in 46%. The local guidelines recommended : wearing gloves for all contacts with body fluids (94%) ; washing/disinfecting hands after removing gloves (91%) and use of alcohol-based solutions (66%) or medicated/antiseptic soap (43%) for decontamination of non-soiled hands. Use of alcohol-based solutions varied by region from 41% in S to 100% in N vs use of medicated soap from 77% in S to 11% in N region ( $p < 0.01$ ).

In 87% of hospitals, the laboratory notified Alert Organism (AO) to the IC team as follows: methicillin resistant *S. aureus* (MRSA): 89%, glycopeptide resistant *Enterococci* (GRE): 60%, 3<sup>rd</sup> generation cephalosporins resistant *K. pneumoniae* (C3RKP): 61%, carbapenem resistant *A. baumannii* (CRAB): 48%, *C. difficile* (CDIFF): 43%, gentamicin resistant *P. aeruginosa* : 38%. Alert system for MRSA varied by region from 67% in S to 100% in N region ( $p < 0.01$ ). For MRSA, active screening of carriers in patients was performed in 56% of hospitals and in health care workers in 47%. Screening for other AO was performed by 5% to 17% of hospitals. Contact isolation precautions were used for the care of MRSA patients in the majority of centres (gloves:85% ; gown:74%) with significant regional differences. For other AO, contact precautions were used by < 52% centres. In addition, placement of colonised patient in single rooms varied by organism, from 67% (MRSA) to 33% (CRAB). For MRSA patients additional measures were : use of mask (45%), mupirocin decolonisation of patients (78%) and cohort care (46%). The major implementation problems were lack of isolation rooms (93 %) and lack of skilled staff (82%), ranging from 43% in N to 92% in S-SE regions ( $p < 0.01$ ).

Linear regression modelling of IC policies as predictor of MRSA prevalence adjusted for antibiotic consumption, case-mix and hospital size indicated strong evidence that 2 policies were associated with lower resistance rates: (1) recommending alcohol-based solution for hand hygiene (mean difference 10.3 %, 99%CI 1.2%-10.3%) and (2) recommending placement of MRSA patients in single room (mean difference 11.2 %, 99%CI 1.4%-20.9%) whereas hospitals having problems implementing AO isolation policies had higher resistance (mean difference 12%, 99%CI 3.8%-20.1%).

Other IC policies showed weaker evidence of association with low resistance rates.

These results indicate a wide variation of IC resources, policies and practices in European hospitals. The Southern and Eastern regions had less resources and less extensive programmes than the Northern and Western regions. The promotion of hand hygiene is well developed but with different modalities. Audit and feedback of IC policies and surveillance data is limited. AO surveillance and control is mostly focused on MRSA with different modalities by region. Both alcohol hand disinfection and MRSA isolation policy appeared associated with lower prevalence rates. This diversity of approaches underlines the need to define the minimum components of infection prevention policies, to strengthen resources to allow their implementation and to develop criteria for AO control programmes based on regional/local priorities.

# Role of molecular typing in controlling the spread of antibiotic-resistant bacteria

*Kevin J. Towner, Queen's Medical Centre, Nottingham, UK  
on behalf of the ESCMID Study Group for Epidemiological Markers (ESGEM)*

Accumulated susceptibility data and other surveillance information will not, in itself, enable the timely recognition of particular epidemic multi-resistant bacteria on a pan-European basis. Rapid molecular typing techniques have become essential tools for monitoring the geographical spread of particular virulent, epidemic, or antibiotic-resistant pathogens. However, significant barriers to data exchange include a lack of standardisation, a lack of reproducibility, the fact that certain methods are confined to reference laboratories, and difficulties in transporting cultures. ARPAC Workpackage 6 therefore investigated the possibility of establishing an electronic data exchange network for rapid local detection and epidemiological tracing of specific clones of antibiotic-resistant pathogens throughout the EU. In addition, the Workpackage collected information on typing methods being used currently by participating European hospitals.

Based on the typing methods currently available in hospital laboratories throughout Europe, the Workpackage first defined standard operating procedures (SOPs) based on the generation of DNA typing fingerprints from the most important ALERT organisms specified by the ARPAC consortium. Further details of these will be presented in Workshop 4. The SOPs can be used by participating laboratories to generate DNA fingerprints for electronic exchange via the Internet and, following validation, can be archived and stored on central interactive typing databases. The databases are based on BioNumerics software and are accessible to all participating laboratories. This allows local isolates of ALERT organisms to be compared with isolates reported from other laboratories throughout Europe.

## **Overall, the Workpackage reached three main conclusions:**

- DNA fingerprinting techniques can be used at the local level on a day-to-day basis, with selected isolates being sent to reference laboratories for inclusion in databases
- databases based on fingerprint patterns can be effective with rigorous (and labour-intensive) standardisation
- databases based on sequence analysis provide unambiguous comparisons, but are currently not feasible for use by routine diagnostic laboratories dealing with large numbers of specimens and immediate cross-infection control problems

Surveillance combined with typing will contribute to recognition and a greater understanding of specific cross-infection and epidemiological problems, but only if these investigations are followed by targeted interventions.

**Workshop 1**  
**Surveillance of Antimicrobial**  
**Resistance**

**Abstracts**

# Resistance determinants as targets for antibiotic selection

*Rafael Cantón. Hospital Universitario Ramón y Cajal, Madrid, Spain*

The European Conference on the "Role of Research in Combating Antibiotic Resistance" held last year in Rome stressed the importance of resistance determinants as a target for the study of antimicrobial resistance in addition to the study of resistant pathogens and/or specific resistant clones. The European Study Group for Antimicrobial Resistance Surveillance (ESGARS) has recently included genes or gene combinations encoding mechanisms of resistance as resistance surveillance targets. Even more recently genes surrounding resistance genes (pieces) have been recognized as important factors in the evolution of resistance. The hospital setting is an excellent scenario for the study of emergence, evolution, and persistence of multi-drug-resistant (MDR) organisms. Resistance determinants can be fixed in bacterial pathogens within the so called gene capture units, which are important actors for the horizontal or lateral gene transfer. Plasmids, integrons, transposons, and phage related sequences have been recognized to act as integrative and supporting structures for resistance determinants. Efforts are being performed for the understanding of mechanisms leading to the integration of different pieces in such structures and genetic processes for the dissemination of these complex structures. In contrast, less attention has been paid to the control of selection processes affecting persistence of such structures and/or bacterial pathogens carrying these constructions. ARPAC Alert Organisms include excellent examples for the study of resistance determinants and the possibility to analyse the influence of antibiotic selection processes. Extended spectrum  $\beta$ -lactamase (ESBL) and cephamycinase producing organisms are frequently resistant to other antimicrobials, including aminoglycosides, tetracyclines and/or sulphonamides. More recently, fluoroquinolone resistance has been identified as fuelling the dissemination of ESBL producing organisms, particularly those producing CTX-M enzymes. Co-resistance determinants can be present as aggregative elements in organisms carrying these enzymes or can be linked in the same genetic structure (e.g. integron structures). The co-selection process can be easily understood, even in well designed strategies such as antimicrobial cycling. Intervention strategies should be designed not only to reduce the transmission of resistant organisms but also to decrease the gene pool of resistant determinants. Selective intensity of different antimicrobials should be measured in the hospital setting and correlated with the presence of primary and secondary resistance mechanisms to avoid the spread and persistence of MDR organisms and resistance determinants.

## **Critical appraisal of antimicrobial surveillance studies**

Herman Goossens, University of Antwerp, Belgium

Abstract not available

## **Integrating local, regional, national and supranational surveillance.**

Vincent Jarlier, CHU Pitié-Salpêtrière, Paris, France

Abstract not available

## **Future of antimicrobial resistance surveillance in Europe**

Giuseppe Cornaglia, Istituto di Microbiologica, Verona, Italy

Abstract not available



**Workshop 2**  
**Antibiotic Policies in**  
**European Hospitals**

**Abstracts**

# How effective are antibiotic control measures?

*Dilip Nathwani, Ninewells Hospital & Medical School, Dundee, UK*

A number of strategies have been advocated to promote optimal antibiotic prescribing in hospitals. Many of these interventions have been used, either in isolation or usually in combination with one or more measures, with variable success. In general the understanding of the effectiveness of these interventions to date is the following: 1) No one intervention is effective all the time; 2) different interventions work in different settings; 3) different methods of implementing the intervention work in some but not all setting; 4) the impact of different interventions is variable on a variety of clinical, prescribing, microbiological and economic outcomes. These will be discussed in the presentation.

Would a more rigorous scientific and evidence based approach (advocated by the EPOC group of the Cochrane collaboration [www.update-software.com/cochrane/](http://www.update-software.com/cochrane/)) to evaluating the true impact of these intervention on a variety of clinical, microbiological and fiscal outcomes provide clinicians and organisations more definitive steer about the most effective strategy or the method of implementation? Furthermore, what should be the overall strategic goals or standards for antibiotic prescribing in hospitals?

This presentation will:

- a) review the generic measures used to promote better prescribing
- b) review the systematic review of the literature undertaken by a working party of BSAC and HIS with the aim of evaluating the current evidence base on the effectiveness of interventions to change antibiotic prescribing in inpatients. The methodology and protocol and early results from this work were published in 2003 (*Ramsay C et al. JAC 2003; 52: 764-771*). The full analysis were presented on behalf of the group by Dr Erwin Brown at ICAAC, Washington October 2004. The results presented here are based on a report produced by Professor Peter Davey and members of this group, with their permission.
- c) review the strategic goals and standards of care for antibiotic prescribing and policy for hospitals recently developed in Scotland.

# How effective are antibiotic control measures?

*Ian M. Gould, Aberdeen Royal Infirmary, UK  
(for the ARPAC Steering Group)*

170 European ARPAC hospitals provided answers to the questionnaire on Antibiotic Stewardship. This work was carried out under the auspices of the ESCMID Study Group on Antibiotic Policies. There was a wide distribution of practices amongst European ARPAC hospitals but the only significant geographic differences were for antibiotic formularies and restricted lists ( $p=0.012$ ). 146 (86%, 1 missing) had a drugs and therapeutics committee (DTC) which met at least 3 monthly in 96 hospitals and was usually multidisciplinary. 81% ( $n=137$ ) of DTCs included a pharmacist, 70% ( $n=118$ ) a microbiologist (micro) or infectious disease (ID) specialist, 64% ( $n=108$ ) an ICU physician and 44% (74) an infection control (IC) specialist. Only 53% ( $n=88$ , 4 missing) had a separate antibiotic committee but again this was usually multidisciplinary, including a pharmacist in 48.8% ( $n=83$ ) and a micro/ID specialist in 53% ( $n=89$ ). 38% ( $n=65$ ) and 35% ( $n=59$ ) included an ICU physician and IC specialist respectively (1 missing). 87 hospitals (52%, 9 missing) had antibiotic prescribing as a strategic goal of the hospital and 51 (30%) had an antibiotic management team although only in 40 (24%, 57 missing) was there an antibiotic utilisation co-ordinator.

77% ( $n=131$ , 3 missing) had a written antibiotic formulary but only 61% ( $n=103$ , 26 missing) operated a restricted antibiotic list. The formulary was updated at least every 2 years in 87 (41 missing) and in 97 (57%, 31 missing) there was an authorisation procedure in place for access to restricted list antibiotics. This involved the patients consultant in 32 (19%, 2 missing), the micro/ID specialist in 71 (42%), the pharmacist in 43 (25%) and "others" in 23 (14%). Pharmaceutical companies (PCs) had input into the content of the AP in only 20 hospitals (12%, 9 missing) although they sponsored its printing in 39 (23%, 35 missing). In only 51 hospitals (30%, 3 missing) did PC representatives have to report to the pharmacy department before visiting doctors and in 71 (42%, 6 missing) hospitals the PC reps were permitted to leave drug samples on the wards. In 81 (48%, 32 missing) hospitals the PCs provided sponsorship for dinners and parties and in 151 (89%, 15 missing) they provided sponsorship for attendance at meetings. Cost details of antibiotics were only reported by the laboratory in 20 hospitals (12%). 59 hospitals (35%, 9 missing) routinely reported antibiotic susceptibilities to non-formulary drugs. There were financial restrictions on prescribing of antibiotics in 57 hospitals (34 %, 5 missing). These were imposed by government in 32 (19%, 2 missing) and locally in 49 (29%). There were very few other significant differences in the application of restrictions. Hospitals with a greater proportion of long stay beds had less restricted lists in place ( $p=0.018$ ), were less likely to have improvement of antibiotic prescribing as a strategic goal ( $p=0.051$ ) and less likely to have a written antibiotic formulary ( $p=0.001$ ). This latter restriction was also less likely the more paediatric beds a hospital had ( $p=0.037$ ). There was also a relationship between having a DTC and the proportion of ICU beds ( $p=0.045$ ).

Few restrictions were associated with significantly lower antibiotic consumption. These included written formularies and 3rd generation cephalosporins ( $p=0.026$ ) and a DTC and carbapenems ( $p=0.076$ ).

In conclusion, restrictive and organisational measures to control antibiotic prescribing are widely practised in ARPAC hospitals although there is significant room for their expansion. There are only weak associations with antibiotic consumption.

## What is the formula for successful antibiotic guidelines?

*Dilip Nathwani, Ninewells Hospital & Medical School, Dundee, UK*

Evidence based clinical practice guidelines have been defined as systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances. In short, they are designed to help clinicians do the right thing. Importantly they must also reflect the routine working practices of most doctors for them to be accepted as a gold standard that most doctors will accept or admire. So what makes an antibiotic or infection guideline successful?

One of the key components of a successful or good guideline is the rigour of the development process. Unfortunately, most of the guidelines produced by specialist societies do not meet this basic principles of guideline development. One important study reported that 67% did not report any description of the type of stakeholders, 88% gave no information on searches for published studies and 82% did not give any explicit grading of the strength of the recommendations. Of the 431 eligible guidelines considered between January 1988 and July 1998 very few appeared to be for infection although the exact numbers were not explicit in the paper. Another study revealed that the methodological quality of guidelines is generally poor and often exhibits great variation and conflicting recommendations. This study of 279 guidelines published from 1985 to 1997 revealed a mean (SD) adherence to methodological standards on guideline development of 51.1%. There is clearly a need for a common, international, valid and transparent approach to develop good clinical practice guidelines. The AGREE (Appraisal of Guidelines, Research and Evaluation for Europe; [www.agreecollaboration.org](http://www.agreecollaboration.org)) collaboration have developed a European agreed generic methodology to assess the quality of guidelines and the guideline development process. The Scottish Intercollegiate Guideline Network (SIGN, [www.sign.ac.uk](http://www.sign.ac.uk)) has long adopted the majority of these criteria and has recently updated many aspects of SIGN methodology which are consistent with the agree criteria. SIGN 50 is an excellent and commendable resource to the guideline process for any group wishing embark upon this. A more recent global and collective organization (Guideline international network; <http://www.g.i.n.net>) provides interested groups/individuals a forum for sharing good quality international guidelines (>2000), links to relevant organizations & networking facility, on line guideline development methodology, critical appraisal tools, implementation support and strategies as well as updated news and activities.

A more recent comparison of the quality of 100 guidelines from 11 different countries using the above appraisal tool confirmed a significant improvement in guideline development from around the globe but once again the data emphasises the importance of a continuing international effort to globalise this process. Antibiotic guideline developers in the infection community worldwide need to be encouraged to broadly embrace this process and consider these issues when planning future guidelines. The current guidelines for hospital and ventilator associated pneumonia being undertaken by a working group of BSAC appear to have taken on board these important considerations.

*Guideline Implementation:* It is important that for antibiotic guidelines to be most effective the strategy for dissemination and implementation needs to be considered at the development process and adequately resources. How these guidelines are implemented has an emerging evidence base: evidence based implementation, which is considered here. The determinants of changing physician behaviour are multi-factorial and appear to be dependant around bring about an improvement in knowledge, a change in attitude and a number of organisational, social and personal factors.

*Guideline Content:* A recent working group of the Scottish Medicine Consortium (<http://www.scottishmedicines.org.uk/>) have produced national recommendations related

to Anti-microbial Prescribing Policy and Practice in Scotland. This document includes guidance on what should hospital guidelines include and the important standards or criteria to audit compliance with these guidelines/policies. This guidance may stimulate debate about a European Policy for anti-microbial management as wells as development of a generic template for antibiotic policies/guidelines across Europe.

## What's the formula for successful antibiotic guidelines?

*Barry Cookson, Health Protection Agency, London, UK  
(for the ARPAC Steering Group)*

### ARPAC Antibiotic Policy Analyses:

The ARPAC antibiotic policy questionnaires were designed by an expert group using previous questionnaires (e.g. UK BSAC and HARMONY) and other experiences within the group. An antibiotic policy was present in 59% of 165 Hospitals, with different unit policies being found in 48% of 118 responses. The policy was drawn up by a National Committee in 10% (of 166), a Drugs & Therapeutics Committee in 18% (166), an Antibiotic Committee in 30% (166), a Pharmacy in 16% (166) and a CMM/ID Physician in 37% (166). It was portable in 60% of 109 Hospitals and had a revision date in 47% of 105 Hospitals. Policies varied in their year of publication and no of pages. Many other parameters will be outlined, but importantly local resistance data was referred to in 57% (107) and a change in antibiotic following receipt of laboratory results in 76% (108). The policy was available on an Intranet in 20% (109). Computerised monitoring of prescriptions occurred in 25% (113). Cycling was only performed in 13% (110). Empirical treatment and prophylactic parameters will be covered comprehensively. Voluntary prophylaxis stop dates were in 21% (158) and compulsory stoppage in 9% (157): for antibiotic treatment the data were 15% (158) and 6% (159) respectively. Parenteral/oral switch was mentioned in 67% (108). Various aspects of laboratory analyses will be outlined. Significant relationships were found between 3rd Generation Cephalosporins ( $p$ ; 0.04) and Glycopeptide ( $p$ ; .028) usage and computerised prescribing. There were no other relationships found between specific parameters and prescribing (true?). A subjective policy prescribing scoring system was thus agreed within the group and will be made available on the day. The relationships between these and descriptive hospital data (e.g. region and teaching hospital status) and antibiotic usage will be described.

# Can the laboratory influence clinical use?

*Hans J. Kolmos, Odense University Hospital, Denmark*

The influence of the microbiology laboratory on antibiotic prescribing is dependent on three key factors: Firstly, microbiology facilities must be easily available. Microbiology laboratories should be integrated in hospitals close to patients and clinicians, and if necessary, the laboratories should provide an after-hours service. Secondly, the laboratories should be staffed with medically and clinically trained microbiologists, who can liaise with the clinicians and play an active role in decisions on antibiotic prescribing. Thirdly, timely reporting of test results is essential. Laboratories should emphasize new rapid techniques, and general practitioners should be encouraged to office based testing.

Antimicrobial susceptibility testing should be based on validated techniques, and break points should follow accepted standards. Disc diffusion techniques provide reliable results if standardised, and are still good for routine purposes. Reporting of antimicrobial susceptibility should be interpretative, leaving the clinician with a simple choice: S or R. Selective release of susceptibility data may be employed as a way promote the use of recommended agents and restrict the use of others. Periodic preparation of statistics on resistance data and feedback to clinicians is a useful tool to adjust antibiotic policies, but is no substitute for a daily proactive clinical liaison service.

# Can the laboratory influence antibiotic use?

*Ian M. Gould, Aberdeen Royal Infirmary, UK  
(for the ARPAC Steering Group)*

170 European ARPAC hospitals provided answers to the questionnaire on Antibiotic Stewardship. This work was carried out under the auspices of the ESCMID Study Group on Antibiotic Policies.

75% (n=127, 3 missing) hospitals provided an emergency out of hours microbiology laboratory service. 86% (n=147) provided blood culture results on a semi continuous basis, 73% (n=124) provided summary S/I/R data to guide empiric treatment. This was sent to individual physicians in 54 hospitals (32%), individual units in 64 (38%) and to the whole hospital in 59 (35%). This data was provided annually in 86 (51%) and more frequently in 37 (22%).

Susceptibility test results were reported routinely for restricted agents in 88 hospitals (52%, 15 missing) and for non-formulary agents in 59 (35%, 9 missing). 114 (67%, 13 missing) reported non-formulary agents where there was resistance to formulary agents. 89 (52%, 10 missing) reported MIC values.

Prescribing advice was available in normal working hours from micro/ID specialists in 91% of hospitals (n=155, 5 missing) and out of hours in 71% (n=121). Daily ward rounds to advise on therapy were carried out by micro/ID specialist in 70 (41%) hospitals.

In conclusions, most ARPAC hospitals have active laboratory based antibiotic stewardship programmes although there is no evidence from the ARPAC database that these reduce antibiotic consumption.

## **Do education and audit optimise prescribing?**

*Inge C. Gyssens, Erasmus MC University Medical Center, Rotterdam  
The Netherlands.*

Inappropriate antibiotic use has consequences for the quality of care, costs and antimicrobial resistance. Although there is epidemiological evidence that overuse has been linked with increasing resistance, there is a scarcity of data about the consequences of inappropriate (under)use for the development of resistance. Educational intervention programmes aim at improving not only the knowledge of indications for use, but also at optimal dosing regimens in terms of efficacy and toxicity. Various formats have been described for hospital and community settings. Prescribers at all levels have been exposed to evidence based guidelines, lectures, grand rounds, audits, newsletters for feed back and face to face academic detailing. Guidelines should be implemented fully to result in success. In the community, the public has also been targeted in some national programs. Recent examples are the dissemination of flyers and commercials and special programs for children. For professionals, peer education is considered the most successful and its effectiveness is enhanced when the message delivered by local opinion leaders. Education as a sole intervention has not always been successful. No single educational intervention has ever been effective in all settings. Evaluation of impact is hampered by methodological flaws of intervention studies. In the future, better study methodology should lead to better insight to formulate recommendations.

## **Do education and audit optimise prescribing?**

*Jos van der Meer, University Hospital Nijmegen, The Netherlands  
(for the ARPAC Steering Group)*

This part of the ARPAC study was co-ordinated by the ESCMID Study Group on Antibiotic Policies and involved analysis of responses from 170 ARPAC hospitals. Data were collected for the year 2001.

In the two years prior to 2001, 80% of hospitals (n=136, 5 missing) had carried out education on antibiotic use and 72% (n=123, 12 missing) on the consequences of resistance. 44% (n=75, 15 missing) carried out these activities at least once per year, 11% (n=19) at least every 3 months and in 18% (n=31) these activities were continuous. 79 hospitals (46%, 11 missing) directed these initiatives to individuals and 124 (73%) to groups of staff. Implementation of educational initiatives was by micro/ID/IC specialists in 147 hospitals (86%, 7 missing), by the DTC in 35 (21%), pharmacy in 34 (20%), pharmaceutical companies in 53 (31%), commercial advertising agencies in 5 (3%) and others in 13 (8%).

The targets were heads of departments in 98 hospitals (58%, 7 missing), senior prescribers in 136 (80%), junior prescribers in 126 (74%), nurses in 35 (21%), pharmacists in 45 (26%) and undergraduates in 51 (30%)

Audits were performed at least twice per year in 20 hospitals (12%), once per year in 49 (29%) and not at all in 17 (10%) but 84 hospitals (49%) did not answer the question.

DTCs were involved in audit in 23 hospitals (14%, 7 missing), antibiotic committees in 34 (20%) surgeons in 10 (6%), physicians in 15 (9%), pharmacists in 37 (22%) and CM/ID specialists in 57 (34%). Individual prescribers received feedback in 14 hospitals (8%), units in 42 (25%) and whole hospitals in 34 (20%). Audit feedback was by personal letter in 10 hospitals (6%) oral communication in 29 (17%), during meetings in 43 (25%) and by a single report to the whole hospital in 26 (15%). Individual performance was only compared to whole hospital performance in 16 hospitals (9%) but 70 responders did not complete this question.

In conclusion, educational initiatives were common in ARPAC hospitals and diverse in nature. Audit activities were much more rarely performed. Hospitals performing educational initiatives had consistently lower antibiotic consumption figures although p-values were only marginally significant.

**Workshop 3**  
**Antibiotic Prescribing and**  
**Consumption in European**  
**Hospitals**

**Abstracts**

## How should antibiotic consumption be measured?

*Ron Polk, Virginia Commonwealth University School of pharmacy,  
Richmond, VA. USA*

Many national and international organizations have forcefully argued that data regarding antibiotic consumption--at all levels-- should be made available. The method used to express antibiotic consumption is less important than just doing it. We do not really understand if there are differences within classes of drugs and their propensity to promote bacterial resistance. When total antibiotic consumption is measured within a hospital or health care system, including the breakdown by individual class and agent, then it is possible for an institution to "benchmark" and compare their usage to similar institutions to get an idea if usage is more or less than the norm. The easiest data to obtain will be "whole hospital" data. In many cases this will be sufficient. However, it is clear that in many hospitals-but not all-there are major differences in rates of resistance between different units within the hospital. It is still unclear what measures are most appropriate to establish that one hospital is "similar" to another then it comes to benchmarking antibiotic use. The method used to measure antibiotic consumption depends on the use to which it will be put. For example, it is reasonably clear that comparison of antibiotic use across hospitals is most easily accomplished by comparing DDD/1000 patient days (DDD/1000PD). However since this is an evolving science, we must remain open to alternative and possibly improved measures of expressing antibiotic use.

# How should antibiotic consumption be measured (The ARPAC perspective)

*Fiona M. MacKenzie, Aberdeen Royal Infirmary, UK  
(for the ARPAC Steering Group)*

140 European ARPAC hospitals provided antibiotic use data. This work was carried out under the auspices of the ESCMID Study Group on Antibiotic Policies.

Although there are various units of measurement of antibiotic use, ARPAC chose to use the WHO recommended defined daily doses (DDD) / 100 patient days (PD) in conjunction with the ATC J01 classification system. Hospitals were supplied with an Excel spreadsheet (ABC calc) and asked to enter pharmacy stock data and the number of bed-days for 2001. The spreadsheet provided the DDD values and made automatic calculations to present the data as DDDs/100 BD for the J01 sub-classes.

More hospitals were able to provide data for the whole hospital than for individual specialties. It is unclear how accurate the data supplied might be as accuracy is dependent on the source of the data and the means by which antibiotics are dispensed / distributed by the pharmacy. There is some indication that the pharmacy is not the only source of antibiotics in some Eastern European countries. This will be discussed further. There was a marked variation in the ability of various countries to supply data. The number of usable datasets from the regions north, south-east, south, west and centre / east (regions 1-5) were 19, 8, 52, 27 and 34 respectively. There was also a marked variation in the quality of the data supplied. Many hospitals were collating antibiotic use data for the first time and required considerable help. Consequently, this was the most labour intensive part of the ARPAC project for both participating hospitals and for ARPAC.

The number of different antibiotics for which each hospital supplied data was calculated (oral and IV forms were differentiated). There were significant geographical variations and median numbers of antibiotic prescribed for regions 1-5 were 52, 44, 48, 36 and 46 respectively. Taking all 140 hospitals into account, there was a significant, positive relationship between numbers of antibiotics prescribed and total antibiotic use. The numbers of antibiotics prescribed gives an indication of the number of antibiotic on the hospitals' formularies.

Feedback from ARPAC participants indicated that many did not know how to benchmark their antibiotic use data and requests have been made for the return of individual hospital data along with median country, region and complete project data. These will be fed back to participants in due course.

# How Does Consumption Relate to Resistance?

*Dominique L. Monnet,<sup>1</sup> José María López-Lozano<sup>2</sup>*

*<sup>1</sup>Statens Serum Institut, Copenhagen, Denmark,*

*<sup>2</sup>Hospital Vega Baja, Alicante, Spain*

Data on each individual patient's exposure to antibiotics and subsequent emergence of resistance represent the strongest evidence that antibiotic consumption is responsible for antibiotic resistance. However, in most hospitals, only aggregated microbiology and pharmacy data are available to study this relationship. Scatterplots and correlations of consumption vs. resistance levels may be helpful for hospital comparisons, but have shown their statistical limitations. When using aggregated data, variations of antibiotic consumption followed by variations of resistance in the same direction represent the strongest evidence of a cause-effect relationship between these two parameters.

Our experience with multivariate time series analysis shows that it is possible to obtain short-term predictions of resistance through ongoing monitoring of consumption and resistance. For most antibiotic - micro-organism combinations explored in several hospitals that tested this new method, an increase in consumption of a specific antibiotic or antibiotic class was followed by an increase in resistance to this antibiotic or antibiotic class with a delay of less than 6 months. Similarly, decreases in consumption were generally followed by decreases in resistance with delays inferior to 6 months. However, these decreases were not sustained and, on the longer term, resistance levels often showed an increasing trend.

It is essential that hospitals in Europe perform on-going monitoring of both antibiotic resistance and consumption. Because changes in resistance may occur rapidly following changes in consumption, it is essential that this monitoring is performed at short time intervals, e.g. months. Once the monitoring system is implemented efforts should be made to stratify data by medical specialty, hospitalisation unit or ward. Computerised antibiotic prescriptions and analysis of emergence of resistance in individual patient as a consequence of antibiotic exposure are desirable, but remain a long term goal for most hospitals.

## How Does Consumption Relate to Resistance?

Christian Brandt, Statens Serum Institut, Copenhagen, Denmark  
(for the ARPAC Steering Group)

The ARPAC study enrolled 192 hospitals from all European regions that provided data on antimicrobial resistance and consumption. Among participating hospitals there were great variations in both antimicrobial consumption and resistance. Preliminary results are presented in the table below.

Antibiotic consumption (DDD/100 beddays)						
Antibiotic-resistant bacteria (%)	3rd gen. cephs. (3GC)	Carbapenems	Aminoglycosides	Fluoroquinolones	Glycopeptides	Total
3GC-R	0.016	-0.013	<b>0.353**</b>	<b>-0.249*</b>	0.027	<b>-0.301*</b>
<i>K. pneumoniae</i> , Imipenem-R	<b>0.269*</b>	<b>0.297*</b>	0.213	0.081	<b>0.314**</b>	-0.052
<i>P. aeruginosa</i> Carbapenem-R	0.227	<b>0.261*</b>	<b>0.400**</b>	0.054	0.220	0.139
<i>A. baumannii</i> Fluoroquinolone-R	<b>0.278*</b>	0.223	0.230	<b>0.257*</b>	<b>0.259*</b>	0.156
<i>E. coli</i> Vancomycin-R	<b>0.392**</b>	0.242	<b>0.276*</b>	0.202	<b>0.342**</b>	<b>0.352**</b>
enterococci (VRE) Methicillin-R	<b>0.387**</b>		0.149	0.206		<b>0.262*</b>
<i>S. aureus (MRSA)</i>						

Despite correlations that seem consistent, ARPAC data clearly show their limitations in analyzing this relationship between consumption and resistance. Additionally, data were collected on one single year and these correlations do not prove a causal relationship between these two parameters. Nevertheless the present data can be used by ARPAC hospitals to compare their levels of consumption and resistance. In the future, hospitals and multi-centre projects like ARPAC should aim at collecting longitudinal surveillance data to study the impact of variations in consumption on resistance.

## **Can the pharmacy influence antibiotic use?**

*Ron Polk, Virginia Commonwealth University School of pharmacy,  
Richmond, VA. USA*

Since antimicrobial drugs are dispensed from the pharmacy, it is intuitively obvious that pharmacy can and should have an important influence on antibiotic use. Indeed it is likely that the pharmacy department is playing an important role in virtually every institution where antibiotic therapy is managed. The level of involvement might typically range through a wide spectrum of activities, beginning with mostly passive contributions to providing drug cost information though a requirement of pharmacist initiated prior approval for selected drug to be dispensed. At the present time, computer guided antibiotic selection is unusual, but there appears to be an emerging consensus that this will be an exceedingly important mechanism to shape therapy in the future. There is limited data that providing feedback of antibiotic consumption data to hospitals can result in changes in therapy, but this is largely anecdotal and much work in this area remains to be done.

## **Can the pharmacy influence antibiotic use?**

*Vladimir Krcmery, St. Elisabeth Cancer Institute, Bratislava, Slovak Republic  
(for the ARPAC Steering Group)*

170 European hospitals provided answers to the questionnaire on Antibiotic Stewardship relating to the situation in 2001. This work was carried out under the auspices of the ESCMID Study Group on Antibiotic Policies (ESGAP).

A wide range of antibiotic stewardship measures were practiced in the ARPAC European hospitals in 2001, although there remains great scope for expansion of those overseen by pharmacy departments. Financial limitations were only imposed in 34% of hospitals. Antibiotics were dispensed from the pharmacy department for each patient in only 39% of hospitals. Automatic stoppage of treatment and prophylaxis was practiced in less than 20% of hospitals. Only 15% had computerised prescribing and 20% carried out computerised audit. Emergency advice was offered and ward rounds carried out in only 20-30% of hospitals.

There were significant geographical differences in the pharmacy services provided by European hospitals but no evidence has been obtained by the ARPAC project that pharmacy activities in antibiotic stewardship reduced the amount of antibiotics prescribed.

## How can antibiotic prescribing be harmonised?

*Giorgio Zanetti, University Hospital, Lausanne, Switzerland*

There are strong arguments against standardisation of antibiotic policies among European hospitals. Each hospital is faced with its own pattern of antimicrobial resistance. Moreover, hospitals are in many respects independent entities regarding the epidemiology of resistance.

Harmonisation of antibiotic policies, in contrast, refers to agreement on a set of common principles regarding the appropriate use of antibiotics. It may then be translated into hospital-specific policies, provided it goes beyond obvious general considerations and addresses practical issues. Common approaches provide a better expertise in implementation of antibiotic management programs and a better knowledge of their efficacy. Examples of aspects in antibiotic use that are amenable to harmonisation include perioperative prophylaxis (regimen, duration, and minimal standards for efficacy), diagnostic procedures, selection of patients and regimens for empirical therapy, and choice of reserve antibiotics.

Several problems may arise with harmonisation of antibiotic prescribing. It should be flexible enough to allow innovative approaches. It must not neglect values at stake with the use of antibiotics that may be weighted differently across Europe, such as risk acceptance or trade-off between individual and collective interests. Finally, evidence is often lacking to make strong recommendations on appropriate antibiotic use, which opens avenues for future research.

# How can antibiotic prescribing be harmonised?

*Ian M. Gould, Aberdeen Royal Infirmary, UK  
(on behalf of the ARPAC Steering Group)*

This study was carried out under the auspices of the ESCMID Study Group on antibiotic prescribing (ESGAP).

The top 10 most commonly prescribed antibiotics in ARPAC European hospitals were, in descending order, 1) amoxicillin with an enzyme inhibitor, (IV), 2) amoxicillin with an enzyme inhibitor (oral), 3) ciprofloxacin (oral), 4) cefuroxime (IV), 5) amoxicillin (oral), 6) metronidazole (IV), 7) ceftriaxone, (IV), 8) clarithromycin (oral), 9) co-trimoxazole (oral) and 10) ciprofloxacin IV.

Hospitals were asked to state the first choice of antibiotic empiric treatment for eight clinical scenarios according to their antibiotic policy. They were also asked to state the first choice of prophylactic antibiotics for five clinical scenarios according to their policy. There were marked differences in responses between regions, which will be presented. For example, the North favoured narrow spectrum penicillins for the treatment of community-acquired pneumonia while other regions favoured cephalosporins or broad spectrum penicillins. For pyelonephritis, the North favoured  $\beta$ -lactams and aminoglycosides, the West quinolones. These choices are not clearly related to the prevalence of ARPAC resistant Alert organisms. Despite marked differences in the prevalence of the ARPAC Alert organisms, the most common choices for prophylaxis of surgical operations were fairly consistent throughout the different regions with first and second generation cephalosporins being favoured.

There are possibilities for harmonisation of choices for treatment and prophylaxis based on current prescribing practices and Alert organism prevalence. The advantages and disadvantages of harmonisation of drug choices will be discussed.



**Workshop 4**  
**Containment of Antimicrobial**  
**Resistance; Role of Infection**  
**Control Policies and Molecular**  
**Typing**

**Abstracts**

# **How to organize effective infection control programmes in healthcare facilities?**

*Andreas Voss, University Medical Center St. Radboud, Nijmegen, The Netherlands  
Carl Suetens, Institut Scientifique de la Santé Publique, Bruxelles, Belgium*

No Abstracts available

# What is the Role of Targeted Surveillance and Control of Resistant “Alert” Organisms?

Marc J. Struelens, Dominique. Wagner, ULB-Hopital Erasme, Brussels, Belgium

## 1. How to identify relevant alert organism (A.O.) to include in local surveillance, alert and control programme?

A majority (88%) of European hospitals participating to the ARPAC survey have implemented laboratory based surveillance of antimicrobial resistant A.O.s. with notification to the infection control team, for the following organisms : methicillin resistant *S. aureus* (MRSA) (87.7%), glycopeptide resistant *Enterococci* (GRE)(53.8%), 3<sup>rd</sup> generation cephalosporins resistant *K. pneumoniae* (C3R-KP) (42.5%), and carbapenem resistant *A.baumannii* (CR-AB) (40.6%).

This can be placed in perspective with median (interquartile range) resistance rates: MRSA 20.8(6.4-35.8)%: GRE 0.2(0.0-1.3)%; C3R-KP 8.3(2.3-25.9)% and CR-AB 2.3(0.0-12.5)%, with 17-500-fold difference of median rates by European geographical region. For MRSA, active screening of carriers was done in patients in 55% of hospitals and in health care workers (HCW) in 48%. The proportion of centres performing screening was higher in N and W regions. Screening of patients for other A.O. was performed by 7% to 17% of hospitals depending on the organism.

Linear regression modelling of IC policies as predictor of MRSA prevalence adjusted for antibiotic consumption, case-mix and hospital size suggested that the following factors were weakly associated with lower resistance rates: MRSA alert system to inform IC team (mean difference 13.5 %, 99%CI -1.3% to 28.9%); and screening of health care workers for MRSA (mean difference 6.9 %, 99%CI -1.8% to 15.5%).

*Essential requirements should be to develop MRSA surveillance and alert programme with active patient screening in all European hospitals, given its widespread distribution, epidemic character and attributable morbidity/mortality. The optimal modalities of active MRSA surveillance (culture or DNA amplification) require further study.*

*Surveillance of other alert organism should be based on local and regional assessment of transmissibility and attributable morbidity/mortality.*

## 2. What is the role of AO control measures such as isolation and barrier precautions, cohorting and carrier decolonization ?

For the care of MRSA patients, contact precautions were used in a majority of ARPAC centres (single room:55%; gloves :60% ; gown :51% ) as well mupirocin decolonisation of patients (76%) while a minority recommended use of mask (32%), and cohort care (32%). Significant differences ( $p < 0.001$ ) were noted by region, with proportion of centres recommending placement in single room from 30% in SE to 100% N region, gloves in 29% SE to 100% N, gown in 40% SE to 100% N, mask in 21% S to 100% N and mupirocin decolonization in 21% S to 79% N.

Contact precautions were used by fewer centres for other AOs: GRE (gloves and gown :39%), C3R-KP (gloves :57% ; gown :37%), CR-AB (gloves :37% ; gown :31%).

Linear regression modelling adjusted for antibiotic consumption, case-mix and hospital size suggested that the following factors were associated with lower MRSA rates in ARPAC hospitals : placement of MRSA patients in single room (mean difference 11.2 %, 99%CI 1.4% to 20.9%); use of gown (mean difference 13.1%, 99%CI 0.2% to 25.9%);use of gloves (mean difference 13.4%, 99%CI -3.1% to 29.9%) Hospitals having problems implementing AO isolation policies had higher resistance (mean difference 12%, 99%CI 3.8% to 20.1%).

*Essential requirements should be to place MRSA colonized patients in single room and apply glove and gown barrier precautions for patient care. Sufficient resources in terms of skilled health care staff and isolation rooms should be available. Topical decolonization of MRSA nasal carriers with mupirocin should be attempted when no risk factors preclude eradication.*

*The rationale for and cost-effectiveness of using contact precautions for other AOs should be determined by local and multi-centre studies; implementation should be considered and evaluated in all institutions and regions where outbreaks are caused by epidemic strains of AOs*

# What is the role of targeted surveillance and control of resistant “ALERT” organisms?

Stephan Harbarth, Geneva University Hospitals, Switzerland

With the help of computerized information systems, susceptibility test results of clinical specimens sent to routine clinical microbiology laboratories have been used for decades to follow trends in antimicrobial resistance rates. Yet, there is ongoing controversy about the most important alert organisms that should be surveyed and the role of active surveillance cultures to detect asymptomatic carriage. Moreover, only few studies have attempted so far to link the occurrence of resistant alert organisms to specific clinical outcomes, in order to better determine the disease burden related to antimicrobial resistance.

For most European hospitals the difficult question is not whether active surveillance cultures are a good, evidence-based control measure; rather: how much is enough and which units should be included (ICU surveillance only or hospital-wide surveillance)? In my presentation, I will show data that support the hypothesis that the colonization pressure (proportion of patients positive with an alert organism at admission) may play an important role in deciding which microorganism should be included in the targeted surveillance program. Certainly, institution-specific programs should be developed for surveillance of methicillin-resistant *S. aureus* (MRSA) and other clinically important pathogens (yet, one size does not fit all!). Moreover, surveillance programs should be established at the national level, in order to rapidly detect the spread of emerging nosocomial pathogens (e.g. PVL-producing, community-acquired MRSA, vancomycin-resistant enterococci, carbapenem-resistant *Acinetobacter baumannii*).

# What is the role of molecular typing in containing antibiotic resistance?

*K.J. Towner<sup>1</sup> / L. Dijkshoorn<sup>2</sup>*

*<sup>1</sup>Queen's Medical Centre, Nottingham, UK; <sup>2</sup>Leiden University Medical Center, NL*

Microbial typing can be done for different reasons and at different levels, including the local hospital level, the regional or the (supra)national level. Probably the most frequent reason at the local level is to identify cases of cross-infections caused by antibiotic-resistant strains. Typing can also be done to investigate the diversity in the population. Finally, microbial typing can be done to study the relationship between epidemiological markers, antibiotic resistance, epidemicity and pathogenicity mechanisms.

Many different methods are available for typing microorganisms. The first part of this Session will present the data gathered by ARPAC on typing methods being used currently by participating hospital laboratories around Europe for typing ALERT organisms. Additional evidence regarding the possible impact of typing on the overall incidence of antibiotic-resistant ALERT organisms will also be presented.

The second part of the Session will review the typing methods that are considered suitable for possible database construction. Traditional methods include phenotypic characterisation by biotyping and antibiogram typing. Frequently used genotypic methods of increasing complexity are RAPD analysis, macrorestriction fragment analysis using pulsed field gel electrophoresis (PFGE) or high resolution genomic fingerprinting by AFLP. A recent development is the introduction of sequence-based methods to assess relatedness of strains. In the past decade several networks using different methods have been set up to investigate the spread of important pathogens. These pilot databases have demonstrated the feasibility of the database approach at a European level.

The third part of the Session will consider the practical steps and laboratory effort required to set-up typing databases (standardisation, validation, problems). What measures are required to make the database approach a reality?

# Construction and operation of typing databases and the ARPAC demonstration databases

*J. Green<sup>1</sup> / K. Levi<sup>2</sup> / K.J. Towner<sup>2</sup>*

*<sup>1</sup>Health Protection Agency, Colindale, UK;*

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The first part of this Session will consider the construction and management of typing databases. Surveillance of the aetiological agents of infectious disease requires a trans-European approach in order to fully understand transmission mechanisms and sources of infection, especially since there is ever-increasing travel and commerce, both within and between countries of the EU. Utilisation of on-line databases to share epidemiological and molecular typing data on microbial pathogens is not a new concept, and there are several successful models including the 'Salmgene' (international Salmonella surveillance through PFGE strain typing and differentiation <http://www.salmgene.net>) and 'Foodborne Viruses in Europe' ([www.eufoodborneviruses.co.uk](http://www.eufoodborneviruses.co.uk)) projects. Much has been learnt from the establishment of these early models, and although there are still technological challenges to overcome, we are now much better placed to develop efficient, versatile and robust databases suited to the needs of microbial typing. Examples will be given in the presentation.

Sharing of microbial typing data, generated using whatever technique (PFGE, AFLP, DNA sequencing) is dependent to a greater or lesser extent (usually greater) on use of a standardised common protocol. Lessons learned previously have shown, however, that this is not enough. An agreed standardised method of band assignment, for example, is also essential if data are to be comparable, as are agreed data quality standards and formats. How the database is managed both technically and administratively, e.g., issues relating to curatorship, access of participants and non-participants, processes for publications derived from the database, etc., are all issues that may affect the willingness of participants to submit their data, and thus affect the utility of the database. Both technical and management issues will be illustrated in the presentation.

The second part of the Session will describe the methods used for typing the ALERT organisms defined by the ARPAC project. The operation of the pilot demonstration ARPAC databases will be illustrated, and initial findings on the population structures revealed by this preliminary work will be presented.

The potential for effective and versatile online databases as a significant tool in tracking the spread of pathogenic microorganisms across Europe is ever-increasing. Careful planning is essential, however, in order to maximise the potential benefits of such a development. The final part of this Session will discuss how typing databases might be organised at the European level, and will consider what recommendations should be made to the EU to promote further progress in this area.