

EAHP Policy Statement on Antimicrobial Resistance

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Antibiotics (and other antimicrobials) are widely used to treat infections in patients across Europe and the world. They treat living bacteria (or other organisms) to prevent serious infections. Prior to their development, infections such as pneumonia and cellulitis were commonly fatal and antibiotics have dramatically decreased mortality of these infections ^[1].

However, their widespread inappropriate use decreases their utility due to the emergence of resistant strains, and this is an area of high concern for hospital pharmacists working in hospitals within Europe in respect to upholding patient outcomes and welfare.

For example, according to the most recent report from the EU Commission (DG Health and Consumers/DG Sanco) “*antimicrobial resistance (AMR) results each year in **25 000 deaths** and related costs of over **€1.5 billion** in healthcare expenses and productivity losses*”^[2].

The historical roots of the problem are not new. In 1956 Jawetz documented that the pharmaceutical industry was investing heavily in the promotion of anti-infectives and by 1970, 50% of hospital antibiotic use was inappropriate ^[3-5] But the effects over time have been cumulative.

Specifically the bacteria that previously were susceptible to the first introduced antibiotic (penicillin and its derivatives known as *beta lactam* antibiotics) are increasingly becoming more resistant; including the emergence of various strains resistant to all *beta lactam* based antibiotics and other drugs used, including the fluoroquinolones, and aminoglycosides..

There is increased incidence of resistance identified with a number of strains of bacteria including meticillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant *Staphylococcus aureus* (VRSA), vancomycin resistant *Enterococci* (VRE) and worryingly 3rd generation cephalosporins and carbapenem resistance in clinically important Gram negative bacilli (e.g., *Escheirchia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*)^[6].

Europe has taken action towards resolving the lack of surveillance of antimicrobial resistance and consumption including hosting a major EU conference ‘The Microbial Threat’ in 1998. The outcomes of this conference are referred to as ‘The Copenhagen Recommendations’. These recommendations paved the way to a number of EU funded projects on antimicrobial consumption, antimicrobial stewardship and antimicrobial resistance. Less than ten years after ‘The Copenhagen Recommendations’ the EU issued an

updated European Council (EC) Recommendation (2009/C 151/01 of 9 June 2009) on patient safety ^[7, 8] featuring antimicrobial use.

The escalating threat of antimicrobial resistance is a **global public health concern** and now seriously jeopardises the effectiveness of standard treatments, rendering some ineffective for their approved indications ^[9].

Unlike drugs used in the treatment of chronic non-communicable diseases, which do not become ineffective with usage, antibiotics do become ineffective within a few years of clinical use. This implies that antibiotic development is not as profitable so the pharmaceutical industry is deserting the anti-infective branch of Research & Development (R&D) making the antibiotic pipeline drier ^[10]. The drought in novel antimicrobial agents makes the need for antibiotic stewardship initiatives even more urgent and important.

- **Improving stewardship of antimicrobials through hospital pharmacist management**

Antibiotic stewardship programs have developed over the last decades, as has the number of specialist antimicrobial pharmacists ^[11] and when programs have been implemented they are effective at improving clinical outcomes, preventing antimicrobial resistance and decreasing adverse events such as *Clostridium difficile* infections ^[12]. These positive impacts have been brought about by the hospital pharmacist providing direct interventions (for example, in reviewing antibiotic duration, advising on the cessation of inappropriate treatment, counselling on restricted use of certain antibiotics). They helped to provide improved education about antibiotic use to other healthcare professionals and system managers (e.g. coordinating guidelines and avoiding long term prophylaxis), implement policies/procedures leading to a reduction in consumption and good prescribing practice ^[1]. Furthermore, a reduction in the use of resistogenic antibiotics (e.g., fluoroquinolones and 2nd & 3rd generation cephalosporins) has had a positive impact on *Clostridium difficile* Infection (CDI), MRSA as well as Extended-Spectrum-Beta-Lactamase (ESBL) incidence in many European countries. For example in Scotland multidisciplinary teams consisting of antimicrobial pharmacists; infectious disease physicians and microbiologists have been introduced as part of a holistic approach to the problem.

Pharmacists specialised in the area of infectious diseases/antimicrobials are well placed to provide expert high-level advice within health systems about combating antimicrobial resistance. There is also a role for all pharmacists working in all sectors to provide appropriate advice about antibiotic medicines: to patients; prescribers; and those with responsibility for the functioning of health systems more generally.

A 2-year (2006-2008) project entitled: Implementing antibiotic strategies for appropriate use of antibiotics in hospitals in member states of the European Union (ABS-INTERNATIONAL), co-financed by the European Union through the Programme of Community Action in the field of Public Health looked into the effect of antibiotic stewardship in 9 partner EU countries^[13]. Regular (e.g. on an annual basis) Point-Prevalence Surveys (PPS) of antimicrobial prescribing in European Hospitals have shown to be able to identify targets for quality improvement. Furthermore, any resulting intervention could be evaluated by follow-up PPS's^[14, 15].

EAHP calls for national governments and health system managers to promote and develop the resource that is within their midst in terms of combating antimicrobial resistance: the hospital pharmacists, and their specialised background and knowledge in the area of appropriate antibiotic use. Roles should be expanded in this regard, and the hospital pharmacist embedded in the heart of national strategic responses to the antimicrobial resistance crisis.

- **The need for new incentives to develop antibiotics**

There is, and has been over a number of years a lack of investment in the development of new antibiotics and currently there are only a few products that are at later stages of development^[2]. In the absence of new effective antimicrobials, there is a risk that resistance will increase and some infections may no longer be able to be treated effectively^[9]. There is now an urgent need for increased research and development^[6, 16].

Although some efforts have been made by the European Commission (e.g. through the Innovative Medicines Initiative [IMI]) and national governments to combat this development bottleneck, EAHP considers that more still needs to be done. The Infectious Disease Society of America has also undertaken the 10x20 initiative^[17] which is very similar to the ND4BB (new drugs for bad bugs)[18] undertaken by the IMI which incorporates the COMBACTE project^[19].

As a new Commission is created for the 2014-2019 period, EAHP calls for an urgent review of the current research environment for new antibiotics, and development of fresh proposals for pan-European action on the matter.

- **The need to tackle misuse of antibiotics in the veterinary sector**

The misuse use of antimicrobials in the veterinary, agriculture and aquaculture sectors, including the under dosage to uninfected animals, and overuse of prophylactic strategies, is serving to make the problem of antimicrobial resistance worse^[2]. Despite various European and national regulations, between European countries there remains wide variation and

unexplained difference in the sales of antimicrobials in the veterinary sector ^[2]. Furthermore, there is a void of information on the amount and indication of antibiotic use in animal husbandry as many European countries did not take part in the European Medicines Agency (EMA) project entitled European Surveillance of Veterinary Antimicrobial Consumption (ESVAC)^[20].

Misuse of antibiotics in the veterinary sector is particularly concerning for the hospital sector in relation to the increased prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) and its links with new emerging strains from pigs. For example, in 2009 a joint ECDC, EFSA and EMA report declared, “*the extensive use of antimicrobials for prevention of disease appears to be an important factor for the spread of MRSA*”.

EAHP therefore supports further clarification, tightened definition and improved enforcement of European regulations designed to reduce antibiotic misuse in the veterinary sector, and urges that this take place within the next Commission mandate 2014-19.

In summary

EAHP calls for:

- national governments and health system managers to take proactive steps to develop and benefit from the key resource that is within their midst in terms of combating antimicrobial resistance: the hospital pharmacist, and their specialised background and knowledge in the area of appropriate antibiotic use. Roles should be expanded in this regard, and the hospital pharmacist embedded in the heart of national strategic responses to the AMR crisis;
- an urgent review of the current research environment for new antibiotics, and development of fresh proposals for pan-European action on the matter; and,
- further clarification, tightened definition and improved enforcement of European regulations designed to reduce antibiotic misuse in the veterinary sector.

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