

Mapping antibiotic use and resistance in the Netherlands: SWAB and NethMap

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ABSTRACT

The worldwide emergence of antimicrobial resistance has elicited responses from national and international organisations, including the World Health Organisation and the European Union. In the Netherlands, the non-profit foundation SWAB was jointly started by several professional medical societies to coordinate the Dutch efforts in preventing and reversing the trend of emerging resistance. SWAB publishes guidelines on the prudent use of antibiotics in this and other journals. The results of SWAB's surveillance systems for antibiotic consumption and resistance were recently summarised in its NethMap 2003 document. Attention should now be focused on elucidating the major determinants of antibiotic use and resistance emergence, and designing effective intervention strategies to reverse the trend of resistance emergence.

The emergence of resistance to commonly used antimicrobial agents among medically important microorganisms poses a threat to the health of the public. Antimicrobial resistance generally increases the morbidity and mortality of patients suffering from infection and thereby increases the cost of healthcare delivery. Physicians aware of the emergence of resistance find themselves forced to change their antibiotic prescribing policies, not only in patients with proven infection, but also in patients with suspected infection. The economic impact of the emergence of antimicrobial resistance can, therefore, not be overstated. Resistance emergence drives the spiral of applying newer, ever more expensive, antimicrobial agents that have the built-in paradox of being less prone to existing resistance mechanisms and

consequently pose a further selection pressure on the population of medically important microbial species in hospitals and the community.

Although it is clear that there is not a perfect correlation between *in vitro* resistance and therapeutic failure – the host's innate and specific immunity systems play important roles here – there is now little doubt that resistance takes a heavy toll on society in terms of costs, morbidity and mortality. The emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) in virtually all parts of the world is a good case study, a paradigm of the problem. Recent analyses of the impact of MRSA on clinical medicine has shown MRSA infection to be more difficult to cure, to be associated with higher levels of morbidity and mortality and to incur much greater costs for the health-care system compared with infection due to methicillin susceptible strains of *S. aureus* (MSSA). It is also evident that in regions or countries where MRSA has emerged to clinically significant levels (>5-10%) the medical community has responded by switching their (empiric) antibiotic policies from the relatively inexpensive, safe and effective class of β -lactam antibiotics to much more expensive, less safe and potentially less effective classes of antimicrobial agents. In 2002, vancomycin-resistant clones of MRSA were detected reducing our choices further. Genetically it appears that resistance genes are acquired by those *Staphylococcus aureus* clones that are also successful as human pathogens. So where do we go from here?

In 1992 the Institute of Medicine of the United States of America published a landmark report regarding the

emergence of infectious diseases and the threats these emerging diseases pose to the health in the United States. The report recommended that the World Health Assembly take the lead in promoting the development and implementation of a comprehensive global infectious diseases surveillance system. Indeed, the World Health Organisation (WHO) responded and formulated their global strategy for the containment of emerging and re-emerging infectious diseases shortly thereafter. The major elements of the WHO strategy were:

1. development and implementation of surveillance systems for antimicrobial agents;
2. promoting the surveillance of antimicrobial resistance among microbial pathogens;
3. upgrading of microbiology laboratories and microbiological expertise in many parts of the world;
4. to foster applied research into the determinants of emerging infections;
5. to emphasise prevention and control, rather than treatment of diseases.

In 2001 the WHO recognised that special efforts should be directed at containing the rapid emergence of resistance against antimicrobial agents and published their global strategy on the containment of antimicrobial resistance. This strategy largely concurs with the recommendations formulated at the same time by the European Union to address the menace of antimicrobial resistance.

Awareness raised by these authorities and by the national and international professional societies in the biomedical sciences has led many countries, including the Netherlands, to review and amend their strategies regarding the management of infectious diseases.

The decision to form a Dutch Working Party on Antibiotic Policy was taken in 1996 by three societies of professionals involved in the management of infectious diseases in the Netherlands. Thus, the Netherlands Society for Infectious Diseases, the Netherlands Society for Medical Microbiology and the Netherlands Society of Hospital Pharmacists pooled their resources in this working party, locally known by its acronym: the SWAB (Stichting Werkgroep Antibiotica Beleid). SWAB's mission

is to manage, limit and prevent the emergence of resistance to antimicrobial agents among medically important species of micro-organisms in the Netherlands, thereby contributing to the proper care of patients in this country. This year SWAB produced its first surveillance report called NethMap 2003 (freely available at www.swab.nl). NethMap 2003 describes use of and resistance to antibiotics in bacteria isolated from humans in the Netherlands in the period 1997 until 2001. It mimics similar reports from the Scandinavian countries Denmark (DANMAP), Sweden (SWEDRES), Norway (NORM-VET) and Finland (FINRES). Interestingly, these are the same European countries that have so far been able to resist the emergence of antibiotic resistance where most other European countries have clinically seen a rapid increase in their resistance rates. NethMap 2003 reports relatively low levels of consumption and resistance over the years, but also signals trends in use and the emergence of resistance in some species against macrolides and fluoroquinolones.

As a consequence of the recommendations of the European Commission, all EU countries will need to produce such surveillance reports. These efforts are supported by national and European professional societies, and will in the coming years deliver a sharper image on the differences in antimicrobial use and resistance across Europe. As a continent, Europe seems to lead the way in managing the threat of antimicrobial resistance, where similar efforts in the USA, Japan and other parts of the world are fragmented or nonexistent. However, major tasks lie ahead for European countries as well. We have to know what the crucial determinants of antibiotic use are and explain the large differences in the current levels of antibiotic use among the EU member states. Also, for each relevant combination of antibiotic and microbial species we need to know what risk factors determine resistance emergence. Apart from better managing the use of antibiotics, the spread of resistant clones may make it necessary to upgrade our infection prevention efforts as well. Subsequently, we have to devise strategies to intervene with medical practices and deal with socioeconomic pressures that help drive the resistance spiral. NethMap will be monitoring our successes and failures.