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EXTENDED ABSTRACT

Emergence & spread of Multiresistant Organisms: Can Infection Control measures help?

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Introduction

Antimicrobial resistance has been recognised since the earliest days of antibiotic use. It results in increased morbidity and mortality, and raises the costs of health care.

The remarkable ability of bacteria to develop resistance by a variety of mechanisms is influenced by the widespread, sometimes indiscriminate and frequently unnecessary use of antimicrobials in a variety of settings.

A major review presented in the BMJ in 1998 included examples of inappropriate antibiotic use.[1] Areas identified in human medication, agricultural use, and animal feeds were summarised,[2] as shown in Table I, and indicated that between 20% and 80% were either unnecessary, or at least highly questionable.

Examples of inappropriate use include the use of antibiotics for non life threatening conditions such as acne, the practice of using wide spectrum antibiotics as "magic bullets", and the incorporation of antibiotics in pesticides, animal feeds, and household goods such as soaps, plastics and cleaning liquids.

Faced with these challenges, it is not surprising that bacteria have responded by developing resistance to these antibiotics by a variety of different mechanisms such as the acquisition of resistance via plasmids, transposons or through genetic mutations. The mechanisms of resistance are ingenious and varied, and include changes in the antibiotic target sites, the production of detoxifying enzymes, or simple decreased uptake, amongst others.

Table I: Background to resistance

Where antibiotics are used	Types of use	Questionable use
Human use (50%)	20% Hospital 80% Community	20-50% unnecessary
Agricultural use (50%)	20% Therapeutic 80% Prophylactic/growth promotion	40-80% Highly questionable

The clinical impact of antibiotic resistance should not be underestimated. In addition to increased morbidity and mortality, infections with multiresistant organisms result in extended hospital stay, increased rates of admission to ICUs, and the consequent loss of bed days.

Further to these clinical concerns, the emergence of widespread antibiotic resistance has a major economic impact. In 2001, McGowan reviewed data presented by the USA, and estimated the annual cost of infections caused by multi-resistant bacteria to be in the region of U.S. $ 4 to 5 billion.[3]

Cargill *et al*,[4] reporting at the International Society of Technology Assessment in Health Care meeting in 1999 modelled the incremental cost of dealing with *Haemophilus influenzae* resistant to ampicillin ffor the period 1997-2006, and estimated the costs of managing this problem would raise from £6.4 m to £8.7m.

Global spread

Emergence of resistance is not just a problem in developed countries. International surveillance systems have helped to recognise it as a concern the world over.

The European Antimicrobial Resistance Surveillance System (EARSS) is a network of national centres that collects data from microbiology laboratories in 31 European countries.[5] Annual reports, based on validated data, are published providing information on trends in antimicrobial resistance. Information by specific bacterial organisms is produced, and year-by-year data is available on a country-by country basis. Whilst inter country comparisons may have some sampling biases, this comprehensive data base provides a bench mark for countries wishing to assess their rates against international data.

The Antibiotic Resistance Surveillance and Control in the Mediterranean Region (ARMed) project extends European surveillance to southern and eastern Mediterranean countries, and includes studies which relate antibiotic consumption to resistance.[6]

The spread of chromosomally- borne CTX-M Extended Spectrum Beta Lactamase (ESBLs) producing organisms has been mapped out by D Livermore from the Health Protection Agency, England (D Livermore, personal communication), as shown in Figure 1, and highlights the universality of the antibiotic resistance problem.

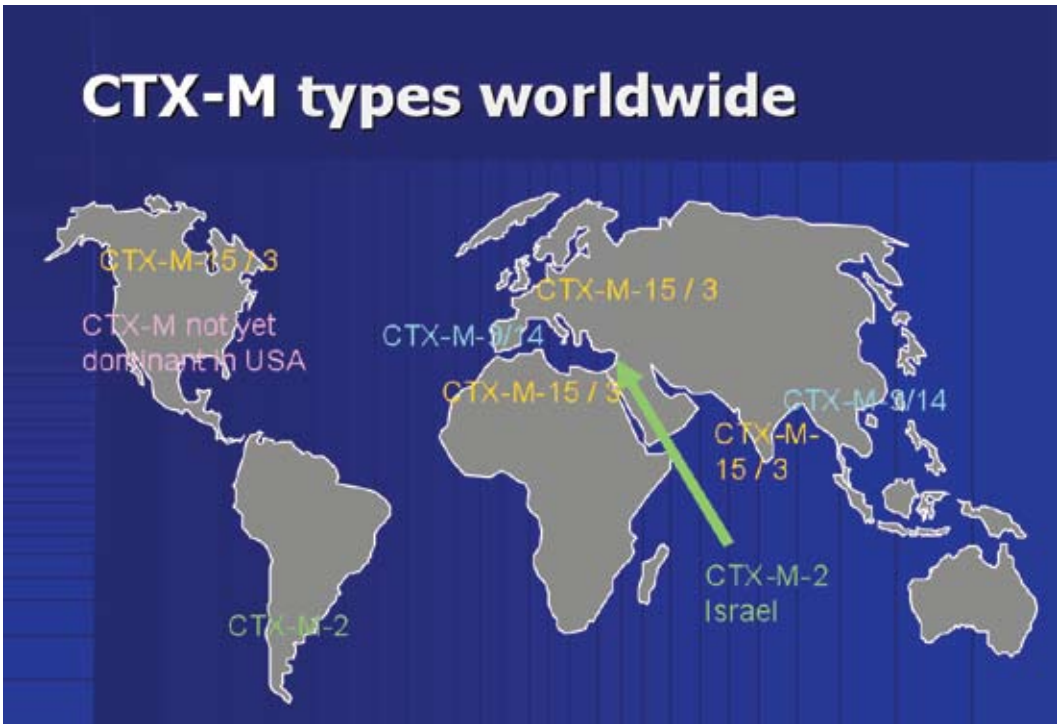

Figure 1: Spread of CTX-M ESBLs worldwide

Can infection control help?

The Society for Healthcare Epidemiology of America (SHEA) and Infectious Diseases Society of America (IDSA) stated in their Guidelines for Prevention that… "a comprehensively applied infection control programme will interdict the dissemination of resistant strains".[7]

Effective control requires a multipronged and integrated approach, as shown in Figure 2.

In addition to local proactive surveillance programmes which help to identify early the emergence of resistant strains institutional and health care settings are expected to develop their own guidelines and protocols for the use of antimicrobials, based on the best evidence available, and taking into account local sensitivity data.

Limitation of antibiotic use, based on microbiology restricted antibiotic reporting, restricted hospital formularies, and cyclic antibiotic rotation programmes have all been proposed as contributing to the control of resistance, in conjunction with local education and audit activities.

Hospitals should also establish regular programmes for the monitoring, auditing and updating of these policies.[7,8]

In the UK, the appointment of antibiotic pharmacists, working alongside microbiologists, infection prevention and control practitioners, and ward based clinicians, has had a major positive impact on the reduction of antibiotic related diarrhoea due to *Clostridium difficile*, and helped to develop and implement local antibiotic management initiatives.

In the setting of health care institutions, basic infection control measures such as hand hygiene, adequate and thorough cleaning, and isolation must be in place, and rapidly implemented when a multiresistant organism either causing clinical infection or colonisation is identified.

Beyond these measures, it is important to realise that antibiotic stewardship programmes have an international as well as a local dimension, and they will not be effective unless they are supplemented by wider educational initiatives.

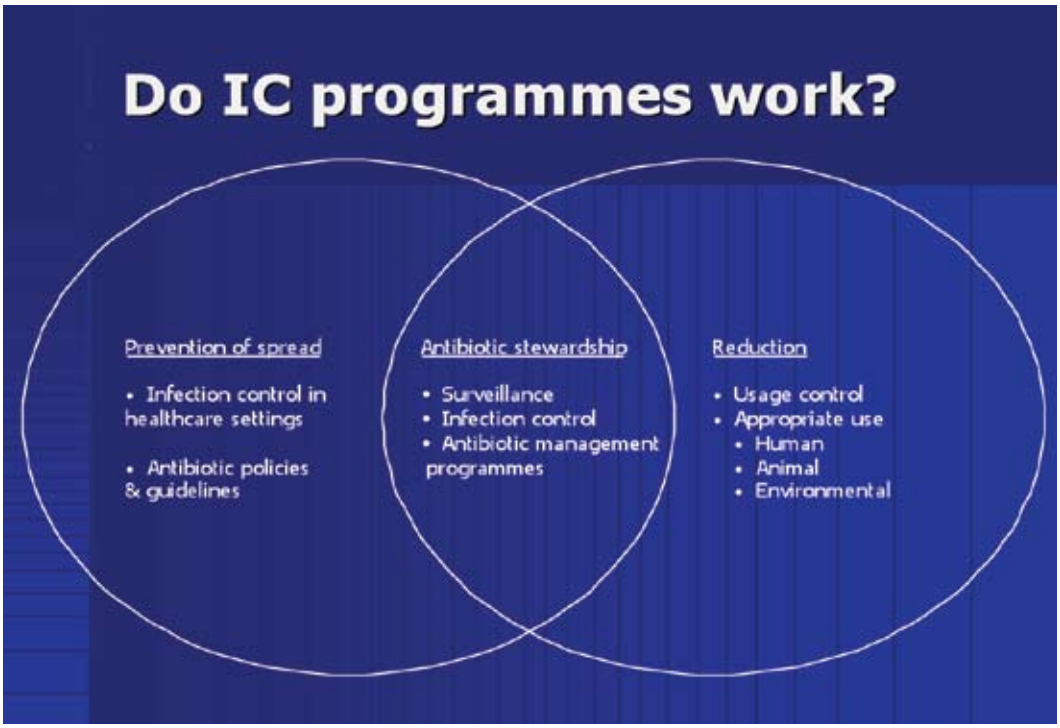

Figure 2: Do infection control programmes work?

The World Health Organization (WHO) , in its 2001 "Global Strategy for Containment of Antimicrobial Resistance" report,[8] promoted the education of patients and the general community, including the press and media, as the first step, followed by awareness raising and education of prescribers and dispensers.

International programmes also depend on the establishment of effective national surveillance programmes, supplemented by international collaboration and data exchange. At national levels, a regulatory frame work is suggested, with the establishment of effective registration schemes for dispensing outlets, and authorised prescribers. Legislative action to ensure pharmaceutical companies comply with national and international codes of practice, including advertising; and reduction of economic incentives should be considered.[8]

The ban of antibiotic use in animal husbandry solely for the purposes of growth promotion, and limitation of their use in agriculture as an adjuvant to pesticides are important steps.

Finally, actions which seek to promote further research, based on collaboration between governments, experts and industry, and aimed primarily at the search for new drugs and vaccines, are key to ensure we rely less on antibiotics, and work towards the future provision of safe and effective alternative antimicrobial agents.

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