

## Antimicrobial resistance

*Is a major threat to public health*

There is an incoming tide of concern about the problems of antimicrobial resistance. For several years alarm has been expressed in the United States,<sup>1</sup> and the past 12 months have seen two World Health Organisation meetings prompted by increasing anxieties about the role of antimicrobials in animal husbandry<sup>2</sup>; a report by Britain's House of Lords on antimicrobial resistance; and a report from the US Institute of Medicine on emerging infections.<sup>3</sup> This week the Danish Chief Medical Officer, Einar Krag, has called together colleagues from the European Union and their advisors for a conference on "the microbial threat" to "assess the strategies to prevent and control the emergence and spread of antimicrobial resistant micro-organisms." Is all this activity warranted? We believe it is: in the words of the House of Lords' report, "Resistance to antibiotics ... constitutes a major threat to public health and ought to be recognised as such more widely than it is at present." This issue of the *BMJ* is helping to broadcast this message.

The causes of these problems and gloomy portents are not difficult to find. In the past 50 years people in both the developed and developing worlds have accepted antibiotics as their right—to obtain a prescription at the first sign of a trivial infection or treat themselves with a handful of cheap antibiotics. We cannot conceive a return to the pre-antibiotic days, yet the unbridled use of these agents in man and animals is inexorably propelling us in that direction.

Most antibiotic use is in two areas: in humans in the community, and in animals for growth promotion and prophylaxis (see table). The data in the table suggest that up to 75% of antibiotic use is of questionable therapeutic value.<sup>3</sup> What seems less controversial is the long term risk of spraying fruit trees in some parts of the world with antibiotics and adding 50-60 kg of an antimicrobial to each acre of salmon farm.<sup>4</sup> Bacteria have evolved very sophisticated means of exchanging DNA, both within their own genus and species and across them. The widespread use of antibiotics will tilt the delicate balance between us and the bacteria.

There seems to be an inevitability about this problem. Society demands easy answers to its health problems. The increasing resistance problems of recent years are probably related to the use of increasingly broad spectrum agents (cephalosporins and fluoroquinolones) and crowding of the most vulnerable members of society in day care centres and nursing homes. These problems are compounded by the world wide phenomena of pressure on health care systems

### Use of antibiotics<sup>3</sup>

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

for greater efficiency, with higher bed occupancies and stretched nursing and medical care. Added to this are pressures to allow over the counter use of antibiotics in western countries so as to reduce healthcare costs. To effect change much will be required by the medical profession, politicians, the pharmaceutical industry, and not least patients.

Without doubt antibiotic prescribing in humans and animals must be prudent, but by how much must antibiotic use be reduced (10-50%?) and to what extent will this affect antibiotic resistance in different bacteria? Will we see a return to more susceptible populations or just keep the current problem in check? Some see the problem as particularly gloomy.<sup>3</sup> There are suggestions that as resistant bacteria increase and the available antibiotics decrease transmission from inpatients to the larger population will increase and become a problem to the general public.

Certainly, the veterinary profession will be required to change practices, and we commend the House of Lords' views on the control of valuable agents in animal husbandry. There are some encouraging signs that this may be occurring; at least in developed countries, fish farming is using new techniques such as immunisation instead of antimicrobials. The Swedish experience in reducing the reliance on growth promoters shows that progression can be made without reducing production. Initial problems in the form of increased morbidity and mortality in pig and poultry production were overcome by enhancing the rearing systems.<sup>5</sup> There is a need to keep a sharp eye on the development of resistance in animals, but not at the expense of inaction.

Secondly, both patients and doctors must reduce their expectations. Antibiotics are commonly prescribed, mainly for the respiratory tract, where the vast majority of infections are caused by viral pathogens. The pressures on both patient and doctor are easily understood: an anxious parent, a sick child, and a doctor faced with diagnostic uncertainty. The solutions are not straightforward. Patients must be educated that most such infections do not require antibiotics—that

they may actually be harmful to them and their families (through their effect on beneficial bacteria in the body) and to society at large (through encouraging resistance). All this requires considerable effort and time, not easily achieved in a five minute consultation. The American Academy of Paediatrics has made a start in giving guidance to parents.<sup>6</sup> Advances in rapid diagnosis will help to remove uncertainties.

The coming years will undoubtedly see the introduction of strict clinical guidelines on antibiotic prescribing. At present there is a tendency to concentrate on which antibiotic to use rather than question whether an antimicrobial is useful at all. More firm guidance is also required on the optimum length of treatment. In many parts of the world simple cystitis is still treated for 5-7 days and the more common chest infections for up to 14 days. The drug regulatory authorities therefore have their part to play in insisting that relevant clinical trials support the licence of an antimicrobial.

There is much discussion world wide about surveillance schemes for antimicrobial resistance.<sup>7</sup> The major problem is gaining useful denominator data—that is, how to obtain an accurate picture of resistance in a community, be it in hospital or general practice. In hospital it is moderately straightforward, since ward based surveys can be undertaken, but in general practice we have little accurate information. As resistance rates of common pathogens can vary greatly over short distances,<sup>8</sup> such surveillance must be undertaken both nationally, so that meaningful broad based policies can be devised, and locally, so that relevant clinical guidelines can be developed.

Greater insights are required into how resistance genes spread, especially in the community, where there is a paucity of information. Infection control procedures in child and elderly care units require enhancing. Scientific funding bodies across the European Union should realise that if we are to understand the levers which control antibiotic resistance more fundamental research will require funding. The House of Lords report highlights the problems of funding research in this area of medicine,<sup>5</sup> which in the past has mainly come from the pharmaceutical industry.

Finally, the pharmaceutical industry, which until recently has been ahead of the resistance race, will also be well advised to increase its commitment to

antimicrobial research. Indeed, now that several bacterial genomes have been sequenced, there are signs that this is occurring.<sup>9</sup> In this issue, we trust that these and other matters have been confronted. We wish the European Union medical officers' conference well. The problems they are addressing are real and can be approached only by concerted action as bacteria respect no country's borders. The past decade has seen the progressive intercontinental spread of methicillin resistant *Staphylococcus aureus*<sup>10</sup> and penicillin resistant *Streptococcus pneumoniae*,<sup>11</sup> and there are concerns about increasing resistance of *Salmonella typhi*.<sup>12</sup> Parochial approaches are therefore doomed to failure.

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## Antimicrobial resistance: a veterinary perspective

*Antimicrobials are important for animal welfare but need to be used prudently*

**B**acterial disease is a major constraint on the efficient production of animal derived food and causes ill health and suffering in both food producing and companion animals. In some production systems the spread of bacterial disease may be accelerated by the proximity of the animals. Bacterial disease may be controlled in some situations by eradication, maintenance of animals of specified health status, vaccination, and good hygiene. Nevertheless, antimicrobial chemotherapy remains vitally impor-

tant for treating and in some cases preventing bacterial disease. Many bacterial diseases of animals are potentially fatal; others cause pain and distress. Appropriate use of antimicrobials will cure some sick animals and speed the recovery of others, and may improve the welfare of treated animals and reduce the spread of infection to other animals or, in the case of zoonotic disease, to humans. The challenge is to use antimicrobials wisely, minimising the risk of resistance.