Antimicrobial Resistance in Scandinavia after Termination of Antimicrobials for Growth Promotion

Introduction

In the Scandinavian countries (Denmark, Finland, Norway and Sweden), antimicrobial growth promoters (AGP) were gradually introduced during the 1960s for use in chicken, beef and pig production. In the early 1970s there were doubts in Sweden about the growth-promoting effect in calves (Johnson and Jacobsson, 1973). The risk of antibiotic resistance was also discovered (Wierup et al., 1975). As a result, the use of AGP in calf and beef production had more or less come to an end before 1986, when all use of AGP was banned. All antimicrobials were then re-classified as veterinary medicines in Sweden and were available only by veterinary prescription.

About ten years later, when the risks of antibiotic resistance were increasingly apparent in other countries and in the EU, AGP were gradually removed in the other Scandinavian countries too (Grave et al., 2006).

These precautionary actions taken by the Scandinavian countries were a major incentive in the EU and internationally for a focus on the use of antibiotics and in particular AGP. A WHO risk assessment on the use of antimicrobials in foods identified areas of concern in 1997 (WHO, 1997). Later, the WHO published global principles and strategies for the containment of antimicrobial resistance (WHO, 2000; WHO 2001a), as well as on monitoring the use of antimicrobials in food animals for the protection of human health (WHO, 2001b). In the EU, the Scientific Steering Committee of the European Commission (1999) adopted an opinion and recommendations on antimicrobial resistance, with special focus on the usage of antimicrobials for growth promotion, which resulted in the EU ban from July 1 1999 on the use of bacitracin, avoparcin, spiramycin, tylosin and virginiamycin as AGP. A total EU ban on the use of all antibiotics for growth promotion was introduced from 2006. The OIE and individual countries and organisations also focused on the subject.

This chapter describes the usage of antimicrobials and the resistance pattern following the ban on AGP in the Scandinavian countries.

Data Sources

In Sweden, the usage of antimicrobials in animals has been monitored since 1980 and antibiotic resistance has been monitored on a regular basis since 2000 (SVARM, 2007). Corresponding monitoring programmes on the use of antimicrobial agents and antimicrobial resistance are also in place in the other Scandinavian countries and the results are published annually for Denmark (DANMAP, 2007), Norway (NORM NORM-VET, 2007) and Finland (FINRES-Vet, 2007).
Consumption of Antimicrobials

Antibiotic Resistance

Sweden
On a national basis, the current annual usage (2008) in Sweden is approximately 65% lower than before the AGP ban (Figure 28.1). Directly following the ban on AGP, the total use of antibiotics increased but during the period 1988 to 1994 it remained stable at approximately 30 tonnes of active ingredient per year, a level approximately 35% below that before the new legislation was introduced. The consumption has since further decreased and in 2008 was about 16.4 tonnes, the bulk (47%) being penicillin intended for treatment of individual animals. The decreased use of antimicrobials is also evident when calculations are based on dose units instead of weight of active substance and related to changes in number of animals (Greko, 1998). Of special interest in the context of development of antibiotic resistance is the use of antimicrobials for group or flock medication. In 1984 about 65% of the total amount used was formulations intended for such use, whereas in 2008 this figure was about 16%, while 60% was used for injections and 24% for oral medication of individual animals.

Denmark
Overall, the total consumption of antibiotics in food animal production in Denmark decreased by 47% from 1994 to 2004 (Figure 28.2). About 80% of the total consumption is used in pigs and during the period studied pig production steadily increased from 20.7 million head in 1994 to 25.1 million head in 2004.

Norway
The annual usage of veterinary antimicrobial drugs in Norway decreased gradually by 40% from 1995 to 2001, and has thereafter remained stable (Figure 28.3). The patterns of use have gradually become more favourable as the proportion of penicillin use has increased.

Finland
The total volume of antimicrobial products used in veterinary medicine in Finland has declined consistently over recent years: by 27% from 1995 to 2002 (FINRES-Vet, 2007). Beta-lactams accounted for 60%, trimethoprime-
sulphonamide for 18% and tetracyclines for 15% of the total veterinary antimicrobial sales in 2002. Penicillins sensitive to beta-lactamase accounted for 85% of the veterinary penicillin preparations sold. The proportions of antimicrobials used in medicated feed in 2002 accounted for only 4%, of which about two-fifths each were used for fur animals and fish, and one-fifth for pigs.

The monitoring in the Nordic programmes is principally directed towards zoonotic bacteria, indicator bacteria and to some extent pathogenic bacteria. In the results presented (Figures 28.4 to 28.9), data from some other EU countries are presented for comparison.

As the ionophores used as coccidiostats (not covered by the AGP ban) also have a preventive effect on outbreaks of necrotic enteritis, a study was performed on the resistance to those drugs in Clostridium perfringens in Sweden, Norway and Denmark (Johansson et al., 2004). It was found that all isolates tested (102 from 1996-2001) were susceptible to the ionophor narasin and in a similar study in Belgium all 47 isolates tested were found to be susceptible to monensin, lasalocid, salinomycin, maduramycin and narasin (Martel et al., 2004).

Antibiotic resistance in zoonotic bacteria is exemplified here by Salmonella Typhimurium isolated from pigs, cattle and poultry in Sweden, Denmark and the Netherlands. A clear difference can be seen in the prevalence of resistance to all the antimicrobials tested between the countries, Sweden having the most favourable situation (Figure 28.4).
Antibiotic resistance in indicator bacteria is exemplified here by *Escherichia coli* and *Enterococcus faecium* isolated from healthy slaughter pigs and broiler chickens (Figure 28.5 to Figure 28.8). Again, a similar picture as above can be seen.

The levels of resistance in the above three groups of bacteria (animal pathogens, zoonotic agents and indicator bacteria) are generally similar in Sweden, Norway and Finland and higher in Denmark. However, in all the Scandinavian countries the level is lower than in some other EU countries previously reported to have a higher use of antimicrobials (EMEA, 1999).

Figure 28.9 shows the resistance to tetracycline in *E. coli* from healthy pigs and the sale of tetracycline in four countries. As can be seen, the prevalence of resistance is rather proportional to the amounts sold.

No monitoring of indicator bacteria occurred in Sweden prior to the 1986 ban on AGP and such data are only available from Denmark. In that country, after the ban on AGP a dramatic reduction occurred in the animal reservoir of enterococci resistant to avoparcin, avilamycin and virginiamycin previously used as growth promoters, as shown in Figure 28.10.

**Conclusions**

The prevalence of antibiotic resistance in indicator bacteria, animal bacterial pathogens or zoonoses is considerably lower in the Scandinavian countries than in some other countries in the EU reported to have a higher use
of antimicrobials. Within the Scandinavian countries this prevalence is generally also highest in Denmark. These results most likely reflect the magnitude of exposure, as it is generally recognised that the risk of bacterial strains acquiring resistance to antibiotics increases with their exposure to such substances. As an example, Sweden, with a relatively very low prevalence of antibiotic resistance, banned the use of AGP 20 years ago and controlled use of antimicrobials was started even earlier, as well as organised actions for the prevention of infectious diseases in livestock production.

The termination of the use of AGP has not significantly influenced the resistance pattern in Norway, Finland and Sweden and the prevalence is maintained at a relatively low level. However, it is interesting that following the withdrawal of AGP in Denmark, a dramatic reduction occurred in the animal reservoir of enterococci resistant to avoparcin, avilamycin and virginiamycin, antimicrobials previously used as growth promoters. This effect is likely to be the result of the withdrawal of the selection pressure for strains resistant to AGP. The same event might also have occurred in the other Scandinavian countries but was not recorded due to lack of data before the ban.

The low prevalence of resistance in Salmonella in Sweden (Figure 28.4) reflects not only a limited use of antimicrobials, but also that Sweden has long applied a
zero tolerance control policy for *Salmonella* contamination (EFSA, 2006; EFSA, 2007). That policy limits the exposure of *Salmonella* to antimicrobials and reduces the spread of multiresistant strains, as salmonella infections in animals are not given antibiotic treatment.

It should be emphasised that the reduction in the use of antimicrobials and the relatively favourable situation for antibiotic resistance is not only a result of the withdrawal of AGP. As can be seen from the annual reports from all the Scandinavian countries, large efforts and industry-based campaigns have been devoted to implementation of optimal disease preventive management routines and proper use of antimicrobials, e.g. guidelines on antimicrobial drug therapy in food animals as described in other chapters of this book by Wierup (Chapter 25) and Pettigrew and Baker (Chapter 27). One of the main messages was critical selection of cases for antimicrobial therapy. In Denmark a decrease in the use of antimicrobials was seen when, as applied earlier in the other Scandinavian countries, a ban was introduced on economic incentives to veterinary surgeons for prescribing antibiotics to producers (Kjeldsen and Callesen, 2006).

The impact on animal health and production of AGP withdrawal is reported elsewhere (Wierup, 2001; WHO/CPE/ZFK/2003; Kjeldsen and Callesen, 2006) following the withdrawal of AGP. The major growth promoting effect was thus found to be the control of enteric infections by the AGP. However, evaluations of controlled data generated in these countries demonstrated that in finisher swine production (> 25 to 30 kg) and in broiler production, no or limited negative effects were found (Wierup and Wegener, 2006).

In summary, the experiences from Denmark, Finland, Norway and Sweden show that termination of AGP has significantly decreased the overall usage of antimicrobials and the risk of future problems with antibiotic resistance. It has also considerably reduced the animal reservoir of enterococci resistant to antibiotics previously used for growth promotion and decreased the risk of human exposure via the food chain of genes coding for resistance to antimicrobials. Naturally, some antibiotic resistance in animal bacterial pathogens occurs in the Scandinavian countries, which is the reason for establishing a continuous monitoring programme of antimicrobial resistance, as well as a focus on prudent use of antimicrobials in food animal production.
References


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DANMAP 2001 Consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, foods and humans in Denmark. ISSN 1600-2032. F. Bager, H.-D. Emborg and O. E. Heuer, Danish Veterinary Institute, Copenhagen, Denmark. Available at www.danmap.org

DANMAP 2002 Consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, foods and humans in Denmark. ISSN 1600-2032. H.-D. Emborg and O. E. Heuer, Danish Veterinary Institute, Copenhagen, Denmark. Available at www.danmap.org <http://www.danmap.org>

DANMAP 2004 Consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, foods and humans in Denmark. ISSN 1600-2032. H.-D. Emborg, O. E. Heuer and P. B. Larsen, Danish Veterinary Institute, Copenhagen, Denmark. Available at www.danmap.org <http://www.danmap.org>


SVARM 2003 Swedish Veterinary Antimicrobial Resistance Monitoring. ISSN 1650-6332. B. Bengtsson, C. Greko and M. Karlsson, National Veterinary Institute, Uppsala, Sweden. Available at www.sva.se

SVARM 2004 Swedish Veterinary Antimicrobial Resistance Monitoring. ISSN 1650-6332. B. Bengtsson, C. Greko and M. Pringle, National Veterinary Institute, Uppsala, Sweden. Available at www.sva.se

SVARM 2007 Swedish Veterinary Antimicrobial Resistance Monitoring. ISSN 1650-6332. B. Bengtsson, C. Greko and U. Grönlund-Andersson, National Veterinary Institute, Uppsala, Sweden. Available at www.sva.se


WHO/CPE/ZFK/2003.1. Impact of antimicrobial growth promoter termination in Denmark. The WHO international panel’s evaluation
of the termination of the use of antimicrobial growth promoters in Denmark, Foulum, Denmark, 6-9 November 2002


References

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