The Swedish Experience of the 1986 Year Ban of Antimicrobial Growth Promoters, with Special Reference to Animal Health, Disease Prevention, Productivity, and Usage of Antimicrobials

MARTIN WIERUP

ABSTRACT

In Sweden the use of antimicrobial growth promoters (AMGP) was banned in 1986. The experiences gained from that ban are presented. In production of slaughter pigs, specialized beef, and turkeys, no negative clinical effects were reported as a consequence of the ban. In broiler chicken production, expected problems with necrotic enteritis were prevented by a continuous use of antibiotics, largely to the same extent during the first 2 years after the ban. Following the implementation of results from experimental activities during that period, the general usage of antimicrobials could be stopped and expected problems with outbreaks of necrotic enteritis was prevented. In piglet production, significant clinical problems emerged that created a demand for antibiotic-medicated feed at therapeutic dosages. During the subsequent 4-year period, the use of antibiotics increased, involving up to 75% of the pigs. Thereafter, the use of antibiotics decreased because of improved management, and could be halved in 1993 followed by a gradual further decrease supported by the addition of zinc oxide to the feed. In 1998, compared to 1994, the total use of zinc decreased by 90%. In 1998/1999, only 5% of weaning piglet producing herds used antibiotic medicated feed and 17% used zinc. The AMGP ban has shown that under good production conditions it is possible to reach good and competitive production results for the rearing of poultry, calves, and pigs without the continuous use of AMGP. As a result of the ban and a focus on disease prevention and correct use of antimicrobials, the total use of antibacterial drugs to animals in Sweden decreased by approximately 55% during the last 13-year period, and a relatively low prevalence of antimicrobial resistance has been maintained.

INTRODUCTION

In Sweden, antimicrobial growth promoters (AMGP) have been banned since 1986 and only allowed, as for other antimicrobials, to be used after veterinary prescription in therapeutic doses for the purpose of curing or preventing disease. That ban can be seen as a continuation of the long tradition for organized control of infectious diseases in animal production existing in Sweden. These controls have, besides a relatively favorable health situation in the animal production, led to a low usage of antimicrobials and also to a relatively low prevalence of antimicrobial resistance. This paper presents the experiences gained from the ban of AMGP.

MATERIALS AND METHODS

When not referred to specific references, the data and judgment presented are based on a broad evaluation by all significant stakeholders concerned and presented at a seminar arranged by the Royal Swedish Academy of Agriculture and Forestry. The actions taken to prepare and motivate producers and practitioners for the change in use pattern of antibiotics and to introduce disease preventive measures needed because of the ban are also described, as well as the clinical experiences. The results are given for each type of animal production concerned. The total pattern of the consumption of antibiotic drugs before and after the ban is especially focused. Finally, the si-
multaneously ongoing international trends, especially within EU on the usage of AMGP, are presented.

RESULTS

Types of production concerned

Broiler production: AMGP (nitrovin) started to be used in the 1970s. Its use almost completely eliminated existing problems with necrotic enteritis caused by toxin from Clostridium perfringens. However, some sporadic outbreaks of the disease occurred and it was evident that those were related to the type of AMGP and/or coccidiostat used. Nitrovin was gradually replaced by avoparcin and later on by virginiamycin.

When the use of AMGP was to be banned, this was expected to have clinical consequences because of necrotic enteritis. Thus, efforts including research projects and field studies were undertaken to find ways to control necrotic enteritis in the absence of AMGP. These actions were initiated by the industry and developed through close collaboration between the producers, the feed industry, and veterinarians.

It was concluded that many factors, such as the construction and climate of stables, hygiene, management, and feed could contribute to the outbreak of necrotic enteritis.5-11 The results gained were summarized as follows: (1) additions of enzymes acting on carbohydrates and the addition of certain probiotics to develop an adequate intestinal bacterial flora reduced the incidence of necrotic enteritis; (2) dietary levels of protein were reduced and amino acids were added, which also resulted in improved stable hygiene and animal health; (3) feeding of whole wheat did not influence the prevalence of C. perfringens but stimulated the skeletal muscle activity and reduced moisture in animal bedding; (4) coccidiostats of the ionophore type used to prevent coccidiosis also protected against certain gut infections.

The results and experiences gained were continuously implemented. The most important change was to reduce the protein content in the feed and to have a composition richer in fiber and supplemented with enzymes. Cases of necrotic enteritis today can often be related to overriding the recommended level of protein in the feed. The feeding regimens employed were developed through close collaboration between the feed industry and the producers. In connection with the ban on AMGP, strong emphasis was also placed on improving animal environments because many diseases, including necrotic enteritis, have a multifactorial background. Notably airflow was inadequate in several units, which affected animal health negatively.

It was strongly felt by the parties concerned that the ban was implemented too quickly, and enough time to adjust to the new situation was not given. This created initial difficulties, reflected in about 90% of broiler chickens being continuously treated with virginiamycin at a dose of 20 ppm during the first year of the ban and in 1987 the corresponding treatment frequency was 100%. Prior to the ban virginiamycin was dosed at 10 ppm.

During 1987, an alternative to the prophylactic use of virginiamycin was introduced. This involved a 2-day treatment with phenoxy methyl penicillin in drinking water in cases of outbreaks. In the beginning of 1988, that treatment had largely replaced the use of virginiamycin. The amount of active ingredient of antibiotics used for treatment of necrotic enteritis subsequently decreased from about 2 tons of virginiamycin in 1987 to 100 kg of phenoxy methyl penicillin in 1988.52 Since 1995, the amounts of antibiotics to prevent or cure outbreaks of necrotic enteritis is practically negligible, and today, on that very rare occasion when outbreaks of the disease occur, tylosin is used.

It should be noticed that coccidiostats of the ionophore type now used have antibacterial effects and act prophylactically against necrotic enteritis and may improve growth rate. However, despite this, the sanitary situation of broiler chicken rearing gained in Sweden would not have been reached without the above-mentioned enforcement.

Contributing to the successful adaptation of the broiler production to the new situation in 1986, and to the continuously ongoing efforts to improve animal health, was the creation of a classification system for breeding farms and production farms. According to that system, a special bonus is given for good animal management and care, which improves the total level of quality of the production. The main reason was that the basic population density in chicken production is 20 kg per square meter. Producers who satisfy specified requirements according to the classification system were permitted a higher limit—up to 36 kg per square meter. In that way, the best growers can be rewarded by being allowed higher populations without risking that this will be done at the expense of animal welfare. The system with differentiated population densities makes it possible for poultry growers to make investments to reach the top classification for population density. If they provide good livestock care, they can reach a production level that is economically competitive, while still retaining the best animal welfare. Growers with low standards are, on the other hand, forced out of business.55

The control of Salmonella, which, on initiative from producers, started already in 1970,13 as well as the efforts to control also the intestinal colonization by Campylobacter, which started in 1987,3 were certainly also of importance for successful adaptation. These controls, which both started as a result of health problems in chicken consumers, have improved the general health situation and also facilitated further organized actions. The fact that the poultry and especially the chicken producer only to a very limited extent have been covered by the subsidies and economic guarantees, which has been the case for other sectors of the animal production such as milk and pork, is probably also of importance. They were, thus, used to a free-market situation and had to be responsible for their own economy.

The relatively low number of chicken producers in Sweden also facilitated organized and fast actions. They generally all also had a relatively uniform production system. The number of producers was less than 200 at the time of the ban, when their total annual production was 37 million chickens. This has increased to 68 million in 1998 (out of which 11% are exported) and the producers have decreased to 175.

Turkey production: The situation for turkey production units was similar to that for broiler chicken production units. Before 1986, AMGP were used solely as a prophylactic agent against necrotic enteritis and not as a growth promoter. The ban did not result in observed clinical problems or reduced growth rate.
Egg production: Before the ban, no AMGP were used in egg production. The use of zinc bacitracin had been discussed because it was used to improve production in other countries. In the egg production sector, the ban in 1986 did not influence production. Neither are the animals treated with coccidiostats during the egg production period, but problems with coccidiosis can be seen during the growing stage and are then usually concentrated to farms where the level of animal hygiene is not satisfactory. When laying hens are transported from a rearing unit to a producing unit, they are sometimes given coccidiostats (amprolium). The availability of vaccine against coccidiosis has reduced the need of coccidiostats in floor raising of laying hens.

Pig production: Before 1986, practically all piglets were given the AMGPs olaquindox or meadox (50 ppm) from the start of their feeding period until they were delivered to the finishing units at an age of 10–12 weeks. Thereafter as finishing pigs, they were given AMGP (avoparcin or virginimycin) until slaughter at the age of about 7 months.

The ban on AMGP did not create obvious clinical problems for growing/finishing pigs, which in 1984, consumed 7.8 tons of active ingredient of virginimycin. Since 1997, the mean daily weight gain in herds joined to production control systems is above 850 grams and not known to be larger in countries where AMGP is used.

However, for piglet production, significant problems initially emerged as a consequence of the removal of olaquindox, which at that time was used for weaning piglets. Robertsson and Lundehain examined the incidence of disease, mortality, and growth rate in piglets from 220 producing units during 1986 and compared it with 1985. The study showed that the post-weaning mortality in the first year after the ban was significantly higher, about 1.5 percentage units compared with 1985. Similarly, the age at 25 kg increased by 5–6 days. Preweaning mortality and the number of piglets produced per sow and year, however, did not show significant differences between 1986 and 1985. An extended rearing period after the ban is also obvious from the National Pig Record by which the age of pigs tested at 30 kg increased by about 2 days from 1986 and onwards.

Despite the lack of alternative strategies at the time when the ban was introduced, the pig sector, in contrast to the broiler chicken sector, did not generally continue to use antibiotics on prescription in therapeutic doses. The use of olaquindox to weaning pigs was therefore reduced by 82% (amount of active ingredient per pig produced) from 1985 to 1986 and by 33% from 1985 to 1987. Thereafter, however, more antibiotics were prescribed and the total amount used during the subsequent years, 1988 and 1989, was 5 and 6%, respectively, higher than in 1985. Considering that the dosage prescribed from 1986 was about three times higher than the AMGP dosage employed previously, a smaller fraction of weaning pigs was treated with olaquindox after the ban or 12% in 1986, 55% in 1987, 75% in 1988, and 76% in 1989. Thereafter, the use was continuously reduced during a 4-year period, and in 1993 it was 35%. From 1993 to 1994, a further reduction occurred supported by the introduction of zinc oxide (see below), and in 1995 the proportion of pigs treated with olaquindox was 12%. During the period studied, the annual production was approximately 4 million pigs.

In a study from 1994, Holmgren and Lundehain analyzed the results from 55 piglet-producing herds in the southwestern part of Sweden and concluded that the prescription of medicated feed to weaning pigs was clinically motivated and followed the recommended guidelines. From that study, it is also obvious that the need for medicated feed differs markedly between herds and that these differences could be ascribed to housing and management systems. The production results were strongly related to the degree of segregated rearing systems and to the level of hygiene. In herds rearing post-weaning pigs on deep litter bedding, both segregation and degree of hygiene were better, and the use of antibiotic was three to four times lower than in herds with pigs in traditional post-weaning pens. The study also underlines the difficulties in preventing weaning diarrhea in units that lack or have limited facilities to arrange satisfactory sectioning and hygiene. Clinical problems emerging in the different herds could seldom be further prevented through single prophylactic environmental or rearing adjustments. In many cases, more thorough changes in production planning and in housing were needed.

After the ban on AMGP, numerous measures have been undertaken and are continuously being undertaken to optimize the rearing and production system and to employ available techniques concerning sectioning, age grouping, and planned production. The ban of AMGP also created a development toward new rearing systems. The weaning of piglets on deep litter beds in large groups is one example, and the so-called birth to slaughter system, which is based on production in the same pen from birth to slaughter, is another. The adjustment of old buildings and pens to the new production system is expensive. Before such an adjustment is done, antibiotics are used to combat weaning diarrhea in exposed herds. Holmgren and Lundehain also found that the use of antibiotics prevented low production results in such herds.

Efforts have also been undertaken to adjust pig feed to the new situation. The most prominent changes have been lowering of the protein content, use of the protein content, use of water-soluble fibers, and supplementation with acids. The anti-secretory factor to prevent liquid penetration to the gut induced by enterotoxin has also been used as a preventive measure.

Since the end of 1993, zinc oxide has been used to prevent weaning diarrhea as previously was employed in other countries in Europe. Since 1992, it is permitted in Sweden to feed pigs starting 2 weeks before weaning with a feed containing 2,000 ppm of zinc oxide. Zinc oxide was found to have a preventive effect on weaning diarrhea equal to the effect reached when using olaquindox. The use of zinc became widespread, but due to actions taken, the usage has from 1994 to 1998 decreased by approximately 90%. In a separate study during 1998–1999 of 350 herds in different parts of the country, it was found that 17% used zinc and 5% antibiotics to wean pigs.

The Swedish Animal Health Service has introduced a program for intensive education of producers in implementing optimal management conditions at weaning.

In summary, it is evident that the best production result can be gained without the continuous use of AMGP. However, all pig-producing herds do not have optimum conditions for production. This is reflected by the fact that certain production results seen before the ban of AMGP still have not been reached. The available data from production control data from herds used for evaluation of the ban in 1985–1986 have also been evalu-
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(Based on Wierup et al., 1987; Björnerot et al., 1996; Odensvik and Greko, 1998; Odensvik, 1999; and Odensvik, 2000.)

\(^a\)According to NLN, Guidelines on ATCvet classification (1995).

\(^b\)Calculated to equivalents of benzyl penicillin.
ated for 1997. A comparison of the average values for 1997 with those for the first year after the ban (1986–1987) reveals post-weaning mortality to have decreased by 1–2 percentage units and the age at 25 kg to be reduced by 3.5–4.5 days. The losses in these production parameters seen after the ban have thus not yet been fully recovered on a national basis. However, the progressive producers report better production results than before the ban of AMGP.38

In connection with the ban of AMGP, it became obvious that clear guidelines on how to prescribe antibiotics as medicated feed were lacking. Such guidelines were developed by the Swedish Society for Veterinary Medicine in 1990.34 In the guidelines, it is emphasized that prescription of antibiotics should always be accompanied by recommendations on prophylactic measures because the need for medicated feed seems to occur repeatedly in the same units. The experiences from the clinical problems that emerged indicate that single prophylactic environmental or rearing corrective measures seldom are enough to correct the situation. Often more thorough and radical changes involving planning of production and housing were necessary.

It is also interesting to note the relatively slow start in compensatory actions undertaken in the pig compared with broiler production. In addition to the fact that the broiler industry in contrast to the pig industry anticipated clinical problems following the ban, this most likely also reflects that there were very few broiler producers compared with weaner pig producers, which at the time of the ban were approximately 10,000. Their production systems, as well as their production facilities, were in addition, not as uniform as in the poultry industry.

Education of veterinarians and producers was done through the Swedish Animal Health Service, but intensive education of the pig producers and veterinarians on how to prevent post-weaning diarrhea started up first during 1998–1999. At that time, efforts were also in place to decrease the use of zinc as a possible replacement for AMGP. The motivation at that time also increased with the decreasing payment to the producer due to worldwide overproduction.

Specialized beef production: Already in the 1960s and 1970s, different antibiotics were used as AMGP in concentrate and milk replacers for calves. The antibiotics used in low doses (50 ppm) in the 1970s were bacitracin, manganbacitracin, zincbacitracin, flavomycin, oleandomycin, and spiramycin. The purpose was to improve the growth rate of the animals. The effect was, however, often doubtful, and documented improvements in animal growth were only sometimes seen in repeated experiments (e.g., ref. 40). The use of AMGP in specialized beef production had more or less come to an end before the ban in 1986. Negative clinical or other effects as a consequence of the ban have not been reported. None of the AMGP used in calves is today used as therapeutics. Guidelines have been worked out when it is justified to treat all calves in a batch instead of individual treatments.

Use of antibacterial drugs

The total usage of antibacterial drugs in animals in Sweden prior to and after the ban against use of antibiotic growth promoters has been studied in detail since 1980.7,27,28,30,41,42 In Table 1 and Fig. 1, the data since 1980 are presented. In contrast to previously presented data up to 1995, in this summary procaine has been excluded from the amount of procaine penicillin and data on the total consumption have been changed accordingly.

The total use of antibacterial drugs from 1980 to 1984 increased from 41.3 to 50.6 tons of active ingredient and decreased by 49% (24.8 tons) from 1984 compared with 1986, when the use of AMGP was banned and veterinary prescriptions for all use of antibiotics were introduced. The distribution of antibacterial drugs from the feed factory decreased by 70% (from 31 to 9.5 tons) during the same period. During the following years, the total use of antibiotics increased but was then, during 1988–1994, stable at approximately 30 tons of active ingredient per year, a level approximately 35% below the level before the new legislation was introduced. The consumption then further decreased to 20.6 and 18.2 tons of active ingredient during 1996–1999. This means that the total use of an-
tibacterial drugs in animal production has decreased by approximately 55% compared with the usage before the ban of AMGP. This decrease is also at least of that magnitude when calculations are measured by dose units instead of weight of active substance of the antimicrobials (Greko 1998). Table 2 presents the sales of antimicrobials divided into formulations intended for treatment of individual animals and for group treatment.

The situation in the EU

In relation to AMGP, the legislation in the EU countries during the period described above principally followed the recommendations of the Swann Committee from 1969 in that use of AMGPs (with some exceptions) was restricted to those not used for therapy. Generally, there was little debate on the use of AMGPs, with the exception that in a few countries their possible relation to intestinal colonization by Salmonella was discussed. This was focused especially on avoparcin, which was found to increase such colonization in broiler chickens. When, in 1995, Sweden and Finland joined the EU, these two countries were allowed to continue with their legislation on AMGPs (total ban in Sweden since 1986) until December 31, 1998, when they had to provide detailed scientific support for a possible further use of their legislation. The report from Sweden was presented in 1997. Prior to this date, the AMGPs were again focused when Denmark in 1995 stopped the use of avoparcin based on a claim that there could be a transfer of vancomycin-resistantenterococcus (VRE) from animals to humans. Similar decisions were later taken also by Germany as well as in countries outside the EU. As a result of an evaluation, the EU Commission in 1997 suspended the use of avoparcin. Later, Denmark also stopped virginimycin because it caused cross-resistance to macrolides and lincosamides. In individual countries like the Netherlands, Denmark, and the United Kingdom, larger evaluations of antibiotic resistance in relation to the use of antimicrobials including AMGPs were presented. Of special importance was the WHO report on the medical impact of the use of antimicrobials in food animals. Stakeholders including the pharmaceutical industry also participated in these studies. As a result of these discussions, the EU Commission from July, 1999, banned the use of the following four antimicrobials as AMGP: zincbacitracin, virginiamycin, spiramycin, and tylosin phosphate.

Subsequently the EU Scientific Steering Committee (SSC) made a comprehensive evaluation on antibiotic resistance as a possible result of the use of antimicrobials in both human and veterinary medicine as well as in animal husbandry (AMGP) and in plant protection. The evaluation and the subsequent numerous recommendations were adopted by SSC on May 28 and presented at an International Conference in July, 1999. The main recommendations in relation to AMGP were to stop the use of those antimicrobials that are used for therapy or can cause cross-resistance to such drugs. The need to implement disease preventive methods was emphasized, as well as an overall statement focused on the need to decrease all use of all antimicrobials.

In summary, in the EU a scientifically based consensus has been achieved on which actions are needed to meet the problems with antimicrobial resistance. In several individual EU countries, industry-based actions are currently under way to handle the ban of the four AMGPs named above. In addition, as a part of the EU zoonoses directive, a few countries also follow and annually report the use of antimicrobials and parameters on antimicrobial resistance.

DISCUSSION AND CONSIDERATIONS ON FUTURE STRATEGIES

The results from Sweden as described above, have been confirmed in departmental evaluations both domestically and on an international basis (e.g., refs. 16,24,33,36,43). More recently,

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(From Odensvik and Greko, 1998; Odensvik, 1999; and Odensvik, 2000.)

<sup>a</sup>As benzylpenicillin.

<sup>b</sup>Amount given also includes QJ01R, combinations.
results from withdrawal of AMGP have been reported also from Denmark.\textsuperscript{1,6} Those results are very similar to the ones found in Sweden, indicating that the latter results are of a more general application. From Denmark, it has also been found that the increased prevalence of antibiotic resistance seen as a result of the use of AMGP decreased following the exclusion of AMGP.\textsuperscript{3} This is a further reason to stop or phase out the use of AMGP as recommended, e.g., by WHO\textsuperscript{43} and the EU.\textsuperscript{14}

A change in attitude toward a more prudent use of antimicrobials, including withdrawal of AMGP and the implementation of disease preventive measures, thus can result in a considerable decrease in the overall use of antimicrobials. In Sweden, that decrease is more than 50%, and similar results are also reported from Norway\textsuperscript{18} and Finland.\textsuperscript{2}

The results also demonstrate that it is possible to achieve competitive production result without a continuous use of antibiotics as AMGP. However, even if a ban of AMGP generally does not need to be accompanied by increased production costs, it is likely that this initially and to some extent also permanently is the case, e.g., for weaner pig production.\textsuperscript{6} This is a challenging situation when operating in a free market. To that extent, we as scientists, as formulated by the former head of WHO zoonoses division, Dr. Konrad Bögel, have to answer the question of whether we are willing to give higher priority to disease prevention and control than to economic consideration of cheap animal mass production, which, incidentally, does not appear to be at all essential from nutritive points of view.\textsuperscript{8}

Motivation of producers and veterinarians toward a more prudent use of antimicrobials should be based on education. A major argument for a prudent use is that antimicrobials probably are the most valuable drugs in animal production and access to effective antimicrobials is of basic importance. In the future, we otherwise may run into a situation where certain antimicrobials will be limited to human use, as recently has been suggested for the quinolones.\textsuperscript{24}

It also seems to be advisable to build up a system with an economic inducement for the producer to undertake actions. The situation from broiler production in Sweden, described above, is one example. Another is an extra cost/tax for AMGP-containing feed, as applied in Denmark.

It is also necessary to control the usage of antimicrobials and combine this with a surveillance of antibiotic resistance. Today, data on the usage of antimicrobials are, surprisingly enough, lacking in most countries, and in the absence of that information it is not possible to control their usage.

In conclusion, the use of antimicrobials should not be considered as an isolated issue and the only way to control infectious diseases. Instead the use should be seen as one of the many disease-preventive measures that can be used in animal production (Wierup 2000).\textsuperscript{39} The use of antimicrobials should principally be the last of those methods and not as a replacement of them.

REFERENCES


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