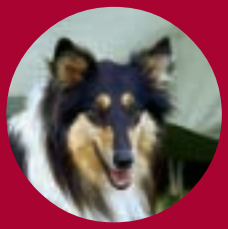
SVARM 2000

Swedish Veterinary Antimicrobial Resistance Monitoring




NATIONAL VETERINARY INSTITUTE UPPSALA, SWEDEN

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Printed by Wikströms, Uppsala, Sweden
ISSN - 1650-6332

Procuded by the Information Department
Graphic production by Gudrun Orava
Photographs by Bengt Ekberg

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Preface

The rapid development and spread of antimicrobial resistance is an increasing threat to human and animal health. It has long been recognised that better data on antimicrobial resistance and antimicrobial usage constitutes a basis for strategies aiming at containing the problem. The ultimate goal is to preserve the effectiveness of available drugs for the benefit of future generations of animals and people. Resistant bacteria or resistance genes can spread between different populations of animals and humans. Hence, the ideal programme should on a regular basis provide data on resistance and use of antimicrobials in all relevant sectors. Such integrated programmes are still not common. However, initiatives to monitor resistance in defined areas are taken in an increasing number of countries.

The main objectives of programmes monitoring antimicrobial resistance in bacteria of animal origin are to detect (undesired) trends, provide a basis for policy recommendations, measure the effects of interventions and generate exposure data for risk assessments. Comparability of data collected over time and between countries is essential in order to maximise the usefulness of generated data. A working group within the EU (ARBAO) has suggested minimum criteria for monitoring programmes.

This is the first yearly report from the Swedish Veterinary Antimicrobial Resistance Monitoring (SVARM). Antimicrobial susceptibility data for intestinal bacteria of healthy animals, zoonotic bacteria and animal pathogens are presented. Statistics on use of antimicrobials for animals is also included. Attempts have been made to comment on the results in relation to earlier reports.

When assessing the data, it is important to bear in mind that results presented in reports from different countries or laboratories may not be directly comparable. One major obstacle, amongst others, is that each country uses its own breakpoints for designating bacterial isolates as resistant. In order to give a good overview and to facilitate interpretation of the results, the distributions of the minimum inhibitory concentrations (MIC) of the antimicrobials tested are presented. Furthermore, the prevalence of resistance patterns or phenotypes of the strains is given. The occurrence of certain resistance phenotypes is discussed.

The data on antimicrobial resistance in animal pathogens is mostly derived from diagnostic submissions and must therefore be interpreted with caution. These types of submissions may be biased towards recurrent clinical cases or therapy failures. Thus, the prevalence of resistant strains may be overestimated.

It must also be made clear that the relationship between the amounts used of a certain antimicrobial and development of resistance is complex. Apart from antimicrobials, many factors such as population density, hygiene, and movement of animals will influence the level of resistance. However, there is strong scientific evidence that the use of an antimicrobial will eventually result in decreased susceptibility among exposed bacteria.

In our opinion, a fully effective programme should include monitoring of foodborne bacteria and bacteria isolated from humans. It is our ambition to co-ordinate SVARM with activities in these areas. Moreover, the statistics on use of antimicrobials will be more useful once it will be possible to split the data per animal species.

Summary

The general situation regarding antimicrobial resistance in the bacteria of animal origin studied in SVARM is favourable. Resistance does occur, but in an international perspective the levels are low. This probably reflects a long tradition of prudent use of antimicrobials, in combination with a favourable animal health status.

During the analysis of data on antimicrobial resistance in SVARM, several areas have been identified in which further studies are needed in order to clarify the link between observed levels of resistance and use of antimicrobials. One such field is co-selection of resistance. Use of one antimicrobial can lead to an increase of resistance not only to itself, but also to other unrelated antimicrobials. Studies of the resistance patterns of individual isolates indicate that co-selection may explain the occurrence of resistance to drugs that are not used in a specific animal species.

Consumption of antimicrobials

Use of antimicrobials for animals was restricted to veterinary purposes in 1986; i.e. their use for growth promotion was banned. Antimicrobials for use in animals are only available on veterinary prescription and guidelines on use have been issued. Between the years 1996 and 2000, the overall use of veterinary antimicrobials has declined with approximately 3.5 metric tons (17%). In year 2000, the figure of total sales of antimicrobials used in animals was 17.1 tons. A switch to use of more potent substances such as the quinolones cannot explain the decline.

Most of the antimicrobials are used for treatment of individual animals. In year 2000, only 16% of the total sales of antimicrobials for systemic treatment were products intended for treatments of groups of animals via feed or water. It can be assumed that the bulk of this latter category of drugs is used in pigs. In chickens, the amount of antimicrobials prescribed is low with the exception of the ionophoric coccidiostats.

Knowledge on how and to what extent antimicrobials are used is vital for analysis of trends in levels of resistance. The statistics from Sweden, going back 20 years, are an important asset. A gradual decrease of the overall use is noted. However, the analysis is hampered by the fact that the amounts used cannot be directly assigned to specific species of animals. Hopefully data on use per animal species will be available in the near future.

Resistance in zoonotic bacteria

The status regarding antimicrobial resistance in *Salmonella* isolated from Swedish animals is favourable. No undesired or unexplained trends have been observed since this monitoring of resistance was initiated 1978. It is obvious that introduction of specific phagetypes of *S.* Typhimurium (e.g. DT104, DT 193) greatly influences the levels of resistance. However, these phagetypes are rare in Swedish animals. The favourable situation is probably, apart from restrictive use of antimicrobials in animal production, largely due to the Swedish *Salmonella* control programme. Through the programme, occurrence of *Salmonella* in Swedish food producing animals is detected and measures are taken to counteract spread of the infection.

Data on *Salmonella* isolated from imported food and animal feed and from human cases of salmonellosis, would provide a broader view of antimicrobial resistance in *Salmonella* encountered in Sweden. Hopefully, such comparisons will be possible in the future.

In SVARM 2000, resistance to antimicrobials in *Campylobacter* spp. has not been studied. The intention is to include also this group of bacteria in years to come.

Resistance in indicator bacteria

Escherichia coli and *Enterococcus* spp. from healthy animals (cattle less than 12 months old, fattening pigs and broiler chickens) were chosen as indicators of the selective pressure exerted by antimicrobial agents used in the specific animal populations. These bacteria are unlikely to cause disease but constitute a reservoir of transferable resistance genes that can spread to bacteria with potential to cause disease in animals or humans.

Among the indicator bacteria, the levels of resistance were generally low in relation to levels reported in comparable monitoring programmes in other countries. In isolates from cattle, resistance was rare in both *E. coli* and *Enterococcus* spp. This is in accordance with the limited use of antimicrobials in the sampled category of cattle.

Higher levels of resistance were found among isolates from pigs and chickens, mostly to drugs used for therapy. However, indications of co-selection of resistance to drugs not used in the specific animal species were observed. This deserves further study.

Resistance to antimicrobials that were formerly used for growth promotion is low. Notably, using non-selective media no resistance to vancomycin among enterococci (VRE) was detected. Using more sensitive techniques, only two samples yielded VRE. In both cases it was *E. faecium,* isolated from chickens and the isolates carried the *vanA* gene.

Resistance in animal pathogens

Extraction of data on susceptibility in animal pathogens from the database at SVA has provided means of presenting data on antimicrobial susceptibility in important animal pathogens. This also allows for analysis of trends over the period from 1992 to 2000. Conclusions from this material must however be made cautiously as the materials might be biased towards treatment failures or otherwise problematic cases.

Resistance to the combination trimethoprim-sulfonamide among *Streptococcus zooepidemicus* from horses has increased markedly in later years. Further studies in this field are needed to exclude confounding factors in the material. The high and uniform sensitivity of *S. zooepidemicus* to penicillin indicates that penicillin is the drug of choice for treatment of infections with this pathogen. In *Rhodococcus equi* the frequency of acquired resistance is low. Among *E. coli* from the genital tract of mares, levels of resistance to ampicillin, streptomycin and trimethoprim-sulfonamide were relatively high but without obvious trends.

Frequencies of resistance to antimicrobials used for therapy, i.e. trimethoprim-sulfonamide, tetracyclines and streptomycin, among *E. coli* from pigs were relatively high but stable. However, resistance to drugs that are used very sparingly (ampicillin) or not at all (chloramphenicol) was also observed. This latter occurrence is probably explained by co-selection by other drugs.

All isolates of *Brachyspira hyodysenteriae* tested were susceptible to tiamulin but two isolates had a decreased susceptibility. This deserves attention, as there are few therapeutic alternatives available for treatment of the infection. The future development should therefore be closely monitored.

Among *Staphylococcus intermedius* from dogs, few isolates were susceptible to penicillin. Resistance levels to macrolides/lincosamides and tetracyclines were high and possibly increasing. No methicillin resistant isolates were found.

Occurrence of resistance among *E. coli* from the urinary tract of dogs was relatively less common but resistance to most therapeutic alternatives was detected. Taken together, the figures emphasise the need for susceptibility testing to provide a basis for an informed choice of antimicrobial for therapy.

The antimicrobial susceptibility of *Pasteurella* spp. from the respiratory tract of calves was most favourable. Acquired resistance to drugs used in therapy of respiratory infections was not detected. In an international perspective, the situation is remarkable and it is e.g. notable that all isolates were susceptible to penicillins.

Acknowledgements

The work with SVARM has involved several people who in various ways have made this report possible. We would like to express our gratitude to all those who during different stages of the work have contributed and in particular to:

Meat inspection personnel from the National Food Adminstration and abattoir staff for collecting samples from slaughtered animals for the study of indicator bacteria.

Patrik Öhagen, Dept of Ruminant Medicine and Veterinary Epidemiology, SLU for expert help on statistical matters.

Personnel at the Department of Bacteriology, SVA, and in particular to Drs Viveca Båverud and Erik Eriksson for valuable discussions and advice on various matters and for helping out in assembling the materials on *Salmonella* and animal pathogens.

Colleagues at the different animal departments at SVA for valuable discussions, advice and constructive criticisms of manuscripts.

Personnel at the National Food Administration, for providing statistics on animals slaughtered.

Sammanfattning

Läget avseende resistens mot antibiotika hos de bakterier från djur som undersökts i SVARM är gott. Resistens förekommer i viss utsträckning, men sammantaget är nivåerna lägre än i många andra länder. Detta är förmodligen en följd av Sveriges tradition av försiktig användning av antibiotika i kombination med ett gynnsamt sjukdomsläge.

Under arbetet med SVARM har flera områden identifierats där ytterligare studier behövs för att bättre förklara sambandet mellan bruk av specifika antibiotika och observerad resistensnivå. Ett sådant område är co-selektion, vilket innebär att användning av ett specifikt antibiotikum ökar förekomsten av resistens inte bara mot detta medel utan även mot andra obesläktade antibiotika. Studier av resistensmönster hos enskilda bakterieisolat antyder att co-selektion kan förklara förekomsten av resistens mot antibiotika som inte används till djurslaget ifråga.

Användning av antibiotika

Användning av antibiotika till djur begränsades till terapeutiskt bruk 1986. Detta innebar ett förbud mot att använda antibiotika i tillväxtbefrämjande syfte. Antibiotika får i dagsläget endast ges till djur efter veterinär förskrivning.

Rekommendationer för hur antibiotika ska användas har utarbetats. Under perioden 1996 till 2000 har användningen av antibiotika för veterinärt bruk minskat med cirka 3,5 ton (17%). Den totala förbrukningen år 2000 var 17,1 ton aktiv substans. Minskningen kan inte förklaras av att förskrivningen förändrats i riktning mot substanser med högre aktivitet per viktsenhet.

Den största mängden antibiotika används för behandling av enskilda djur. Endast 16% av den totala förbrukningen var år 2000 preparat för behandling av grupper av djur genom inblandning i foder eller vatten. Sannolikt används merparten av dessa medel för behandling av grisar. Förskrivningen av antibiotika till kyckling är mycket begränsad, med undantag för jonoforer som används för att förebygga parasitsjukdomen koccidios hos slaktkyckling. Kunskap om hur, och i vilken omfattning, antibiotika används är av avgörande betydelse för att man ska kunna analysera orsaker till trender i förekomst av resistens.

I detta sammanhang är den svenska statistiken, som går tillbaka 20 år i tiden, en ovärderlig tillgång. Tyvärr begränsas dess värde av att man inte direkt kan hänföra förbrukade mängder till specifika djurslag. Förhoppningsvis kommer statistiken i en snar framtid att kunna indelas efter djurslag.

Resistens hos zoonotiska bakterier

Resistensläget hos *Salmonella* isolerade från svenska djur är gynnsamt. Inga oönskade eller oförklarliga trender har observerats sedan resistens övervakningen påbörjades 1978.

Andelen resistenta isolat påverkas i hög grad av förekomsten av multiresistenta stammar av *S.* Typhimurium t.ex. fagtyperna DT 104 och DT 193. Dessa fagtyper är dock ovanliga hos svenska djur.

Det goda läget kan delvis förklaras av en restriktiv användning av antibiotika i svensk animalieproduktion. Av större betydelse är förmodligen det svenska salmonellakontrollprogrammet. Genom kontrollprogrammet upptäcks salmonellasmitta i djurbesättningar och åtgärder vidtas för att förhindra spridning av smittan.

En mer fullständig bild av läget inom landet skulle erhållas om motsvarande uppgifter fanns tillgängliga om resistensläget bland salmonella isolerade från importerade livsmedel och foder, liksom från fall av salmonellainfektion hos människa. Det är därför önskvärt att även dessa områden kartläggs i framtiden. I årets SVARM har antibiotikaresistens hos *Campylobacter* spp. inte studerats. Avsikten är dock att denna grupp bakterier ska undersökas och redovisas under kommande år.

Resistens hos indikatorbakterier

Escherichia coli och *Enterococcus* spp. från friska djur (nötkreatur upp till 12 månaders ålder, slaktsvin och slaktkyckling) har valts som indikatorer för det selektionstryck som utövas av antibiotika som används i en djurpopulation. Dessa bakterier orsakar sällan sjukdom men de utgör en reservoar för överförbara resistensgener vilka kan spridas vidare till bakterier med förmåga att framkalla sjukdom hos djur och människor.

Förekomsten av resistens bland indikatorbakterier var överlag låg jämfört med vad som anges i rapporter från jämförbara övervakningsprogram i andra länder.

Hos såväl *E. coli* som hos *Enterococcus* spp. från nötkreatur var resistens ovanlig. Detta stämmer väl med att antibiotika används i begränsad omfattning till nötkreatur i den studerade åldersgruppen. Resistens var vanligare bland isolat från slaktsvin och slaktkyckling.

Viss förekomst av resistens mot antibiotika som inte används till dessa djurslag tyder på att co-selektion av resistens förekommer. Detta förhållande bör undersökas närmare.

Resistens mot antibiotika som tidigare använts som tillväxtbefrämjare är ovanlig. Särskilt bör noteras att inga isolat av vancomycinresistenta enterokocker (VRE) påvisats vid odling utan anrikning. Vid användning av känsligare, specifika odlingstekniker (anrikning) påvisades VRE endast i två prover. I båda fallen rörde det sig om *E. faecium* från prov från slaktkyckling och bakterierna var bärare av *vanA* genen.

Resistens hos sjukdomsframkallande bakterier från djur

Sammanställning av data från databasen vid SVA har gjort det möjligt att presentera uppgifter avseende antibiotikakänslighet hos kliniskt betydelsefulla bakterier. Det är dessutom möjligt att analysera trender under perioden 1992 till 2000. Slutsatser baserade på materialet bör dock dras med försiktighet, eftersom dess sammansättning inte är helt känd. Isolat från infektioner där behandling misslyckats och från speciellt problematiska fall kan vara överrepresenterade.

Andelen resistens mot kombinationen trimetoprim-sulfa bland *Streptococcus zooepidemicus* från hästar har ökat kraftigt under senare år. Det är oklart om ökningen är en följd av ökad användning av trimetoprim-sulfa till hästar, eller om den beror av att materialets sammansättning inte är likformig från år till år. Detta bör klarläggas närmare. *S. zooepidemicus* har genomgående en hög känslighet för penicillin. Detta antibiotikum bör därför vara ett givet förstahandsval för behandling av streptokockinfektioner. Hos *Rhodococcus equi* var förvärvad resistens sällan förekommande. Däremot var resistens mot ampicillin, streptomycin eller trimetoprim-sulfa vanlig hos *E. coli* från könsorgan hos sto, men inga uppenbara trender kunde noteras. Hos *E. coli* från tarminfektioner hos gris var andelen isolat med resistens mot antibiotika som används för behandling (trimetoprim-sulfa, tetracykliner och streptomycin) relativt hög. Dessutom förekommer resistens mot medel som sällan (ampicillin) eller inte alls (kloramfenikol) används. Detta kan vara en effekt av co-selektion.

Inget isolat av *Brachyspira hyodysenteriae* var resistent mot tiamulin, men två av isolaten var mindre känsliga för medlet än övriga. Detta bör uppmärksammas, eftersom det finns få alternativ för behandling av infektioner med denna bakterie. Utvecklingen framöver bör följas noga.

Bland *Staphylococcus intermedius* från hundar var få isolat känsliga för penicillin. Det var också vanligt med resistens mot makrolider/linkosamider och tetracyklin, och troligen har andelen ökat senare år. Inga meticillinresistena isolat påvisades.

Hos *E. coli* från urinvägar hos hund var resistens något mindre vanlig, men resistens mot flertalet behandlingsalternativ påvisades.

Resultaten understryker betydelsen av att val av terapi vid infektioner med dessa bakterier görs med ledning av resistensbestämning.

Läget avseende antibiotikakänslighet hos *Pasteurella* spp. från luftvägarna hos kalvar var mycket gott. Förvärvad resistens mot medel som används vid behandling påvisades inte. I ett internationellt perspektiv är situationen mycket gynnsam. Det är t.ex. anmärkningsvärt att alla isolat var känsliga för penicillin.

Tack

Arbetet med SVARM har involverat många personer som på olika sätt gjort det möjligt att sammanställa denna rapport. Vi vill tacka alla de som bidragit och särskilt följande personer:
Köttbesiktningspersonal från Statens livsmedelsverk och annan personal vid slakterier för insamling av prov från slaktdjur för undersökningen av indikatorbakterier.
Patrik Öhagen, Institutionen för idisslarmedicin och epidemiologi, SLU, för experthjälp angående statistiska frågeställningar.
Personal vid Avdelningen för bakteriologi, SVA, och särskilt laboratorieveterinärerna Viveca Båverud och Erik Eriksson, för värdefulla diskussioner och råd och för all hjälp vid samanställningen av materialen avseende *Salmonella* och djurpatogener.
Kollegor vid SVAs olika djurslagsavdelningar för värdefulla diskussioner, råd och konstruktiv kritik av manuskript.
Personal vid Statens livsmedelsverk för hjälp att sammanställa slaktdjursstatistik.

Use of antimicrobials

Use of antimicrobials

The occurrence of resistance to antimicrobials in bacteria today is likely to be a reflection of the selective pressure exerted by antimicrobials over a longer period. As this is the first yearly report of SVARM, figures on use of antimicrobials over the last two decades are reviewed in addition to recent figures on sales.

In Sweden, antimicrobials for use in animals are only available on veterinary prescription. In 1986, the Feedstuffs Act restricted the use of antimicrobials to veterinary purposes, i.e. their use as growth promoters was banned.

Data must be examined in relation to changes in animal populations and of animal health. Therefore, some brief notes on these subjects have been included in the section on historical use of antimicrobials.

Use of antimicrobials – the figures for 2000

Material included

Drug statistics are based on sales figures provided by Apoteket AB (the National Corporation of Swedish Pharmacies). Data on the total amount in kg active substance of antimicrobials authorised for veterinary use sold from wholesalers to pharmacies has been calculated.

These figures include antimicrobials for all animal species (food producing animals, fish, pets and horses etc) and formulations for systemic, intramammary and obstetric use, as well as intestinal anti-infectives. It is assumed that the amount sold is also used during the observation period.

Further, statistics on prescription of drugs to poultry and other birds are included. Substance classes for which total prescription during a single year was below one kg active substance were excluded. Details on methodology used are found in Appendix 2 and statistics on animal populations in Appendix 1.

Overall use

The total sales of different classes of antimicrobials for veterinary use in kg active substance are shown in Table AC I. The overall use of veterinary antimicrobials has declined with approximately 3.5 tons between the years 1996 and 2000. A switch to use of more potent substances such as, e.g., the quinolones, cannot explain the decline. In contrary, the quinolones have had a rather even usage over the last years.

Drugs authorised for human use but prescribed for animals are not included in this report. Such drugs are primarily prescribed in small animal medicine, but this use is slightly declining. Probably, this can be attributed to an increased number of products authorised for veterinary use.

Antimicrobials that show increasing sales figures between 1999 and 2000 are the aminopenicillins and the cephalosporins. These antimicrobials are predominantly used for treatment of dogs and cats. Before 1997, no cephalosporins were authorised for use in pets. Off label prescription of drugs authorised for use in humans was therefore common. Thus, the recorded increase might reflect choice of recently authorised veterinary drugs rather than drugs authorised for human use and prescribed off-label to pets.

In 2000, drugs classified as quinoxalines or streptogramins were no longer available. In 1997 olaquindox (a quinoxaline), was taken off the market and by the end of 1999 also virginiamycin (a streptogramin), disappeared.

Table AC I. The total amount of antimicrobial drugs authorised for veterinary use expressed as kg active substance (sales statistics from Apoteket AB).

ATCvet code	Substance class	Year				
		1996	1997	1998	1999	2000
QG01AA, QJ01A	Tetracyclines	2 698	2 558	2 897	2 251	1 754[2]
QJ01CE, QJ01R, QJ51R	Penicillins[1]	8 818	8 781	8 547	8 692	8 254
QJ01CA, QJ01CR	Aminopenicillins	835	841	824	809	852
QJ01D	Other beta-lactam antimicrobials	–	53	133	245	315
QA07AA, QJ01G, QJ01R, QJ51R	Aminoglycosides	1 164	1 077	930	846	797
QA07AB, QJ01E	Sulfonamides	2 198	2 151	2 345	2 403	2 338
QJ01E	Trimethoprim and derivatives	339	352	390	397	390
QJ01F	Macrolides, lincosamides	1 649	1 747	1 846	1 467	1 352
QJ01MA	Fluoroquinolones	173	179	175	155	156
QJ01XX92, QJ01XX94	Pleuromutilins	1 142	1 094	1 032	847	871
QJ01MB	Quinoxalines	1 098	534	–	–	–
QJ01XX91	Streptogramins	525	288	150	125	–
Total		**20 639**	**19 655**	**19 269**	**18 237**	**17 079**

[1] Calculated as benzyl-penicillin; [2] Drugs marketed with special licence are included.

Both short and long acting formulations of antimicrobials for intramammary use show declining sales figures (by 29 and 21%, respectively Table AC II). The population of dairy cattle has decreased by 11% since 1995. To be noted is that one of the short acting intramammaries is also authorised for other indications than mastitis.

Table AC II. Antimicrobials for intramammary use (QJ51) calculated as number of single-dose applicators between 1996 and 2000 (sales statistics from Apoteket AB).

Type of intramammary	Year				
	1996	1997	1998	1999	2000
Short acting	248 412	246 480	212 080	182 320	176 160
Long acting	349 112	344 000	322 364	308 020	275 852

Most of the antimicrobial drugs are used for treatment of individual animals (Table AC III). In fact, few antimicrobials formulated for administration to a group of animals via food or drinking water are available. The proportion of such drugs of the total sales of antimicrobials authorised for systemic treatment of animals was 28% in 1996. In 2000, this figure had declined to 16%. All groups show a steady decline over the period. Thus, the decrease is not due to a shift to drugs with higher potency. Group treatment of calves is not common practice in Sweden.

Very small amounts are used for poultry (see below). Hence, it can be assumed that the bulk of the sales of drugs for group treatment is aimed for treatment of enteric and respiratory infections in pigs. The number of fattening pigs produced was stable from 1995 until 1999 but dropped by 11% in 2000. Thus, the decrease from 1996 until 1999 is likely to reflect a true decrease in use of antimicrobials of this type. In contrast, the changes between 1999 and 2000 are fully explained by the drop in numbers of swine.

Prescription of antimicrobials for birds

The number of prescriptions for poultry and other birds, and total amounts prescribed in kg active substance, is shown in table AC IV. A total of 7 547 prescriptions over 5 years (range 1089-1869) were included. Only 7% of these were for broilerchickens and 23% for hens (including layers, breeders and replacement birds).

The species of bird was not specified in 31% of the prescriptions. Around 80% of prescriptions of tetracyclines where the category of bird was not specified were packages with small quantities intended for treatment of individual animals, indicating that they were intended for exotic pet birds.

The majority of the prescriptions were intended for smaller numbers of birds. For example, 81% of the prescriptions of sulfonamides were for the smallest available package of a product formulated for water medication. The quantity in this package is sufficient to treat a total of 125 kg bodyweight for three days. Thus, it is likely that most of the prescriptions of sulfonamides were intended for backyard flocks. However, these prescriptions represent only 33% of the total amount in kg active substance. For the other substance classes, this is even more pronounced as >70% of the amounts derive from prescriptions for quantities sufficient to treat more than 500 kg bodyweight for three days. Trends in the total amounts prescribed are therefore likely to reflect changes in usage in production units of commercial size.

Coccidiostats of the ionophore group are used in most commercially reared chickens for slaughter. Apart from this, the amounts of antimicrobials prescribed for poultry are low. A decline in total amounts prescribed of tetracyclines and fluoroquinolones was noted. For the sulfonamides, there was a slight increase. The amount of macrolides prescribed varies slightly between the years. However, the figures indicate a very low incidence of treatment. As an example the highest figure for chickens is 1.7 kg. This quantity is enough to treat 27 000 chickens of 10 days of age for three days, indicating that less than 0.05% of the chickens slaughtered that year were treated with macrolides.

Table AC III. The amount of antimicrobial drugs in kg active substance authorised for individual and group treatment, respectively. Intramammaries (QJ51) are not included. The calculation is based on sale statistics from Apoteket AB.

ATCvet code	Substance class	Individual treatment					Group treatment				
		1996	1997	1998	1999	2000	1996	1997	1998	1999	2000
QA07A	Intestinal anti-infectives	863	706	649	607	587[4]					
QJ01A	Tetracyclines	596	663	656	695	634	2 089	1 881	2 230	1 545	1 111[4]
QJ01C	Penicillins[1,2]	9 560	9 530	9 287	9 424	9 037					
QJ01D	Cephalosporins	–	53	133	245	315					
QJ01E	Sulfonamides & trimethoprim	2 033	2 107	2 335	2 376	2 336					
QJ01F	Macrolides & lincosamides	675	652	645	559	531	975	1 096	1 201	908	821
QJ01G	Aminoglycosides[2]	650	617	535	528	474					
QJ01M	Fluoroquinolones	147	147	150	144	150	27	32	25	11	7
QJ01M	Quinoxalines						1 098	534			
QJ01X	Other antimicrobials[3]	73	65	64	52	56	1 594	1 317	1 119	920	815

[1] Calculated as benzyl-penicillin; [2] The amount includes QJ01R, combinations; [3] Tiamulin, valnemulin, virginiamycin; [4] Drugs marketed with special licence are included.

Table AC IV. Amount of antimicrobials for veterinary use prescribed to birds 1996-2000 per substance class and animal category. Substance classes for which total amount prescribed was below 1 kg each of the years were excluded.

Substance class and category	Number of prescriptions					Kg active substance				
	1996	1997	1998	1999	2000	1996	1997	1998	1999	2000
QJ01A Tetracyclines										
Chickens	17	13	10	2	12	4.4	1.5	0.7	0.3	0.2
Hens	122	121	101	78	47	7.6	4.7	7.4	7.5	8.2
Other poultry[1]	127	146	98	115	76	9.8	13.3	7.5	9.9	5.5
Exotic birds	400	353	311	271	239	1.5	1.6	1.4	0.8	0.7
Unspecified[2]	378	309	258	235	196	16.5	7.7	4.2	6.1	4.8
Total	**1044**	**942**	**778**	**701**	**570**	**39.7**	**28.8**	**21.2**	**24.5**	**19.4**
QJ01M Fluoroquinolones										
Chickens	9	9	8	5	0	2.7	1.7	1.5	0.9	0.0
Hens[3]	9	11	11	2	6	9.2	14.7	12.2	2.8	2.2
Other poultry	41	26	20	32	21	0.3	0.6	0.4	0.3	0.5
Exotic birds	25	27	22	19	10	1.6	1.4	1.1	1.0	0.1
Unspecified	24	26	25	18	21	0.9	0.8	2.5	0.4	0.3
Total	**108**	**99**	**86**	**76**	**58**	**14.9**	**19.2**	**17.7**	**5.5**	**3.2**
QJ01F Macrolides and lincosamides										
Chickens	3	5	2	2	5	1.0	2.2	0.9	0.3	1.7
Hens	11	7	12	13	13	0.8	4.0	11.7	1.8	3.9
Other poultry	2	7	10	7	21	0.2	0.5	1.0	4.4	6.3
Exotic birds	2	3	1	1	1	0.2	0.2	0.1	0.1	0.1
Unspecified	8	12	14	10	11	2.0	5.1	1.6	0.8	1.8
Total	**26**	**34**	**39**	**33**	**51**	**4.2**	**12.0**	**15.3**	**7.5**	**13.9**
QP51AG Sulfonamides										
Chickens	95	79	98	64	53	13.7	13.6	21.0	15.2	22.7
Hens	304	265	250	196	146	39.1	36.6	47.8	57.1	32.9
Other poultry	123	130	133	110	96	18.1	15.4	18.3	16.0	13.7
Exotic birds	0	1	1	0	0	0.0	<0.1	<0.1	0.0	0.0
Unspecified	169	154	149	162	124	29.1	18.9	19.0	36.4	47.9
Total	**691**	**629**	**631**	**532**	**419**	**99.0**	**84.2**	**109.7**	**123.9**	**116.9**
QP51AH Ionophoric antibiotics (coccidiostats)										
						11 643	10 805	9 941	9 562[4]	9 368[4]

[1]Ducks, geese, turkeys, ratites, peacocks, pigeons, partridges, pheasants; [2]Species not specified, given as "birds" or "poultry": [3]Columns with kg active substance includes a package of fluoroquinolones sold with special marketing licence; [4] Regulated and classified as feed additives (dir 70/524/EEC) from 1999, figures for 1999 and 2000 from the Feed Control of the Board of Agriculture.

Use of antimicrobials for animals 1980-2000

Material included

The total consumption of antimicrobials for use in animals in Sweden has been studied in detail (Wierup *et al.*, 1987 and 1989; Björnerot *et al.*, 1996; Odensvik and Greko 1998; Odensvik 1999 and 2000). The statistics are based on sales figures from Apoteket AB. For feed additives not authorised as pharmaceutical specialities, data was gathered from the National Board of Agriculture. The figures presented include antimicrobials for all animal species (food animals, fish, pets and horses).

A breakdown of the figures into sales of products formulated for individual treatment (injectables, tablets) and products for group treatment (medication via feed or water) have been presented since 1993. For earlier years, raw data has been reanalysed in order to provide an estimate of the latter group. However, the figures from the early 80s must be interpreted with caution as classification and regulation was slightly different at that time. Details on animal numbers are found in Appendix 1.

Animal populations and health

The general situation with regard to animal health in Sweden is favourable. A geographically advantageous location in combination with a history of strict import control has kept the country free of several animal diseases that are present in many European countries.

A number of disease control programmes have been successfully implemented. Control of viral diseases is likely to influence the need for treatment with antimicrobials, as there would be fewer cases of secondary bacterial infections. Salmonellosis has been subject to measures of control since the early 60s. Today, the prevalence in live animals and animal products is very low, less than 0.05% in beef and pork and 0.1% for poultry at slaughter (Zoonoses in Sweden, 2001).

Cattle

Since 1980, the number of dairy cows has decreased by 35%. The average herd size has increased substantially. The number of beef cows has increased, especially in the early 90s. In the 90s, several programmes to control specific infectious diseases were initiated. The bovine population is now free of infectious bovine rhinotracheitis and bovine leucosis. The prevalence of herds infected with bovine viral diarrhoea has decreased substantially. The main indication for treatment of cattle with antimicrobials is mastitis. In most cases, the drug is administered systemically (as injections). The incidence of treatment has been rather stable over the years, but both dose and length of treatment have been increased.

Swine

The number of slaughtered pigs has varied over the years but has decreased overall. In 1999, it was 8% lower than in 1980. Between 1999 and 2000 there was a sharp drop. Today, most of the pigs are reared in age-segregated systems aiming to minimise the spread of infectious diseases.

Sweden has remained free of porcine respiratory and reproductive syndrome (PRRS) and transmissible gastroenteritis (TGE). A programme aimed to control Aujezky's disease has led to the eradication of the disease in the 90s. Athrophic rhinitis has also been controlled.

The major indications for use of antimicrobials in pig production are enteric and respiratory problems. The former are mainly weaning diarrhoea and swine dysentery. In many cases, treatment of these diseases involves treatment of the whole group of animals where the infection has been diagnosed. Antimicrobials are supplied for a defined period of time through feed or water.

Broiler chickens

The number of broiler chickens decreased somewhat in the early 80s but has since more than doubled. Through bioscrening measures production has remained free of mycoplasmosis, and most other infectiousdiseases. As in other countries, control of coccidiosis in chickens still relies primarily on the use of coccidiostats.

Subsequent to the withdrawal of antibacterial feed additives, streptogramins were prescribed as prophylactics for necrotic enteritis. From 1988, this practice was abandoned and in cases of clinical outbreaks, antimicrobials were prescribed therapeutically. Today, such outbreaks are rare.

A disease that may cause problems periodically is colibacillosis. Overall, therapeutic treatment of chickens with antimicrobials is uncommon.

Overall use

The total usage of antimicrobials is presented in table AC V. As the different substances are not equal in their biological activity per weight unit, total figures might be misleading. If a more active substance would replace a substance requiring high dosages for full efficacy, a false impression of a reduction could be given. Therefore, each substance group should be evaluated separately. Notwithstanding, an analysis of the total figures may indicate trends in the material.

Before 1986, the average total usage per year was 45.1 metric tons. Of this, 17.1 tons was used for growth promotion. When use of antimicrobials as feed additives was banned in 1986, the sales dropped sharply to 25.8 tons. This was 3 tons more than accounted for by a mere withdrawal of feed additives. In pig production, increased mortality due to diarrhoeal diseases was recorded. Neither veterinarians, nor farmers were prepared for the situation and the need for prescription policies was apparent.

Between 1988 and 1994, such policies were established and the sales stabilised around 30 tons. From 1995, a steady decline in total sales has been recorded. In 2000, the figure was 17.1 tons, representing a decrease since 1980-84 by 62%.

Table AC V. Total quantity of antimicrobial substances (kg active substance) for use in animals 1980-2000. Based on sales statistics from Apoteket AB and statistics from the Board of Agriculture.

ATCvet code	Substance class	Year					
		1980	1984	1988	1992	1996	2000
QG01AA, QJ01A	Tetracyclines[1]	9 819	12 955	4 691	8 023	2 698	1 754
QJ01B	Chloramphenicol	47	49	35	–	–	–
QJ01CE, QJ01R, QJ51R	G-and V penicillins[2]	3 222	4 786	7 143	7 446	8 818	8 254
QJ01CA, QJ01CR	Aminopenicillins	60	714	655	837	835	852
QJ01D, QJ51CA	Other betalactam-antibiotics	9	2				315
QA07AA, QJ01G, QJ01R, QJ51R	Aminoglycosides	5 274	5 608	3 194	2 139	1 164	797
QA07AB, QJ01E	Sulphonamides	6 600	4 325	3 072	2 362	2 198	2 338
QJ01E	Trimetoprim and derivatives	134	186	250	284	339	390
QJ01F	Macrolides and lincosamides[1]	603	887	1 205	1 710	1 649	1 352
QJ01MA	Fluoroquinolones				147	173	156
QJ01XX92, QJ01XX94	Pleuromutilins[1]			124	268	1 142	871
	Other substances[1, 3]	861	1 637	1 567	1 634	–	–
QJ01MB	Quinoxalines[1]	6 250	9 900	7 164	4 917	1 098	–
QJ01XX91	Streptogramins[1]		8 800	1 088	1 275	525	–
–	Antimicrobial feed additives[1, 4]	8 380	700				
	Total	41 259	50 549	30 189	31 043	20 639	17 079

[1] Subtance classes that are mainly used for groups or flock medication (i.e. feed or water); [2] Calculated to equivalents of benzyl-penicillin; [3] Mainly nitroimidazoles, QP51AA; [4] Quinoxalines and streptogramins are given separately, substances included are avoparcin, bacitracin, nitrovin, oleandromycin and spiramycin.

Drugs for treatment of individual animals

The use of penicillins has increased markedly (Table AC V). In this class, only formulations suitable for treatment of single animals are presently authorised. Products for injection dominate. It is assumed that the main part is used for treatment of mastitis in dairy cattle and various infections in horses. As mentioned, both dosage and length of treatment has increased with respect to mastitis. Use of penicillin alone has replaced most of the use of the combination of penicillin and dihydrostreptomycin, as consumption of the latter has decreased considerably. The change is in accordance with current policy recommendations where use of narrow spectrum antimicrobials is advocated.

The aminopenicillins are mainly used in pets. The use of this class has increased steadily over the period of observation. This is also true for the cephalosporins and lincosamides. Both these groups were introduced on the veterinary market in the early 90s. Before this, cephalosporins and macrolides authorised for use in humans were prescribed to pets. Thus, the increase could, at least partly, be a reflection of veterinary authorised drugs replacing off-label prescription of drugs authorised for humans. More information on the use of antimicrobials for pets is found in Odensvik *et al.* 2001.

The fluoroquinolones are mainly used for treatment of individual animals. Following their introduction, overall sales increased until the mid-90s and thereafter, a decrease is noted. However, the subset of this use that consists of products for use in dogs or cats has increased steadily over the 90s.

A steady increase in use of trimethoprim-sulfonamides is recorded. This might partly be explained by an increased use in horses, subsequent to the introduction of formulations for oral use in that species in the late 80s.

Drugs for treatment of groups

Of special interest when considering the risk for development of resistance is the consumption of antimicrobials intended for group or flock medication (Table AC VI). Before 1986, antimicrobial feed additives were used both for chickens and pigs but rarely for calves. From 1988, an overwhelming part of the sales of products for inclusion into feed or water has been for treatment of pigs. When interpreting the data, it is important to bear in mind that the numbers of pigs has varied and has mostly been 5-10% lower than in the early 80s.

After the ban of antimicrobial feed additives in 1986, a decrease in use of tetracyclines was observed. However, between 1988 and 1993, an increase was again noted. As this could not be connected to an altered disease situation, investigations were initiated. It was found that the increase could almost entirely be explained by the prescriptions of one veterinarian to one herd. The total tetracycline consumption is today around one tenth of that in the early 80s.

Swine dysentery is the main indication for use of macrolides and pleuromutilins. The latter class was introduced in 1988 and its use has since increased markedly. An increase is also noted for the macrolides. The nitroimidazoles were taken off the market in 1995 and it can be assumed that they were replaced by the two former groups of antimicrobials. Overall, the increased use of these drugs is believed to reflect an increase in the incidence of treatment of swine dysentery. It has been estimated that today, around 10% of slaughtered pigs have been treated for this disease (Wallgren 1998).

Table AC VI. Sales of formulations of antimicrobials intended for treatment of animals through feed or water (flock or group medications) expressed as kg active substance. Based on statistics from Apoteket AB.

ATC group	Substance group	1980	1984	1988	1992	1996	2000
QJ01A	Tetracyclines[1]	9 270	12 300	4 177	7 461	2 089	1 111
QJ01C	Penicillins	–	–	186	9	–	–
QJ01F	Macrolides and lincosamides	308	607	751	1 139	975	821
QJ01M	Fluoroquinolones	–	–	–	10	27	7
QJ01M	Quinoxalines	6 250	9 900	7 164	4 917	1 098	–
QJ01X	Streptogramins	–	8 800	1 088	1 275	525	–
QJ01X	Pleuromutilins	–	–	101	229	1 069	815
QP51A	Nitroimidazoles	791	1 440	1 557	1 563	–	–
–	Antibacterial feed additives[2]	8 380	700	–	–	–	–
	Total	24 999	33 747	15 025	16 602	5 783	2 754

[1] 1980-1984 only quantities mixed in feed at feed mills (Wierup et al 1989); [2] Antibacterial feed additives other than quinoxalines and streptogramins (avoparcin, bacitracin, nitrovin, oleandomycin, spiramycin).

Fluoroquinolones were introduced on the market in the late 80s. Less than 20% of the sales have been formulations intended for medications through feed or water. These have been authorised for use in poultry and pigs. After their introduction, consumption increased to around 30 kg. From 1999 only the product intended for medication of poultry remains on the market and figures have dropped accordingly.

The use of substances formerly authorised as feed additives and subsequent to the ban authorised as pharmaceutical specialities (quinoxalines and streptogramins) decreased substantially over the 90s in spite of higher doses being given for therapy than for growth promotion. The use of streptogramins (i.e. virginiamycin) decreased gradually and from 1999, no product of this group is available. The major quinoxaline, olaquindox, was exclusively used in pigs. In 1988, its use as pharmaceutical speciality for prevention of weaning diarrhoea was at a level approaching that pre-ban.

However, as the dosage used was three times higher than before, fewer animals were exposed. After this, the use decreased gradually and from July 1997 olaquindox is no longer available in Sweden. In 1992, zinc oxide was authorised for incorporation into piglet feed at 2000 ppm of zinc for prevention of weaning diarrhoea. Currently, this type of medicated feed is only available on veterinary prescription. This practice is being phased out and the consumption has declined to 8% of its maximum amount.

Coccidiostats

The combination of amprolium and ethopabate has been the main drug used for prevention of coccidiosis in chickens reared for laying pullets in Sweden. In the 90s, vaccination has largely replaced the use of coccidiostats for prevention of coccidiosis in replacement breeders. In the broiler productio n, the ionophore anticoccidials have been favoured. Narasin is, by far, the most widely applied product.

Resistance in zoonotic bacteria

Resistance in zoonotic bacteria

The monitoring program will encompass zoonotic bacteria isolated from animals of Swedish origin. This year the report only presents data on *Salmonella enterica.* Future reports will also include data on antibacterial susceptibility among *Campylobacter coli* and *Campylobacter jejuni.*

Salmonella

Isolates included

Salmonellosis in animals is a notifiable disease in Sweden and confirmation at SVA of all cases is mandatory. From these isolates, one from each animal species (warm-blooded wild and domesticated) involved in each notified incident were included.

In Sweden, monitoring of antimicrobial susceptibility among *Salmonella* of animal origin has been performed regularly since 1978. Although the antimicrobials included in the test panels have varied, microdilution methods have been used in all these surveys. For comparison, data from previous years are therefore presented together with data for 2000.

Results and comments

A total of 67 isolates were investigated (Table S I). Of these, 46 were *S.* Typhimurium, three *S.* Dublin, one *S.* Enteritidis and the remainder, 18 isolates, were other serovars. Of the *S.* Typhimurium isolates only 7% were from cattle, and as much as 37% originated from pets and horses (Table S III). The distributions of MICs of the antimicrobials tested are shown in Table S IIA and S IIB.

Overall, only five isolates (8%) were classified as resistant to any of the antimicrobials tested. Of these isolates four were *S.* Typhimurium and one was *S.* Yoruba. The *S.* Yoruba isolate was resistant to sulfamethoxazole alone. Of the four *S.* Typhimurium isolates three were resistant to only one antimicrobial (nalidixic acid or streptomycin). The fourth *S.* Typhimurium isolate however, was resistant to seven of the tested antimicrobials (amoxicillin/clavulanic acid, ampicillin, chloramphenicol, florfenicol, streptomycin, sulfamethoxazole and oxytetracycline). This isolate emanated from a cat and was of the phage type DT 104.

The occurrence of resistance among *S.* Typhimurium in 2000 and in previous years is shown in Table S IV. The proportions of different animal sources vary between the different time periods. In the materials from the years 1978-88 all the isolates were from cattle. Since, the proportion of cattle isolates has gradually decreased but isolates from major food producing animals constituted over 50% of the materials in all years except in 1999 (Table S III).

Resistance to most antimicrobials among *S.* Typhimurium is low and relatively stable over the years but there appears to be a decline in streptomycin resistance. Phage typing of *S.* Typhimurium isolates was included in the surveys from 1997. It is evident that resistance to ampicillin, chloramphenicol, tetracycline and trimethoprim-sulfonamides can be strongly linked to specific phage types. In the years 1997-2000 resistance to more than one antimicrobial was found in 17 isolates. Of these, nine were of phage type DT 104 and three of phage type DT 193. The DT 104 isolates had the typical resistance pattern ampicillin, chloramphenicol, streptomycin, sulfonamide and tetracycline (ACSSuT), in some cases with resistance also to the combination trimethoprim-sulfonamide. The phage type DT 193 isolates had the pattern ampicillin, cephalothin, streptomycin, sulfonamide and tetracycline in some cases resistance also to trimethoprim-sulfonamide. Appearance of these phage types, albeit sparse, in the materials greatly influences the prevalence of resistance.

As the material consists of one isolate from each incident of *Salmonella* in Sweden, including those detected in food-producing animals in the *Salmonella* control programme, it is thought to be representative for *Salmonella* prevalent in animals in the country. In the light of this, the overall situation of antimicrobial resistance in *Salmonella* is favourable. There is no evident spread of multiresistant clones among domesticated animals within the country, probably a result of the strategies in the Swedish *Salmonella* control programme.

Campylobacter

Data on antimicrobial susceptibility among *Campylobacter* spp. is not included this year. In the future, occurence of resistance among *Campylobacter coli* and *Campylobacter jejuni* will be monitored in isolates from cattle, pigs and chickens sampled at slaughter. Earlier data on Swedish isolates of *Campylobacter* spp. were cited in Antimicrobial Feed Additives (SOU 1997:132) also accessible at http://jordbruk.regeringen.se.

Table S I. Number of isolates of *Salmonella enterica* tested for antimicrobial susceptibility in 2000 presented by serotype and source of isolate.

Serotype	Phage type	Sheep	Dog	Horse	Cat	Cattle	Swine	Poultry	Wild birds	Ostrich	Total
S. Typhimurium	12						3				**3**
	15a					1					**1**
	40			2	10		8	1	2		**23**
	41			1		2	4	2			**9**
	104				1						**1**
	NST				3		1	3	1		**8**
	Not typed	1									**1**
S. Dublin						3					**3**
S. Enteritidis							1				**1**
S. Infantis			1								**1**
S. Livingstone								2			**2**
S. Mbandaka								1			**1**
S. Senftenberg			1					1			**2**
S. subspecies IIIb		1									**1**
S. Virchow			1								**1**
S. Yoruba							1	1			**2**
S. Duesseldorf				1	1	2					**4**
S. Jangwani						1					**1**
S. Ebrie										1	**1**
S. Havana								1			**1**
Total		**2**	**3**	**4**	**15**	**9**	**18**	**12**	**3**	**1**	**67**
Percent of total		**3%**	**4%**	**6%**	**22%**	**13%**	**27%**	**18%**	**4%**	**2%**	

Table S II. Distribution of MICs for *Salmonella enterica* (A) and for *Salmonella* Typhimurium (B) from animals in 2000.

A *Salmonella enterica* **n = 67**	**Breakpoint resistance** (mg/L)	**% Resistant**	**Distribution (%) of MIC[2]** (mg/L)															
Substance			**≤0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**>512**
Amoxi/Clavulan[1]	>8/4	2						83.6	13.4	1.5		1.5						
Ampicillin	>8	2						34.3	61.2	3.0				1.5				
Apramycin	>32	0						1.5	1.5	9.0	52.2	32.8	3.0					
Ceftiofur	>2	0				1.5	40.3	55.2	3.0									
Chloramphenicol	>8	2							6.0	77.6	14.9	1.5						
Enrofloxacin	>0.5	0		65.7	28.4	6.0												
Florfenicol	>16	2							13.4	73.1	11.9		1.5					
Gentamicin	>8	0					4.5	32.8	50.7	11.9								
Nalidixic acid	>16	3									55.2	41.8	3.0					
Neomycin	>32	0						7.5	79.1	11.9	1.5							
Streptomycin	>32	3								1.5	16.4	55.2	23.9	1.5	1.5			
Sulfamethoxazole	>256	3												46.3	44.8	6.0		3.0
Oxitetracycline	>8	2						7.5	50.7	40.3					1.5			
Trimethoprim	>8	0				9.0	61.2	26.9	3.0									

B *Salmonella* **Typhimurium n = 46**	**Breakpoint resistance** (mg/L)	**% Resistant**	**Distribution (%) of MIC[2]** (mg/L)															
Substance			**≤0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**>512**
Amoxi/Clavulan[1]	>8/4	2						76.1	19.6	2.2		2.2						
Ampicillin	>8	2						26.1	69.6	2.2				2.2				
Apramycin	>32	0						2.2	2.2	6.5	50.0	39.1						
Ceftiofur	>2	0					34.8	60.9	4.3									
Chloramphenicol	>8	2							4.3	87.0	6.5	2.2						
Enrofloxacin	>0.5	0		58.7	34.8	6.5												
Florfenicol	>16	2							15.2	80.4	2.2		2.2					
Gentamicin	>8	0					4.3	32.6	50.0	13.0								
Nalidixic acid	>16	4									50.0	45.7	4.3					
Neomycin	>32	0						4.3	78.3	15.2	2.2							
Streptomycin	>32	4									8.7	58.7	28.3	2.2	2.2			
Sulfamethoxazole	>256	2												45.7	43.5	8.7		2.2
Oxitetracycline	>8	2						8.7	50.0	39.1					2.2			
Trimethoprim	>8	0				10.9	56.5	28.3	4.3									

[1] Concentration of amoxicillin given, tested with clavulanic acid in concentration ratio 2/1; [2] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration.

Table S III. Occurrence of resistance to antimicrobials and source of isolates in *Salmonella* Typhimurium from animals 1978 to 2000.

Substance	Breakpoint resistance (mg/L)	Percent resistance						
		1978-86 (n = 117)	1987-88[1, 2] (n = 8)	1989-92 (n = 79)	1993-96 (n = 87)	1997-98 (n = 50)	1999 (n = 101)	2000 (n = 46)
Amoxicillin/Clavulanic acid	>8/4	–	–	–	–	–	–	2
Ampicillin	>8	2	0	3	8	12	5	2
Apramycin	>32	–	–	–	–	–	–	0
Ceftiofur	>2	–	–	–	–	–	–	0
Cephalothin	>16	–	–	1	0	0	3	–
Chloramphenicol	>0.5	–	4	3	6	12	2	2
Enrofloxacin	>0.5	–	–	0	1	0	0	0
Florfenicol	>16	–	–	–	–	–	–	0
Gentamicin	>16	–	–	0	0	0	0	0
Nalidixic acid	>16	–	–	–	–	–	–	4
Neomycin	>32	–	0[3]	0	0	12	0	0
Oxitetracycline	>8	14	14	3	7	12	5	2
Streptomycin	>32	78	78	25	13	20	6	4
Trimethoprim	>8	–	–	–	–	–	–	0
Trimethoprim/Sulfmethoxazole	>0.5/9.5	0	0	1	1	8	3	–
Percent of isolates from:								
Cattle, sheep, pigs, poultry		100	100	59	55	56	23	57
Horses, cats, dogs		–	–	15	22	16	53	37
Wildlife		–	–	26	23	28	24	7

[1] Only isolates from cattle; [2] 1988 includes isolates to September, isolates from October-December 1988 given under 1989; [3] Breakpoint for resistance >8 mg/L.

Resistance in indicator bacteria

Resistance in indicator bacteria

The prevalence of acquired resistance to antimicrobials among bacteria of the normal enteric microflora can serve as an indicator of the selective pressure exerted by use of antimicrobial agents in exposed populations. Although these bacteria are unlikely to cause diseases, they form a reservoir of transferable resistance determinants from which resistance genes can spread to bacteria responsible for infections in animals or humans. Thus, surveillance of resistance among indicator bacteria in the normal enteric microbiota can be of great value to detect trends and to follow the effects of interventions. In SVARM, *Escherichia coli* and *Enterococcous* spp. were chosen as indicator bacteria. Isolates from cattle up to 12 months of age, from fattening pigs and from broiler chickens are included in the monitoring programme.

Of special interest in monitoring antimicrobial susceptibility among indicator bacteria is the occurrence of specific patterns of resistance, the different resistance determinants observed in single isolates. Such patterns, or resistance phenotypes, can indicate the presence of linked resistance genes. The danger of such elements is evident in the sense that a single transfer event conveys resistance to several antimicrobials to the recipient bacterium (co-transfer). Use of one antimicrobial can thereby select for resistance to other unrelated antimicrobials (co-selection).

Isolates included

E. coli and *Enterococcous* spp. were isolated from samples of intestinal content (caecum or colon) from healthy cattle, pigs and broiler chickens sampled at slaughter. However, 140 samples from cattle were faecal samples collected in live animals on the farm of origin. Each isolate from cattle and pigs represents a unique herd. In the chicken material, each isolate represents a unique flock but not always a unique herd. Antimicrobials included in the test panels and concentration ranges used are given in Table EC II and ENT II. For details on methodology, including sampling strategy, see Appendix 3.

Escherichia coli

Results and comments

The material includes 293 isolates of *E. coli* from cattle, 260 from pigs and 274 from chickens (Table EC I). Isolates were obtained from about 90% of the samples cultured. The isolation frequencies were of the same magnitude in the three animal species sampled. For samples from cattle and pigs, the figures tally with those in the Danish monitoring programme (DANMAP 99). From samples from chickens, however, the isolation frequency in the Danish programme is substantially lower, 55%, despite similar methods of isolation. In DANMAP 99, cloacal swabs were used but in SVARM caecal contents were cultured. Thus, it is possible that the observed difference is due to the type of material cultured.

Cattle

Among isolates from cattle, resistance to streptomycin was the most prevalent trait (5%) (Table EC II). Resistance to nalidixic acid, chloramphenicol, tetracycline or sulfonamides was about 1%. Only five of 293 isolates (2%) were resistant to more than one antimicrobial (Table EC III). Four of the antimicrobials tested were represented in the resistance patterns.

The most prevalent resistance phenotype, with three or more antimicrobials represented in the pattern, was streptomycin-sulfonamides-tetracycline, which was found in two isolates. Of the 15 isolates resistant to streptomycin (Table EC IV), four were co-resistant to sulfonamides (Table EC III).

Pigs

Resistance to streptomycin was the most common trait (13%) among isolates from pigs (Table EC II). Lower resistance levels, 3-7%, were found to amoxicillin/clavulanic acid, ampicillin, tetracycline, sulfonamides or trimethoprim. Only occasional isolates, about 1%, were resistant to chloramphenicol, gentamicin or neomycin. Twenty-five isolates (10%) were resistant to more than one antimicrobial with seven of the tested substances represented in the patterns (Table EC III).

The most prevalent resistance phenotype with three or more antimicrobials represented was the combination streptomycin-sulfonamides-tetracycline, which was found in four isolates. All these isolates were also resistant to one or more of the other antimicrobials tested. Interestingly, seven of the eight isolates resistant to ampicillin (Table EC IV) were also resistant to streptomycin, sulfonamides or trimethoprim. Use of ampicillin is very limited in Swedish pig production. Thus, the occurrence of ampicillin resistance might be explained by linkage with other resistance genes.

Chickens

In the material from broiler chickens, resistance against sulfamethoxazole was the most common (12%) (Table EC II). Resistance to amoxicillin/clavulanic acid, ampicillin, tetracycline, nalidixic acid or streptomycin were less frequent (4-8%). Less than 2% of the isolates were resistant to chloramphenicol, enrofloxacin, gentamicin, neomycin or trimethoprim.

Twenty-five isolates (9%) were resistant to more than one antimicrobial with nine of the tested substances represented in the patterns (Table EC III).

Table EC I. Prevalence of *Escherichia coli* in samples of intestinal content from cattle, pigs and chickens, 2000.

Animal species	Number of samples cultured	Number of isolates	% positive	Number tested for antimicrobial susceptibility
Cattle	322	294	91	293
Pigs	372	321	86	260
Chickens	302	274	91	274

The most prevalent resistance phenotype, with three or more antimicrobials represented, was the combination streptomycin-sulfonamides-ampicillin, found in six isolates. Five of these isolates were also resistant to trimethoprim. Sulfonamides are used, albeit sparingly, in chicken production to treat outbreaks of coccidiosis. It is possible that this use to some extent co-selects for resistance to other antimicrobials.

General comments

Overall, the figures appear to be low. The lowest levels of resistance were found in cattle, which is consistent with a limited use of antimicrobials in the sampled category of animals.

Occurrence of resistance is slightly higher in pigs, where for example trimethoprim and tetracyclines are used to treat various infections. The figures are notably lower than those found for *E. coli* from diagnostic samples. However, in both materials resistance to streptomycin and tetracycline are the most common traits. This indicates that the pool of resistance genes present in pathogenic *E. coli* extends to the inherent flora of the whole target animal population.

Occurrence of resistance in the material from broiler chickens was about the same level as that of pigs for most antimicrobials. This is somewhat unexpected, as antimicrobials, apart from cocciodiostats, are very seldom used in chicken production (see Use of antimicrobials).

Table EC II. Occurrence of resistance (%) among isolates of *Escherichia coli* from cattle, pigs and chickens, 2000.

Substance	**Range tested** (mg/L)	**Breakpoint resistance** (mg/L)	**% Resistant. 95% confidence interval inside brackets**		
			Cattle n = 293	**Pigs** n = 260	**Chickens** n = 274
Amoxicillin/Clavulanic acid[1]	2/1-16/8	>8/4	0 (0.0-1.3)	3 (1.3-6.0)	5 (2.6-8.0)
Ampicillin	0.25-32	>8	0 (0.0-1.3)	3 (1.3-6.0)	5 (2.6-8.0)
Apramycin	0.25-32	>32	0 (0.0-1.3)	0 (0.0-1.4)	0 (0.0-1.3)
Ceftiofur	0.25-2	>2	0 (0.0-1.3)	0 (0.0-1.4)	0 (0.0-1.3)
Chloramphenicol	2-16	>8	<1 (0.0-1.9)	<1 (0.0-2.1)	<1 (0.1-2.6)
Enrofloxacin	0.03-4	>0.5	0 (0.0-1.3)	0 (0.0-1.4)	2 (0.4-3.7)
Florfenicol	2-16	>16	0 (0.0-1.3)	0 (0.0-1.4)	0 (0.0-1.3)
Gentamicin	0.25-32	>8	0 (0.0-1.3)	<1 (0.0-2.1)	<1 (0.0-2.0)
Nalidixic acid	1-128	>16	<1 (0.1-2.4)	0 (0.0-1.4)	4 (2.3-7.5)
Neomycin	1-128	>32	0 (0.0-1.3)	1 (0.2-3.3)	<1 (0.1-2.6)
Streptomycin	2-256	>32	5 (2.9-8.3)	13 (9.2-17.8)	4 (2.3-7.5)
Sulfametoxazole	64-512	>256	1 (0.4-3.5)	7 (4.2-10.7)	12 (8.1-16.0)
Tetracycline	0.5-64	>8	1 (0.4-3.5)	7 (4.2-10.7)	8 (4.8-11.5)
Trimethoprim	0.12-16	>8	0 (0.0-1.3)	5 (2.4-7.9)	<1 (0.1-2.6)

[1] Concentration of amoxicillin given, tested with clavulanic acid in concentration ratio 2/1 (amoxicillin/clavulanic acid).

Table EC III. Number of isolates of *Escherichia coli* resistant to two or more antimicrobials, presented by animal species and resistance phenotype. "R" in hatched fields indicates resistance.

Cattle n = 293	**Pigs** n = 260	**Chickens** n = 274	**Total** n = 827	**Resistance pattern**[1]									
				Sm	**Su**	**Am**[2]	**Tr**	**Tc**	**Cm**	**Nm**	**Ef**	**Nal**	**Gm**
		1	1	R	R	R			R				
	3		3	R	R	R	R						
	1		1	R	R	R		R		R			
	1	1	2	R	R	R	R	R		R			
	1		1	R	R	R	R	R					
2	1	1	4	R	R			R					
		1	1	R	R			R	R		R	R	
		1	1	R	R			R		R		R	
1	3	3	7	R	R								
	2		2	R	R		R						
	1		1	R	R				R				
1			1	R	R							R	
		1	1	R				R				R	
		1	1		R			R				R	
		1	1					R				R	
		3	3								R	R	
		2	2		R	R							
	1		1			R	R						
1	7	1	9	R				R					
	1		1	R			R			R			
	1		1	R			R						
	1	6	7		R			R					
	1	1	2		R		R						
		1	1		R			R					R
Total													
5	25	25	55										

[1] Sm: streptomycin; Su: sulfonamides; Am: ampicillin; Tr: trimethoprim; Tc: tetracycline; Cm: chloramphenicol; Nm: neomycin; Ef: enrofloxacin; Nal: nalidixic acid; Gm: gentamicin; [2] Denote resistance also against amoxicillin/clavulanic acid.

Table EC IV. Distribution of MICs for *Escherichia coli* from cattle (n = 293), pigs (n = 260) and chickens (n =274), 2000.

Substance	Breakpoint resistance (mg/L)	Animal species	% Resistant	Distribution (%) of MICs[2] (mg/L)															
				≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Amoxicillin/ Clavulan. acid[1]	>8/4	Cattle	0							11.6	70.3	18.1							
		Pigs	3							6.9	74.2	15.8	0.4	2.7					
		Chickens	5							6.2	77.7	11.3		4.7					
Ampicillin	>8	Cattle	0						1.4	18.8	78.8	1.0							
		Pigs	3						0.4	31.2	64.6	0.8			3.1				
		Chickens	5						1.8	23.4	69.3	0.7			4.7				
Apramycin	>32	Cattle	0								7.2	44.4	38.6	9.9					
		Pigs	0					0.4		0.4	3.1	32.7	53.8	9.6					
		Chickens	0							0.4	2.6	25.2	55.1	16.8					
Ceftiofur	>2	Cattle	0				24.9	72.0	3.1										
		Pigs	0				30.8	65.8	3.5										
		Chickens	0				11.3	74.5	14.2										
Chloramphenic.	>8	Cattle	<1							1.0	37.9	60.8	0.3						
		Pigs	<1							1.9	50.0	47.7		0.4					
		Chickens	<1								27.0	72.3		0.7					
Enrofloxacin	>0.5	Cattle	0	29.4	69.3	1.0		0.3											
		Pigs	0	25.0	71.9	3.1													
		Chickens	2	19.3	75.2	1.1	0.7	2.2	1.5										
Florfenicol	>16	Cattle	0							0.7	23.5	70.6	5.1						
		Pigs	0							1.2	43.8	54.2	0.8						
		Chickens	0								13.9	85.0	1.1						
Gentamicin	>8	Cattle	0					2.4	37.2	49.8	9.9	0.7							
		Pigs	<1					1.5	19.6	55.0	21.9	1.5	0.4						
		Chickens	<1						14.6	52.2	30.7	2.2	0.4						
Nalidixic acid	>16	Cattle	<1							0.7	22.5	70.3	5.8		0.3		0.3		
		Pigs	0							1.9	26.2	68.8	3.1						
		Chickens	4								23.7	66.8	5.1			1.1	3.3		
Neomycin	>32	Cattle	0						5.8	61.4	30.7	2.0							
		Pigs	1						4.6	56.9	34.6	2.7				0.4	0.8		
		Chickens	<1						1.1	51.5	40.5	6.2			0.7				
Streptomycin	>32	Cattle	5							0.7	13.0	67.2	14.0		1.4	1.0	1.7	1.0	
		Pigs	13								6.9	53.1	24.2	2.7	3.5	3.8	3.1	2.7	
		Chickens	4								2.9	59.9	32.1	0.7	0.7	0.7	1.1	1.8	
Sulfametoxazole	>256	Cattle	1												42.3	54.6	1.7	0.3	1.0
		Pigs	7												57.7	35.4			6.9
		Chickens	12												32.5	54.4	1.5		11.7
Tetracycline	>8	Cattle	1						8.9	57.7	30.7	1.4			0.3	1.0			
		Pigs	7					0.8	8.1	70.0	13.5	0.8	0.4	0.8		5.8			
		Chickens	8						5.1	59.9	27.0	0.4		0.4		7.3			
Trimethoprim	>8	Cattle	0			3.1	9.2	34.8	42.3	8.9	1.7								
		Pigs	5			0.8	10.0	59.2	23.5	1.2	0.8		0.4	4.2					
		Chickens	<1			2.6	8.0	55.5	32.1	1.1				0.7					

[1] Concentration of amoxicillin acid given, tested with clavulanic acid in concentration ratio 2/1 (amoxicillin/clavulanic acid); [2] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration.

Enterococci

Results and comments

The material includes 277 isolates from cattle, 241 from pigs and 261 from chickens (Table ENT I). The proportion of isolates of *E. faecalis, E. faecium* or *E. hirae* varied between the three animal species (Table ENT I). *E. hirae* was the most prevalent species in cattle and pigs and *E. faecium* in chickens. Other species of enterococci isolated were predominantly *E. mundtii* isolated from 2-8% of the samples. In addition, *E. gallinarum, E. durans, E. avium* and *E. casseliflavus* were isolated in lower numbers.

In 2-6% of the samples, enterococci not confirmed to belong to any of these species were isolated. Isolation frequencies of *E. faecalis* and *E. faecium* roughly tally with those reported from Denmark except for *E. faecium* in samples from chicken where only 17% of the cultured samples were positive in the Danish study (DANMAP 99).

All enterococci

Overall, levels of antimicrobial resistance among all enterococci were lowest among isolates from cattle and highest among isolates from chickens (Table ENT II). Only tetracycline resistance was of appreciable magnitude (5%) among cattle isolates. Tetracycline resistance was the most prevalent (27%) trait among isolates from pigs followed by erythromycin resistance (11%). In isolates from chickens, resistance to narasin was very common (72%) but relatively high levels of resistance to tetracyclines, bacitracin or erythromycin (19-37%) were also found. Flavomycin and virginiamycin are not included in the overall comparison as the inherent susceptibility to these substances differs between species of enterococci.

No isolate in the material was resistant to vancomycin. However, all samples were also cultured in enrichment-broth containing vancomycin. From these cultures, two vancomycin resistant isolates were obtained. The isolates were from chickens and identified as *E. faecium* with MIC for vancomycin of >128 mg/L. Genotyping with PCR revealed that both isolates carried the *vanA* gene-cluster. The isolates were also resistant to narasin and in addition, one to tetracyclines and the other to erythromycin and virginiamycin.

Cattle

Among specific species of enterococci, resistance was rare in *E. hirae* from cattle (Table ENT III). In *E. faecalis* and *E. faecium* resistance was also rare with flavomycin or tetracycline resistance in *E. faecalis* the most prevalent (14%). Considering the small number of isolates of *E. faecalis* these figures must however be interpreted with caution.

Resistance to more than one antimicrobial was detected in only four isolates among *E. faecalis* and *E. faecium* (Table ENT V and VI). All four isolates had tetracyclines included in the resistance pattern, in combination with streptomycin, erythromycin or virginamycin. No isolate was resistant to three or more antimicrobials.

Pigs

In isolates from pigs, levels of resistance to single antimicrobials were of similar magnitude among *E. faecium* and *E. hirae* with tetracycline resistance being the predominant trait (10-15%) (Table ENT III). Notably, resistance to bacitracin in isolates from pigs was only found in *E. faecium* albeit in a low frequency (4%). Among *E. faecalis,* resistance to tetracyclines or erythromycin was common (68 and 36% respectively) and considerably higher than in *E. faecium* and *E. hirae*. In addition, streptomycin and neomycin resistance was more prevalent (13 and 7% respectively) in *E. faecalis* than in the other two species of enterococci.

Resistance to more than one antimicrobial occurred in 22 of 56 isolates of *E. faecalis* but only in one of 48 *E. faecium* isolates (Table ENT V and VI). Among *E. faecalis* six antimicrobials were included in the resistance patterns. The most prevalent phenotype, with resistance to three or more antimicrobials, was erythromycin-streptomycin-neomycin resistance, which was found in three isolates. In addition, the only multiresistant isolate of *E. faecium* in pigs was of this phenotype. Notably, of the 56 isolates of *E. faecalis*, 20 were resistant to erythromycin and of these, 18 were tetracycline resistant (Table ENT II and V). The finding indicates a link between resistance to erythromycin and tetracyclines in *E. faecalis* from pigs.

Table ENT I. Prevalence of enterococci in samples of intestinal content from cattle, pigs and chickens, 2000. Species not identified as *Enterococcus faecalis, E. faecium* or *E. hirae* are given as "other species".

Animal species	Number of samples cultured	Total number of isolates. Percent positive samples given in brackets.	Number tested for antimicrobial susceptibility	*Enterococcus* species isolated. Number of isolates and percent of total isolates in brackets.			
				E. faecalis	*E. faecium*	*E. hirae*	Other species
Cattle	415	277 (67%)	277	22 (8%)	71 (26%)	127 (46%)	57 (21%)
Pigs	460	241 (52%)	241	56 (23%)	48 (20%)	106 (44%)	36 (13%)
Chickens	317	261 (82%)	261	47 (18%)	151 (58%)	28 (11%)	35 (13%)

Table ENT II. Occurrence of resistance (%) among isolates of *Enterococcus* spp. from cattle, pigs and chickens, 2000.

Substance	Range tested (mg/L)	Breakpoint resistance (mg/L)	% Resistant 95% confidence interval inside brackets.		
			Cattle n = 277	Pigs n = 241	Chickens n = 261
Ampicillin	0.25-32	>8	0 (0.0-1.3)	<1 (0.0-2.6)	0 (0.0-1.4)
Avilamycin	0.5-32	>8	2 (0.6-4.2)	<1 (0.1-3.0)	0 (0.0-1.4)
Bacitracin[1]	0.5-32	>32	<1 (0.1-2.6)	2 (0.5-4.7)	20 (14.9-24.9)
Erythromycin	0.25-32	>4	3 (1.0-5.1)	11 (8.1-17.3)	19 (14.6-24.5)
Flavomycin	2-128	>32	NR[2]	NR[2]	NR[2]
Gentamicin	0.5-32, 512	>512	0 (0.0-1.3)	0 (0.0-1.7)	0 (0.0-1.4)
Narasin	0.12-16	>2	1 (0.4-3.7)	2 (0.5-4.7)	72 (65.8-77.0)
Neomycin	2-128, 1024	>1024	<1 (0.0-2.0)	3 (1.0-6.0)	0 (0.0-1.4)
Streptomycin	2-128, 1024	>1024	<1 (0.1-2.6)	4 (2.3-8.4)	2 (0.9-4.9)
Tetracycline	0.25-32	>8	5 (3.1-8.8)	27 (23.9-36.5)	37 (30.9-43.0)
Vancomycin	1-128	>16	0 (0.0-1.3)	0 (0.0-1.7)	0 (0.0-1.4)
Virginiamycin	0.5-64	>8	NR[2]	NR[2]	NR[2]

[1] MIC in U/mL, see Appendix 3 for details; [2] Not relevant as susceptibility in some species of *Enterococcus* is inherently low.

Chickens

In isolates from broiler chickens, levels of resistance were largely similar in the three species of enterococci (Table ENT II). Resistance to narasin was the most prevalent trait (43-89%) but erythromycin resistance was also frequent (12-30%). Among *E. faecalis* and *E. faecium* resistance to tetracyclines and bacitracin was common (20-60%).

Of the 47 isolates of *E. faecalis,* 20 were resistant to more than one antimicrobial (Table ENT V). Six antimicrobials were included in the resistance patterns. The most prevalent phenotype with three or more antimicrobials in the pattern was tetracycline-erythromycin-narasin resistance. Notably, of the 47 isolates of *E. faecalis* from chickens 14 were resistant to erythromycin and of these, 12 were resistant also to tetracycline (Table ENT II and V).

Among *E. faecium*, 75 of 151 isolates were resistant to more than one antimicrobial (Table ENT VI). Six antimicrobials were included in the resistance patterns. The most prevalent phenotypes with three or more antimicrobials in the patterns were tetracycline-narasin-bacitracin, which was found in 14 isolates, and tetracycline-erythromycin-narasin in eight isolates. It is notable that 72-93% of isolates resistant to tetracyclines, erythromycin, bacitracin or virginiamycin were also resistant to narasin (Table ENT II and VI). The apparent association of resistance is probably not of genetic origin but due to the high proportion of narasin resistant isolates in the material. However, in accordance with the findings in *E. faecalis*, there appears to be a link between resistance to virginiamycin and tetracyclines and between erythromycin and tetracyclines. Hence, of 151 isolates of *E. faecium*, eight of 12 isolates resistant to virginiamycin were also tetracycline resistant, and of 18 isolates resistant to erythromycin, 11 were resistant to tetracyclines (Table ENT II and VI).

General comments

When comparing levels of resistance across animal species it is evident that resistance to narasin, virginiamycin and bacitracin occur almost exclusively among isolates from chickens and for the latter substance, predominantly among *E. faecalis* and *E. faecium* (Table ENT IV).

Regarding narasin, the results probably reflect an extensive use as cocciodiostat in chickens. Resistance to bacitracin and virginiamycin can however not be explained as caused by a selective pressure as these substances have not been used in Swedish broiler production since the mid 80s. Hence, the observed levels of bacitracin and virginiamycin resistance in isolates from chickens might be a remnant of the past use of these antimicrobials. It might also be a consequence of co-selection of resistance traits.

No evidence of such co-selection is however available and the issue deserves further study. A similar reasoning is applicable for resistance to erythromycin or tetracycline in isolates from chickens as these substances are scarcely used in broiler production (see Use of antimicrobials). However, resistance to erythromycin or tetracyclines among isolates from pigs (Table ENT IV) may be a consequence of the therapeutic use of these antimicrobials.

Table ENT III. Occurrence of resistance (%) among *Enterococcus faecalis, E. faecium* and *E. hirae* presented by source of isolates and bacterial species. Range of dilutions tested and breakpoints for resistance are given in Table ENT II.

Substance	Cattle			Pigs			Chickens		
	E. faecalis n = 22	*E. faecium* n = 71	*E. hirae* n = 127	*E. faecalis* n = 56	*E. faecium* n = 48	*E. hirae* n = 106	*E. faecalis* n = 47	*E. faecium* n = 151	*E. hirae* n = 28
Ampicillin	0	0	0	0	0	0	0	0	0
Avilamycin	5	3	<1	0	2	<1	0	0	0
Bacitracin	0	1	0	0	4	0	23	20	7
Erythromycin	5	6	0	36	2	4	30	12	25
Flavomycin	14	NR[1]	NR[1]	2	NR[1]	NR[1]	11	NR[1]	NR[1]
Gentamicin	0	0	0	0	0	0	0	0	0
Narasin	0	1	2	2	2	2	43	79	89
Neomycin	0	0	0	7	2	<1	0	0	0
Streptomycin	5	0	0	13	2	<1	9	<1	4
Tetracycline	14	6	<1	68	10	15	60	38	7
Vancomycin	0	0	0	0	0	0	0	0	0
Virginiamycin	NR[1]	1	0	NR[1]	2	0	NR[1]	8	11

[1] Not relevant as susceptibility in some species of *Enterococcus* is inherently low.

Table ENT IV. Occurrence of resistance (%) in *Enterococcus* spp. presented by bacterial species and source of isolates. Range of dilutions tested and breakpoints for resistance are given in Table ENT II.

Substance	***E. faecium***			***E. faecalis***			***E. hirae***		
	Cattle n = 71	Pigs n = 48	Chickens n = 151	Cattle n = 22	Pigs n = 56	Chickens n = 47	Cattle n = 127	Pigs n = 106	Chickens n = 28
Ampicillin	0	0	0	0	0	0	0	0	0
Avilamycin	3	2	0	5	0	0	<1	<1	0
Bacitracin	1	4	20	0	0	23	0	0	7
Erythromycin	6	2	12	5	36	30	0	4	25
Flavomycin	NR[1]	NR[1]	NR[1]	14	2	11	NR[1]	NR[1]	NR[1]
Gentamicin	0	0	0	0	0	0	0	0	0
Narasin	1	2	79	0	2	43	2	2	89
Neomycin	0	2	0	0	7	0	0	<1	0
Streptomycin	0	2	<1	5	13	9	0	<1	4
Tetracycline	6	10	38	14	68	60	<1	15	7
Vancomycin	0	0	0	0	0	0	0	0	0
Virginiamycin	1	2	8	NR[1]	NR[1]	NR[1]	0	0	11

[1] Not relevant as susceptibility in some species of *Enterococcus* is inherently low.

Table ENT V. Number of isolates of *Enterococcus faecalis* resistant to two or more antimicrobials, presented by animal species and resistance phenotype. "R" in hatched fields indicates resistance.

Cattle n = 22	Pigs n = 56	Chickens n = 47	Total n = 125	Resistance pattern[1]						
				Tc	**Em**	**Sm**	**Na**	**Ba**	**Nm**	**Fl**
		2	2	R	R	R	R	R		
		1	1	R	R	R	R			
	1	1	2	R	R		R			
		2	2	R	R		R	R		
		5	5	R	R			R		
	2		2	R	R	R			R	
	15	1	16	R	R					
		2	2	R			R			
		1	1	R			R			R
		1	1	R				R		
	1		1	R		R			R	
1	2		3	R		R				
		1	1		R		R			R
		1	1		R		R	R		
	1		1		R	R			R	
		2	2				R			R
Total										
1	22	20	43							

[1] Tc: tetracycline; Em: erythromycin; Sm: streptomycin; Na: narasin; Ba: bacitracin; Nm: neomycin; Fl: flavomycin.

Table ENT VI. Number of isolates of *Enterococcus faeccium* resistant to two or more antimicrobials, presented by animal species and resistance phenotype. "R" in hatched fields indicates resistance.

Cattle n = 71	Pigs n = 48	Chickens n = 151	Total n = 270	Resistance pattern[1]						
				Tc	Em	Vi	Sm	Na	Ba	Nm
		1	1	R	R	R		R	R	
		2	2	R	R			R	R	
		1	1	R	R				R	
		5	5	R	R			R		
2		2	4	R	R					
		2	2	R		R		R	R	
		9	9	R				R	R	
		5	5	R		R		R		
		25	25	R				R		
1			1	R		R				
		1	1		R	R	R			
		5	5		R			R		
	1		1		R		R			R
		3	3			R		R		
		14	14					R	R	
Total										
3	1	75	79							

[1] Tc: tetracycline; Em: erythromycin; Vi: virginiamycin; Sm: streptomycin; Na: narasin; Ba: bacitracin; Nm: neomycin.

Table ENT VII. Distribution of MICs for *Enterococcus faecalis* from cattle (n=22), pigs (n=56) and chickens (n=47), 2000.

Substance	Breakpoint resistance (mg/L)	Animal species	% Resistant	Distribution (%) of MICs[2] (mg/L)													
				≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	>8	Cattle	0		13.6	18.2	59.1		9.1									
		Pig	0				37.5	62.5										
		Chicken	0			8.5	70.2	19.1	2.1									
Avilamycin	>8	Cattle	5				13.6	36.4	36.4	9.1	4.5							
		Pig	0					48.2	51.8									
		Chicken	0			2.1		80.9	14.9	2.1								
Bacitracin[1]	>32	Cattle	0			9.1	9.1	9.1	27.3	27.3	4.5	13.6						
		Pig	0			1.8	1.8		1.8	17.9	64.3	12.5						
		Chicken	23				8.5	2.1	4.3	23.4	36.2	2.1	23.4					
Erythromycin	>4	Cattle	5		13.6	18.2	9.1	31.8	22.7				4.5					
		Pig	36		1.8	7.1	3.6	33.9	17.9		1.8		33.9					
		Chicken	30			10.6	21.3	27.7	10.6	4.3	4.3	4.3	17.0					
Flavomycin	>32	Cattle	14					4.5	63.6	9.1	9.1				13.6			
		Pig	2					23.2	64.3	8.9		1.8			1.8			
		Chicken	11					6.4	63.8	12.8	4.3	2.1		2.1	8.5			
Gentamicin	>512	Cattle	0				4.5	4.5	9.1	40.9	40.9							
		Pig	0					1.8	3.6	8.9	69.6	16.1						
		Chicken	0				2.1		6.4	36.2	44.7	10.6						
Narasin	>2	Cattle	0	9.1	31.8	40.9	13.6	4.5										
		Pig	2	3.6	10.7	67.9	16.1				1.8							
		Chicken	43	4.3	19.1	21.3	6.4	6.4	14.9	23.4	2.1	2.1						
Neomycin	>1024	Cattle	0					4.5		4.5	4.5	36.4	22.7	27.3				
		Pig	7								1.8	3.6	7.1	41.1			39.3	7.1
		Chicken	0							6.4	6.4	17.0	31.9	34.0			4.3	
Streptomycin	>1024	Cattle	5								4.5	13.6	40.9	27.3			9.1	4.5
		Pig	13									3.6	26.8	53.6			3.6	12.5
		Chicken	9						2.1		2.1	8.5	51.1	27.7				8.5
Tetracycline	>8	Cattle	14			13.6	27.3	45.5			4.5	9.1						
		Pig	68		1.8	1.8	14.3	14.3			3.6	23.2	41.1					
		Chicken	60			2.1	25.5	12.8			12.8	21.3	25.5					
Vancomycin	>16	Cattle	0				27.3	63.6	9.1									
		Pig	0				5.4	80.4	14.3									
		Chicken	0				19.1	68.1	12.8									
Virginiamycin	NR[3]	Cattle	–			9.1	9.1	18.2	13.6	22.7	22.7	4.5						
		Pig	–					1.8	3.6	7.1	80.4	7.1						
		Chicken	–			4.3	2.1	6.4	8.5	19.1	48.9	10.6						

[1] MIC in U/mL, see Appendix 3 for details; [2] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration; [3] Not relevant as susceptibility in *E. faecalis* is inherently low.

Table ENT VIII. Distribution of MICs for *Enterococcus faecium* from cattle (n=71), pigs (n=48) and chickens (n=151), 2000.

Substance	Breakpoint resistance (mg/L)	Animal species	% Resistant	Distribution (%) of MICs[2] (mg/L)														
				≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	>8	Cattle	0		4.2	1.4	12.7	63.4	16.9	1.4								
		Pig	0		6.3	10.4	18.8	58.3	6.3									
		Chicken	0		5.3	19.2	19.9	23.8	23.8	7.9								
Avilamycin	>8	Cattle	3				8.5	22.5	49.3	16.9	1.4	1.4						
		Pig	2				2.1	16.7	39.6	39.6	2.1							
		Chicken	0			0.7	4.0	32.5	57.0	6.0								
Bacitracin[1]	>32	Cattle	1			2.8	25.4	21.1	5.6	12.7	12.7	18.3	1.4					
		Pig	4				6.3	2.1	4.2	12.5	12.5	58.3	4.2					
		Chicken	20			2.0	10.6	4.6	4.0	25.8	22.5	10.6	19.9					
Erythromycin	>4	Cattle	6		5.6	53.5	14.1	9.9	11.3		2.8		2.8					
		Pig	2		2.1	14.6	6.3	25.0	50.0				2.1					
		Chicken	12		2.6	19.9	20.5	31.8	13.2	0.7	2.0		9.3					
Flavomycin	NR[3]	Cattle	–						1.4	14.1	5.6	1.4		1.4	76.1			
		Pig	–						2.1				2.1		95.8			
		Chicken	–						0.7	4.0	3.3	2.6	1.3	2.0	86.1			
Gentamicin	>512	Cattle	0					4.2	5.6	56.3	31.0	2.8						
		Pig	0					4.2	39.6	39.6	14.6	2.1						
		Chicken	0					6.6	33.1	51.0	9.3							
Narasin	>2	Cattle	1	5.6	26.8	23.9	39.4	2.8	1.4									
		Pig	2	2.1	2.1	37.5	54.2	2.1		2.1								
		Chicken	79		0.7	6.6	3.3	9.9	23.2	53.6	2.6							
Neomycin	>1024	Cattle	0					4.2		8.5	15.5	49.3	21.1	1.4				
		Pig	2					2.1	2.1	37.5	35.4	10.4	8.3				2.1	2.1
		Chicken	0						9.3	45.7	27.2	11.3	4.6	2.0				
Streptomycin	>1024	Cattle	0							1.4	2.8	52.1	38.0	5.6				
		Pig	2								14.6	62.5	18.8	2.1				2.1
		Chicken	<1							0.7	14.6	59.6	21.9	2.6				0.7
Tetracycline	>8	Cattle	6		1.4	5.6	62.0	23.9	1.4			2.8	2.8					
		Pig	10			4.2	47.9	35.4	2.1		2.1		8.3					
		Chicken	38		0.7	6.0	47.0	6.0	1.3	1.3	8.6	10.6	18.5					
Vancomycin	>16	Cattle	0				77.5	16.9	4.2	1.4								
		Pig	0				77.1	22.9										
		Chicken	0				79.5	14.6	4.6	1.3								
Virginiamycin	>8	Cattle	1			21.1	21.1	33.8	16.9	5.6			1.4					
		Pig	2			20.8	16.7	25.0	12.5	22.9	2.1							
		Chicken	8			11.3	29.1	31.1	4.0	16.6	6.6	1.3						

[1] MIC in U/mL, see Appendix 3 for details; [2] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration; [3] Not relevant as susceptibility in *E. faecium* is inherently low.

Table ENT IX. Distribution of MICs for *Enterococcus hirae* from cattle (n=127), pigs (n=106) and chickens (n=28), 2000.

Substance	Breakpoint resistance (mg/L)	Animal species	% Resistant	Distribution (%) of MICs[2] (mg/L)														
				≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	>8	Cattle	0		11.8	3.9	15.0	46.5	21.3	1.6								
		Pig	0		46.2	15.1	17.9	17.9	2.8									
		Chicken	0		28.6	10.7	17.9	39.3	3.6									
Avilamycin	>8	Cattle	<1				2.4	27.6	56.7	12.6	0.8							
		Pig	<1			1.9	11.3	31.1	34.0	20.8	0.9							
		Chicken	0				3.6	39.3	57.1									
Bacitracin[1]	>32	Cattle	0				27.6	41.7	24.4	2.4	2.4	1.6						
		Pig	0			1.9	33.0	45.3	16.0	0.9	1.9	0.9						
		Chicken	7				32.1	14.3	7.1	17.9	7.1	14.3	7.1					
Erythromycin	>4	Cattle	0		36.2	60.6	0.8	2.4										
		Pig	4		32.1	61.3		2.8					3.8					
		Chicken	25		21.4	35.7	7.1	3.6	7.1				25.0					
Flavomycin	NR[3]	Cattle	–					0.8	2.4	8.7	3.9	0.8	1.6	1.6	80.3			
		Pig	–								0.9			0.9	98.1			
		Chicken	–						17.9	25.0		3.6	3.6		50.0			
Gentamicin	>512	Cattle	0					4.7	8.7	52.8	27.6	6.3						
		Pig	0						7.5	54.7	35.8	1.9						
		Chicken	0					25.0	17.9	25.0	21.4	10.7						
Narasin	>2	Cattle	2		15.0	36.2	44.1	3.1	1.6									
		Pig	2	7.5	26.4	20.8	40.6	2.8	1.9									
		Chicken	89			7.1	3.6		32.1	50.0	7.1							
Neomycin	>1024	Cattle	0						3.1	11.8	25.2	28.3	22.0	8.7			0.8	
		Pig	<1							4.7	33.0	28.3	31.1	1.9				0.9
		Chicken	0					7.1	21.4	14.3	14.3	17.9	17.9	7.1				
Streptomycin	>1024	Cattle	0								6.3	22.8	60.6	10.2				
		Pig	<1									25.5	66.0	6.6			0.9	0.9
		Chicken	4								17.9	35.7	21.4	21.4				3.6
Tetracycline	>8	Cattle	<1			8.7	43.3	44.9	2.4				0.8					
		Pig	15			12.3	39.6	32.1	0.9			0.9	14.2					
		Chicken	7			7.1	82.1	3.6			3.6		3.6					
Vancomycin	>16	Cattle	0				88.2	11.8										
		Pig	0				86.8	13.2										
		Chicken	0				89.3	10.7										
Virginiamycin	>8	Cattle	0			20.5	9.4	47.2	7.9	15.0								
		Pig	0			38.7	12.3	30.2	6.6	12.3								
		Chicken	11				7.1	60.7	3.6	17.9	10.7							

[1] MIC in U/mL, see Appendix 3 for details; [2] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration; [3] Not relevant as susceptibility in *E. hirae* is inherently low.

Resistance in animal pathogens

Resistance in animal pathogens

Data on antimicrobial susceptibility in animal pathogens were, if not otherwise stated, obtained from the database at SVA. Results presented emanate from isolates tested for antimicrobial susceptibility at the routine bacteriological examination of clinical submissions or post-mortem examinations. Samples were cultured by routine methods and isolates tested for antimicrobial susceptibility by a microdilution method (VetMIC™). Different panels of VetMIC with varying antimicrobials and dilutions were used depending on bacterial species. For further details, see Appendix 3.

Horse

Isolates included

Antimicrobial susceptibility in *Streptococcus zooepidemicus* and *Rhodococcus equi* isolated from bacteriological samples from the respiratory tract and in *Escherichia coli* isolated from samples from the female genital tract are presented.

Results and comments

When interpreting the data, it must be kept in mind that all isolates emanate from diagnostic submissions and that no selection of isolates based on individual animal or stable was possible. The material is likely to represent the central-east part of Sweden rather than the whole country. Further, the material is probably biased towards treatment failures and recurrent infections. Assessment of trends of resistance frequencies is based on the assumption that this bias is of similiar magnitude throughout the period studied.

Among *S. zooepidemicus* from 2000, resistance to the combination trimethoprim-sulfonamide is widespread and appears to have increased markedly since 1992 (Table Horse I).

In the end of the 80s, formulations of trimethoprim-sulfonamides for oral use in horses were introduced on the Swedish market. This has probably contributed to an increased use of this substance class in horses. Thus, the increased frequency of resistance is likely to be a reflection of an increased use. *S. zooepidemicus* has an inherent low susceptibility to aminoglycosides (gentamicin, neomycin) and therefore, assessment of trends is not relevant for these substance groups. In the context of choice of antimicrobial for therapy, the uniform susceptibility to penicillin among *S. zooepidemicus* must be emphasised.

R. equi has an inherent low susceptibility to most antimicrobials (Table Horse II). Classification as resistant is therefore not relevant. Only for erythromycin and the aminoglycosides (e.g. gentamicin), the inherent susceptibility is such that the MIC range is below concentrations that can be obtained during therapy. Erythromycin and lately gentamicin has been used for therapy in combination with rifampin. The frequency of acquired resistance to either of the two first substances is still very low.

In *E. coli,* frequency of resistance to streptomycin is high (20-31%) (Table Horse III). For ampicillin and trimethoprim-sulfa, the figures are relatively high (11-19%). Interestingly, only 7% of the isolates are resistant to tetracycline. This is low in comparison to figures obtained for *E. coli* from diagnostic submissions from other animal species and might be a reflection of the limited use of tetracyclines in horses. No obvious trends can be detected in the material.

Table Horse I. Occurrence of resistance among *Streptococcus zooepidemicus* from horses the years 1992-93, 1996 and 2000 and distribution of MICs among the isolates from 2000. All isolates are from diagnostic submissions of samples from the respiratory tract.

Substance	Breakpoint resistance (mg/L)	Percent resistant			Distribution (%) of MICs[1] 2000 (mg/L)										
		1992-93 n = 100	1996 n = 160	2000 n = 301	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	>16	0	0	0		97.3	0.7			1.7	0.3				
Chloramphenicol	>8	1	<1	<1[2]						23.0	74.3	2.0	0.3	0.3	
Clindamycin	>4	2	1	<1[3]					97.3		2.0	0.7			
Erythromycin	>4	1	1	<1[2]				98.7		1.0		0.3			
Gentamicin	NR[3]	–	–	–					0.3		4.0	6.3	37.5	51.8	
Neomycin	NR	–	–	–						0.3	1.0	2.3	1.3	8.0	87.0
Penicillin	>8	0	<1	0[4]	98.0	0.7		0.3	1.0						
Spiramycin	>16	1	1	<1[4]							94.6	4.3	0.7		0.3
Tetracycline	>8	4	2	4[4]					25.1	3.7	66.2	1.0	1.0	3.0	
Trim-Sulfa[7]	>8	0	2[6]	49[5]		9.7	1.7	21.5	8.7			9.4	49.0		

[1] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration; [2] 300 isolates tested; [3] Not relevant as the inherent susceptibility is such that the MIC range is above concentrations that can be obtained during therapy; [4] 299 isolates tested; [5] 298 isolates tested; [6] 159 isolates tested; [7] Tested in concentration ratio 1/20 (trimethoprim/sulfamethoxazole), concentration of trimethoprim given.

Table Horse II. Occurrence of resistance among *Rhodococcus equi* from horses the years 1992-96 and 1997-2000 and distribution of MICs among the isolates from 1997-2000. All isolates are from diagnostic submissions of samples from the respiratory tract.

Substance	Breakpoint resistance (mg/L)	Percent resistant		Distribution (%) of MICs[1] 1997-2000 (mg/L)												
		1992-96 n = 46	1997-00 n = 73	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ampicillin	NR[2]	–	–						2.8	26.4	40.3	25.0	5.6			
Chloramphenicol	>8	33	25							19.2	56.2	23.3	1.4			
Clindamycin	NR	–	–					4.1	24.7	54.8	16.4					
Enrofloxacin	NR	–	–				27.3	57.6	12.1	3.0						
Erythromycin	>4	2	1				87.7	9.6	1.4		1.4					
Gentamicin	>16	2	0[4]					84.7		15.3						
Neomycin	>32	0	0						97.3	1.4		1.4				
Penicillin	NR	–	–					11.0	19.2	32.9	21.9	15.1				
Spiramycin	>16	52	70								6.8	23.3	52.1	17.8		
Streptomycin	>32	4[3]	2[5]					7.7	58.5	18.5	9.2	4.6		1.5		
Tetracycline	NR	–	–					1.4		5.5	43.8	45.2	4.1			
Trim-Sulfa[6]	>8	17	8		2.7	4.1	15.1	32.9	16.4	5.5	15.1	8.2				

[1] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration; [2] Not relevant as the inherent susceptibility is such that the MIC range is above concentrations that can be obtained during therapy; [3] 45 isolates tested; [4] 72 isolates tested; [5] 65 isolates tested; [6] Tested in concentration ratio 1/20 (trimethoprim/sulfamethoxazole), concentration of trimethoprim given.

Table Horse III. Occurrence of resistance among *Escherichia coli* from horses the years 1992-96 and 1997-2000 and distribution of MICs among the isolates from 1997-2000. All isolates are from diagnostic submissions of samples from the female genital tract.

Substance	Breakpoint resistance (mg/L)	Percent resistant		Distribution (%) of MICs[1] 1997-2000 (mg/L)									
		1992-96 n = 176	1997-00 n = 323	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	>8	19	11					32.8	49.8	6.5	0.9	9.9	
Chloramphenicol	>8	5	6					5.3	43.7	45.5	3.1	2.5	
Enrofloxacin	>0.5	2	1		97.2	1.5	0.6	0.3	0.3				
Gentamicin	>8	3	4				55.4		38.7	1.5	0.6	3.7	
Neomycin	>32	2	3					65.9	5.0	25.1	0.9	0.3	2.8
Nitrofurantoin	>32	2	2								95.7	2.5	1.9
Streptomycin	>32	31	20					3.1	2.8	57.9	15.5	0.6	20.1
Tetracycline	>8	7	7				5.9	9.6	75.2	2.2	0.6	6.5	
Trim-Sulfa[3]	>8	12[2]	15	79.2	0.6	3.1	0.6	0.3		1.2	14.9		

[1] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration; [2] 175 isolates tested; [3] Tested in concentration ratio 1/20 (trimethoprim/sulfamethoxazole), concentration of trimethoprim given.

Pig

Isolates included

Data on antimicrobial susceptibility in *Escherichia coli* and *Actinobacillus pleuropneumoniae* from pigs for the years 1992-2000 were obtained from the database at SVA and emanates from isolates from clinical submissions or post mortem examinations. *E. coli* was isolated from samples from the gastro-intestinal tract (gut content, faecal samples or mesenteric lymph nodes) and *A. pleuropneumoniae* from the respiratory tract (nasal swabs and lung, including regional lymph nodes) of pigs.

The *E. coli* material from 1989-91 also includes isolates from clinical submissions to SVA. The material was however entered into a separate data file and includes results for all *E. coli* that were isolated from pigs irrespective of type of material sampled.

Isolates of *Brachyspira hyodysenteriae* emanate from clinical submissions of pig faecal samples. All isolates of *B. hyodysenteriae* obtained in pure culture year 2000 were tested for susceptibility using a specially adapted broth dilution method (see Appendix 3 for details).

Results and comments

Isolates from all parts of Sweden are included. However, when interpreting data it must be borne in mind that the isolates emanate from diagnostic submissions. No selection of isolates based on individual herds was possible. Further, it is probable that the bulk of isolates is from herds with diarrhoeal (*E. coli* and *B. hyodysenteriae*) or respiratory (*A. pleuropneumoniae*) problems. In the year 2000, over 1000 isolates of *E. coli* from pigs were serotyped at the SVA. Susceptibility tests were requested for no more than 1/10 of the isolates, indicating a bias towards isolates from herds with diarrhoeal problems. Assessment of trends for *E. coli* is made under the assumption that this bias is of similar magnitude throughout the period studies.

No obvious trends in occurrence of resistance among *E. coli* can be discerned (Table Pig I). Frequencies of resistance to tetracycline and trimethoprim-sulfonamides are around 30% and 15%, respectively. Both these groups of antimicrobials are used in pig production, the latter especially for treatment of enteric infections. Use of streptomycin in pig production is thought to be low and limited to injectables, in combination with penicillin, or to oral treatment of neonatal diarrhoea. Therefore, the high frequency of resistance to streptomycin is probably not a reflection of the use of the substance in pig production. Instead, the level of resistance might be explained by resistance genes to streptomycin being linked to genes for resistance to sulfonamides, trimethoprim and/or tetracyclines. Similarly, co-selection of linked genes coding for resistance to several drugs is a plausible explanation for the surprisingly high frequencies of resistance to ampicillin and chloramphenicol (around 10%), as these antimicrobials are used to a very limited extent (ampicillin) or not at all (chloramphenicol) in pig production in Sweden. The presented results tally with those of previous investigations from Sweden (Melin *et al.*, 1996 and 2000).

Table Pig I. Occurrence of resistance among *Escherichia coli* in pigs the years 1989-91, 1992-96 and 1997-2000 and distribution of MICs among the isolates from 1997-2000. All isolates are from the gastro-intestinal tract, isolated in samples for diagnostic submissions or from post mortem investigations.

Substance	Breakpoint resistance (mg/L)	Percent resistant			Distribution (%) of MICs[1] 1997-2000 (mg/L)									
		1989-91 n = 248	1992-96 n = 301	1997-00 n = 399	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	>8	7	15	13					40.1	40.9	6.5	0.3	12.3	
Chloramphenicol	>8	11	7[3]	13					5.3	41.6	39.8	1.0	12.3	
Enrofloxacin	>0.5	1[2]	4	3		95.2	1.8	1.8	0.5	0.8				
Gentamicin	>8	1	0[3]	1[4]				52.5		44.5	2.0	1.0		
Neomycin	>32	5	6	5					61.7		31.1	1.3	1.0	5.0
Nitrofurantoin	>32	4	4	5								79.7	15.8	4.5
Streptomycin	>32	44	40	34					5.0		43.1	13.0	5.0	33.8
Tetracycline	>8	28	30	32				3.5		62.2	2.8	2.5	29.1	
Trim-Sulfa[5]	>8	15	15	12[4]	70.6		13.3	3.0			0.8	12.3		

[1] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration; [2] 227 isolates tested; [3] 300 isolates tested; [4] 398 isolates tested; [5] Tested in concentration ratio 1/20 (trimethoprim/sulfamethoxazole), concentration of trimethoprim given.

Only a very limited number of isolates of *A. pleuropneumoniae* have been tested for antimicrobial susceptibility over the years (Table Pig II). However, the data tally with previous reports on antimicrobial susceptibility in this pathogen (Landén *et al.,* 2000), showing no indications of acquired resistance to relevant antimicrobials in Swedish isolates of *A. pleuropneumoniae.* Nonetheless, a somewhat higher rate of specific diagnostics of the infection and subsequent susceptibility testing is desirable if emerging resistance is to be detected early enough to counteract its spread.

The breakpoints for antimicrobial resistance for *B. hyodysenteriae*, suggested in Table Pig III, are based on the MIC distribution for the tested isolates. The level of resistance to tylosin was high, 72%, and appears to have increased substantially since 1988-90 when 20% of the isolates had MICs >16 mg/L with an agar dilution technique (Gunnarsson *et al,*. 1991). Considering tiamulin, two isolates deviated from the susceptible population. The MIC for these two isolates was 1 mg/L. When monitoring antimicrobial susceptibility in *B. hyodysenteriae*, special attention should be paid to emergence of such isolates with decreased susceptibility.

Table Pig II. Occurrence of resistance and distribution of MICs among *Actinobacillus pleuropneumoniae* in pigs the years 1992-00. All isolates are from the respiratory tract, isolated in samples from diagnostic submissions or from post mortem investigations.

Substance	Breakpoint resistance (mg/L)	Percent resistant	Distribution (%) of MICs[1] 1992-2000 (mg/L)												
		n = 18	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ampicillin	>16	0		16.7	33.3	44.4		5.6							
Chloramphenicol	>8	0						88.9	11.1						
Clindamycin	NR[2]	–					5.6	11.1	50.0	33.3					
Enrofloxacin	>2	0			94.4		5.6								
Erythromycin	NR	–				5.6		11.1	27.8	55.6					
Gentamicin	NR	–					11.1		27.8	33.3	16.7	11.1			
Neomycin	NR	–									50.0	38.9	11.1		
Nitrofurantoin	>32	0									100.0				
Penicillin	>8	0	16.7		22.2	33.3	22.2		5.6						
Spiramycin	NR	–							5.6			33.3	61.1		
Streptomycin	NR	–								11.1	33.3	44.4	11.1		
Tetracycline	>8	11					38.9	33.3	11.1	5.6	5.6	5.6			
Trim-Sulfa[3]	>8	0		41.2	23.5	11.8			17.6	5.9					

[1] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration; [2] Not relevant as the inherent susceptibility is such that the MIC range is above concentrations that can be obtained during therapy; [3] Tested in concentration ratio 1/20 (trimethoprim/sulfamethoxazole), concentration of trimethoprim given.

Table Pig III. Occurrence of resistance among *Brachyspira hyodysenteriae* in pigs and distribution of MICs among the isolates year 2000. Isolates emanate from diagnostic submissions of faecal samples.

Substance	No. of isolates tested	Breakpoint resistance (mg/L)	Percent resistant	Distribution (%) of MICs[1] (mg/L)														
				≤0.016	0.031	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	>256
Clindamycin	37	>0.5	68		2.7	10.8	13.5	5.4		5.4	8.1	8.1	45.9						
Erythromycin	36	>32	75									5.6	8.3	5.6	5.6			2.8	72.2
Tiamulin	50	>2	0	2.0	12.0	30.0	34.0	18.0		4.0									
Tylosin	50	>16	72								2.0	10.0	12.0	4.0				20.0	52.0
Valnemulin	34	>1	0	17.6	32.4	44.1	2.9	2.9											
Virginiamycin	36	>8	6							8.3	41.7	44.4		5.6					

[1] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration.

Dog

Isolates included

Antimicrobial susceptibility in *Staphylococcus intermedius*, isolated from bacteriological samples from skin, and in *E. coli* isolated from urine are presented.

Results and comments

The data presented emanate from diagnostic submissions and might include repeat isolates from the same patients. It is probable that isolates from dogs in the central-eastern part of Sweden are over-represented. Further, it is also probable that there is a bias towards isolates from dogs with recurrent disease or from therapeutic failures. Inference regarding trends in resistance is based on the assumption that these biases are of a similar magnitude throughout the study period.

Among *S. intermedius,* the frequency of resistance to penicillin (β-lactamase production) is high over the period (>75%) (Table Dog I). In fact, similar rates were reported already in 1978. Thus, β-lactam antibiotics are not likely to be efficient for treatment of recurrent pyodermas in dogs. However, this group of antimicrobials is widely used for other indications. About half of the antimicrobials prescribed for dogs and/or cats in Sweden are β-lactam antimicrobials, mostly penicillin and aminopenicillins (Odensvik *et al.*, 2001). This may explain the stable maintenance of this resistance determinant in canine staphylococci.

Resistance against macrolides (erythromycin and spiramycin), lincosamides (clindamycin) and tetracycline is high (23–33%) and seems to have increased over the monitored period (Table Dog I). The observation concurs with earlier reported findings (Sternberg, 1999). In staphylococci, *erm* genes commonly convey resistance to macrolides. Constitutive expression of such genes also conveys resistance to lincosamides. In the present material, 72% of the macrolide-resistant isolates were also resistant to lincosamides indicating a high frequency of constitutively expressed *erm* genes. Further, 68% of the isolates resistant to macrolides-lincosamides were also resistant to tetracycline (14% of the total material from 2000). This is consistent with earlier observations from similar materials (Hansson *et al.*, 1997). Macrolides and lincosamides are commonly prescribed to dogs (Odensvik *et al.*, 2001) and it is plausible that the observed increase in resistance is related to this use.

Among *E. coli,* the levels of resistance are slightly lower than among *S. intermedius* (Table Dog II). However, resistance against ampicillin, streptomycin, tetracycline or the combination trimethoprim-sulfamethoxazole occur in 10-20% of the isolates. With the possible exception of streptomycin, all these antimicrobials are commonly used for pets. Resistance frequencies to substances of low use (gentamicin, neomycin and nitrofurantoin) are low (<5%).

Table Dog I. Occurrence of resistance among *Staphylococcus intermedius* in dogs the years 1992-93, 1995 and 2000 and distribution of MICs for the isolates from 2000. All isolates are from diagnostic submissions of samples from skin.

Substance	Breakpoint resistance (mg/L)	Percent resistant			Distribution (%) of MICs[1] 2000 (mg/L)									
		1992-93 n = 204	1995 n = 94	2000 n = 145	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Cephalothin	>16	0	0	0						99.3		0.7		
Chloramphenicol	>8	3[4]	2	4					2.8	62.1	31.0	1.4	2.8	
Clindamycin	>4	12	13	22				73.1		4.8	22.1			
Erythromycin	>4	19	25	30			59.3	10.3	0.7		29.7			
Gentamicin	>16	0	0	0[3]				95.8		2.8	1.4			
Neomycin	>32	<1	1	0					73.8	0.7	22.1	2.8	0.7	
Nitrofurantoin	>32	1	0	<1								98.6	0.7	0.7
Oxacillin	>1	1	0	1			97.9	0.7	1.4					
Penicillin		77[2,5]	71[2]	75[2]										
Spiramycin	>16	20	25	30						37.2	31.7	1.4		29.7
Tetracycline	>8	24	25	33				64.8		2.1		2.1	31.0	
Trim/Sulfa[6]	>8	1[4]	0	<1[3]	35.7		40.6	21.7			1.4	0.7		

[1] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration; [2] denotes β-lactamase production; [3] 143 isolates tested; [4] 203 isolates tested; [5] 200 isolates tested; [6] Tested in concentration ratio 1/20 (trimethoprim/sulfamethoxazole), concentration of trimethoprim given.

The frequency of resistance to fluoroquinolones (enrofloxacin) is surprisingly high throughout the observed period (7-9%). However, it must be observed that the breakpoints chosen for this report are based on microbiological criteria. Thus, using breakpoints based on pharmacokinetics of these drugs (>2mg/L) to define resistance, the frequency is only 3%.

Nonetheless, as sales of fluoroquinolones for dogs and cats have increased steadily during the 90s (Odensvik *et al.*, 2001), the development must be monitored closely. No obvious trends in occurrence of resistance can be discerned in the material and the results are consistent with data presented in a study from 1993 (Franklin *et al.*, 1993).

Table Dog II. Occurrence of resistance among *Escherichia coli* in dogs the years 1992-93, 1995 and 2000 and distribution of MICs for the isolates from 2000. All isolates are from diagnostic submissions of urinary samples.

Substance	Breakpoint resistance (mg/L)	Percent resistant			Distribution (%) of MICs[1] 2000 (mg/L)									
		1992-93 n = 150	1995 n = 96	2000 n = 185	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	>8	19	24	20[3]					25.4	43.8	10.8	1.1	18.9	
Chloramphenicol	>8	17	20	7					7.0	44.1	41.9	1.6	5.4	
Enrofloxacin	>0.5	7[2]	5	9		87.6	3.2	4.8	1.1	3.2				
Gentamicin	>8	1[2]	2	3[3]				27.6		67.6	1.6	1.6	1.6	
Neomycin	>32	3	3	5					60.8	3.2	30.1	0.5	0.5	4.8
Nitrofurantoin	>32	2	3	2								96.2	2.2	1.6
Streptomycin	>32	16	28	17					3.2	0.5	61.3	16.1	1.6	17.2
Tetracycline	>8	16[2]	22	13				10.2	3.2	71.5	2.2	0.5	12.4	
Trim-Sulfa[4]	>8	8	12	12	76.9	0.5	7.5	2.2	0.5			12.4		

[1] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration; [2] 149 isolates tested; [3] 184 isolates tested; [4] Tested in concentration ratio 1/20 (trimethoprim/sulfamethoxazole), concentration of trimethoprim given.

Cattle

Isolates included

Data on antimicrobial resistance in *Pasteurella* spp. emanate from a field study on respiratory pathogens in calves conducted 1997 to 2000 (Bengtsson and Viring, 2000). In the study, 314 calves, 1-7 months old, from 43 different herds in the central and southern parts of Sweden were sampled. Bacteriological samples were taken from the nasal cavity (swabs) and from the lower respiratory tract (tracheo-bronchial lavage).

In 178 calves, sampling was performed twice with four weeks interval. Calves with and without clinical signs of respiratory disease were sampled. Samples were cultured at SVA according to standard methods. In total 168 isolates of *Pasteurella* spp. were obtained from nasal swabs and 86 from the lower respiratory tract. Isolates were tested for antimicrobial susceptibility with a microdilution method (VetMIC™).

Results and comments

Occurrence of antimicrobial resistance among isolates of *Pasteurella* spp. was rare (Table Cattle I). Resistance against penicillin and tetracycline, the substances commonly used for therapy of respiratory disease in calves, was not detected. Similar results were obtained in a study in 1988 (Franklin *et al.*, 1988). As the isolates do not emanate from herds where therapy failure is common, the results might not reflect the situation in herds where response to therapy is poor.

However, in a small material of *Pasteurella* spp., where susceptibility data were extracted from the database at SVA, no isolates were resistant to penicillin or tetracycline, but resistance to the combination trimethoprim-sulfamethoxazole occurred in 19% and resistance to streptomycin in 25% of the isolates. The material consisted of 28 isolates from post mortem investigations of calves with respiratory disease in the years 1992-00. It is conceivable that the isolates largely emanated from therapeutic failures. Consequently, there is no indication that therapeutic failures are due to resistance against penicillin or tetracycline.

Table Cattle I. Occurrence of resistance and distribution of MICs among *Pasteurella* spp. isolated from nasal swabs or tracheo-bronchial lavage from the respiratory tract of calves the years 1997-00.

Substance	Breakpoint resistance (mg/L)	Percent resistant	Distribution (%) of MICs[1] 1997-2000 (mg/L)												
		1997-00 n = 254	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ampicillin	>16	0		29.5	54.3	14.6	0.8	0.4	0.4						
Cephalothin	>16	0							100.0						
Enrofloxacin	>2	<1			98.0	1.6			0.4						
Penicillin	>8	0	29.9	50.4	18.5	1.2									
Spiramycin	NR[2]	–							0.8	3.5	8.7	33.9	53.1		
Streptomycin	>32	4						15.4	37.0	24.4	15.7	3.9	1.6		2.0
Tetracycline	>8	0				30.7	54.3	11.8	3.1						
Trim-Sulfa[3]	>8	1	71.3	7.9	7.5	5.5	3.9	0.4	2.0	0.4	1.2				

[1] Hatched fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration; [2] Not relevant as the inherent susceptibility is such that the MIC range is above concentrations that can be obtained during therapy; [3] Tested in concentration ratio 1/20 (trimethoprim/sulfamethoxazole), concentration of trimethoprim given.

Appendix 1: Demographic data

Statistics on animal numbers and agricultural holdings with animals are provided by Statistics Sweden in collaboration with the Board of Agriculture. Figures are based either on total census or on samples of the populations. The countings are made in June and/or December. Statistics are published annually as a Yearbook of Agricultural Statistics. Figures on number of animals slaughtered in 2000 and number of chickens slaughtered all years was provided by the National Food Administration.

The number of dairy cows has decreased by 35% since 1980 (Table AP1 I). Most of the decrease took place from 1985 to 1987 and from 1990 to 1991. The number of beef cows has more than doubled since 1980. The increase was most marked in the beginning of the 90s. The number of dairy herds has decreased by 70% since 1980 (Table AP1 II). The herd size for both beef and dairy cows has more than doubled since 1980. The average size for dairy herds in 1999 was 32 cows.

The total number of pigs slaughtered decreased during the 80s but was rather constant over most of the 90s (Table AP1 III). From 1999 until 2000, the number dropped by 9%. The recent decrease is explained by decreased profitability. The number of holdings with pigs has decreased by about 75% since 1980 (Table AP1 II). The marked reduction in the beginning of the 90s is largely explained by the introduction of sow-pool systems. The average number of sows per herd has tripled and was in 1999 55 sows.

The production of chickens for slaughter has almost doubled from 1980 until 2000 (Table AP1 III).

Table AP1 I. Number of livestock (in thousands) from 1980-2000[1]. The figures represent census figures from counts of all, or samples of the population in the given years.

	1980	1985	1990	1995	1999	2000
Cattle						
Dairy cows	*656*	*646*	*576*	*482*	*449*	*428*
Beef cows	*71*	*59*	*75*	*157*	*165*	*167*
Other cattle > 1 year	*614*	*570*	*544*	*596*	*600*	*589*
Calves < 1 year	*595*	*563*	*524*	*542*	*499*	*500*
Total, cattle	**1 935**	**1 837**	**1 718**	**1 777**	**1 713**	**1 685**
Pigs						
Boars	*12*	*11*	*9*	*8*	*4*	*4*
Sows	*278*	*249*	*221*	*237*	*220*	*202*
Fattening pigs >20 kg [2]	*1 254*	*1 127*	*1 025*	*1 300*	*1 240*	*1 146*
Piglets <20 kg [3]	*1 170*	*1 113*	*1 009*	*769*	*651*	*566*
Total, pigs	**2 714**	**2 500**	**2 264**	**2 313**	**2 115**	**1 918**
Sheep						
Ewes and rams	*161*	*173*	*161*	*195*	*194*	
Lambs	*231*	*252*	*244*	*266*	*244*	
Total, sheep	**392**	**425**	**405**	**462**	**437**	
Laying hens						
Hens	*5 937*	*6 548*	*6 392*	*6 100*	*5 648*	
Chickens reared for laying	*2 636*	*2 159*	*2 176*	*1 812*	*2 202*	
Total, hens	**8 573**	**8 708**	**8 568**	**7 912**	**7 850**	

[1] Source: Yearbook of Agricultural Statistics, Sweden 1981, 1986, 1991, 1996 and 2000. For 1980 and 1985 only cattle and sheep at premises with more than 2 ha counted; [2] Before 1995, the figure denotes pigs above 3 months of age; [3] Before 1995, the figure denotes pigs below 3 months of age.

Table AP1 II. Number of holdings with animals from 1980-1999[1].

	1980	1985	1990	1995	1999
Cattle					
Dairy cows	*44 100*	*30 100*	*25 900*	*17 700*	*14 000*
Beef cows	*12 400*	*10 300*	*10 900*	*17 100*	*14 300*
Other cattle >1 year	*63 200*	*52 700*	*42 700*	*39 200*	*32 200*
Calves <1 year	*62 300*	*52 000*	*42 000*	*36 500*	*29 200*
Total, cattle	70 500	58 900	47 300	42 000	34 000
Sheep, excluding lambs	10 100	10 500	9 700	10 000	8 200
Pigs	26 100	19 900	14 300	10 800	6 000
Laying hens	23 600	17 500	12 900	9 600	6 400
Chickens reared for laying	5 100	2 700	1 900	1 400	800
Without cattle, sheep, pigs or hens	32 300	35 400	36 700	33 600	36 800

[1] Source: Yearbook of Agricultural Statistics, Sweden 1981, 1986, 1991, 1996 and 2000.

Table AP1 III. Number of animals slaughtered (in thousands) from 1980-2000[1].

	1980	1985	1990	1995	1999	2000
Cattle						
Cattle >1 year	*574*	*584*	*523*	*502*	*482*	*492*
Calves < 1 year	*130*	*138*	*70*	*46*	*39*	*39*
Total, cattle	704	722	592	548	521	531
Pigs	4 153	4 283	3 659	3 763	3 815	3 247
Sheep	302	328	280	145	198	208
Chickens (broiler)	40 466	36 410	38 577	60 300	66 145	68 616

[1] Source: National Food Administration

Appendix 2: Materials and methods, use of antimicrobials

Wholesaler data

Antimicrobial drugs used in veterinary medicine in Sweden are only available on veterinary prescription. Furthermore, antimicrobial drugs have to be dispensed through pharmacies, which in turn are supplied solely by two drug wholesalers. Sales statistics are available from Apoteket AB (The National Corporation of Swedish Pharmacies).

These statistics describe the amount of medicinal products sold from the wholesalers to the pharmacies. As the pharmacies stock a limited number of veterinary drugs, the wholesalers´statistics can be used as an approximation on the actual usage of antimicrobials. Wholesalers´ data have a very high degree of completeness. This is explained by the fact that the wholesalers represent the entire drug distribution network, i.e., there are no other sources of antimicrobials for use or prescription by veterinarians. Sweden has a long tradition in drug consumption statistics. Apoteket AB, former Apoteksbolaget AB, has since 1976 followed the consumption of drugs for use in humans mainly by using wholesalers´ statistics.

However, it has never been determined in detail whether Apoteket AB is responsible or not for producing sales statistics of veterinary medicinal products. Further, no governmental authority has yet been given the responsibility to gather or supervise such data. Notwithstanding, SVA and Apoteket AB have collaborated over the years and data on the total use of antimicrobials for animals in Sweden are available since 1980 (Wierup *et al.*, 1987 and 1989; Björnerot *et al.*, 1996; Odensvik and Greko 1998; Odensvik 1999 and 2000).

Classification of drugs

Veterinary medicinal drugs are classified according to the Anatomical Therapeutic Chemical veterinary classification system (ATCvet). The system is based on the same main principles as the ATC classification system for substances used in human medicine. In both the ATC and ATCvet systems, drugs are divided into groups according to their therapeutic use. First, they are divided into 15 anatomical groups, classified as QA-QV in the ATCvet system (without Q in the human system), on basis of their main therapeutic use. Thereafter subdivision is made according to therapeutic main groups, which is followed by a further division in chemical/therapeutic subgroups.

Antimicrobials are classified in the QJ group - general anti-infectives for systemic use. However, antimicrobials can also be found in other groups such as QA (alimentary tract and metabolism), QD (dermatologicals), QG (genito-urinary system), QP (antiparsitic) and QS (sensory organs) depending on the therapeutic use (Nordic council of medicines, 1999).

Inclusion criteria

With the exception of dermatologicals, all veterinary antimicrobial drugs authorised for use in animals were included (i.e., ATC codes QA, QG and QP). Veterinary drugs are preparations authorised for use in animals only. Human drugs may be authorised not only for humans, but for animals as well. This latter category is not included in the statistics. However, no such drugs are authorised for use in the major food producing animal species, and the volume sold is very limited.

Prescription data

Electronic records of veterinary prescriptions are kept by the pharmacies in connection with the dispensing process. These records include information on animal species, prescribed drug, strength, formulation, package size and number of packages dispensed. Since 1996, these data are recorded in a centralised data system owned by Apoteket AB.

It should be emphasised that the information in the database does not include names of animal owners or veterinarians. This system was used to select data on prescriptions of antimicrobials for birds of different categories.

Distribution of veterinary medicines in Sweden

Marketing of drugs in Sweden is regulated by the Medicinal Products Act, which applies both to human and veterinary drugs. According to the Act, a medicinal product may not be sold until it has been granted marketing authorisation by the Medical Products Agency (MPA). The MPA has issued provisions concerning authorisation, distribution and prescription of veterinary medicinal products.

The state-owned Apoteket AB has exclusive rights regarding retail sales of medicines in Sweden. Apoteket AB operates according to guidelines set out in an agreement with the State. According to the Act only pharmacies run by Apoteket AB are permitted to sell prescription only medicines. This implies that veterinarians in Sweden are not permitted to sell drugs, although they may for practical reasons hand over medicines for emergency use. Veterinarians are, however, under no conditions permitted to make a profit from dispensing medicines.

Appendix 3: Materials and methods, resistance monitoring

Sampling strategy

Zoonotic bacteria

Isolates of *Salmonella* from warm-blooded animals (wild and domesticated) are included. Salmonellosis in animals is a notifiable disease in Sweden and confirmation at SVA of all cases, including those collected in the Swedish *Salmonella* control programme, is mandatory. The first isolate from each animal species in each notified incident is included in the material. Therefore, the material is thought to be representative for *Salmonella* prevalent among animals in Sweden.

Indicator bacteria

Indicator bacteria, *Escherichia coli* and *Enterococcus* spp., were isolated from samples of intestinal content (caecum or colon) from healthy fattening pigs, broiler chickens and cattle up to 12 months old. Samples were collected at slaughter except 140 samples from cattle, 43% of the total number of samples from cattle. These were faecal samples from healthy live animals collected at the farm of origin.

To obtain a representative material of randomly selected samples from the three animal species, the number collected at each abattoir was determined in proportion to the number of animals slaughtered at the abattoir each year. Five abattoirs for chickens, five for pigs and 14 for cattle participated in the collection of samples. The abattoirs represented in the monitoring programme are geographically separated and accounted for 85, 63 and 72 percent, respectively, of the total slaughter in Sweden during 1998-1999.

Sampling was performed weekly, with exceptions for holidays and summer vacations, by meat inspection staff or abattoir personnel. Each sample collected from pigs and cattle represents a unique herd whereas each sample from chickens represents a unique flock, but not necessarily a unique herd. By these measures, bacterial isolates included are from healthy individuals randomly selected among Swedish herds/flocks.

Animal pathogens

With the exception of *Pasteurella* spp. from cattle, isolates of animal pathogens included emanate from routine bacteriological examinations of clinical submissions or post-mortem examinations at SVA.
Isolates included are *Streptococcus zooepidemicus* and *Rhodococcus equi* from the respiratory tract of horses and *E. coli* from the genital tract of mares. From pigs, *E. coli* from the gastro-intestinal tract (gut content, faecal samples or mesenteric lymph nodes), *Actinobacillus pleuropneumoniae* from the respiratory tract (nasal swabs and lung, including regional lymph nodes) and *Brachyspira hyodysenteriae* isolated from faecal samples are presented. Further, from dogs *Staphylococcus intermedius* isolated from skin samples and *E. coli* isolated from samples of urine are included. *Pasteurella* spp. from cattle were collected in a field study on respiratory pathogens (see Resistance in animal pathogens for details).

Isolation and identification of bacteria

Zoonotic bacteria

Salmonella

Salmonella was isolated and tentatively identified at SVA or at regional laboratories according to standard procedures. All samples within official control programmes are cultured according to the procedures laid down by the Nordic Committee in Food Analysis, 1999).

Confirmation and serotyping of isolates is performed at the Department of Bacteriology, SVA following to standard procedures according to Kaufmann and White. Phagetyping of *S.* Typhimurium and *S.* Enteritidis is performed by Swedish Institute for Infectious Disease Control (SMI), Stockholm.

Indicator bacteria

Escherichia coli

Intestinal content (caecum or colon) from cattle, pigs and chicken was diluted (1/10) in phosphate/sodium chloride buffer, spread onto MacConkey agar and incubated overnight at 37˚C. One large red colony typical for *E. coli* was sub-cultivated on blood agar. *E. coli* was identified by positive reactions for indole and p-nitrophenyl-β-D-glucopyranosiduronic acid (PGUA). Only isolates fulfilling these criteria were included and tested for susceptibility. Isolates were stored at -70˚C.

Enterococci spp.

Intestinal content (caecum or colon) from cattle, pigs and chicken was diluted (1/10) in phosphate/sodium chloride buffer and cultured both on solid media without vancomycin and selectively enriched in broth supplemented with vancomycin.

Culture without vancomycin: 0.1 mL of the diluted faecal material was spread onto Slanetz-Bartley (SlaBa) agar and incubated 48 hours at 37˚C. One colony, randomly chosen, was sub-cultured on bile-esculin agar and blood agar (37˚C, 24-48 hours). In case of dubious results, the isolate was tested with pyrrolidonyl arylamidase (PYR). Only isolates with positive reaction in the PYR-test were included. Bile-esculine positive colonies were tested for antimicrobial susceptibility and identified to species using the following biochemical tests: mannitol, sorbitol, arabinose, saccharose, ribose, methyl-α-D-glucopyranoside and raffinose. Results were interpreted according to Devriese *et al.* (1993).

Enrichment in broth with vancomycin: 5 mL of the diluted faecal material (see above) was inoculated in 5 mL enrichment broth (Enterococcosel) supplemented with 16 mg/L vancomycin (final concentration: 8 mg/L vancomycin) and incubated in 37˚C, 24 hours. 0.1 mL was spread onto SlaBa agar supplemented with 8 mg/L vancomycin and incubated in 37˚C, 48 hours.

One colony, randomly chosen, was sub-cultivated on bile-esculin agar and blood agar (37˚C, 24-48 hours). Bile-esculin positive colonies were tested for antimicrobial susceptibility and at the same time species identified as above. Isolates were stored at -70˚C.

Isolates resistant to vancomycin were genotyped with PCR for the *vanA* gene. Identification of the genes *vanB*, *vanC-1* and *vanC-2/3* and species *E. faecium* and *E. faecalis* was also possible in the same PCR reaction (Dutka-Malen *et al.*, 1995).

Animal pathogens

Animal pathogens were isolated and identified at the Dept. of Bacteriology, SVA following standard procedures.

Susceptibility testing

Antimicrobial susceptibility testing was performed by a microdilution method, VetMIC™, where antimicrobials were dried in serial twofold dilutions in microtitre wells. Different panels were used depending on which bacterial species that was tested, see Table AP3 I. VetMIC™ is produced and validated at the Dept. of Antibiotics, SVA. The tests were performed following the standards for microdilution of the National Committee of Clinical Laboratory Standards (NCCLS, 1999).

For susceptibility testing of *Brachyspira hyodysenteriae,* a specially developed VetMIC™ panel was used. The antimicrobials were dried in serial twofold dilutions in the wells of tissue culture trays. The wells were filled with 0.5 mL of a suspension of bacteria in Brain Heart Infusion broth with 10% fetal calf serum. The trays were incubated in an anaerobic atmosphere for four days on a shaker. Minimum inhibitory concentration (MIC) is registered as the lowest concentration of the antimicrobial that inhibits bacterial growth. An isolate is regarded as resistant to a specific antimicrobial when the MIC is distinctly higher than those of inherently susceptible strains of the bacterial species in question. In other words, microbiological criteria were used to define resistance. Where appropriate, the breakpoints suggested by NCCLS (1999) for animal pathogens were also taken into consideration. The breakpoints defining resistance are shown in Table AP3 I.

Bacitracin values in this report are given in units/mL. In an attempt to convert unit/mL to mg/L we discovered that there appears to be some confusion in the matter. The bacitracin compound used in SVARM is obtained from Sigma and meets the standards set by the United States Pharmacopoeia (USP), stating that one unit is equivalent to 26 µg of the US standard. However, according to the International Standard Preparations, one international unit is equivalent to 13.51 µg. On the other hand, if the bacitracin is of a very high degree of purity, though unstable, it correspond to 66(-70) units/mg, that is, one unit is equivalent to approximately 15µg. Feedingstuff grade of bacitracin correspond to 42-50 units/mg (one unit = 20-24 µg) (Otten *et al.*, 1975).

Quality assurance system

The Dept. of Antibiotics and the Dept. of Bacteriology at SVA using VetMIC™ for antimicrobial susceptibility tests are accredited to perform the method according to SS-EN ISO/IEC 45001 by the Swedish Board for Accreditation and Conformity Assessment (SWEDAC).

As quality control for susceptibility tests of zoonotic and indicator bacteria, *Escherichia coli* ATCC 25922 and *Enterococcus faecalis* ATCC 29212 were included at least on a weekly basis. Relevant control strains were also included and evaluated at least once weekly for animal pathogens. The Dept. of Antibiotics participates in several proficiency tests for antimicrobial susceptibility testing. These are arranged either as national or international studies. Likewise, the Dept. of Bacteriology participates in proficiency tests concerning isolation and identification of *Salmonella enterica* and general clinical veterinary bacteriology and susceptibility tests.

Data handling

Data on isolates of *Salmonella* and animal pathogens are routinely registered in an Oracle database at SVA. Records include source of cultured sample, antimicrobial susceptibility etc. From this database, relevant data for calculations and analysis were extracted to an Access database.

Data on samples for cultivation of indicator bacteria were recorded in an Access database on arrival of samples. Recorded data were animal species, date of sampling, abattoir and herd of origin. For samples from chickens, also flock of origin was recorded. Subsequently, results of laboratory investigations were recorded in the same database. Calculations and analysis of data were performed in the computer programs Access and Excel.

Concerning confidence limits

When the prevalence of antimicrobial resistance is close to zero, e.g. when one out of 120 isolates are resistant, the question arises how to calculate the prevalence of resistance and its confidence intervals. In the example, the prevalence could be estimated to 0.83% while the 95% confidence interval is trickier. The normal approximation to the binomial distribution would give a lower confidence of -0.8% and an upper confidence limit of 2.5%. The lower limit is nonsensical and indicates the unsuitability of the normal approximation in this case.

There are several ways out of the dilemma; one is to calculate the exact binomial confidence limits, which would be possible in some cases (small number of isolates). Another alternative is to run Monte-Carlo simulations based on the beta-distribution which is possible but quite laborious for a huge set of data since each prevalence estimate has to be simulated 10 000 times.

Finally the relationship between the F-distribution and, the beta-distribution the binomial distribution can be used. This gives the formulae that enables calculations of the confidence intervals (Rao, 1965). Using this approach, the confidence intervals in the example would be 0.021% and 4.6%.

In conclusion, the normal approximation to the binomial distribution might be unsuitable when the prevalence is close to 0% or close to 100% since the approximation might lead to confidence intervals lower than 0% or higher than 100%. Moreover, when the prevalence of resistance is less than 5% using the link between the F-distribution and the binomial distribution yield different confidence intervals compared to those obtained from the normal approximation and should accordingly be preferred.

In SVARM the link between the F-distribution and the binomial distribution was used to calculate confidence limits for observed levels of resistance in indicator bacteria *(Escherichia coli* and *Enterococcus* spp.) from cattle, pigs and broiler chickens.

Table AP3 I. Breakpoints and range of dilutions (mg/L) used for antimicrobial susceptibility testing of bacteria. Isolates with MIC values higher than the given figures are considered resistant.

Substance	*E. coli* (indicator), *Salmonella* spp.		*E. coli* (pathogens)		Staphylococci[1], Streptococci[1], *Actinobacillus* spp.[1], *Rhodococcus equi*[1]		Enterococci		*Brachyspira hyodysenteriae*		*Pasteurella* spp.	
	Breakpoint	Range	Breakpoint	Range	Breakpoint	Range	Breakpoint	Range	Breakpoint	Range	Breakpoint	Range
Amoxicillin & Clavulanic acid[2]	>8/4	2/1-16/8										
Ampicillin	>8	0.25-32	>8	2-16	>16	0.12-16	>8	0.25-32			>16	0.12-16
Apramycin	>32	0.25-32										
Avilamycin							>8	0.5-32				
Bacitracin[3]							>32	0.5-32				
Ceftiofur	>2	0.25-2										
Cephalothin					>16	4-16					>16	4-32
Chloramphenicol	>8	2-16	>8	2-16	>8	2-16						
Clindamycin					>4	1-4			>0.5	0.031-4		
Enrofloxacin	>0.5	0.03-4	>0.5	0.25-2	>2	0.25-2					>2	0.25-2
Erythromycin					>4	0.5-4	>4	0.25-32	>32	2-256		
Flavomycin							>32	2-128				
Florfenicol	>16	2-16										
Gentamicin	>8	0.25-32	>8	1, 4-16	>16	1, 4-16	>512	0.5-32, 512				
Nalidixic acid	>16	1-128										
Narasin							>2	0.12-16				
Neomycin	>32	1-128	>32	2-32	>32	2-32	>1024	2-128, 1024				
Nitrofurantoin			>32	4-32	>32	16-32						
Oxacillin					>1	0.5-1						
Penicillin					>8	0.06-8					>8	0.06-8
Spiramycin					>16	4-32						
Streptomycin	>32	2-256	>32	2-32	>32	1-128	>1024	2-128, 1024			>32	1-128
Sulfamethoxazole	>256	64-512										
Tetracycline	>8	0.5-64	>8	1-16	>8	1-16	>8	0.25-32			>8	0.5-64
Tiamulin									>2	0.016-2		
Trimethoprim	>8	0.12-16										
Trimethoprim & Sulfamethoxazole[4]			>8	0.12-8	>8	0.12-8					>8	0.06-8
Tylosin									>16	2-256		
Valnemulin									>1	0.016-2		
Vancomycin							>16	1-128				
Virginiamycin							>8	0.5-64	>8	0.25-16		

[1] All substances are not tested for all bacterial species, see tables in Resistance in animal pathogens for details; [2] Concentration of amoxicillin given, tested with clavulanic acid in concentration ratio 2/1; [3] MIC in U/mL;
[4] Concentration of trimethoprim given, tested with sulfamethoxazole in concentration ratio 1/20.

Appendix 4: Antimicrobial agents authorised

Antimicrobial agents authorised for veterinary use in Sweden year 2001 are listed in Table AP4 I.

Only substances licensed for systemic, oral, intrauterine or intramammary use are included (ATCvet codes QJ, QG, QA and QP). Data from FASS VET. 2001. For explanation of ATCvet code, see Appendix 2.

Table AP4 I. Antimicrobial agents authorised for therapeutic use in cattle, pigs, poultry, horses, dogs and cats in Sweden, 2001. Routes of administration are indicated.[1]

Antimicrobial agent	ATCvet code	Animal species					
		Cattle	Pigs	Poultry	Horses	Dogs	Cats
Tetracyclines							
Doxycycline	QJ01A A02					O	O
Oxytetracycline	QJ01A A06, QG51A A01	I O U	I O U	O		O	O
Beta-lactams, penicillins							
Ampicillin	QJ01C A01	O	O		O	O	O
Amoxicillin	QJ01C A04		I			I O	O
Penicillin G	QJ01C E01	I	I		I		
Penicillin G, procaine	QJ01C E09	I	I		I	I	I
Penicillin V	QJ01C E02					O	O
Amoxicillin/Clavulanic acid	QJ01C R02					I O	I O
Beta-lactams, cephalosporins							
Cephalexin	QJ01D A01					O	
Cefadroxil	QJ01D A09					O	O
Ceftiofur	QJ01D A90	I					
Sulfonamides + Trimethoprim							
Sulfadiazine/Trimethoprim	QJ01E W10	I	I		I O	O	O
Sulfadoxine/Trimethoprim	QJ01E W13	I	I		I		
Sulfonamides							
Formosulfatiazole	QA07A B90	O	O		O	O	O
Sulfaklozin	QP51A G04			O			
Macrolides							
Spiramycin	QJ01F A02	I					
Tylosin	QJ01F A90	I	I O	O		I	I
Lincosamides							
Clindamycin	QJ01F F01					O	O
Aminoglycosides							
Gentamicin	QJ01G B03				I U	I	I
Dihydrostreptomycin (DHS)	QA07A A90	O U	O U		O U	O	O
Fluoroquinolones							
Enrofloxacin	QJ01M A90	I	I	O		I O	I O
Danofloxacin	QJ01M A92	I	I				
Marbofloxacin	QJ01M A93					O	O
Orbifloxacin	QJ01M A95					O	
Pleuromutilins							
Tiamulin	QJ01X X92		I O				
Valnemulin[2]	QJ01X X94		O				
Combinations							
Penicillin G, procaine/DHS	QJ01R A01, QJ51R C23	I M	I		I	I	I
Penicillin G, benzatin/DHS	QJ51R C24	M					
Penicillin G, ester/Framycetin	QJ51R C25	M					
Penicillin G, ester/DHS	QJ51R C25	M					

[1] O = oral; I = injection; U = intrauterine; M = intramammary; [2] Authorisation temporarily withdrawn october 2000.

Appendix 5: References

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