# SVARM 2008

## Swedish Veterinary Antimicrobial Resistance Monitoring

SVA

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**Editors**
Björn Bengtsson, Stina Englund, Christina Greko and Ulrika Grönlund Andersson
Department of Animal Health and Antimicrobial Strategies, National Veterinary Institute (SVA)
SE-751 89 Uppsala, Sweden

**Authors**
Björn Bengtsson, Karin Bergström, Stina Englund, Christina Greko, Ulrika Grönlund Andersson, Oskar Nilsson and Ulrika Windahl
*Department of Animal Health and Antimicrobial Strategies, SVA*

**SVARM laboratory working group**
Kerstin Ekström, Maria Finn, Margareta Horn af Rantzien, Eva Hübbinette, Annica Landén and Eva Säker
*Department of Animal Health and Antimicrobial Strategies, SVA*


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Reprints can be ordered from
Department of Animal Health and Antimicrobial Strategies
National Veterinary Institute
SE-751 89 Uppsala
Sweden
Phone: +46 (0) 18 67 40 00
Fax: +46 (0) 18 30 91 62
e-mail: sva@sva.se

# Content



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# Preface

**WELCOME** to the ninth Swedish report combining results from the monitoring of antimicrobial resistance and antimicrobial usage in both veterinary and human medicine: SVARM and SWEDRES. These joint reports facilitate comparisons of resistance levels and incidence of use in the two areas.

Data in this and previous reports indicate that the Swedish strategies in human and veterinary medicine have been comparatively successful in containing resistance. But antimicrobial resistance continues to increase in many parts of the world. Resistance emerging in one country can rapidly spread to others through trade and travel, which underlines the need for international collaboration in all fields. The need for continued collective efforts in all sectors was iterated in the European Union's Council Conclusions on Antimicrobial Resistance (10 June 2008).

In veterinary medicine, the emergence and spread of multiresistant methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) among dogs in Sweden and elsewhere continues to be a serious problem, as the options left for treatment are scant.

An outbreak of methicillin-resistant *S. aureus* (MRSA) among horses admitted to an equine hospital attracted considerable attention, not least from media. This was also true for the first cases of MRSA in dogs reported in 2006 and 2007. On a positive note, the attention has led to a generally increased awareness of the problems with antimicrobial resistance. In small animal medicine, matters related to antimicrobial policy and hospital hygiene have been intensively discussed both nationally and locally. The pronounced decrease in sales of antimicrobials for dogs over the last two years highlighted in this report is probably the result of these combined efforts.

In Sweden, the strategic programme against antimicrobial resistance is co-ordinated by Strama. A secretariat to support a network with a similar remit, Strama VL, was initiated at SVA during 2008. Strama VL will provide a platform for all stakeholders to exchange of information, analyze problems, pinpoint solutions and initiate prioritized activities. Our hope is that the information in SWEDRES and SVARM, is translated into further investigations and action in order to preserve our increasingly threatened, but still favourable, situation.

# Summary

**THE 2008 REPORT** from SVARM shows that the situation regarding antimicrobial resistance in bacteria of animal origin remains favourable from an international perspective. But the emergence of methicillin resistant *Staphylococcus pseudintermedius* (MRSP) in dogs illustrates that the situation can rapidly change in an unfavourable direction. However combined efforts to counter this development have resulted in an overall decrease in use of antimicrobials for dogs. Prudent use of antimicrobials reduces the selection pressure for resistance and is one of the cornerstones to mitigate antimicrobial resistance.

**The total amount of antimicrobials** used for animals was 16 365 kg in 2008, which is similar to year 2005 and among the lower figures this decade. The amount of antimicrobials for in-feed or in-water medication has decreased by 93% since 1984 and is today but 15 % of the total sales. The sales of products for medication of individual animals have remained relatively unchanged over the last decade. The sales of fluoroquinolones has decreased by 16% over the last three years which is explained by decreased use both of injectable products (mainly for food producing animals) and of products for oral medication of individual animals (mainly for dogs).

**The sales of antimicrobials for dogs** have decreased by 11% since 2006, measured as total number of prescriptions dispensed. Downward trends are noted for the major groups; cephalosporins (-32%), fluoroquinolones (-21%) and aminopenicillins with clavulanic acid (-9%). The findings of methicillin resistant staphylococci in 2006 attracted considerable attention, not least in the media. This in turn triggered national and local initiatives on hygiene and prescribing policies, which probably led to the observed changes in prescribers' behaviour.

**Methicillin resistant *Staphylococcus aureus* (MRSA)** were confirmed in three dogs and seven horses in 2008. Since first reported in 2006, there have been ten cases in dogs, one in a cat and eight in horses until the end of April 2009. So far MRSA has not been found in food producing animals in Sweden and was not detected in holdings with breeding pigs screened 2008. As from January 2008, MRSA in animals are notifiable in Sweden.

***Salmonella*** is rare in Swedish animals and most incidents involve susceptible strains. There are no indications of increased occurrence of resistance. In 2008, 85% of the strains were susceptible to all antimicrobials tested and only six of 85 strains from food producing animals and one of 20 strains from companion animals were multiresistant. Resistance to third generation cephalosporins was not observed but fluoroquinolone resistance was confirmed in one isolate from a pig sampled at slaughter. That strain was not reisolated from pigs from the herd of origin.

***Campylobacter jejuni*** from broilers were susceptible to all antimicrobials tested but in hippurate negative isolates from slaughter pigs, presumptive ***Campylobacter coli***, fluoroquinolone resistance was common (29%). This agrees with previous data from SVARM and is possibly linked to use of fluoroquinolones in piglet producing herds. In slaughter pigs, treatment with injectable fluoroquinolones is probably uncommon and oral administration through feed or water is not authorized.

**Resistance in indicator bacteria,** i.e. *Escherichia coli* and *Enterococcus* spp. from the intestinal flora of healthy animals, are believed to reflect the antimicrobial selective pressure in an animal population. In indicator bacteria from sheep, resistance was rare in agreement with a limited use of antimicrobials in this animal species. In pigs, resistance to antimicrobials used in pig production was not uncommon but occurrence is low in an international perspective and without obvious trends. Screening of samples from pigs show that *Escherichia coli* with transferable resistance to third generation cephalosporins is at most rare.

This year data on indicator bacteria from food is introduced in SVARM. Fifty samples of pork from retail were cultured in a pilot study. Resistance was most uncommon but the small number of samples preclude valid conclusion. In future a larger number of samples will be cultured.

**Vancomycin resistant enterococci (VRE)** were isolated from 28% of 107 samples of caecal content from broilers cultured on media supplemented with vancomycin. This is a similar prevalence as in 2006 and 2007, which shows that the increase in prevalence of VRE in broilers observed 2000-05 has levelled off.

***Escherichia coli*** from clinical submissions were often resistant to ampicillin, streptomycin, tetracycline or trimethoprim-sulphonamides, irrespective of source (pig, horse, dog or cat). In addition, resistance to enrofloxacin was common (10%) in *E. coli* from urine samples from dogs. Multiresistance commonly involved these substances with prevalence ranging from 5% in isolates from horses to 14% in isolates from pigs. One multiresistant *E. coli* isolated from the genital tract of a mare was ESBL-producing.

In ***Brachyspira* spp.** from pigs, resistance to tiamulin occurred in *B. pilosicoli* but was not observed in *B. hyodysenteriae*. The majority of *B. pilosicoli* and *B. hyodysenteriae* were resistant to tylosin.

Resistance was rare in ***Actinobacillus pleuropneumoniae*** and in ***Pasteurella* spp.** from the respiratory tract of pigs as well as in ***Pasteurella* spp**. from the respiratory tract of calves.

***Staphylococcus aureus*** from milk of dairy cows with subclinical mastitis were mostly susceptible to antimicrobials. Only two isolates (2%) were resistant to penicillin through beta-lactamase production.

In ***Aeromonas salmonicida*** subsp. ***achromogenes, Flavobacter columnare*** and ***Flavobacter psychrophilum*** from farmed fish, deviating high MICs to nalidixic acid, tetracycline or florfenicol in some isolates indicate acquired resistance to these antimicrobials.

***Streptococcus zooepidemicus*** from the respiratory tract of horses were uniformly susceptible to penicillin, but resistance to trimethoprim-sulphonamides was common.

Most ***Staphylococcus pseudintermedius*** from dogs were resistant to penicillin. Resistance to clindamycin, erythromycin, fusidic acid, streptomycin or tetracycline was also common (between 22 and 28%). About one third of *S. pseudintermedius* were multiresistant and 14% were resistant to at least five antimicrobials.

## Acknowledgements

Several people have in various ways been involved in the work with SVARM. We would like to express our gratitude to all who have contributed to this report and in particular to:
Karin Granath at Stockholm Stad Miljökontor for organizing the collection of pork at retail for the study of indicator bacteria in food.

**Methicillin resistant *Staphylococcus pseudintermedius* (MRSP)** in Swedish dogs were first confirmed 2006. Since, the number of confirmed cases has increased and in 2008 about 100 isolates of MRSP were confirmed at SVA. Isolates were from all parts of Sweden and mainly from dogs. As from January 2008, MRSP are notifiable in Sweden.

# Sammanfattning

**SVARM 2008** visar att läget avseende antibiotikaresistens hos bakterier från djur är fortsatt gynnsamt ur ett internationellt perspektiv. Men ökad förekomst av meticillinresistent *Staphylococcus pseudintermedius* (MRSP) hos hundar illustrerar hur situationen snabbt kan förändras i en ogynnsam riktning. Det är dock glädjande och hoppfullt att initiativ för att motverka denna utveckling sammantaget har resulterat i en minskning av den totala försäljningen av antibiotika till hundar. Ansvarsfull användning av antibiotika reducerar selektionstrycket för resistens och är en grundförutsättning för att motverka antibiotikaresistens.

**Försäljningen av antibiotika** till djur var totalt 16 365 kg under 2008, vilket är i samma storleksordning som 2005. Volymen antibiotika för inblandning i foder eller vatten har minskat med 93 % sedan 1984 och utgör idag endast 15 % av den totala försäljningen. Försäljningen av produkter för individuell behandling av djur har varit relativt stabil under de senaste tio åren. Försäljningen av fluorokinoloner har minskat med 16 % de senaste tre åren vilket förklaras av minskad användning både av medel för injektion (främst livsmedelsproducerande djur) och för behandling av enstaka djur via munnen (främst hundar).

**Försäljningen av antibiotika för hundar** har minskat med 11 % sedan 2006, mätt som totalt antal dispenserade recipen. Nedåtgående trender noteras för några av de största grupperna; cefalosporiner (-32 %), fluorokinoloner (-21 %) och aminopenicilliner med klavulansyra (-9 %). Fynd av meticillinresistenta stafylokocker under 2006 väckte stor uppmärksamhet, inte minst i media. Detta ledde till ett stort antal initiativ nationellt och lokalt kring frågor om hygien och antibiotikaförskrivning vilket i sin tur troligen påverkat förskrivarnas beteende.

**Meticillinresistent *Staphylococcus aureus* (MRSA)** påvisades hos tre hundar och sju hästar under 2008. Sedan det första fallet hos svenska djur 2006 har MRSA konfirmerats hos tio hundar, en katt och åtta hästar fram till och med april 2009. Hittills har MRSA inte påvisats från animalieproducerande djur i Sverige. I en riktad undersökning av avels- och smågrisproducerandebesättningar 2008 påvisades inte MRSA. Sedan 1 januari 2008 är fynd av MRSA hos djur anmälningspliktigt.

***Salmonella*** är ovanligt hos svenska djur och de fall som inträffar orsakas oftast av antibiotikakänsliga stammar. Det finns inga tecken på en ökad förekomst av resistens. Under 2008 var 85 % av isolaten känsliga för alla testade antibiotika och bara sex av 85 isolat från livsmedelsproducerande djur och ett av 20 isolat från sällskapsdjur var multiresistenta. Resistens mot tredje generationens cefalosporiner påvisades inte men ett isolat från en slaktad gris var resistent mot fluorokinoloner. Den senare stammen återfanns inte hos djur i ursprungsbesättningen.

*Campylobacter jejuni* från slaktkyckling var känsliga för alla antibiotika som testades. Däremot var, liksom tidigare, fluorokinolonresistens vanlig (29 %) bland hippurat negativa isolat från slaktsvin, sannolikt ***Campylobacter coli***. Detta beror förmodligen på användning av kinoloner i smågrisproducerande besättningar eftersom slaktsvin sällan behandlas med injektion av kinoloner och preparat för behandling av grisar via foder eller vatten inte är registrerade i Sverige.

**Resistens hos indikatorbakterier** (*Escherichia coli* och *Enterococcus* spp.) från tarmfloran hos friska djur anses återspegla selektionstrycket från användning av antibiotika i en djurpopulation. Indikatorbakterier från får var sällan resistenta vilket stämmer med att får sällan behandlas med antibiotika. Resistens var vanligare hos indikatorbakterier från slaktsvin men förekomsten är låg i ett internationellt perspektiv och det finns inga tydliga trender. I huvudsak förekom resistens mot antibiotika som används till svin. Alla prov från slaktsvin undersöktes specifikt för *Escherichia coli* med överförbar resistens mot tredje generationens cefalosporiner men sådan resistens misstänktes endast i ett prov.

För första gången rapporteras i SVARM uppgifter om indikatorbakterier från livsmedel. Femtio prov av svinkött insamlat i butik undersöktes i en pilotundersökning. Resistens var ovanlig men eftersom få prov undersöktes är resultaten svåra att värdera. Fortsättningsvis kommer ett större antal prov att undersökas årligen.

**Vankomycinresistenta enterokocker (VRE)** isolerades från 28 % av 107 prov av tarminnehåll från slaktkyckling. Proven odlades på odlingsmedier med tillsats av vankomycin. Andelen positiva prov är densamma som 2006 och 2007 vilket tyder på att ökningen fram till 2005 har brutits.

***Escherichia coli*** från kliniska prov från grisar, hästar, hundar och katter var ofta resistenta mot ampicillin, streptomycin, tetracyklin eller trimetoprim-sulfa. Hos *E. coli* från urinprover från hund var också resistens mot enrofloxacin vanlig (10 %). Frekvensen multiresistens varierade beroende på djurslag och var lägst (5 %) hos isolat från hästar och högst (14 %) hos isolat från grisar.

Hos ***Brachyspira pilosicoli*** från grisar förekom resistens mot tiamulin men däremot inte bland ***B. hyodysenteriae***. Majoriteten av såväl *B. pilosicoli* som *B. hyodysenteriae* var resistenta mot tylosin.

***Actinobacillus pleuropneumoniae*** och ***Pasteurella* spp.** från grisars luftvägar liksom ***Pasteurella* spp.** från kalvars luftvägar var känsliga för de flesta antibiotika.

Resistens hos ***Staphylococcus aureus*** från mjölk från mjölk-

kor med subklinisk mastit var ovanligt. Endast två isolat (2 %) producerade beta-laktamas och därmed resistens mot penicillin.

Bland ***Aeromonas salmonicida*** subsp. ***achromogenes, Flavobacter columnare*** och ***Flavobacter psychrophilum*** från odlad fisk förekom isolat med avvikande höga MIC-värden mot nalidixansyra, tetracyklin eller florenikol. Detta tyder på att några isolat förvärvat resistens mot dessa antibiotika.

***Streptococcus zooepidemicus*** från luftvägarna hos hästar var genomgående känsliga för penicillin men resistens mot trimetoprim-sulfa var vanlig.

***Staphylococcus pseudintermedius*** från hundar var i stor utsträckning resistenta mot penicillin. Resistens mot klindamycin, erytromycin, fusidinsyra, streptomycin eller tetracyklin var också vanlig (mellan 22 och 28 %). En knapp tredjedel av *S. pseudintermedius* var multiresistenta och 14 % var resistenta mot minst fem antibiotika.

## Tack

Många personer har på olika sätt varit involverade i arbetet med SVARM. Vi vill tacka alla som bidragit och särskilt Karin Granath vid Stockholm Stad Miljökontor för hjälp att organisera insamlingen av prov i butiker för undersökning av indikatorbakterier i fläskkött.

**Meticillinresistenta *S. pseudintermedius* (MRSP)** från svenska hundar konfirmerades för första gången 2006. Sedan dess har antalet påvisade fall av MRSP ökat kraftigt och under 2008 konfirmerades ungefär 100 isolat vid SVA. De flesta isolaten kommer från hundar och är från i stort sett hela Sverige. Sedan 1 januari 2008 är fynd av MRSP anmälningspliktigt.

# Use of antimicrobials

**THROUGH** an initiative by SVA and Apoteket AB (the National Corporation of Swedish Pharmacies), statistics on total sales of antimicrobials for use in animals in Sweden are available since 1980. For a review of the figures from 1980–2000 as well as references to publications on which that review is based, see SVARM 2000.

### Material included

In Sweden, antimicrobials for use in animals are only available on veterinary prescription and all pharmaceuticals are dispensed by pharmacies. In 1986, the Feedstuffs Act restricted the use of antibiotics for veterinary medicinal purposes, i.e. their use as growth promoters was no longer authorised.

Drug statistics are based on sales figures provided by Apoteket AB and represent the total sales of antimicrobials authorised for veterinary use, calculated to kg active substance. These figures include antimicrobial formulations for all animal species (food producing animals, pets and horses etc) for systemic, intramammary and obstetric use, and intestinal anti-infectives. Drugs authorised for human use but prescribed for animals are not included. Such antimicrobials are almost exclusively prescribed in small animal medicine. Between 2005 and 2008, 6–8% of the total number of prescriptions for dogs was of products for human use (ATC group J01; see highlight 'Decreased sales of antimicrobials for dogs').

Up to and including year 2002, the source of the statistics has been sales of drugs from wholesalers to pharmacies. From year 2003, the statistics are based on the amounts of drugs dispensed by pharmacies and a new system for retrieval of data was introduced. In both systems, data represent an approximation on the real usage of antimicrobials, assuming that the amount sold is also used during the observation period.

Ionophoric antimicrobials given to control coccidiosis are currently classified as feed additives, and are not included in the overall statistics based on sales from pharmacies. However, figures on the sales of these products, based on statistics collected by the Board of Agriculture from feed mills, are given under the section on group treatment (Table AC III).

Details on animal numbers are found in Appendix 1, on methodology in Appendix 2 and on antimicrobial agents with general marketing authorisation in Sweden in Appendix 4.

### Overall use of antimicrobials

The total yearly sales of antimicrobials over the last decade are presented in Table AC I. Figures on antimicrobials used as feed additives before 1986 are not included, but are for completeness given in Table AC III and Figure AC III.

Changes in the number of animals may affect trends in statistics on use of antimicrobials. The decrease in number of dairy cows continues and the figure was 12% lower in 2008 than in 2004. The number of beef cows, however, has increased by 14% in the same period. The number of pigs slaughtered in 2008 was 10% lower than in year 2004 but in the last three years there has been little change. The number of slaughtered broilers was roughly unchanged.

As noted in SVARM 2007, the lower total figures on sales of antimicrobials for animals shown for years 2003–2005 are uncertain, as there was a change in the system for data retrieval in year 2003. It is possible that initially, sales of some products sold with special licence prescription were not captured by searches in the new system. This problem has been addressed, and from year 2006 all products dispensed should be captured in the searches.

The potency of different antimicrobials is not equal and therefore each class should be evaluated separately. Nonetheless, the overall figures may indicate trends in the material. In SVARM 2007, an increase in total sales between years 2003 and 2007 was noted. This trend may now be broken, as the amount sold in 2008 was 500 kg lower than in 2007 (4%). The overall decrease is partly explained by a drastic decrease in sales of antimicrobials for dogs since 2006. The amount dispensed by pharmacies for dogs (out-patient use) was 188 kg

**TABLE AC I.** Yearly sales of antimicrobial drugs for veterinary use expressed as kg active substance. Based on sales statistics from Apoteket AB.

| ATCvet code | Antimicrobial class | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| QJ01AA, QG01A | Tetracyclines[a] | 2 251 | 1 754 | 1 453 | 1 415 | 1 307 | 1 329 | 1 562 | 1 516 | 1 853 | 1 649 |
| QJ01-CE, -R, QJ51 | Penicillin G-and V[b] | 8 692 | 8 254 | 8 414 | 8 179 | 7 579 | 7 814 | 7 571 | 7 860 | 7 582 | 7 758 |
| QJ01-CA, -CR | Aminopenicillins | 809 | 852 | 752 | 767 | 870 | 875 | 911 | 920 | 927 | 939 |
| QJ01D, QJ51CA | Other betalactams | 245 | 315 | 474 | 676 | 832 | 928 | 1 009 | 1 217 | 954 | 820 |
| QA07AA, QJ01-G, -R, QJ51R | Aminoglycosides and polymixins[a] | 846 | 797 | 770 | 753 | 645 | 606 | 762 | 750 | 718 | 643 |
| QA07AB, QJ01E | Sulphonamides | 2 403 | 2 338 | 2 485 | 2 477 | 2 326 | 2 462 | 2 535 | 2 543 | 2 427 | 2 303 |
| QJ01E | Trimethoprim & derivatives | 397 | 390 | 414 | 414 | 381 | 406 | 437 | 450 | 438 | 416 |
| QJ01F | Macrolides & lincosamides | 1 467 | 1 352 | 1 510 | 1 412 | 1 124 | 1 095 | 1 080 | 1 254 | 1 520 | 1 096 |
| QJ01MA | Fluoroquinolones | 155 | 156 | 182 | 185 | 184 | 187 | 184 | 195 | 180 | 169 |
| QJ01XX-92, -94 | Pleuromutilins | 847 | 871 | 841 | 988 | 744 | 387 | 338 | 459 | 506 | 572 |
| QJ01XX91 | Streptogramins[c] | 125 | - | - | - | - | - | - | - | - | - |
| Total | | 18 237 | 17 079 | 17 295 | 17 266 | 15 992 | 16 089 | 16 389 | 17 164 | 17 106 | 16 365 |

[a] Includes drugs marketed with special licence prescription for years 2000-2006; [b] Calculated as benzyl-penicillin; [c] From 1986 sold only on veterinary prescription at therapeutic dosages.

and 460 kg lower in 2008 compared to 2007 and 2006, respectively (see further under 'Treatment of individual animals' and highlight 'Decreased sales of antimicrobials for dogs'). Also, the sales of some products that are mostly used for medication of pigs via feed or water has decreased since 2007 (see 'Treatment of groups or flocks').

Most of the total sales are products formulated for systemic treatment of individual animals. In 2008, 60% of the sales were products for injection, 24% for oral medication of individual animals (e.g. tablets) and only 16% for medication of groups or flocks via feed or water. The proportion of the total sales of the latter subset has been roughly unchanged over the last decade.

The sales of antimicrobials in QJ01 and QA07 (data in Tables ACII and ACIII) are presented in Figure AC I as relative amounts of each class of products for injection, for oral use in individual animals (tablets, gels etc.) and for oral administration to groups of animals by mixing into feed or water. The tetracyclines, pleuromutilins and macrolides are mainly used for treatment of groups of animals, mostly pigs. Penicillins for systemic use are exclusively sold as injectables, and that type of formulation also dominates for the aminoglycosides. These products

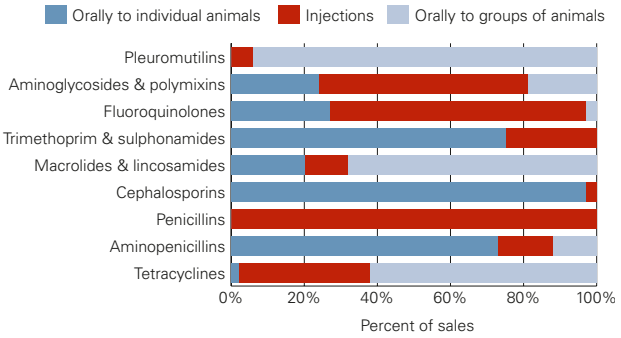



**FIGURE AC I.** Proportions of the total sales of intestinal anti-infectives and antimicrobials for systemic use (QA07 and QJ01) of drugs that are formulated for injection, for oral individual use or for oral use for groups of animals (amounts are given in Tables AC II and AC III).

are probably mainly used for treatment of cattle, in particular dairy cows but also for pigs and horses. The sales of fluoroquinolones are dominated by injectables used for food-producing animals, and products for oral use in dogs and cats. Only 3% of the sales in 2008 were for medication via feed or water.

Sales of broad-spectrum beta-lactam antimicrobials

**TABLE AC II.** Yearly sales of antimicrobial drugs authorised for individual treatment expressed in kg active substance. Only products for systemic use (QJ01) or for use as intenstinal anti-infective (QA07) are included. Based on sales statistics from Apoteket AB.

| ATCvet code | Antimicrobial class | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| QA07A | Intestinal anti-infectives[a] | 607 | 587 | 614 | 594 | 594 | 586 | 496 | 434 | 372 | 364 |
| QJ01A | Tetracyclines | 695 | 634 | 623 | 628 | 606 | 611 | 623 | 609 | 632 | 659 |
| QJ01-CA, -CR | Aminopenicillins | 809 | 852 | 752 | 767 | 870 | 875 | 911 | 909 | 899 | 828 |
| QJ01-CE. -R | Penicillin G and V [b] | 8 615 | 8 185 | 8 343 | 8 127 | 7 536 | 7 769 | 7 493 | 7 777 | 7 504 | 7 671 |
| QJ01D | Cephalosporins | 245 | 315 | 474 | 676 | 832 | 928 | 1 009 | 1 212 | 950 | 817 |
| QJ01E | Sulfonamides & trimethoprim | 2 376 | 2 336 | 2 478 | 2 483 | 2 280 | 2 427 | 2 610 | 2 689 | 2 619 | 2 486 |
| QJ01F | Macrolides & lincosamides | 559 | 531 | 522 | 477 | 430 | 382 | 400 | 417 | 413 | 352 |
| QJ01-G, -R | Aminoglycosides[c] | 528 | 474 | 454 | 460 | 367 | 344 | 362 | 345 | 343 | 318 |
| QJ01M | Fluoroquinolones | 144 | 150 | 169 | 178 | 177 | 180 | 179 | 190 | 177 | 164 |
| QJ01X | Pleuromutilins | 52 | 56 | 48 | 49 | 77 | 32 | 29 | 39 | 36 | 36 |

[a] Drugs marketed with special licence prescription are included from year 2000; [b] Procaine-penicillin calculated to benzyl-penicillin; [c] Does not include QA07A, intestinal anti-infectives.

**TABLE AC III.** Yearly sales of antimicrobial drugs authorised for group treatment and ionophoric anticoccidials sold expressed as kg active substance. Based on sales statistics from Apoteket AB and from the Board of Agriculture

| ATCvet code | Antimicrobial class | 1984 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| QA07A | Intestinal anti-infectives[a] | - | - | - | - | - | - | - | 163 | 170 | 158 | 106 |
| QJ01A | Tetracyclines[b] | 12 300 | 1 545 | 1 111 | 822 | 777 | 695 | 712 | 934 | 903 | 1217 | 986 |
| QJ01C | Penicillins | - | - | - | - | - | - | - | - | 11 | 28 | 146 |
| QJ01F | Macrolides & lincosamides | 607 | 908 | 821 | 988 | 935 | 694 | 713 | 680 | 837 | 1 107 | 744 |
| QJ01M | Fluoroquinolones | - | 11 | 7 | 13 | 7 | 8 | 7 | 5 | 5 | 3 | 5 |
| QJ01M | Quinoxalines[c] | 9 900 | - | - | - | - | - | - | - | - | - | - |
| QJ01XX91 | Streptogramins[c] | 8 800 | 125 | - | - | - | - | - | - | - | - | - |
| QJ01XX92, QJ01XX94 | Pleuromutilins | - | 795 | 815 | 793 | 939 | 667 | 355 | 309 | 420 | 471 | 536 |
| QP51AA | Nitroimidazoles | 1 440 | - | - | - | - | - | - | - | - | - | - |
| | Feed additives[d] | 700 | - | - | - | - | - | - | - | - | - | - |
| QP51AH | Ionophoric antibiotics (coccidiostats)[e] | 7 900 | 11 643 | 9 368 | 10 019 | 8 439 | 10 920 | 10 486 | 11 095 | 12 335 | 12 527 | NA[f] |

[a] Drugs with special licence prescription are included from year 2005; [b] Drugs marketed with special licence prescription are included from year 2000; c Years 1980-1984 sold as feed additives, thereafter on veterinary prescription at therapeutic dosages; d Feed additives other than quinoxalines and streptogramins: avoparcin, bacitracin, nitrovin, oleandomycin and spiramycin; [e] From 1999 regulated and classified as feed additives (dir 70/524/EEC). Figures from 1999 and onwards are from the Feed Control of the Board of Agriculture (www.sjv.se); [f] not available at the time of publication.

FIGURE A

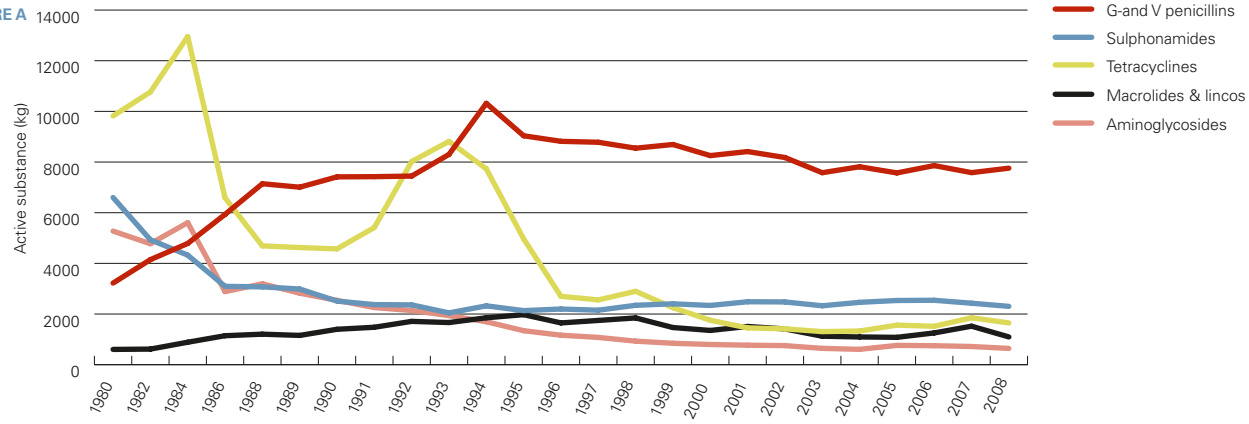



FIGURE B

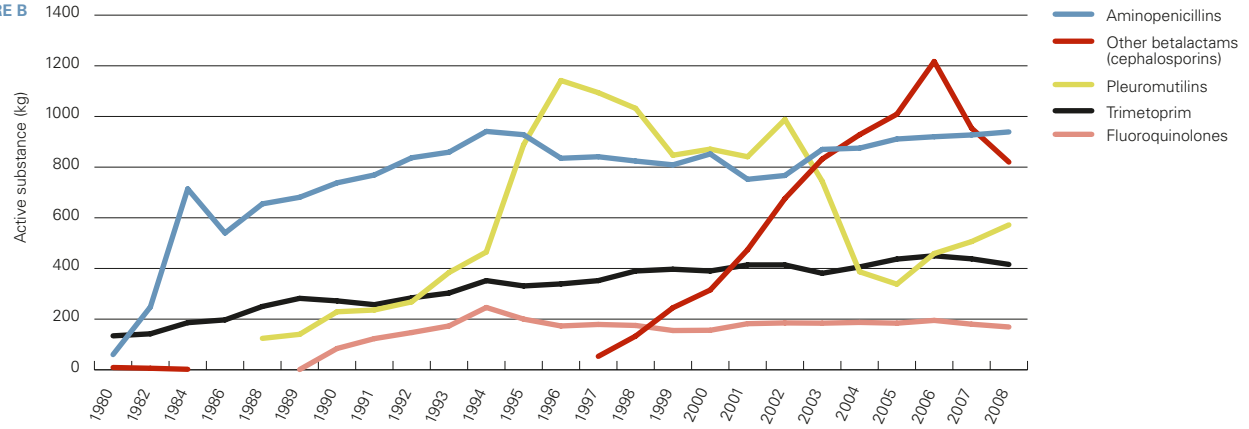



**FIGURE AC II A & B.** Sales of antimicrobials for animals from 1980–2008. Amfenicols, nitromimidazoles, streptogramins, quinoxalines and other feed additives were withdrawn from the market during the time period and are not shown. Note that the scales on the Y-axis are different in figure a and b.

(aminopenicillins with or with out clavulanic acid and cephalosporins) and lincosamides are mainly or exclusively products for oral use in pets. Finally, sales of sulphonamides and trimethoprim are also largely products for oral use in individual animals, mainly for horses. Long term trends total sales of classes that are currently used are illustrated in Figure AC II a & b. Comments on recent trends are found in the following sections.

### Treatment of individual animals

In table AC II, the sales of products for use in individual animals, excluding topical, intrauterine and intramammary use are presented. The total sales in this subset have been relatively unchanged over the last decade.

The sales of intestinal anti-infectives for individual use have declined by 16% over the last three years. Products in this ATCvet category contain either aminoglycosides, polymixins or certain formulations of sulphonamides. The decrease is largely explained by changes in sales of products of the latter type, which today are not generally available on the Swedish market but are sold with special licence prescriptions.

On the Swedish market, the products for systemic use containing penicillins are exclusively products formulated for injection, mostly benzylpenicillin and procaine-penicillin. Since 1998, the sales of this class have decreased by 11%. The main indication for these products is treatment of mastitis in dairy cows. Over the same time period, the number of dairy cows has decreased by 20%. Thus, the overall use per animal may have increased. Alternatively, it is possible that the use of penicillins for other animals than dairy cows (e.g. pigs or horses) has increased.

Until year 2006, the sales of aminopenicillins and cephalosporins increased steadily. Since, the sales have decreased by 8 and 33 percent, respectively. In 2008, 70 and 94% of the sales of these two classes was dispensed for use in dogs (out-patient use). Hence, changes within these groups are almost entirely explained by the amounts prescribed for dogs (see Decreased sales of antimicrobials for dogs).

The sales of sulphonamides and trimethoprim for individual use have increased steadily over time, but have decreased somewhat from year 2006 (8%). In year 2008, 70% of the sales of the combination sulphonamides and trimethoprim were products for oral use in horses (paste or powder). This type of products was introduced on the market in the late 80s, and since, most of the increasing trend in use of trimethoprim and sulphonamides (Figure ACII a & b) is derived from that type of products.

Over the last three years, the sales of fluoroquinolones for therapy of individual animals have decreased by 16%. This is explained both by a marked decrease of products for oral use

in dogs and cats (22% decrease of that subset) and of products for injection (15% decrease of that subset) (see highlight 'Decreased sales of antimicrobials for dogs').

### Treatment of groups or flocks

When considering the risk for development of resistance, the consumption of antimicrobials intended for group or flock medication, e.g. administration via feed or water, is of special interest. Figures on sales of that subset of drugs over the last decade are given in Table AC III. As a reference, figures for 1984, the last year before the termination of use of antimicrobials as feed additives (growth promoting use), are given. More complete data sets for previous years are available in SVARM 2000. From year 2005, products of the class 'intestinal anti-infectives' that are sold with a special licence prescription are included. The active substances in products of that class are currently neomycin and colistin.

Overall, the sales of products intended for medication of groups of animals have decreased by 93% since 1984. This reduction is not only explained by the cessation of growth promoting use, as the corresponding decrease since 1988 is 83% (Figure AC III). Today this subset represents but 15% of the overall sales (total sum of Table AC III divided by total sum of Table I). Products for group treatment are mainly used in pigs except those with penicillins of which about 30% were used for pigs in 2008 and the remainder for poultry, and for those with fluoroquinolones that are mainly used for poultry but also in minor quantities for other species.

In Figure AC III, the development of sales of veterinary medicines and antimicrobial feed additives (before 1986) is shown. Substances grouped as 'others' are the feed additives and other substances that are no longer available on the market (e.g. nitroimidazoles). The figure shows a prominent decrease over the 90s, but between 2005 and 2007, a gradual increase can be noted. In 2008, the total sales were 15% lower than in 2007, indicating that the trend may have been halted.

Two methodological factors could partly contribute to the apparent increase between 2005 and 2007. Firstly, intestinal anti-infectives for medication of groups are included in the statistics from year 2004. Secondly, as noted previously the retrieval system was changed in 2003 and it cannot be excluded that part of the sales of drugs with special licence prescription were initially not captured by the system. However, none of these factors would affect the figures on sales of macrolides or pleuromutilins. The observed increases in these two groups, and also at least partly of the tetracyclines, therefore probably reflect a true increase in use of antimicrobials for group medication.

The use of macrolides and tetracyclines increased from 2004 but for both these classes, a marked drop in sales is noted from 2007 to 2008. Use of oral penicillins (amoxicillin) for pigs could to some extent explain the decrease in tetracyclines as both classes can be used for treatment of acute respiratory infections caused by *Actinobacillus pleuropneumoniae*.

Several factors are likely to contribute to the observed changes in amounts of antimicrobials used for group medication of pigs. Two specific disease problems have probably had an impact, possibly in interaction with an increase in the average herd size. In later years, problems with acute respiratory infections caused by *Actinobacillus pleuropneumoniae* have increased. Further, postweaning multisystemic wasting syndrome (associated with porcine circovirus type 2, PCV2) was diagnosed for the first time in Sweden in year 2003 (Wallgren et al, 2007). In the years following introduction of that infection, antimicrobials were often applied at least in the early stages of infection with the intent to treat concomitant infections. The recent drop in use of macrolides and tetracyclines could reflect increased experience in management of such herds, including vaccination strategies and an awareness that in most cases, antimicrobials have no or limited effect.

The sales of pleuromutilins have increased from year 2004, but the figures are still considerably lower than in earlier years. Pleuromutilins (tiamulin, valnemulin) are authorised for use in pigs with swine dysentery as the main indication. It is probable that efforts to control the disease have resulted in a decreased need to treat swine dysentery, leading to overall declining sales figures since 1998. The reasons for the recent increasing trend are unclear.

Coccidiostats of the ionophore group are used as feed additives to control coccidiosis in the production of chickens for slaughter. Since the late 80s, narasin is by far the most widely applied substance.

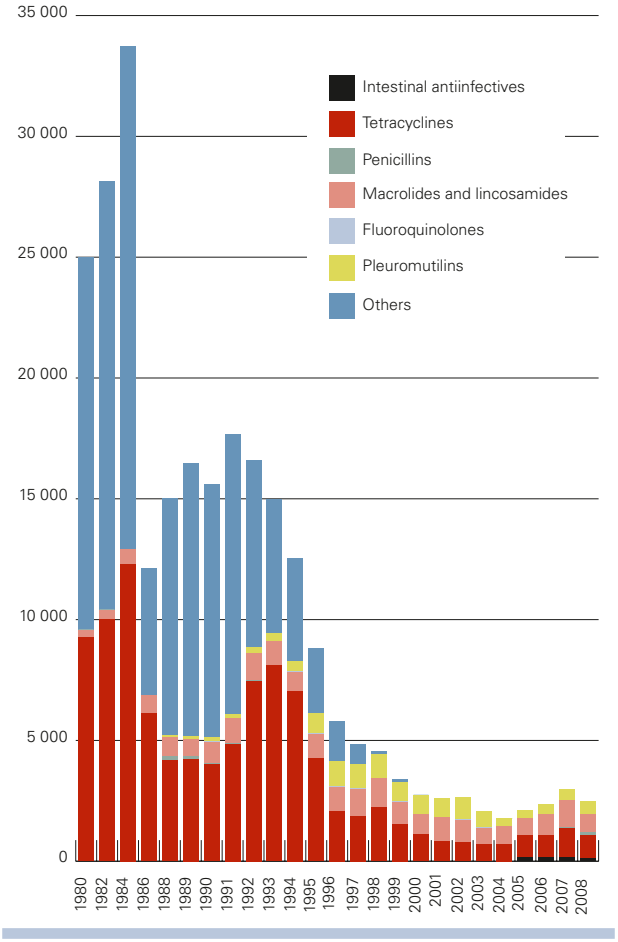



**FIGURE AC III.** Yearly sales of antimicrobial drugs authorised for group treatment measured as kg active substance (based on Table AC III and data from SVARM 2000)

# Decreased sales of antimicrobials for dogs

**AN INCREASE** in the number of prescriptions dispensed for dogs in year 2005 compared to year 1998 was reported in SVARM 2005. The use of beta-lactam antimicrobials with broad spectrum was high in 2005, and the use of fluoroquinolones has been increasing since the mid 90s. As a follow up, the sales of antimicrobials dispensed for systemic use in dogs in the years 2005–2008 are presented in Table AC IV. The dataset includes drugs authorised for systemic oral use in animals (ATC vet code QJ01) as well as for humans (ATC code J01) and corresponds to out-patient care of dogs. The proportion of drugs authorised for use in human medicine was stable and varied between 6–8% of the total sales for dogs in the different study years.

A marked decrease in total sales expressed as total number of prescriptions dispensed for dogs is noted from 2006 to 2008 (-11%; Table AC IV). As shown in Figure AC IV, the decrease is of a similar magnitude or larger when the sales are expressed as number of packages or as kg active substance. Statistics Sweden estimated the total number of dogs in Sweden to 729 000 in year 2006 (SCB, 2006). This figure is lower than the estimates used in SVARM 2005, but is believed to have a higher reliability. Thus, the figures given on numbers of prescriptions/1000 dogs presented in SVARM 2005 were most probably underestimates of the incidence of antimicrobial treatments of dogs. Using the population figure for 2006, around 402 and 357 prescriptions/1000 dogs were dispensed in 2006 and 2008, respectively. The corresponding figures for human out-patient use are 436 and 423 prescriptions/1000 inhabitants.

The most prominent decrease is noted for the cephalosporins, but reductions are also recorded for the fluoroquinolones and 'aminopenicillins with clavulanic acid' (Figure AC V). For all these classes, the downward trend started after 2006. A drop in sales of aminopenicillins is also noted between 2007 and 2008. The only class for which an increase is observed is the 'macrolides and lincosamides'.

The decrease in sales is observed for all units of measurement used, and the observed trends affect certain classes more than others. The canine population is not believed to have decreased in the study years, and assuming that the amounts sold are also used, the figures shown in Table AC IV therefore represent a true decrease in use of antimicrobials for dogs.

In the fall of 2006, the first clinical cases of methicillin resistant *Staphylococcus aureus* (MRSA) and of methicillin resistant *Staphylococcus pseudintermedius* (MRSP) were confirmed by SVA (see corresponding highlights in the chapter on zoonotic bacteria and on animal pathogens, respectively). Regarding MRSP, it soon became evident that one multire-

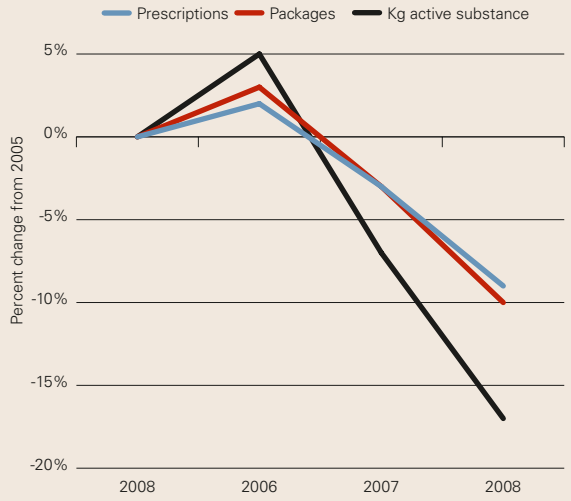



**FIGURE AC IV.** Trends in sales of antimicrobials for systemic use in dogs measured as number of prescriptions, number of packages and kg active substance.

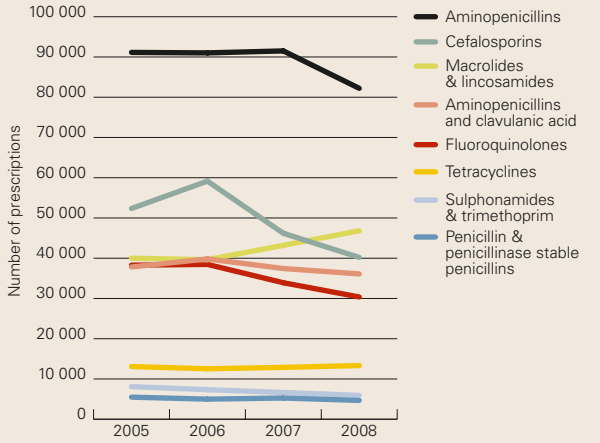



**FIGURE AC V.** Sales of different classes of antimicrobials for systemic use in dogs, number of prescriptions. For ATC groups included in the different classes see Table AC IV.

**TABLE AC IV.** Sales of antimicrobials for systemic use (QJ01 and J01) for dogs in Sweden years 2005-2008. Number of prescriptions dispensed. Data from Apoteket AB.

| ATC(vet)-group | | 2005 | 2006 | 2007 | 2008 | Change 2006-2008 |
|---|---|---|---|---|---|---|
| (Q)J01AA | Tetracyclines | 13 094 | 12 533 | 12 882 | 13 337 | 6% |
| (Q)J01CA | Aminopenicillins | 91 135 | 91 013 | 91 506 | 82 211 | -10% |
| (Q)J01CE | Penicillin & penicillinase stabile penicillins | 5 483 | 4 991 | 5 266 | 4 675 | -6% |
| (Q)J01CR | Aminopenicillins and clavulanic acid | 37 823 | 39 825 | 37 442 | 36 104 | -9% |
| (Q)J01D- | Cefalosporins | 52 359 | 59 152 | 46 196 | 40 203 | -32% |
| (Q)J01EW | Sulphonamides & trimethoprim | 8 098 | 7 340 | 6 640 | 5 917 | -19% |
| (Q)J01F- | Macrolides & lincosamides | 40 003 | 39 634 | 43 202 | 46 820 | 18% |
| (Q)J01MA | Fluoroquinolones | 38 273 | 38 464 | 33 908 | 30 372 | -21% |
| (Q)J01X, (Q)J01R, (Q)J01G | Other | 375 | 333 | 437 | 296 | -11% |
| Total | | 286 643 | 293 285 | 277 479 | 259 935 | -11% |

sistant clone was spreading within and between animal clinics and hospitals. During 2007, statistics on use of antimicrobials for dogs was also published (Pettersson, 2007). These findings were communicated to Swedish veterinarians, but were also given considerable attention in media, including radio, TV and as front page news in major daily newspapers.

The increased attention triggered a number of activities. During 2007 and 2008, experts from SVA gave speeches at seminars and workshops on these topics on more than 50 occasions, spanning from the Swedish Veterinary Congress to local animal hospitals and veterinary clinics around the country. The Swedish Veterinary Society initiated work on a policy on hygiene and a revision of the current guideline for use of antimicrobials in small animal health care. Many hospitals and clinics initiated work on local guidelines on the use of antimicrobials and hygiene. Independently, the Swedish Veterinary Dermatology Study Group issued a new guideline on use of antimicrobials for skin conditions. The importance of good diagnostic workup was iterated, and for some conditions, non-use of systemic antimicrobials was advised. Lincosamides were recommended as drug of choice for first-time pyoderma, and cephalosporins for recurrent pyoderma after bacteriological sampling. The decrease in use of cephalosporins and increase in use of macrolides and lincosamides shown in Figure AC V are well in line with these recommendations.

Taken together, the factors discussed above interacted and led to a generally increased awareness of the problems with antimicrobial resistance. Matters related to antimicrobial policy and hospital hygiene in small animal medicine were intensively discussed both nationally and locally. National and local initiatives, supported by data such as those presented in SVARM, by education and by expert advice probably led to changes in prescribers' behaviour which in turn explains the downward trends recorded for sales of antimicrobials for dogs. The challenge for the future is to keep this discussion going with the aim of further identifying and reducing unnecessary use of antimicrobials and reducing the risk of transfer of resistant bacteria between patients.

# Zoonotic bacteria

**ZOONOSES ARE DISEASES** and infections that can be naturally transmitted between animals and man. Antimicrobial resistance in zoonotic bacteria is therefore of public health concern. In SVARM antimicrobial susceptibility of *Salmonella* and *Campylobacter* from animals are tested. More information on infections with zoonotic bacteria in Sweden is presented in the yearly Swedish zoonoses report, available at www.sva.se.

In SVARM, isolates are classified as susceptible or resistant by epidemiological cut-off values issued by EUCAST (see Appendix 3 for details). This classifies isolates with acquired reduced susceptibility as resistant, which is relevant for monitoring purposes, but it should be understood that this not always implies clinical resistance. To facilitate comparisons when retrospect data are presented, levels of resistance have been recalculated using current cut-off values.

## *Salmonella*

### Isolates included

Findings of *Salmonella* in animals are notifiable in Sweden and isolates from each incident are confirmed at SVA. Antimicrobial susceptibility was tested in one isolate from each involved warm-blooded animal species (wild and domesticated) of incidents notified 2008 and of incidents previously notified but still under restrictions 2008. In addition,

**TABLE SALM I.** Number of *Salmonella enterica* tested for antimicrobial susceptibility year 2008.

| Serovar | Cattle | Pig | Sheep | Poultry | Horse | Dog | Cat | Wildlife | Total |
|---|---|---|---|---|---|---|---|---|---|
| Agona | 1 | | | 5 | | | | | 6 |
| Cubana | | 1 | | | | | | | 1 |
| Dublin | 11 | 2 | | | 1 | | | | 14 |
| Duesseldorf | 1 | | | | | | | | 1 |
| Enterica subsp. diarizonae (IIIb) | 1 | | 2 | 1 | | | | | 4 |
| Enterica subspecies enterica (I) | | 2 | | | | | | 2 | 4 |
| Enteritidis DT 1 | 2 | | | | | | | | 2 |
| Enteritidis DT NST | | | | | | | | 1 | 1 |
| Enteritidis NT | 1 | | | | | | | | 1 |
| Enteritidis, not phagetyped | | | | | | 1 | | | 1 |
| Goldcoast | | 1 | | | | | | | 1 |
| Hessarek | | | | | | | | 1 | 1 |
| Kottbus | | | | | | | | 1 | 1 |
| Livingstone | | | | 1 | | | | | 1 |
| Meleagridis | | 1 | | | | | | | 1 |
| Montevideo | | | | | | 1 | | | 1 |
| Newport | | 1 | | | | | | | 1 |
| Reading | 4 | | 1 | 1 | 3 | 1 | | 4 | 14 |
| Tennessee | | | | | | 1 | | | 1 |
| Thompson | | 1 | | | | | | | 1 |
| Typhimurium DT 1 | 2 | | 1 | | | | | 4 | 7 |
| Typhimurium DT 15a | | | | 1 | | | | | 1 |
| Typhimurium DT 40 | | 7 | | | | | 6 | 1 | 14 |
| Typhimurium DT 41 | 1 | | | | | | | 1 | 2 |
| Typhimurium DT 104 | 2 | 1 | 1 | | | | | | 4 |
| Typhimurium DT 126 | 2 | | | | | | | | 2 |
| Typhimurium DT 151 | 1 | | | | | | | | 1 |
| Typhimurium DT NST | 5 | | | 7 | | 1 | 2 | 1 | 16 |
| Typhimurium DT NST U277 | 1 | 5 | | | | | 1 | | 7 |
| Typhimurium NT | | 1 | | | | | | | 1 |
| Typhimurium, not phagetyped | 4 | 2 | | | | 1 | 1 | 1 | 9 |
| Total | 39 | 25 | 5 | 16 | 4 | 6 | 10[a] | 17 | 122 |
| Percent of total | 32 | 20 | 4 | 13 | 3 | 5 | 8 | 14 | |

[a] Selected from 47 isolates available.

isolates obtained in the salmonella surveillance programme from samples collected at slaughter were tested. If an incident involved more than one serovar or phage type, one isolate of each serovar and phage type was tested. Details on methodology are given in Appendix 3.

### Results and comments

This year, 122 isolates were tested. About two thirds (69%) of the isolates were from major food-producing animals (cattle, sheep, pigs and poultry) and about half (52%) were *S.* Typhimurium (Table Salm I). Occurrence of resistance and distributions of MICs are given in Table Salm II–IV.

The majority of isolates (88%) were susceptible to all antimicrobials tested but 15 isolates were resistant to at least one substance. Of these, five isolates of miscellaneous serotypes and two isolates of *S.* Typhimurium were resistant to one antimicrobial only. One isolate of *S.* Typhimurium from poultry was resistant to streptomycin and sulphonamides. The remaining seven resistant isolates were all *S.* Typhimurium. Of these, one isolate of phage-type DT 151 from cattle and one not phage-typed isolate from a dog were resistant to ampicillin, streptomycin, sulphonamide and tetracycline. Three isolates of *S.* Typhimurium DT 104 from cattle and one isolate from sheep were resistant to these antimicrobials and also to chloramphenicol and florfenicol. These four isolates were from epidemiologically linked herds. Finally one isolate of *S.* Typhimurium DT 104 from pigs was resistant to ampicillin, chloramphenicol, florfenicol, streptomycin, sulphonamide and tetracycline. In addition the isolate was resistant to fluoroquinolones with MIC to ciprofloxacin and nalidixic acid of 0.5 mg/L and 256 mg/L, respectively. This is the first isolate of *S.* Typhimurium from Swedish food-producing animals with confirmed resistance to fluoroquinolones. The finding was made on routine abattoir screening for salmonella of lymph nodes from carcasses but salmonella was not re-isolated from live animals on the farm.

From a public health perspective the prevalence of resistance in *Salmonella* from food-producing animals is more important than resistance in isolates from wild animals or pets. In SVARM, 386 isolates from notified incidents in food-producing animals were tested in the period 2000–08. This includes the vast majority of isolates from notified incidents in food-producing animals in the period. Of these isolates, 180 (47%) were *S.* Typhimurium. About half of these were from pigs (47%), one fourth from cattle (26%) and poultry (25%), respectively and four isolates (2%) were from sheep. Occurrence of resistance and distributions of MICs are given in Table Salm V. Among *S.* Typhimurium from the period 2000–2008, 30 isolates (17%) were resistant to at one least antimicrobial and 23 isolates to more than three substances (Table Salm VI). Among other serovars, 18 isolates (9%) were resistant to at least one antimicrobial and three of these to two substances.

Eighteen of the 180 isolates of *S.* Typhimurium in food-producing animals from 2000–08 involved multiresistant strains, i.e. resistant to at least three antimicrobials. All 18 isolates were among 127 isolates from 2004–08, whereas none of 52 isolates from 2000–03 were multiresistant. The isolates were from 16 separate incidents of which nine involved cattle, two involved pigs only and one incident involved both pigs and cattle. Of the remaining incidents one was in sheep, one in ducks for food production and one in ducks in a hobby flock. Three incidents in 2004 involving cattle were epidemiologically linked through trade of calves. In addition an epidemiological link is suspected between four incidents 2007–2008 involving cattle, pigs and sheep. Epidemiological links between the other incidents are unknown. Resistance phenotypes of the isolates involved are given in Table Salm VI.

Multiresistance in *Salmonella* from Swedish food-producing animals occurred also before 2004. In 1997 to 1999, five of 51 incidents in food-producing animals involved multiresistant *S.* Typhimurium, either DT 104 or DT 193. The cluster of incidents with multiresistant strains in later years is therefore probably coincidental and not an indication of an overall increased occurrence.

From an international perspective, the overall situation

**TABLE SALM II.** Distribution of MICs for all serovars of *Salmonella enterica* (n=122) from animals, 2008.

| Antimicrobial | Resistance (%) | Distribution (%) of MICs[a] (mg/L) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | ≤0.008 | 0.016 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | 64 | 128 | 256 | 512 | 1024 | >1024 |
| Ampicillin | 7 | | | | | | | 9.0 | 80.3 | 4.1 | | | | | | 6.6 | | | | |
| Cefotaxime | 0 | | | | 30.3 | 62.3 | 7.4 | | | | | | | | | | | | | |
| Chloramphenicol | 4 | | | | | | | | | 9.0 | 82.0 | 3.3 | 1.6 | | | | 4.1 | | | |
| Ciprofloxacin | 2 | | | 51.6 | 45.9 | 0.8 | 0.8 | 0.8 | | | | | | | | | | | | |
| Florfenicol | 4 | | | | | | | | | 6.6 | 79.5 | 7.4 | 2.5 | 1.6 | 2.5 | | | | | |
| Gentamicin | <1 | | | | | | | 20.5 | 73.8 | 4.9 | 0.8 | | | | | | | | | |
| Kanamycin | 0 | | | | | | | | 1.6 | 36.1 | 58.2 | 3.3 | 0.8 | | | | | | | |
| Nalidixic acid | <1 | | | | | | | | | 2.5 | 85.2 | 11.5 | | | | | 0.8 | | | |
| Streptomycin | 9 | | | | | | | | | | 4.9 | 15.6 | 52.5 | 18.0 | 3.3 | 2.5 | 1.6 | 1.6 | | |
| Sulphonamide | 7 | | | | | | | | | | | | | 9.8 | 41.8 | 41.0 | 0.8 | | | 6.6 |
| Tetracycline | 6 | | | | | | | | 50.0 | 44.3 | | | 1.6 | 1.6 | 0.8 | 1.6 | | | | |
| Trimethoprim | 0 | | | | | | 32.8 | 63.1 | 4.1 | | | | | | | | | | | |

[a] White fields denote range of dilutions tested. Values above the range denote MICs greater than the highest concentration tested. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Vertical lines indicate cut-off values for resistance.

of *Salmonella* among Swedish animals is favourable. Swedish food-producing animals are virtually free from *Salmonella*, most likely a result of the strategies in the Swedish *Salmonella* control programme, and few incidents involve multiresistant strains. Nevertheless, in view of the public health consequences of multiresistant *Salmonella*, vigilance towards such strains in food-producing animals is warranted.

**TABLE SALM III.** Distribution of MICs for *Salmonella* Typhimurium (n=64) from animals, 2008.

| Antimicrobial | Resistance (%) | Distribution (%) of MICs[a] (mg/L) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | ≤0.008 | 0.016 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | 64 | 128 | 256 | 512 | 1024 | >1024 |
| Ampicillin | 13 | | | | | | | | 85.9 | 1.6 | | | | | | 12 5 | | | | |
| Cefotaxime | 0 | | | | 20.3 | 75.0 | 4.7 | | | | | | | | | | | | | |
| Chloramphenicol | 8 | | | | | | | | | 4.7 | 85.9 | 1.6 | | | | | 7.8 | | | |
| Ciprofloxacin | 3 | | | 48.4 | 48.4 | 1.6 | | 1.6 | | | | | | | | | | | | |
| Florfenicol | 8 | | | | | | | | | 6.3 | 82.8 | 3.1 | | 3.1 | 4.7 | | | | | |
| Gentamicin | 0 | | | | | | | 17.2 | 79.7 | 3.1 | | | | | | | | | | |
| Kanamycin | 0 | | | | | | | | | 32.8 | 64.1 | 1.6 | 1.6 | | | | | | | |
| Nalidixic acid | 2 | | | | | | | | | | 89.1 | 9.4 | | | | | 1.6 | | | |
| Streptomycin | 13 | | | | | | | | | | 1.6 | 17.2 | 51.6 | 17.2 | 1.6 | 4.7 | 3.1 | 3.1 | | |
| Sulphonamide | 13 | | | | | | | | | | | | | 3.1 | 39.1 | 43.8 | 1.6 | | | 12.5 |
| Tetracycline | 11 | | | | | | | | 39.1 | 50.0 | | | 3.1 | 3.1 | 1.6 | 3.1 | | | | |
| Trimethoprim | 0 | | | | | | 25.0 | 71.9 | 3.1 | | | | | | | | | | | |

[a] White fields denote range of dilutions tested. Values above the range denote MICs greater than the highest concentration tested. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Vertical lines indicate cut-off values for resistance.

**TABLE SALM IV.** Resistance (%) and source of isolates in *Salmonella* Typhimurium from animals 1978-2008.

| Antimicrobial | Cut-off value (mg/L) | Resistance (%) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 1978-88[a] (n=125) | 1989-99 (n=317) | 2000-02 (n=108) | 2003 (n=49) | 2004 (n=49) | 2005 (n=85) | 2006 (n=53) | 2007 (n=72) | 2008 (n=64) |
| Ampicillin | >4 | 2[b] | 6[b] | 3 | 0 | 8 | 9 | 17 | 8 | 13 |
| Cefotaxime | >0.5 | - | - | - | - | - | 0 | 0 | 0 | 0 |
| Ceftiofur | >2 | - | - | 0 | 0 | 0 | 0 | 0 | - | - |
| Chloramphenicol | >16 | 4[b] | 5[b] | 3 | 0 | 8 | 9 | 2 | 1 | 8 |
| Ciprofloxacin | >0.06 | - | - | - | - | - | - | 0 | 0 | 3 |
| Enrofloxacin | >0.25 | - | 1 | 0 | 0 | 0 | 1 | - | - | - |
| Florfenicol | >16 | - | - | 3 | 0 | 6 | 8 | 2 | 1 | 8 |
| Gentamicin | >2 | - | 0[b] | 0[c] | 2 | 0 | 0 | 0 | 0 | 0 |
| Kanamycin | >16 | - | - | - | - | - | - | 0 | 0 | 0 |
| Nalidixic acid | >16 | - | - | 4 | 0 | 0 | 1 | 0 | 0 | 2 |
| Neomycin | >4 | 0[b] | 1[b] | 4 | 0 | 0 | 0 | - | - | - |
| Streptomycin | >32 | 74 | 15 | 4 | 2 | 8 | 10 | 11 | 4 | 13 |
| Sulphonamide | >256 | - | - | 3 | 2 | 8 | 10 | 15 | 7 | 13 |
| Tetracycline | >8 | 13 | 6 | 3 | 0 | 8 | 9 | 11 | 4 | 11 |
| Trimethoprim | >2 | - | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Trim/sulph. | >0.5/9.5 | 0 | 3 | - | - | - | - | - | - | - |
| **Percent of isolates from:** | | | | | | | | | | |
| Cattle, sheep, pigs, poultry | | 100 | 46 | 45 | 12 | 33 | 19 | 40 | 53 | 70 |
| Horses, cats, dogs | | | 29 | 36 | 82 | 61 | 58 | 36 | 17 | 16 |
| Wildlife | | | 25 | 19 | 6 | 6 | 23 | 24 | 30 | 14 |

[a] 1988 includes isolates to September, isolates from October-December 1988 given under 1989; [b] Cut-off value for resistance >8 mg/L; [c] Cut-off value for resistance >4 mg/L.

**TABLE SALM V.** Distribution of MICs for *Salmonella* Typhimurium (n=180) from food-producing animals 2000-2008.

| Antimicrobial | Resistance (%) | Distribution (%) of MICs[a] (mg/L) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | ≤0.008 | 0.016 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | 64 | 128 | 256 | 512 | 1024 | >1024 |
| Ampicillin | 13 | | | | | | | 3.3 | 62.8 | 19.4 | 1.7 | | | | 12.8 | | | | | |
| Cefotaxime[b] | 0 | | | | 23.2 | 67.9 | 8.9 | | | | | | | | | | | | | |
| Ceftiofur[c] | 0 | | | | | | | 28.7 | 68.3 | 3.0 | | | | | | | | | | |
| Chloramphenicol | 7 | | | | | | | | | 8.3 | 81.1 | 3.9 | | | | 1.1 | 5.6 | | | |
| Ciprofloxacin[d] | 1 | | | 55.6 | 43.4 | | | 1.0 | | | | | | | | | | | | |
| Enrofloxacin[e] | 0 | | | | 54.3 | 42.0 | 3.7 | | | | | | | | | | | | | |
| Florfenicol | 6 | | | | | | | | | | 90.0 | 3.3 | 0.6 | 6.1 | | | | | | |
| Gentamicin | 2 | | | | | | | 16.1 | 68.9 | 12.8 | 2.2 | | | | | | | | | |
| Kanamycind | 0 | | | | | | | | | 24.2 | 69.7 | 5.1 | 1.0 | | | | | | | |
| Nalidixic acid | 1 | | | | | | | | | 1.1 | 73.9 | 17.2 | 6.7 | 0.6 | | | 0.6 | | | |
| Neomycin[e] | 0 | | | | | | | | | 84.0 | 16.0 | | | | | | | | | |
| Streptomycin | 11 | | | | | | | | | | 0.6 | 16.1 | 57.8 | 14.4 | 3.3 | 2.8 | 3.3 | 1.7 | | |
| Sulphonamide | 14 | | | | | | | | | | | | | | 46.1 | 34.4 | 6.7 | | | 13.8 |
| Tetracycline | 10 | | | | | | | | 29.4 | 53.3 | 7.2 | | 2.2 | 1.1 | 2.8 | 3.9 | | | | |
| Trimethoprim | 0 | | | | | | 30.0 | 61.7 | 8.3 | | | | | | | | | | | |

[a] White fields denote range of dilutions tested. Values above the range denote MICs greater than the highest concentration tested. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Vertical lines indicate cut-off values for resistance; [b] 112 isolates tested; [c] 101 isolates tested; [d] 99 isolates tested; [e] 81 isolates tested

**TABLE SALM VI.** Resistance phenotypes and multiresistance (%) of *Salmonella* Typhimurium (n=180) from food-producing animals years 2000-2008. All isolates tested for susceptibility to ampicillin, ceftiofur/cefotaxime, enrofloxacin/ciprofloxacin, florfenicol, gentamicin, chloramphenicol, nalidixic acid, streptomycin, sulphametoxazole, tetracycline, and trimethoprim. Breakpoints for resistance are given in Table Salm V.

| Resistance pattern[a] | Animal species | Phage type | | | | | | | | | | | | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 104 | 120 | 195 | 193 | 151 | 126 | 99 | 41 | 40 | 15a | 10 | 12 | 9 | 1 | NST | U277 | NT | Not typed | |
| AmFfCmSmSuTcNalCi | Pig | 1 | | | | | | | | | | | | | | | | | | 1 |
| AmFfCmSmSuTc | Cattle | 5 | 1 | | | | | | | | | | | | | | | | 1 | 7 |
| AmFfCmSmSuTc | Pig | 1 | | | | | | | | | | | | | | | | | 1 | 2 |
| AmFfCmSmSuTc | Sheep | 1 | | | | | | | | | | | | | | | | | | 1 |
| AmCmSmSuTc | Cattle | 1 | | | | | | | | | | | | | | | | | | 1 |
| AmSmSuTc | Cattle | | | | | 1 | | | | | | | | | | | | 2 | | 3 |
| AmSmSuTc | Pig | | 1 | | | | | | | | | | | | | | | | | 1 |
| AmSmSuTc | Poultry | | | | | | | | | | | | | | | | | 2 | | 2 |
| AmSu | Cattle | 2 | | | | | | | | | | | | | | | | | | 2 |
| AmSu | Pig | 1 | | | | | | | | | | | | | | | | | | 1 |
| SmSu | Poultry | | | | | | | | | | 2 | | | | | | | | | 2 |
| Nal | Pig | | | | | | | | | | | | 1 | | | | | | | 1 |
| Gm | Cattle | | | | | | | | 1 | | | | | | | | | | | 1 |
| Gm | Pig | | | | | | | | | 1 | | | | | | | | | | 1 |
| Gm | Poultry | | | | | | | | 1 | | | | | | | 1 | | | | 2 |
| Am | Poultry | | | | | | | | | | | | | | | 2 | | | | 2 |
| Susceptible | Sheep | | | | | | | | | | | | | | 1 | | | | 2 | 3 |
| Susceptible | Cattle | 1 | 2 | | | | 2 | | 3 | | 1 | 2 | | | 2 | 15 | | 1 | 4 | 33 |
| Susceptible | Pig | 2 | 3 | | | | | 1 | 7 | 35 | | | 2 | | 1 | 15 | 1 | 3 | 7 | 77 |
| Susceptible | Poultry | | 1 | 1 | 1 | | | | 2 | 3 | | | 1 | 1 | 1 | 23 | 1 | 2 | | 37 |
| Number of isolates | | 15 | 8 | 1 | 1 | 1 | 2 | 1 | 14 | 39 | 3 | 2 | 4 | 1 | 5 | 56 | 2 | 10 | 15 | 180 |
| percent of total | | 8 | 4 | <1 | <1 | <1 | 1 | <1 | 8 | 22 | 2 | 1 | 2 | <1 | 3 | 31 | 1 | 6 | 8 | |
| **Multiresistance** (%) | | | | | | | | | | | | | | | | | | | | |
| Susceptible to all antimicrobials | | 20 | 25 | 100 | 100 | | 100 | 100 | 86 | 97 | 33 | 100 | 75 | 100 | 100 | 95 | 100 | 60 | 87 | 83 |
| Resistant to 1 antimicrobial | | | | | | | | | 14 | 3 | | | 25 | | | 5 | | | | 4 |
| Resistant to 2 antimicrobials | | | | | | | | | | | 66 | | | | | | | | | 3 |
| Resistant to 3 antimicrobials | | 20 | | | | | | | | | | | | | | | | | | |
| Resistant to >3 antimicrobials | | 60 | 75 | | | 100 | | | | | | | | | | | | 40 | 13 | 10 |

[a] Am: ampicillin; Ff : florfenicol; Cm: chloramphenicol; Sm: streptomycin; Su: sulphonamide; Tc: tetracycline; Nal: nalidixic acid; Gm: gentamicin.; Ci: ciprofloxacin.

## Campylobacter

### Isolates included

*Campylobacter* were isolated from intestinal contents from slaughter pigs and broilers. Isolates from pigs were from samples of colon content collected at abattoirs for isolation of indicator bacteria. Isolates from broilers were from caecal content collected at abattoirs within the framework of the 2008 survey on prevalence of *Campylobacter* in broilers initiated by a decision of the European Commission (2007/516/EC). Isolates were identified as *Campylobacter jejuni* or as hippurate-negative thermophilic *Campylobacter* spp. For details on methodology and sampling strategy, see Appendix 3.

### Results and comments

Pig

*Campylobacter* were isolated from 99 (77%) of 129 samples cultured. The majority of isolates, 97, were hippurate-negative thermophilic *Campylobacter* spp. and only two were *C. jejuni*. The isolation frequency is similar to previous studies in SVARM.

Among *Campylobacter* spp. resistance to gentamicin did not occur and only one and two isolates were resistant to erythromycin and tetracycline, respectively (Table Camp I). Resistance to quinolones (ciprofloxacin and nalidixic acid) or streptomycin was common and occurred in about one third and about half of the isolates respectively. Resistance in an isolate was mostly to a single substance but 18 isolates were resistant to both quinolones and streptomycin and of these one isolate was resistant also to erythromycin. In addition one isolate was resistant to tetracycline and streptomycin. Of the two isolates of *C. jejuni* one was resistant to quinolones and the other was susceptible to all antimicrobials tested.

The results for 2008 tally with previous data from SVARM. No trends are discernable in the period since 1999 (Table Camp I). Resistance to quinolones is common among *Campylobacter* spp. although neither quinolones nor fluoroquinolones are authorised or used for treatment of groups of pigs via feed or water in Sweden. Injectables, i.e. enrofloxacin and danofloxacin, are authorised but the extent of usage in pigs is unknown. These drugs are unlikely to be used in fattening pigs older than 12 weeks but probably to some extent in piglets and sows. Selection for quinolone resistance in *Campylobacter* therefore probably occurs in younger pigs and/or sows before pigs are moved to the finishing stage. The high prevalence (39%) of quinolone resistance in *Campylobacter* spp. from piglets <12 weeks old reported in SVARM 2006 supports this hypothesis.

Occurrence of streptomycin resistance in *Campylobacter* spp. is remarkably high (57%) but since previous data on resistance in Swedish isolates are lacking trends in resistance cannot be evaluated. A high prevalence of streptomycin resistance in *C. coli* from pigs and cattle is reported also from other countries (EFSA, 2007). No isolate of *C. jejuni* from Swedish broilers was resistant to streptomycin (see below). Such resistance is reported also in *C. jejuni* from poultry and cattle although it seems to be much less common than in *C. coli* from pigs (EFSA, 2007). This could reflect a difference between species of *Campylobacter* in the ability to acquire resistance determinants. But since *C. coli* is mostly isolated from pigs and *C. jejuni* from poultry and cattle, differences in resistance between the

**TABLE CAMP I.** Distribution of MICs and resistance (%) of hippurate-negative thermophilic *Campylobacter* spp. from slaughter pigs 2008. Data on resistance for 1999, 2003 and 2005 are given for comparison.

| | | | | | Distribution (%) of MICs[a] (mg/L) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Substance** | **1999** (n= 91) | **2003** (n=100) | **2005** (n=97) | **2008** (n=97) | **≤0.06** | **0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **64** | **>64** |
| Ciprofloxacin | 30[b] | 17[b] | 24[b] | 30 | 5.2 | 29.9 | 28.9 | 6.2 | | | 2.1 | 7.2 | 20.6 | | | |
| Erythromycin | 1 | 0 | 0 | 1 | | | | 17.5 | 33.0 | 41.2 | 6.2 | 1.0 | | | | 1.0 |
| Gentamicin | 0 | - | 0 | 0 | | | 2.1 | 10.3 | 86.6 | 1.0 | | | | | | |
| Nalidixic acid | 30 | 17 | 24 | 29 | | | | | | | 23.7 | 32.0 | 14.4 | 1.0 | 6.2 | 22.7 |
| Streptomycin | - | - | - | 57 | | | | | 1.0 | 4.1 | 38.1 | 3.1 | | | 18.6 | 35.1 |
| Tetracycline | 4 | 3 | 4 | 2 | | 38.1 | 43.3 | 11.3 | 5.2 | | | | 1.0 | 1.0 | | |

[a] White 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. Vertical lines indicate cut-off values defining resistance; [b] Enrofloxacin tested.

**TABLE CAMP II.** Distribution of MICs and resistance (%) of *Campylobacter jejuni* from broilers 2008. Data on resistance for 2001, 2002 and 2004 are given for comparison.

| | | | | | Distribution (%) of MICs[a] (mg/L) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Substance** | **2001** (n=91) | **2002** (n=100) | **2004** (n=97) | **2008** (n=38) | **≤0.06** | **0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **64** | **>64** |
| Ciprofloxacin | 2[b] | 0[b] | 5[b] | 0 | 28.9 | 63.2 | 5.3 | 2.6 | | | | | | | | |
| Erythromycin | 0 | 0 | 0 | 0 | | | | 89.5 | 2.6 | 7.9 | | | | | | |
| Gentamicin | - | - | 1 | 0 | | 2.6 | 18.4 | 76.3 | 2.6 | | | | | | | |
| Nalidixic acid | 5 | 0 | 5 | 0 | | | | | | 34.2 | 52.6 | 10.5 | 2.6 | | | |
| Streptomycin | - | - | - | 0 | | | | 5.3 | 71.1 | 23.7 | | | | | | |
| Tetracycline | 0 | 1 | 3 | 0 | | 97.4 | | 2.6 | | | | | | | | |

[a] White 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. Vertical lines indicate cut-off values defining resistan ce; [b] Enrofloxacin tested.

# Strama VL – strategies against antimicrobial resistance

**IN EARLY 2007,** the Swedish parliament decided on a Swedish strategic programme against antimicrobial resistance. The strategy is multifaceted, and involves both human and veterinary medicine (Government bill 2005/06:50). The mission of this programme is to preserve the efficacy of antibiotics for treatment of humans and animals. The strategy involves both human and veterinary medicine.

### A coordinated strategy

The core elements of the Swedish strategy are illustrated in Figure below. Experience from Sweden and other countries shows that effective strategies against antimicrobial resistance should be multifaceted, involving monitoring of use and resistance, prevention and infection control and prudent use of antimicrobials. Continuous information, education and research are key to increase awareness and bridge knowledge gaps. Resistance is a global problem impacting on both public and animal health, and it is therefore essential that countries work together and share experiences. Lastly, for these activities to be fully effective, a platform for exchange of experiences, collaboration and coordination is needed.

In human medicine in Sweden, the coordinating function is filled by Strama (www.strama.se), an organization that is active both locally and nationally. During 2008, a secretariat to support a similar organization, Strama VL (VL stands for veterinary and food), has been operative at the National Veterinary Institute (SVA). Its tasks are to coordinate activities aiming to contain antibiotic resistance within the veterinary and food sector, to be and to take initiatives in prioritized areas. Strama VL was mandated by the Swedish Government, and is to work in close collaboration with Strama.

During 2008, the activities of Strama VL have been focused on strategic planning. Examples of other activities are:

- Publication of a Swedish shorter version of the SVARM report,
- A workshop on antimicrobial treatment of cattle for bovine practitioners in collaboration with SVARMpat, SVA and the Swedish Animal Health Services,
- Statistics on use of antimicrobials for dogs and cats in Sweden,
- A Danish-Norwegian-Swedish collaborative study on sales of antimicrobials for dogs,
- Participation in a number national working groups,
- A risk profile on antimicrobial resistance in collaboration with the Food Agency,
- Participation in scientific working groups in the European Union and in Task Force on Antimicrobial Resistance of the Codex Alimentarius.

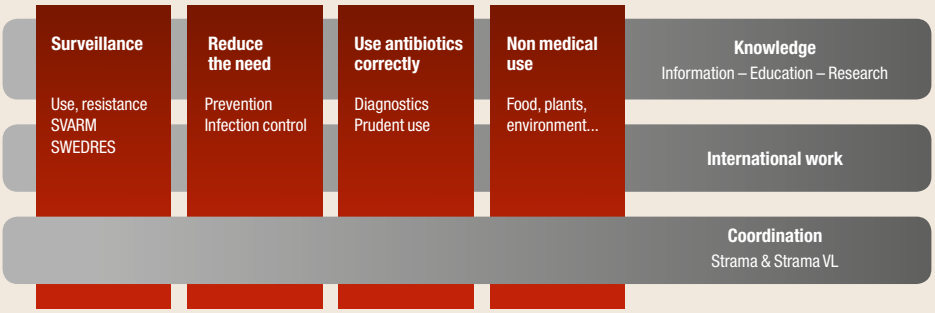



**FIGURE.** Core elements of the Swedish strategy on antimicrobial resistance.

two bacterial species could also be due to differences in selection pressure between poultry, pig and cattle populations.

Streptomycin resistance in *Campylobacter* spp. from Swedish pigs is difficult to explain in the of context selection by use since streptomycin is rarely used in pigs in recent years. Neither is co selection by use of other substance likely since 65% of the streptomycin resistant isolates were resistant only to this antimicrobial. However, similar *aadA2* encoding class 1 integrons, encoding streptomycin/spectinomycin resistance, have been identified in *Campylobacter*, *Escherichia coli* and *Salmonella* (O'Halloran et al., 2004). Accordingly, streptomycin resistance could be a marker for the presence of a transferable resistance element and the issue deserves further study.

### Broiler

In all, 38 isolates of *C. jejuni* and one isolate of hippurate-negative thermophilic *Campylobacter* spp. were tested for antimicrobial susceptibility. None of the isolates was resistant to any of the antimicrobials tested. The results are in good agreement with previous data from SVARM demonstrating that resistance in *C. jejuni* from Swedish broiler is rare (Table Camp II).

Notably, resistance to macrolides (erythromycin) and fluoroquinolones (ciprofloxacin/enrofloxacin) is rare or absent in *C. jejuni* from Swedish broilers. This is in agreement with the limited use of these antimicrobial classes in Swedish broiler production (see "Use of antimicrobials"). It is therefore likely that resistance to ciprofloxacin and erythromycin in *Campylobacter* isolated from humans in Sweden 2007, 45% and 7% respectively (SWEDRES 2007) is a consequence of infections contracted abroad or of consumption of imported foodstuffs.

# Methicillin resistant *Staphylococcus aureus* (MRSA) in Swedish animals – an update

**METHICILLIN RESISTANT** *Staphylococcus aureus* (MRSA) has emerged in several animal species worldwide (EFSA, 2009, CVMP 2009). This is of clinical importance in veterinary medicine because infections in animals can be difficult to treat but of greater concern is the zoonotic aspect, since MRSA can be transferred between animal and man. In human healthcare, MRSA is a serious problem worldwide.

In Sweden MRSA is still rarely isolated in animals. But the situation can rapidly change if livestock associated lineages of MRSA are introduced to populations of intensively reared food-producing animals. Likewise, inadequate infection control in animal health care settings can lead to a rapid spread of MRSA among companion animals and horses. The current situation is summarized below.

### Dogs and cats

The first MRSA from animals in Sweden were isolated from two dogs in 2006. Since, including the first quarter of 2009, MRSA has been confirmed by the National Veterinary Institute (SVA) in 10 dogs and one cat. The cases were diagnosed at four different animal hospitals located in different counties. Twelve isolates were of *spa*-type 032 and had the same antibiogram including high level ciprofloxacin resistance (MIC >4 mg/L) in addition to beta-lactam resistance. All these isolates were from post-operative wound infections. The thirteenth isolate was from a skin wound due to mange in a dog. This isolate was of a different *spa*-type, 127, than the other and also had a different antibiogram including resistance to ciprofloxacin, erythromycin, tetracycline, gentamicin, kanamycin and trimethoprim in addition to beta-lactam resistance. All isolates were negative for genes coding for Panton Valentine Leukocidin toxin (PVL).

Thus, the vast majority of MRSA isolated from dogs and cats in Sweden are of *spa*-type 032 which also is the most common linage in humans in the country (SWEDRES 2008). This is in agreement with findings abroad and supports the observation of others that humans often are a source of infection for small companion animals (EFSA 2009, CVMP 2009).

### Horses

The first finding of MRSA in a Swedish horse was from a study in 2007 where 300 horses were screened by selective culture of nasal swabs (see SVARM 2007). The isolate was of *spa*-type 011 and clonal complex CC398 and resistant to beta-lactam antibiotics, gentamicin, kanamycin, tetracycline and trimethoprim. Clonal complex CC398 is the livestock associated MRSA mostly found in pigs and other food-producing animals but reported also from other animals including horses (EFSA 2009, CVMP 2009).

In the summer of 2008 the first outbreak of MRSA infections in Swedish horses occurred at an equine hospital. Six horses with postoperative wound infections were confirmed with MRSA. During the outbreak an epidemiological tracing by screening contact horses outside the hospital for MRSA was initiated by the Swedish Board of Agriculture. The tracing revealed one horse, without any signs of infection, as carrier of MRSA in the nostrils.

The index case of the outbreak was not established. All MRSA isolates had the same antibiogram including resistance to gentamicin, kanamycin, tetracycline, trimethoprim and beta-lactams. Six of the seven isolates were tested for *spa*-type and all were 011. Both antibiogram and *spa*-type are the same as the isolate of CC398 from the screening study in 2007 (see above). MRSA of *spa*-type 011 have been documented in humans in Sweden but only in a small number of cases (SMI, 2009).

### Food-producing animals

Occurrence of MRSA in food-producing animals is reported from countries around the world, mostly in pigs but a high prevalence has been documented also among veal calves and broilers and MRSA are found in milk from dairy cows (for a review see EFSA, 2009). In production animals, the livestock associated MRSA CC398 dominates.

Reports from other countries on MRSA in animals led to increased awareness also in Sweden and several surveys screening for MRSA in food-producing animals were carried out in recent years. In the fall of 2006 and early spring 2007 slaughter pigs were screened for MRSA in collaboration with the Swedish Animal Health Services. In each of 100 slaughter pig production units distributed across the country, samples were taken from the nostrils from five pigs in five different pens. In previous years, samples of milk from dairy cows have been screened for MRSA on several occasions. Further, in 2003 the Food Production Agency screened *S. aureus* isolated from chicken carcasses. Hitherto, MRSA has not been isolated from food-producing animals in Sweden.

In view of reports of a high prevalence of MRSA in pigs in some European countries the European Commission initiated a baseline study on prevalence of MRSA in pigs to be conducted in 2008. All member states were obliged to screen a proportionate number of holdings with breeding pigs for MRSA using harmonized methodology (Decision 2008/55/EC). Briefly, samples of dust collected inside stables were enriched and cultured on media selective for MRSA.

In Sweden, MRSA was not isolated from any of the samples collected from 208 herds randomly selected among herds meeting the inclusion criteria. This is in agreement with the study on slaughter pigs performed 2006/2007. The results indicate that MRSA currently is at most rare among Swedish pigs.

### Future strategies

In view of the recently emerged situation in some animal populations, the public health significance of MRSA in animals and food was recently assessed by the Panel on Biological Hazards of the European Food Safety Authority (EFSA) (EFSA, 2009). One conclusion of the panel is that livestock-associated lineages, i.e. CC398, can be a major contributor to the overall MRSA burden in countries with a low prevalence of human MRSA infection but is of less

significance in countries where human infections are more common. The panel recommends that the prevalence of MRSA in food producing animals should be periodically monitored since this is essential to determine control strategies and evaluate their effect.

In the EFSA document and also in a reflection paper from the Committee for Medicinal Products for Veterinary Use (CVMP, 2009) control options to mitigate MRSA in food producing and companion animals are discussed. Among such options is improved biosecurity to hinder spread of MRSA to, between and within farms with food-producing animals. Likewise improved infection control in animal health care settings would prevent spread and nosocomial infections in companion animals. A reduction of antimicrobial selection pressure in animal populations by prudent use of antimicrobials is recommended. Of key importance to control transfer of MRSA between humans and animals are basic hygiene measures such as hand washing and disinfection. Other strategies could be to decolonize carriers and clear environments from MRSA but here knowledge is lacking and studies are needed.

Sweden is still a country with a comparatively low prevalence of human MRSA infection although the annual number of reported cases is increasing both in hospitals and in the community (SWEDRES 2008). Moreover, MRSA was only recently isolated from animals in Sweden and the number of confirmed cases is still low. In January 2008, MRSA in animals was made notifiable to the Swedish Board of Agriculture and this year three cases in dogs and seven in horses were reported. Therefore, if instituted immediately efficient measures to hinder spread within animal populations as outlined above could avert a situation where animals constitute a reservoir for MRSA spreading into human health care.

# Indicator bacteria

**THE PREVALENCE** of acquired antimicrobial resistance in bacteria of the enteric microflora of healthy animals indicates the magnitude of the selective pressure from use of antimicrobials in a population. Effect on resistance of changes in use of antimicrobials in an animal population can be evaluated by monitoring resistance among commensal bacteria at regular intervals. In SVARM, *Escherichia coli* and *Enterococcus* spp. from healthy animals serve as indicator bacteria for the normal enteric microflora.

Resistance to more than one antimicrobial in a bacterium (co-resistance) can indicate that resistance genes are located on the same genetic element. Evaluation of resistance patterns, i.e. phenotypes, can give insight in resistance selection since use of one antimicrobial can select for resistance to other, unrelated antimicrobials (co-selection) and a single transfer event can convey resistance to several antimicrobials to a recipient bacterium (co-transfer).

Although most bacteria of the normal enteric microflora are unlikely to cause disease, they can be a reservoir for resistance genes that can spread to bacteria that cause infections in animals or humans. The exposure of humans to the reservoir among production animals is indicated by occurrence of resistant bacteria in food of animal origin. Therefore, occurrence of resistance among indicator bacteria from meat at retail is monitored in SVARM.

In SVARM, isolates of indicator bacteria are classified as susceptible or resistant by epidemiological cut-off values issued by EUCAST (see Appendix 3 for details). This classifies isolates with acquired reduced susceptibility as resistant, which is relevant for monitoring purposes, but it should be understood that this not always implies clinical resistance. Resistance data from earlier SVARM reports are recalculated using current cut-off values.

### Samples cultured and isolates included

**Slaughter pigs and pork**: *Escherichia coli* and *Enterococcus* spp. are from caecal content from healthy slaughter pigs sampled at slaughter and from raw pork of Swedish origin collected at retail. All samples were screened for *E. coli* resistant to third generation cephalosporins by culture on media supplemented with cefotaxime (1mg/L).

**Sheep**: *Escherichia coli* and *Enterococcus* spp. are from rectal swabs of healthy sheep (lambs and ewes) sampled on farms. One ewe and one lamb were sampled on each farm.

**Broilers:** Occurrence of vancomycin resistant enterococci (VRE) in intestinal content from broilers was investigated using culture on media supplemented with vancomycin (16 mg/L).

For details on methodology and sampling strategy, see Appendix 3. Antimicrobials tested and concentration ranges used are given in Table EC IV and ENT VII-IX.

## *Escherichia coli*

### Slaughter pigs and pork

In samples from pigs *Escherichia coli* were isolated from 77% of 452 samples cultured. The majority (79%) of the 349 isolates was susceptible to all 12 antimicrobials tested but 75 isolates (21%) were resistant to at least one substance (Table EC I & EC IV). Resistance to streptomycin was the most common trait (14%) followed by resistance to sulphonamides, tetracyclines, ampicillin, or trimethoprim (6–9%). Four isolates (1%) were resistant to quinolones (nalidixic acid and ciprofloxacin) or kanamycin. Resistance to other antimicrobials occurred in occasional isolates but no isolate was resistant to cefotaxime.

Thirty-nine isolates (11%) from pigs were resistant to more than one antimicrobial and of these 11 isolates were resistant to two and 28 isolates to three or more antimicrobials (Table EC I). The phenotypes of the latter isolates are presented in Table EC II. Notably the resistance traits streptomycin, sulphonamide, ampicillin, chloramphenicol and tetracycline are often associated (Table EC III).

In samples of pork, *Escherichia coli* were isolated from 38% of 50 samples cultured. Eighteen of the 19 isolates were sensitive to all 12 antimicrobials tested but one isolate was resistant to three substances (ampicillin, chloramphenicol and sulphonamide) (Table EC I & EC IV).

When screened for *E. coli* resistant to third generation cephalosporins, all samples of pork were negative but isolates resistant to cefotaxime (MIC 0.5–2 mg/L) were grown from nine samples of intestinal content. All nine isolates were negative for extended spectrum beta-lactamases (ESBLs) when tested by the phenotypic confirmatory test recommended by CLSI and all isolates were resistant to cefoxitin (MICs 8->16 mg/L). On additional testing of the nine isolates by molecular methods, i.e. microarray, for presence of transferable genes coding for ESBL or plasmidic AmpC, $bla_{tem}$ genes was confirmed in one isolate (see Appendix 3 for details). This indicates that in eight of the isolates resistance to third generation cephalosporins was by mutational hyperproduction of AmpC beta-lactamases. However, in the one isolate carrying $bla_{tem}$

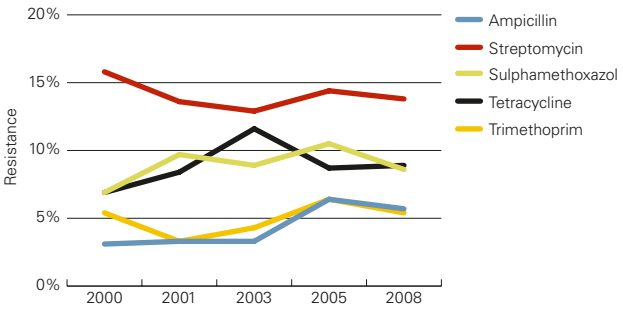



**FIGURE EC I.** Resistance (%) in *Escherichia coli* from pigs 2000, 2001, 2003, 2005 and 2008. For number of isolates see Table EC I. Data from SVARM.

gene(s) further typing is needed to determine if resistance of ESBL type is conferred.

### Sheep

*Escherichia coli* were isolated from 97% of 119 samples cultured. Samples were evenly distributed among the three age categories sampled since about one third were from ewes, suckling lambs or newborn lambs, respectively. Resistance was rare and only 14 isolates (12%) were resistant to one or more antimicrobial (Table EC I). Of these, four isolates were resistant to two or more antimicrobials. Sulphonamide resistance was the most common trait (5%). Four of the resistant isolates were from ewes, four from newborn lambs and two from suckling lambs.

### Comments

In *E. coli* from pigs resistance is not uncommon but occurrence is low in an international perspective. Also resistance is stable and without statistically significant trends in occurrence over the period studied (Chi-square for trend, P>0.05). Quinolone resistance is uncommon, which differ from the situation among *Campylobacter* spp. from pigs where about one third of the isolates are resistant to this antimicrobial class (See Zoonotic bacteria). Overall, resistance was negligible in *E. coli* from pork but the number of isolates is too low for valid conclusions.

Resistance in isolates from pigs mostly occurs to substances currently used in Swedish pig production. But there is probably also co-selection of resistance among *E. coli* in the intestinal microflora since some resistance traits often are associated, e.g. streptomycin, sulphonamide, ampicillin, chloramphenicol or tetracycline. Resistance to chloramphenicol is probably retained in the enteric flora by co-selection since amphenicols have not been used in Swedish pig production for over twenty years.

Likewise, ampicillin resistance is often associated with other traits and has the potential to co-select and, conversely, be co-selected by use of other antimicrobials. Resistance to ampicillin has increased from 3 to 6% in the period studied. The increase is not statistically significant and there is no change since 2005. An increase in resistance to ampicillin is observed also among *E. coli* from diagnostic submissions from pigs (see Animal pathogens). These tendencies could be due to increased use of broad-spectrum penicillins (ampicillin/amoxicillin) in later years. The extent of use in pigs is not known but in Sweden, ampicillin is available for oral use in pigs since the 70s. For injection, it was available until 1992 and again from 1998 when a new product (amoxicillin) was authorized. Due

**TABLE EC I.** Resistance (%) and multiresistance (%) for *Escherichia coli* from slaughter pigs and pork 2008 and from sheep 2006-09. Previous data from SVARM given for comparison.

| | | **Resistance** (%) (95% confidence interval inside brackets) | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **Pigs** | | | | | | | | | | **Pork** | | **Sheep** | |
| **Antimicrobial** | Cut-off value (mg/L) | **2008** n=349 | | **2005** n=390 | | **2003** n=303 | | **2001** n=308 | | **2000** n=260 | | **2008** n=19 | | **2006-09** n=115 | |
| Ampicillin | >8 | 6 | (3.5-8.7) | 6 | (4.2-9.3) | 3 | (1.6-6.0) | 3 | (1.6-5.9) | 3 | (1.3-6.0) | 5 | (0.1-26.0) | 2 | (0.2-6.1) |
| Cefotaxime | >0.25 | 0 | (0.0-1.0) | 0 | (0.0-0.9) | - | | - | | - | | 0 | (0.0-17.6) | 0 | (0.0-3.2) |
| Ceftiofur | >1 | - | | 0 | (0.0-0.9) | 0 | (0.0-1.2) | 0 | (0.0-1.2) | 0 | (0.0-1.4) | - | | - | |
| Chloramph. | >16 | 3 | (1.4-5.2) | 3 | (1.8-5.6) | <1 | (0.1-2.4) | 2 | (0.5-3.8) | <1 | (0.0-2.1) | 5 | (0.1-26.0) | 0 | (0.0-3.2) |
| Ciprofloxacin | >0.06 | 1 | (0.3-2.9) | <1[b] | (0.1-1.4) | <1[b] | (0.2-2.9) | <1[b] | (0.0-1.8) | 0[b] | (0.0-1.4) | 0 | (0.0-17.6) | <1 | (0.0-4.8) |
| Florfenicol | >16 | <1 | 0.0-1.6) | 0 | (0.0-0.9) | 0 | (0.0-1.2) | 0 | (0.0-1.2) | 0 | (0.0-1.4) | 0 | (0.0-17.6) | 0 | (0.0-3.2) |
| Gentamicin | >2 | <1 | 0.0-1.6) | 2 | (0.7-3.7) | 0[c] | (0.0-1.2) | 2[c] | (0.9-4.6) | 2[c] | (0.6-2.4) | 0 | (0.0-17.6) | 3 | (0.5-7.4) |
| Kanamycin | >8 | 1 | (0.3-2.9) | - | | - | | - | | - | | 0 | (0.0-17.6) | 2 | (0.2-6.1) |
| Nalidixic acid | >16 | 1 | (0.3-2.9) | <1 | (0.1-1.4) | 1 | (0.2-2.9) | <1 | (0.0-1.8) | 0 | (0.0-1.4) | 0 | (0.0-17.6) | 0 | (0.0-3.2) |
| Streptomycin | >16 | 14 | (10.3-17.8) | 14 | (11.0-18.2) | 13 | (9.3-17.2) | 13 | (10.0-18.0) | 16 | (11.6-20.8) | 0 | (0.0-17.6) | 3 | (0.5-7.4) |
| Sulphonamide | >256 | 9 | (5.9-12.0) | 11 | (7.7-14.0) | 9 | (6.0-12.7) | 10 | (6.7-13.6) | 7 | (4.2-10.7) | 5 | (0.1-26.0) | 5 | (1.9-11.0) |
| Tetracycline | >8 | 9 | (6.1-12.4) | 9 | (6.1-12.0) | 12 | (8.2-15.7) | 8 | (5.6-12.1) | 7 | (4.2-10.7) | 0 | (0.0-17.6) | <1 | (0.0-4.8) |
| Trimethoprim | >2 | 5 | (3.3-8.4) | 6 | (4.2-9.3) | 4 | (2.3-7.2) | 3 | (1.6-5.9) | 5 | (3.0-8.9) | 0 | (0.0-17.6) | 2 | (0.2-6.1) |
| **Multiresistance**[a] | | | | | | | | | | | | | | | |
| Susceptible to all | | 79 | | 76 | | 77 | | 76 | | 78 | | 95 | | 88 | |
| Resistant to 1 | | 10 | | 10 | | 12 | | 13 | | 11 | | | | 9 | |
| Resistant to 2 | | 3 | | 6 | | 6 | | 6 | | 6 | | | | 2 | |
| Resistant to 3 | | 2 | | 4 | | 3 | | 3 | | 2 | | 5 | | 1 | |
| Resistant to >3 | | 6 | | 4 | | 2 | | 2 | | 2 | | | | 1 | |

[a] Enrofloxacin/ciprofloxacin/nalidixic acid as well as cefotaxime/ceftiofur considered as one substance; [b] Enrofloxacin tested, cut-off value >0.12mg/L; [c] Cut-off value >4 mg/L.

# Vancomycin resistant enterococci (VRE) in broilers

**STUDIES IN SVARM** show that the prevalence of vancomycin resistance among randomly selected enterococci from Swedish farm animals is negligible. However, when samples of intestinal content from broilers are cultured on media containing vancomycin (16 mg/L) the number of samples positive for (i.e. the proportion of Swedish broilers colonised by) vancomycin resistant enterococci (VRE) has increased substantially since 2000. In 2000 less than 1% of tested broilers were positive for VRE whereas from 2006 to 2008 between 27 and 28% of tested broilers were positive each year (Figure). All isolates (n=414) have been *Enterococcus faecium* with MIC for vancomycin of > 64 mg/L and all isolates investigated for resistance genotype with PCR (n=127) carried the *vanA* gene. Furthermore, the majority of isolates (90%) show the same resistance phenotype also including reduced susceptibility to narasin (MIC 4–16 mg/L) and erythromycin (MIC 8–16 mg/L).

The epidemiological relationship of VRE from Swedish broilers isolated within SVARM has recently been investigated using multi locus sequence typing (MLST) and Tn*1546* transposon typing (Nilsson et al. 2009). The investigated strains included the first two VRE isolated in 2000 and 46 isolates selected at random from all (n=338) isolates obtained from January 2001 until June 2007. The MLST analysis showed that all 46 isolates selected at random had the same sequence type (ST310), whereas the two isolates from 2000 had ST13 and ST370 respectively. In addition, all 48 isolates contained the same Tn*1546* transposons, identical to the Tn*1546* transposon of reference strain BM 4147. The result of MLST and Tn*1546* transposon typing together with similarities in resistance phenotype show that a clone of VRE has spread within the Swedish broiler industry. The increas-

to the risk of co-selection prudent use of this antimicrobial is warranted.

Transferable resistance to third generation cephalosporins is at most rare in *E. coli* from Swedish pigs. No isolate with such resistance was detected in randomly selected *E. coli* from pigs or pork. After selective culture on media supplemented with cefotaxime, one isolate carrying $bla_{tem}$ genes was isolated, however. Additional testing by molecular methods is needed to determine if resistance of ESBL type is expressed by the isolate.

Resistance in *E. coli* from sheep is infrequent and there appears to be no difference in resistance among isolates from adult sheep and lambs. Most likely this reflects a limited use of antimicrobials in sheep.

**TABLE EC II.** *Escherichia coli* resistant to three or more antimicrobials presented by resistance phenotype, intestinal content of pigs. "R" in shaded fields indicates resistance. Data from SVARM.

| Year | | | | | Resistance pattern[a] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **2008** n=349 | **2005** n=390 | **2003** n=303 | **2001** n=308 | **2000** n=260 | **Sm** | **Su** | **Am** | **Tc** | **Cm** | **Tm** | **Gm** | **Km** | **Nal** |
| 1 | 1 | | | | R | R | R | R | R | R | | | |
| 2 | 4 | 1 | 1 | 2 | R | R | R | R | | R | | | |
| 1 | | 1 | | 1 | R | R | R | R | | | | | |
| | 1 | | 2 | | R | R | R | | R | | | | |
| 2 | | | 2 | | R | R | R | | R | R | | | |
| 2 | 5 | | 4 | | R | R | R | | | | | | |
| 1 | | | | | R | R | R | | | | | R | |
| 5 | 3 | 2 | 1 | 3 | R | R | R | | | R | | | |
| | 3 | 5 | 3 | 2 | R | R | | R | | | | | |
| 4 | 2 | 2 | | | R | R | | R | | R | | | |
| 1 | 3 | | 1 | 1 | R | R | | | R | | | | |
| 1 | | | | | R | R | | | R | R | | | |
| | 2 | 2 | 2 | 3 | R | R | | | | R | | | |
| | | 1 | | | R | | | R | | R | | | |
| 1 | | | | | R | | | | | | R | R | |
| 1 | | | | | | R | R | R | R | | | | |
| | 2 | | | | | R | R | R | R | R | | | |
| 2 | | | | | | R | R | | R | | | | |
| 2 | 4 | 1 | | | | R | R | | R | R | | | |
| | 1 | | | | | R | | | R | R | | | |
| 2 | | | | | | R | | | | R | | | R |
| | | 1 | | | | | R | R | | | | | R |
| **28** (8.0%) | **31** (7.9%) | **16** (5.3%) | **16** (5.2%) | **12** (4.6%) | Number of isolates (percent of all isolates) | | | | | | | | |

[a] Sm: streptomycin; Su: sulphonamide; Am. Ampicillin; Tc: tetracycline; Cm: chloramphenicol; Tm: trimethoprim; Gm: gentamicin; Km: kanamycin; Nal: nalidixic acid; Ef: enrofloxacin; Ci: ciprofloxacin.

ing proportion of chickens colonised with VRE is unusual since it took place in an apparently non selective environment. Avoparcin, known to select for VRE, has not been used in Sweden for 25 years, and all use of growth promoters was discontinued over 20 years ago. The only antimicrobials used in large scale are ionophores but ionophore resistance is common also among enterococci susceptible to vancomycin. Therefore the use of ionophores is unlikely to select for VRE among Swedish broilers.

Worldwide VRE is an important cause of human nosocomial infections. In Europe the main concern is *E. faecium* carrying the *vanA* gene and especially the hospital adapted VRE pertaining to clonal complex 17 (Werner et al. 2008). So far, the increased proportion of Swedish broilers colonised with ST310 does not seem to have had an important impact on human healthcare. Human VRE cases in Sweden are mainly caused by *E. faecium*, *vanB* and hence encoded by a different resistance gene, although cases with *E. faecium*, *vanA* occur (SWEDRES 2009; Werner et al. 2008).

Additional research regarding the epidemiology of VRE among Swedish broilers has been done. The possibility of a constant introduction of VRE to the broiler houses has, for example, been investigated. Samples from feed-mills, hatcheries and farm produced whole wheat were analysed with selective methods. This included pre enrichment and culture on media containing vancomycin (16 mg/L). However, VRE were not isolated from any of the samples (n=197) investigated (Nilsson et al. 2008).

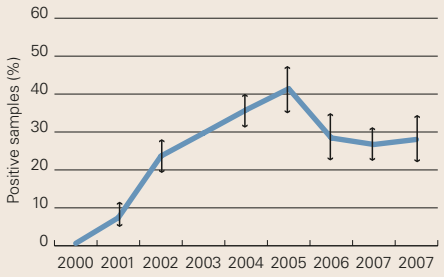



**FIGURE.** Proportion (%) of samples of intestinal content from healthy broilers positive for VRE when cultured on vancomycin supplemented media (16 mg/L), 95% confidence intervals indicated. Number of samples cultured each year has been between 99 and 351.

**TABLE EC III.** Association between resistance traits in *Escherichia coli* from pigs 2000, 2001, 2003, 2005 and 2008. For each antimicrobial the first line gives resistance rates for susceptible isolates (S) and the second line rates for resistant isolates (R). All antimicrobials were not tested all years, therefor all combinations of resistance traits cannot be calculated.

| Single substance susceptibility | | n | Resistance (%)[a] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Am | Cm | Ff | Gm | Nal | Sm | Su | Tc | Tm |
| Ampicillin | S | 1537 | 0.0 | 0.7 | 0.1 | 1.3 | 0.5 | 11.5 | 5.6 | 7.9 | 2.6 |
| | R | 73 | 100.0 | 28.8 | 0.0 | 0.0 | 2.7 | 67.1 | 82.2 | 30.1 | 56.2 |
| Cefotaxime | S | 739 | 6.1 | 3.1 | 0.1 | 1.1 | 0.7 | 14.1 | 9.6 | 8.8 | 6.0 |
| | R | 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Ceftiofur | S | 1261 | 4.2 | 1.7 | 0.0 | 1.5 | 0.4 | 14.1 | 9.2 | 9.0 | 4.9 |
| | R | 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Chloramph. | S | 1579 | 3.3 | 0.0 | 0.1 | 1.3 | 0.6 | 13.2 | 7.3 | 8.8 | 4.1 |
| | R | 31 | 67.7 | 100.0 | 0.0 | 0.0 | 0.0 | 54.8 | 96.8 | 16.1 | 54.8 |
| Ciprofloxacin | S | 345 | 5.8 | 2.9 | 0.3 | 0.3 | 0.0 | 13.9 | 8.1 | 9.0 | 4.9 |
| | R | 4 | 0.0 | 0.0 | 0.0 | 0.0 | 100.0 | 0.0 | 50.0 | 0.0 | 50.0 |
| Enrofloxacin | S | 1256 | 4.1 | 1.7 | 0.0 | 1.5 | 0.0 | 14.1 | 9.2 | 8.9 | 4.9 |
| | R | 5 | 40.0 | 0.0 | 0.0 | 0.0 | 100.0 | 20.0 | 0.0 | 20.0 | 20.0 |
| Florfenicol | S | 1609 | 4.5 | 1.9 | 0.0 | 1.2 | 0.6 | 14.0 | 9.1 | 8.9 | 5.0 |
| | R | 1 | 0.0 | 0.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Gentamicin | S | 1590 | 4.6 | 1.9 | 0.1 | 0.0 | 0.6 | 13.8 | 9.2 | 9.1 | 5.1 |
| | R | 20 | 0.0 | 0.0 | 0.0 | 100.0 | 0.0 | 30.0 | 0.0 | 0.0 | 0.0 |
| Kanamycin | S | 345 | 5.5 | 2.9 | 0.3 | 0.0 | 1.2 | 13.3 | 8.4 | 9.0 | 5.5 |
| | R | 4 | 25.0 | 0.0 | 0.0 | 25.0 | 0.0 | 50.0 | 25.0 | 0.0 | 0.0 |
| Nalidixic acid | S | 1601 | 4.4 | 1.9 | 0.1 | 1.2 | 0.0 | 14.1 | 9.0 | 8.9 | 4.9 |
| | R | 9 | 22.2 | 0.0 | 0.0 | 0.0 | 100.0 | 11.1 | 22.2 | 11.1 | 33.3 |
| Neomycin | S | 1261 | 4.2 | 1.7 | 0.0 | 1.5 | 0.4 | 14.1 | 9.2 | 9.0 | 4.9 |
| | R | 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Streptomycin | S | 1384 | 1.7 | 1.0 | 0.1 | 1.0 | 0.6 | 0.0 | 2.8 | 5.1 | 2.0 |
| | R | 226 | 21.7 | 7.5 | 0.0 | 2.7 | 0.4 | 100.0 | 47.3 | 32.7 | 23.9 |
| Sulphonamide | S | 1464 | 0.9 | 0.1 | 0.1 | 1.4 | 0.5 | 8.1 | 0.0 | 6.9 | 1.4 |
| | R | 146 | 41.1 | 20.5 | 0.0 | 0.0 | 1.4 | 73.3 | 100.0 | 29.5 | 41.8 |
| Tetracycline | S | 1466 | 3.5 | 1.8 | 0.1 | 1.4 | 0.5 | 10.4 | 7.0 | 0.0 | 3.9 |
| | R | 144 | 15.3 | 3.5 | 0.0 | 0.0 | 0.7 | 51.4 | 29.9 | 100.0 | 16.7 |
| Trimethoprim | S | 1529 | 2.1 | 0.9 | 0.1 | 1.3 | 0.4 | 11.2 | 5.6 | 7.8 | 0.0 |
| | R | 81 | 50.6 | 21.0 | 0.0 | 0.0 | 3.7 | 66.7 | 75.3 | 29.6 | 100.0 |

[a] Am: ampicillin; Cm: chloramphenicol; Ff: florfenicol; Gm: gentamicin; Nal: nalidixic acid; Sm: streptomycin; Su: sulphonamide; Tc: tetracycline; Tm: trimethoprim.

**TABLE EC IV.** Distribution of MICs for *Escherichia coli* from pigs (n=349) and pork (n=19) 2008 and from sheep (n=115) 2006-2009. Composite data for pigs from SVARM 2000, 2001, 2003 and 2005 (n=1261) given for comparison.

| Anti-microbial | Year | Sample | Resistance (%) | Distribution (%) of MICs[a] (mg/L) | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | ≤0.008 | 0.016 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | 64 | 128 | 256 | 512 | 1024 | >1024 |
| Ampicillin | 2008 | Pig | 6 | | | | | | | 0.6 | 21.2 | 66.8 | 5.7 | | | | 0.3 | 5.4 | | | | |
| | | Pork | 5 | | | | | | | | 5.3 | 57.9 | 31.6 | | | | | 5.3 | | | | |
| | 2000-05 | Pig | 4 | | | | | | | 0.4 | 8.9 | 49.9 | 36.2 | 0.4 | | 0.2 | 4.0 | | | | | |
| | 2006-09 | Sheep | 2 | | | | | | | 1.7 | 7.8 | 70.4 | 16.5 | 1.7 | 0.9 | | 0.9 | | | | | |
| Cefotaxime | 2008 | Pig | 0 | | | | 76.5 | 21.8 | 1.7 | | | | | | | | | | | | | |
| | | Pork | 0 | | | | 63.2 | 36.8 | | | | | | | | | | | | | | |
| | 2000-05[c] | Pig | 0 | | | | 60.5 | 38.7 | 0.8 | | | | | | | | | | | | | |
| | 2006-09 | Sheep | 0 | | | | 66.1 | 28.7 | 5.2 | | | | | | | | | | | | | |
| Chloram-phenicol | 2008 | Pig | 3 | | | | | | | | | 4.9 | 73.6 | 17.8 | 0.9 | 1.7 | 0.9 | | | 0.3 | | |
| | | Pork | 5 | | | | | | | | | 15.8 | 63.2 | 15.8 | | 5.3 | | | | | | |
| | 2000-05 | Pig | 2 | | | | | | | | | 4.8 | 69.2 | 23.9 | 0.5 | 1.7 | | | | | | |
| | 2006-09 | Sheep | 0 | | | | | | | | | 2.6 | 73.0 | 23.5 | 0.9 | | | | | | | |
| Cipro-floxacin[b] | 2008 | Pig | 1 | | 13.2 | 82.8 | 2.9 | | | 0.3 | 0.9 | | | | | | | | | | | |
| | | Pork | 0 | | 63.2 | 36.8 | | | | | | | | | | | | | | | | |
| | 2006-09 | Sheep | <1 | | 1.7 | 47.8 | 49.6 | 0.9 | | | | | | | | | | | | | | |
| Florfenicol | 2008 | Pig | <1 | | | | | | | | | 1.1 | 53.0 | 43.3 | 2.3 | 0.3 | | | | | | |
| | | Pork | 0 | | | | | | | | | | 57.9 | 42.1 | | | | | | | | |
| | 2000-05 | Pig | 0 | | | | | | | | | | 57.7 | 41.4 | 0.9 | | | | | | | |
| | 2006-09 | Sheep | 0 | | | | | | | | | | 36.5 | 61.7 | 0.9 | | | | | | | |
| Gentamicin | 2008 | Pig | <1 | | | | | | 0.6 | 26.6 | 65.6 | 6.9 | 0.3 | | | | | | | | | |
| | | Pork | 0 | | | | | | | 78.9 | 21.1 | | | | | | | | | | | |
| | 2000-05 | Pig | <1 | | | | | | | 11.3 | 36.7 | 36.9 | 14.2 | 0.9 | 0.1 | | | | | | | |
| | 2006-09 | Sheep | 3 | | | | | | | 13.0 | 68.7 | 14.8 | 1.7 | 0.9 | | | | | | | | |
| Kanamycin[c] | 2008 | Pig | 1 | | | | | | | | 0.6 | 23.8 | 61.3 | 13.2 | 0.9 | 0.3 | | | | | | |
| | | Pork | 0 | | | | | | | | | 57.9 | 42.1 | | | | | | | | | |
| | 2006-09 | Sheep | 2 | | | | | | | | | 8.7 | 68.7 | 20.9 | 1.7 | | | | | | | |
| Nalidixic acid | 2008 | Pig | 1 | | | | | | | | | 48.7 | 48.7 | 0.9 | 0.6 | | | 0.3 | 0.6 | 0.3 | | |
| | | Pork | 0 | | | | | | | | | 5.3 | 78.9 | 15.8 | | | | | | | | |
| | 2000-05 | Pig | <1 | | | | | | | | 0.5 | 20.9 | 51.6 | 25.5 | 1.1 | | 0.1 | 0.1 | 0.2 | | | |
| | 2006-09 | Sheep | 0 | | | | | | | | 0.9 | 47.0 | 50.4 | 0.9 | 0.9 | | | | | | | |
| Strepto-mycin | 2008 | Pig | 14 | | | | | | | | | 0.6 | 19.5 | 58.2 | 8.0 | 2.3 | 3.7 | 4.6 | 2.0 | 1.1 | | |
| | | Pork | 0 | | | | | | | | | | 73.7 | 26.3 | | | | | | | | |
| | 2000-05 | Pig | 14 | | | | | | | | | 0.2 | 12.2 | 50.4 | 23.1 | 3.5 | 2.8 | 3.3 | 2.4 | 2.2 | | |
| | 2006-09 | Sheep | <1 | | | | | | | | | | 13.9 | 67.0 | 16.5 | 1.7 | | | 0.9 | | | |
| Sulpho-namide | 2008 | Pig | 9 | | | | | | | | | | | 30.9 | 39.5 | 20.3 | 0.6 | | | | | 8.6 |
| | | Pork | 5 | | | | | | | | | | | 47.4 | 42.1 | 5.3 | | | | | | 5.3 |
| | 2000-05 | Pig | 9 | | | | | | | | | | | | | | 71.2 | 19.3 | 0.3 | | 9.2 | |
| | 2006-09 | Sheep | 5 | | | | | | | | | | | | 37.4 | 46.1 | 9.6 | 1.7 | | | 5.2 | |
| Tetracycline | 2008 | Pig | 9 | | | | | | | | 54.4 | 36.1 | | 0.6 | 0.6 | 1.1 | 3.7 | 3.4 | | | | |
| | | Pork | 0 | | | | | | | | 57.9 | 42.1 | | | | | | | | | | |
| | 2000-05 | Pig | 9 | | | | | | | 0.2 | 22.0 | 58.5 | 10.0 | 0.3 | 0.3 | 0.9 | 0.8 | 7.0 | | | | |
| | 2006-09 | Sheep | <1 | | | | | | | | 56.5 | 40.9 | 1.7 | | | | 0.9 | | | | | |
| Trimetho-prim | 2008 | Pig | 5 | | | | | | 23.5 | 58.7 | 11.5 | 0.9 | | 0.6 | | | 4.9 | | | | | |
| | | Pork | 0 | | | | | | 10.5 | 78.9 | 10.5 | | | | | | | | | | | |
| | 2000-05 | Pig | 5 | | | | | | 20.7 | 58.2 | 15.1 | 1.0 | 0.5 | 0.2 | 0.1 | 4.2 | | | | | | |
| | 2006-09 | Sheep | 2 | | | | | | 34.8 | 51.3 | 8.7 | 0.9 | | 0.9 | | | 0.9 | | | | | |
| | | | | **≤0.008** | **0.016** | **0.03** | **0.06** | **0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **64** | **128** | **256** | **512** | **1024** | **>1024** |

[a] White 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. Bold vertical lines indicate epidemiological cut-off values for resistance; [b] Not tested 2000-05; [c] 390 isolates tested 2005.

## *Enterococcus*

### Slaughter pigs and pork

Enterococci were isolated from 53% of the 484 samples of caecal content from pigs. *Enterococcus hirae* (44%) was the predominant species followed by *E. faecalis* (27%) and *E. faecium* (15%) (Table ENT I). In samples of pork, *E. faecalis* were isolated from 17 samples (34%) and *E. faecium* from three samples (3%).

#### *Enterococcus faecalis*

In *E. faecalis* from pork, resistance was rare and only tetracycline resistance was observed, occurring in four isolates (24%). In contrast, the majority of isolates from pigs (71%) were resistant to at least one antimicrobial but multiresistance was rare and only two isolates were resistant to three or more antimicrobials (Table ENT II & V).

Tetracycline resistance was the most frequent trait (62%) followed by erythromycin (24%) and streptomycin (13%) (Table ENT II). Cross-tabulation of data indicates an association between these resistance traits (Table ENT VI) and they are also the most common in phenotypes of multiresistant isolates (Table ENT V). No isolate was resistant to ampicillin, bacitracin, linezolid, narasin, vancomycin or virginiamycin.

#### *Enterococcus faecium*

From samples of pork only three isolates of *E faecium* were obtained. All three were susceptible to the antimicrobials studied. In *E. faecium* from pigs, two thirds (64%) of the isolates were susceptible to all antimicrobials tested. Resistance to tetracycline (15%), erythromycin (13%) or bacitracin (10%) were the most common traits. Isolates with phenotypes including all these traits are rare however (Table ENT V) even if they seem to be associated on cross-tabulation (Table ENT VI).

#### *Enterococcus hirae*

This species of Enterococcus is the most common species in intestinal content from pigs at slaughter. Resistance is rare however and 80% of the isolates were susceptible to all antimicrobials tested (Table ENT IV). Resistance to tetracycline (14%) or erythromycin (9%) and streptomycin (5%) were the most common traits. Mostly, resistant isolates were resistant to one antimicrobial only (Table ENT IV). No attempt was made to isolate *E. hirae* from pork.

### Sheep

Enterococci were isolated from 83% of the 117 samples cultured. Of the 97 isolates, 24, 15 and 33 were *E. faecalis*, *E. faecium* and *E. hirae*, respectively. Resistance was rare and only one isolate was resistant to more than one antimicrobial (Table ENT III-V). The small number of isolates precludes valid conclusions on prevalence. Streptomycin resistance occurred in all three species and tetracycline resistance in both *E. faecalis* and *E. faecium*.

### Broilers

Vancomycin resistant enterococci (VRE) were isolated from 30 (28%) of 107 samples cultured on vancomycin supplemented media (16 mg/L). All 30 isolates were *E. faecium* with MIC for vancomycin >128 mg/L. All isolates were susceptible to ampicillin, tetracycline, virginiamycin and linezolid but MICs to narasin (2–4 mg/L) and to erythromycin (8–32 mg/L) are elevated and indicate acquired resistance. Ten isolates examined by PCR all carried the *vanA*-gene.

### Comments

Resistance in enterococci from sheep is uncommon in agreement with the limited use of antimicrobials in this animal species. In isolates from pigs, resistance this year is mostly of the same magnitude as previously and low in an international perspective. Tetracycline resistance is the most prevalent trait in all three species of enterococci. This is in agreement with the use of tetracyclines (doxycycline) for group treatment of diarrhoea or respiratory disease in pigs. Tetracycline is the most common, and only, resistance trait also in *E. faecalis* from pork.

Macrolides (tylosin) are also used for group medication in outbreaks of diarrhoea in pigs, which could explain that resistance to erythromycin is the second most common trait in enterococci. The increase in erythromycin resistance in *E. faecium* observed 2000 – 2005 (Chi-Square for trend P=0.002) was broken in 2008 and resistance is again of the magnitude observed 2001 (Fig ENT I). The increase 2000–2005 was due to isolates with MICs 8–16 mg/L but occurrence of high-level resistance (MIC >32mg/L) is similar over the years studied (Table ENT VIII). Also in *E. faecalis* is erythromycin resistance lower 2008 than previously but in *E. hirae* the situation is converse, resistance is more common 2008 than previously. In this species, the increase is due to a larger proportion of isolates with MICs >64 mg/L.

**TABLE ENT I.** Prevalence of enterococci in caecal content from pigs, 2008. Previous data from SVARM given for comparison.

| Year | No. of samples cultured | Percent positive cultures | Enterococcus species isolated No. of isolates (% of total isolates) | | | |
|---|---|---|---|---|---|---|
| | | | *E. faecalis* | *E. faecium* | *E. hirae* | Other spp. |
| 2008 | 484 | 53% | 68 (27%) | 39 (15%) | 111(44%) | 36 (14%) |
| 2005 | 455 | 58% | 55 (21%) | 47 (18%) | 112 (43%) | 48 (18%) |
| 2003 | 510 | 62% | 87 (28%) | 71 (23%) | 124 (39%) | 33 (10%) |
| 2001 | 470 | 59% | 52 (19%) | 106 (38%) | 77 (28%) | 44 (16%) |
| 2000 | 460 | 52% | 56 (23%) | 48 (20%) | 106 (44%) | 36 (13%) |

Trends in erythromycin resistance in the three enterococcal species do not coincide. Therefore it is unlikely that they are an effect of changes in selection pressure. Moreover, there is no obvious association between resistance and yearly sales of macrolides for group treatment (see Use of antimicrobials). Thus, conclusions on trends must be made cautiously and in light of the limited number of isolates tested each year. This is illustrated by the confidence intervals of occurrence of resistance in Table ENT II-IV. Likewise, fluctuations over time in resistance to bacitracin and virginiamycin in *E. faecium* must be interpreted cautiously. Notably neither of these two antimicrobials are used in Swedish pig production.

Resistance to ampicillin, linezolid, vancomycin or streptogramins (virginiamycin) in enterococci from pigs was not observed in 2008. In SVARM, resistance to ampicillin has been documented in only four isolates of enterococci from pigs since 2000 and resistance to virginiamycin in a limited number of *E. faecium* and *E. hirae*. Vancomycin resistant enterococci carrying the *vanA* or *vanB* genes have never been documented from pigs in SVARM, neither in randomly selected isolates nor by culture of almost 2000 samples on media supplemented with vancomycin. These findings show that in Sweden enterococci in pigs are not an important reservoir of resistance to antimicrobials used for treatment of enterococcal infections in humans.

The prevalence of VRE among broilers, studied by culture on vancomycin supplemented media, has gradually increased from less than one percent in 2000 to a peak of 41% of 99 samples cultured in 2005. This year VRE were isolated from 28% of 107 samples which is similar to the prevalence in 2007 (27%) and 2006 (28%). This indicates that the increase in prevalence observed in the first half of the 2000s has abated. More data on VRE from broilers are presented in the highlight "Vancomycin resistant enterococci from broilers".

**TABLE ENT II.** Resistance (%) and multiresistance (%) of *Enterococcus faecalis* from pigs and pork 2008 and from sheep 2006-09. Previous data from SVARM given for comparison.

| | | **Resistance** (%) (95% confidence interval inside brackets) | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **Pigs** | | | | | | | | | | **Pork** | | **Sheep** | |
| **Antimicrobial** | **Cut-off value** (mg/L) | **2008** n=68 | | **2005** n=55 | | **2003** n=87 | | **2001** n=52 | | **2000** n=56 | | **2008** n=17 | | **2006-09** n=24 | |
| Ampicillin | >4 | 0 | (0.0-6.5) | 0 | (0.0-6.5) | 0 | (0.0-4.2) | 4 | (0.5-13.2) | 0 | (0.0-6.4) | 0 | (0.0-19.5) | 0 | (0.0–14.2) |
| Bacitracin | >32 | 0 | (0.0-6.5) | 2 | (0.0-9.7) | 0 | (0.0-4.2) | 0 | (0.0-6.8) | 0 | (0.0-6.4) | 0 | (0.0-19.5) | 0 | (0.0-14.2) |
| Chloramph. | >32 | 1 | (0.0-9.7) | 5 | (1.1-15.1) | - | | - | | - | | 0 | (0.0-19.5) | 0 | (0.0–14.2) |
| Erythromycin | >4 | 24 | (17.6-42.9) | 33 | (45.9-73.0) | 25 | (16.6-35.7) | 27 | (15.6-41.0) | 36 | (23.4-49.6) | 0 | (0.0-19.5) | 0 | (0.0-14.2) |
| Gentamicin | >32 | 3 | (0.4-12.5) | - | | 14 | (7.3-22.9) | 6 | (1.2-15.9) | 0 | (0.0-6.4) | 0 | (0.0-19.5) | 0 | (0.0-14.2) |
| Kanamycin | >1024 | 3 | (0.4-12.5) | - | | - | | - | | - | | 0 | (0.0-19.5) | 0 | (0.0-14.2) |
| Linezolid | >4 | 0 | (0.0-6.5) | - | | - | | - | | - | | 0 | (0.0-19.5) | 0 | (0.0-14.2) |
| Narasin | >2 | 0 | (0.0-6.5) | 0 | (0.0-6.5) | 1 | (0.0-6.2) | 4 | (0.5-13.2) | 2 | (0.0-9.6) | 0 | (0.0-19.5) | 0 | (0.0-14.2) |
| Streptomycin | >512 | 13 | (7.8-28.8) | 16 | (7.8-28.8) | - | | - | | - | | 0 | (0.0-19.5) | 4 | (0.1–21.1) |
| Tetracycline | >2 | 62 | (63.0-86.8) | 64 | (49.6-76.2) | 63 | (52.2-73.3) | 67 | (52.9-79.7) | 68 | (54.0-79.7) | 24 | (0.1-28.7) | 8 | (1.0–27.0) |
| Vancomycin | >4 | 0 | (0.0-6.5) | 0 | (0.0-6.5) | 1 | (0.0-6.2) | 0 | (0.0-6.8) | 0 | (0.0-6.4) | 0 | (0.0-19.5) | 0 | (0.0–14.2) |
| Virginiamycin | >32 | 0 | (0.0-6.5) | 0 | (0.0-6.5) | 0 | (0.0-4.2) | 0 | (0.0-6.8) | 0 | (0.0-6.4) | 0 | (0.0-19.5) | 0 | (0.0–14.2) |
| **Multiresistance** | | | | | | | | | | | | | | | |
| Susceptible to all above | | 29 | | 25 | | 33 | | 27 | | 29 | | 76 | | 92 | |
| Resistant to 1 | | 46 | | 40 | | 39 | | 48 | | 39 | | 24 | | 4 | |
| Resistant to 2 | | 22 | | 27 | | 18 | | 17 | | 30 | | | | 4 | |
| Resistant to 3 | | 4 | | 8 | | 6 | | 2 | | | | | | | |
| Resistant to >3 | | 3 | | 4 | | 1 | | 2 | | | | | | | |

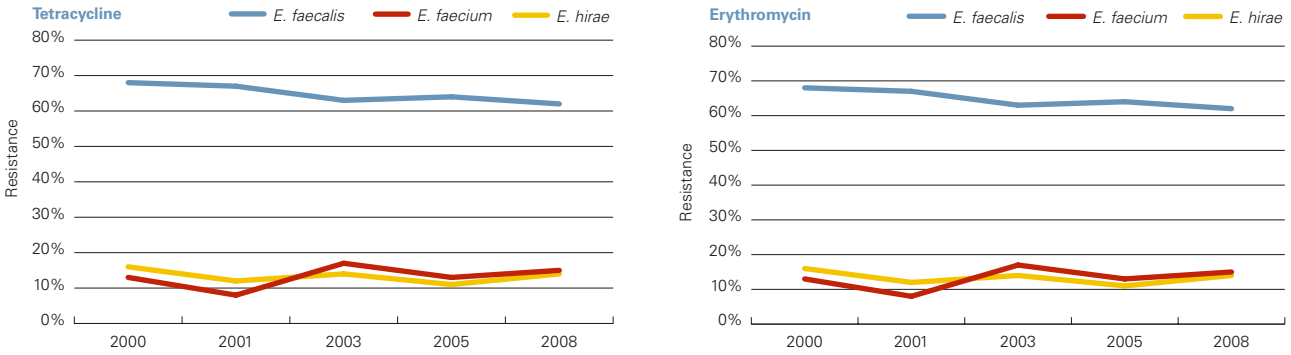



**FIGURE ENT I.** Resistance (%) to selected tetracycline and erythromycin in *Enterococcus faecalis, E. faecium* and *E. hirae* from pigs 2000–2001, 2003, 2005 and 2009. For number of iolates see Table ENT II and III. Data from SVARM.

**TABLE ENT III.** Resistance (%) and multiresistance (%) of *Enterococcus faecium* from pigs and pork, 2008 and from sheep 2006-09. Previous data from SVARM given for comparison.

| | | **Resistance** (%) (95% confidence interval inside brackets) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **Pigs** | | | | | | | | **Pork** | | **Sheep** | |
| **Antimicrobial** | **Cut-off value** (mg/L) | **2008** n=39 | | **2005** n=47 | | **2003** n=71 | | **2001** n=106 | | **2000** n=48 | | **2008** n=3 | **2006-09** n=15 | |
| Ampicillin | >4 | 0 | (0.0-9.0) | 0 | (0.0-7.5) | 0 | (0.0-5.1) | 2 | (0.2-6.6) | 0 | (0.0-7.4) | 0 - | 0 | (0.0–21.8) |
| Bacitracin | >32 | 10 | (2.9-24.2) | 2 | (0.0-7.6) | 13 | (6.0-22.7) | 3 | (0.6-8.0) | 4 | (0.5-14.3) | 0 - | 0 | (0.0-21.8) |
| Chloramph. | >32 | 0 | (0.0-9.0) | 2 | (0.0-7.6) | 0 | (0.0-5.1) | - | | - | | 0 - | 0 | (0.0–21.8) |
| Erythromycin | >4 | 13 | (4.3-27.4) | 21 | (7.0-24.4) | 18 | (10.1-29.3) | 11 | (6.0-18.9) | 2 | (0.1-11.1) | 0 - | 0 | (0.0-21.8) |
| Gentamicin | >32 | 0 | (0.0-9.0) | - | | 1 | (0.0-7.6) | 0 | (0.0-3.4) | 0 | (0.0-7.4) | 0 - | 0 | (0.0-21.8) |
| Kanamycin | >1024 | 0 | (0.0-9.0) | - | | - | | - | | - | | 0 - | 0 | (0.0-21.8) |
| Linezolid | >4 | 0 | (0.0-9.0) | - | | - | | - | | - | | 0 - | 0 | (0.0-21.8) |
| Narasin | >4 | 0 | (0.0-9.0) | 0 | (0.0-5.1) | 0 | (0.0-5.1) | 0 | (0.0-3.4) | 2 | (0.1-11.1) | 0 - | 0 | (0.0-21.8) |
| Streptomycin | >128 | 3 | (0.1-13.5) | - | | 1 | (0.0-7.6) | 5 | (1.5-10.7) | 2 | (0.1-11.1) | 0 - | 7 | (0.2–32.0) |
| Tetracycline | >2 | 15 | (5.9-30.5) | 13 | (3.2-17.5) | 17 | (9.0-27.7) | 8 | (4.0-15.5) | 13 | (4.7-25.2) | 0 - | 7 | (0.2–32.0) |
| Vancomycin | >4 | 0 | (0.0-9.0) | 0 | (0.0-5.1) | 0 | (0.0-5.1) | 0 | (0.0-3.4) | 0 | (0.0-7.4) | 0 - | 0 | (0.0–21.8) |
| Virginiamycin | >4 | 0 | (0.0-9.0) | 13 | (3.2-17.5) | 3 | (0.3-9.8) | 11 | (6.0-18.9) | 25 | (13.6-39.6) | 0 - | 0 | (0.0–21.8) |
| **Multiresistance** | | | | | | | | | | | | | | |
| Susceptible to all above | | 64 | | 62 | | 62 | | 75 | | 60 | | 100 | 87 | |
| Resistant to 1 | | 33 | | 30 | | 28 | | 16 | | 31 | | | 13 | |
| Resistant to 2 | | | | 6 | | 4 | | 6 | | 8 | | | | |
| Resistant to 3 | | 3 | | | | 6 | | 2 | | | | | | |
| Resistant to >3 | | | | 2 | | | | 2 | | | | | | |

**TABLE ENT IV.** Resistance (%) and multiresistance (%) among *Enterococcus hirae* from pigs, 2008 and from sheep 2006-09. Previous data from SVARM given for comparison.

| | | **Resistance** (%) (95% confidence interval inside brackets) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **Pigs** | | | | | | | | | | **Sheep** | |
| **Antimicrobial** | **Cut-off value** (mg/L) | **2008** n=111 | | **2005** n=112 | | **2003** n=124 | | **2001** n=77 | | **2000** n=106 | | **2006-09** n=33 | |
| Ampicillin | >4 | 0 | (0.0-3.3) | 0 | (0.0-3.2) | <1 | (0.0-4.4) | 0 | (0.0-4.7) | 0 | (0.0-3.4) | 0 | (0.0–10.6) |
| Bacitracin | >32 | 0 | (0.0-3.3) | 0 | (0.0-3.2) | 0 | (0.0-2.9) | 0 | (0.0-4.7) | 0 | (0.0-3.4) | 0 | (0.0-10.6) |
| Chloramph. | >8 | 0 | (0.0-3.3) | 0 | (0.0-3.2) | 0 | (0.0-2.9) | - | | - | | 0 | (0.0–10.6) |
| Erythromycin | >2 | 9 | (4.4-15.9) | <1 | (0.0-4.9) | 4 | (1.3-9.2) | 0 | (0.0-4.7) | 4 | (1.0-9.4) | 0 | (0.0-10.6) |
| Gentamicin | >32 | 0 | (0.0-3.3) | - | | <1 | (0.0-4.4) | 1 | (0.0-7.0) | 0 | (0.0-3.4) | 0 | (0.0-10.6) |
| Kanamycin | >1024 | 4 | (1.0-9.0) | - | | - | | - | | - | | 0 | (0.0-10.6) |
| Linezolid | >4 | 0 | (0.0-3.3) | - | | - | | - | | - | | 0 | (0.0-10.6) |
| Narasin | >4 | 0 | (0.0-3.3) | 0 | (0.0-3.2) | 0 | (0.0-2.9) | 0 | (0.0-4.7) | 0 | (0.0-3.4) | 0 | (0.0-10.6) |
| Streptomycin | >128 | 5 | (1.5-10.2) | - | | 2 | (0.2-5.7) | 0 | (0.0-4.7) | 2 | (0.2-6.6) | 3 | (0.1–15.8) |
| Tetracycline | >2 | 14 | (7.8-21.3) | 11 | (5.7-18.0) | 14 | (8.2-21.0) | 12 | (5.5-21.0) | 16 | (9.6-24.4) | 0 | (0.0–10.6) |
| Vancomycin | >4 | 0 | (0.0-3.3) | 0 | (0.0-3.2) | 0 | (0.0-2.9) | 0 | (0.0-4.7) | 0 | (0.0-3.4) | 0 | (0.0–10.6) |
| Virginiamycin | >4 | <1 | (0.0-4.9) | 2 | (0.2-6.3) | 0 | (0.0-2.9) | 1 | (0.0-7.0) | 12 | (6.7-20.1) | 0 | (0.0–10.6) |
| **Multiresistance** | | | | | | | | | | | | | |
| Susceptible to all | | 80 | | 87 | | 82 | | 86 | | 73 | | 97 | |
| Resistant to 1 | | 14 | | 13 | | 15 | | 14 | | 22 | | 3 | |
| Resistant to 2 | | 2 | | | | 2 | | | | 5 | | | |
| Resistant to 3 | | 4 | | | | 1 | | | | 1 | | | |
| Resistant to >3 | | 1 | | | | | | | | | | | |

**TABLE ENT V.** Resistance phenotypes of *Enterococcus faecalis* and *E. faecium*, resistant to three or more antimicrobials, pigs 2008. "R" in shaded fields indicates resistance. Previous data from SVARM given for comparison.

| ***E. faecalis*** | | | | | | | | | | | | | ***E. faecium*** | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Year** | | | | | **Resistance pattern**[a] | | | | | | | | **Year** | | | | | **Resistance pattern**[a] | | | | | | | |
| **2008** n=68 | **2005** n=55 | **2003** n=87 | **2001** n=52 | **2000** n=56 | **Tc** | **Em** | **Gm**[b] | **Am** | **Sm**[c] | **Cm**[c] | **Km**[d] | **Na** | **2008** n=39 | **2005** n=47 | **2003** n=71 | **2001** n=106 | **2000** n=48 | **Tc** | **Em** | **Vi** | **Sm**[b] | **Am** | **Cm**[c] | **Ba** | **Gm**[b] |
| | | | 1 | | R | R | R | R | | | | | 1 | | | | | R | R | R | | | R | | |
| | | 1 | | | R | R | R | | | | | R | | | 1 | | | R | R | R | R | | | | |
| | | 7 | 1 | | R | R | R | | | | | | | 1 | | | | R | R | R | | | | | |
| 1 | | | | | R | R | R | | R | R | R | | | | 1 | | | R | R | | R | R | | | |
| 1 | | | | | R | R | R | | R | | R | | 1 | | 2 | 1 | | R | R | | | | | | R |
| | | | 1 | 1 | R | R | | | | | | R | | | 1 | | | | R | R | R | | | | |
| | 2 | | | | R | R | | | R | | | | | 1 | | | | | | R | R | | | | R |
| | 2 | | | | R | R | | | R | R | | | | | | | | | | | | | | | |
| | | | 1 | | R | | | R | | | | R | | | | | | | | | | | | | |
| **2** (3%) | **4** (7%) | **8** (9%) | **4** (8%) | **1** (2%) | Number of isolates | | | | | | | | **1** (3%) | **1** (2%) | **4** (6%) | **4** (4%) | **0** (0%) | Number of isolates | | | | | | | |

[a] Tc: tetracycline; Em: erythromycin; Gm: gentamicin; Am: ampicillin; Sm: streptomycin; Cm: chloramphenicol; Km: kanamycin; Na: narasin; Vi: virginiamycin; Ba: bacitracin. [b] Not tested 2005. [c] Not tested 2000-03. [d] Not tested 2000-05.

**TABLE ENTVI.** Association between resistance traits in *Enterococcus faecalis* and in *Enterococcus faecium*, respectively. Isolates from pigs years 2000, 2001, 2003, 2005 and 2008. For each antimicrobial the first line gives resistance rates for susceptible isolates (S) and the second line rates for resistant isolates (R). All antimicrobials were not tested all years, therefor all combinations of pairs of resistance traits can not be calculated.

***E. faecalis***

| Single substance susceptibility | | n | Cross resistance (%)[a] Am | Ba | Em | Na | Tc | Va | Vi |
|---|---|---|---|---|---|---|---|---|---|
| Ampicillin | S | 316 | - | 0.3 | 28.2 | 0.9 | 64.2 | 0.3 | 0.0 |
| | R | 2 | 100.0 | 0.0 | 50.0 | 50.0 | 100.0 | 0.0 | 0.0 |
| Avilamycin | S | 244 | 0.8 | 0.0 | 29.1 | 1.6 | 64.8 | 0.4 | 0.0 |
| | R | 6 | 0.0 | 16.7 | 50.0 | 0.0 | 83.3 | 0.0 | 0.0 |
| Bacitracin | S | 317 | 0.6 | - | 28.1 | 1.3 | 64.7 | 0.3 | 0.0 |
| | R | 1 | 0.0 | 100.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Chloramph. | S | 198 | 0.0 | 0.5 | 23.2 | 0.5 | 60.6 | 0.5 | 0.0 |
| | R | 12 | 0.0 | 0.0 | 83.3 | 0.0 | 100.0 | 0.0 | 0.0 |
| Erythromycin | S | 228 | 0.4 | 0.0 | - | 0.4 | 55.7 | 0.4 | 0.0 |
| | R | 90 | 1.1 | 1.1 | 100.0 | 3.3 | 86.7 | 0.0 | 0.0 |
| Flavomycin | S | 206 | 0.5 | 0.0 | 30.1 | 1.5 | 68.4 | 0.5 | 0.0 |
| | R | 9 | 11.1 | 0.0 | 11.1 | 11.1 | 33.3 | 0.0 | 0.0 |
| Gentamicin | S | 297 | 0.3 | 0.3 | 24.9 | 1.0 | 62.6 | 0.3 | 0.0 |
| | R | 21 | 4.8 | 0.0 | 76.2 | 4.8 | 90.5 | 0.0 | 0.0 |
| Kanamycin | S | 66 | 0.0 | 0.0 | 21.2 | 0.0 | 60.6 | 0.0 | 0.0 |
| | R | 2 | 0.0 | 0.0 | 100.0 | 0.0 | 100.0 | 0.0 | 0.0 |
| Linezolid | S | 68 | 0.0 | 0.0 | 23.5 | 0.0 | 61.8 | 0.0 | 0.0 |
| | R | 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Narasin | S | 314 | 0.3 | 0.3 | 27.7 | - | 64.0 | 0.3 | 0.0 |
| | R | 4 | 25.0 | 0.0 | 75.0 | 100.0 | 100.0 | 0.0 | 0.0 |
| Streptomycin | S | 254 | 0.4 | 0.4 | 25.2 | 0.8 | 66.1 | 0.4 | 0.0 |
| | R | 64 | 1.6 | 0.0 | 40.6 | 3.1 | 57.8 | 0.0 | 0.0 |
| Tetracycline | S | 113 | 0.0 | 0.9 | 10.6 | 0.0 | - | 0.9 | 0.0 |
| | R | 205 | 1.0 | 0.0 | 38.0 | 2.0 | 100.0 | 0.0 | 0.0 |
| Vancomycin | S | 317 | 0.6 | 0.3 | 28.4 | 1.3 | 64.7 | - | 0.0 |
| | R | 1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 100.0 | 0.0 |
| Virginiamycin | S | 318 | 0.6 | 0.3 | 28.3 | 1.3 | 64.5 | 0.3 | - |
| | R | 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | - |

***E. faecium***

| Single substance susceptibility | | n | Cross resistance (%)[a] Am | Ba | Em | Na | Tc | Va | Vi |
|---|---|---|---|---|---|---|---|---|---|
| Ampicillin | S | 309 | - | 6.1 | 12.9 | 0.3 | 12.3 | 0.0 | 10.4 |
| | R | 2 | 100.0 | 0.0 | 50.0 | 0.0 | 50.0 | 0.0 | 0.0 |
| Avilamycin | S | 271 | 0.7 | 5.5 | 13.3 | 0.4 | 12.2 | 0.0 | 11.8 |
| | R | 1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Bacitracin | S | 292 | 0.7 | - | 11.6 | 0.3 | 11.3 | 0.0 | 10.3 |
| | R | 19 | 0.0 | 100.0 | 36.8 | 0.0 | 31.6 | 0.0 | 10.5 |
| Chloramph. | S | 156 | 0.0 | 9.0 | 17.3 | 0.0 | 14.7 | 0.0 | 4.5 |
| | R | 1 | 0.0 | 0.0 | 100.0 | 0.0 | 100.0 | 0.0 | 100.0 |
| Erythromycin | S | 270 | 0.4 | 4.4 | - | 0.4 | 11.5 | 0.0 | 9.6 |
| | R | 41 | 2.4 | 17.1 | 100.0 | 0.0 | 19.5 | 0.0 | 14.6 |
| Flavomycin | S | 255 | 0.8 | 5.9 | 12.5 | 0.4 | 12.2 | 0.0 | 11.4 |
| | R | 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Gentamicin | S | 309 | 0.6 | 6.1 | 12.9 | 0.3 | 12.3 | 0.0 | 9.7 |
| | R | 2 | 0.0 | 0.0 | 50.0 | 0.0 | 50.0 | 0.0 | 100.0 |
| Kanamycin | S | 39 | 0.0 | 10.3 | 12.8 | 0.0 | 15.4 | 0.0 | 0.0 |
| | R | 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Linezolid | S | 39 | 0.0 | 10.3 | 12.8 | 0.0 | 15.4 | 0.0 | 0.0 |
| | R | 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Narasin | S | 310 | 0.6 | 6.1 | 13.2 | - | 12.6 | 0.0 | 10.3 |
| | R | 1 | 0.0 | 0.0 | 0.0 | 100.0 | 0.0 | 0.0 | 0.0 |
| Streptomycin | S | 303 | 0.3 | 6.3 | 12.2 | 0.3 | 12.2 | 0.0 | 8.9 |
| | R | 8 | 12.5 | 0.0 | 50.0 | 0.0 | 25.0 | 0.0 | 62.5 |
| Tetracycline | S | 272 | 0.4 | 4.8 | 12.1 | 0.4 | - | 0.0 | 9.2 |
| | R | 39 | 2.6 | 15.4 | 20.5 | 0.0 | 100.0 | 0.0 | 17.9 |
| Vancomycin | S | 311 | 0.6 | 6.1 | 13.2 | 0.3 | 12.5 | - | 10.3 |
| | R | 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | - | 0.0 |
| Virginiamycin | S | 279 | 0.7 | 6.1 | 12.5 | 0.4 | 11.5 | 0.0 | - |
| | R | 32 | 0.0 | 6.3 | 18.8 | 0.0 | 21.9 | 0.0 | 100.0 |

[a] Am: ampicillin; Ba: bacitracin; Em: erythromycin; Na: narasin; Sm: streptomycin; Tc: tetracycline; Va: vancomycin; Vi: virginiamycin.

**TABLE ENT VII.** Distribution of MICs for *Enterococcus faecalis* from pigs (n=68) and pork (n=18), 2008 and from sheep (n=24) 2006-2009. Composite data for pigs from SVARM 2000, 2001, 2003 and 2005 (n=250) given for comparison.

| Anti-microbial | Sample | Year | Resis-tance (%) | Distribution (%) of MICs[a] (mg/L) | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | ≤0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | 64 | 128 | 256 | 512 | 1024 | 2048 | >2048 |
| Ampicillin | Pig | 2008 | 0 | | | | 92.6 | 7.4 | | | | | | | | | | | |
| | Pork | | 0 | | | | 82.4 | 17.6 | | | | | | | | | | | |
| | Pig | 2000-05 | <1 | | 1.2 | 7.2 | 66.0 | 24.4 | 0.4 | 0.4 | 0.4 | | | | | | | | |
| | Sheep | 2006-09 | 0 | | | 12.5 | 83.38 | 4.2 | | | | | | | | | | | |
| Bacitracin | Pig | 2008 | 0 | | | | 2.9 | | 23.5 | 61.8 | 11.8 | | | | | | | | |
| | Pork | | 0 | | | | | | 23.5 | 70.6 | 5.9 | | | | | | | | |
| | Pig | 2000-05 | <1 | | | | 0.8 | 1.6 | 3.6 | 52.4 | 37.2 | 4.0 | 0.4 | | | | | | |
| | Sheep | 2006-09 | 0 | | | | | | 12.5 | 66.7 | 16.7 | 4.2 | | | | | | | |
| Chloramph. | Pig | 2008 | 2 | | | | | | 8.8 | 88.2 | 1.5 | | 1.5 | | | | | | |
| | Pork | | 0 | | | | | | 29.4 | 70.6 | | | | | | | | | |
| | Pig | 2003-05[c] | - | | | | | 1.4 | 13.4 | 66.9 | 9.9 | 8.5 | | | | | | | |
| | Sheep | 2006-09 | 0 | | | | | | 20.8 | 79.2 | | | | | | | | | |
| Erythromycin | Pig | 2008 | 24 | | | 11.8 | 22.1 | 27.9 | 14.7 | | | 1.5 | | 22.1 | | | | | |
| | Pork | | 0 | | | 35.3 | 23.5 | 29.4 | 11.8 | | | | | | | | | | |
| | Pig | 2000-05 | 30 | | | 10.0 | 23.6 | 24.8 | 12.0 | | 0.4 | 0.8 | 28.4 | | | | | | |
| | Sheep | 2006-09 | 0 | | | 4.2 | 33.3 | 41.7 | 20.8 | | | | | | | | | | |
| Gentamicin | Pig | 2008 | 3 | | | | | | | 8.8 | 63.2 | 25.0 | | | | 2.9 | | | |
| | Pork | | 0 | | | | | | 23.5 | 58.8 | 17.6 | | | | | | | | |
| | Pig | 2000-03[d] | 8 | | | | | 0.5 | 2.6 | 9.7 | 50.8 | 28.7 | 7.7 | | | | | | |
| | Sheep | 2006-09 | 0 | | | | | 4.2 | | 4.2 | 75.0 | 16.7 | | | | | | | |
| Kanamycin | Pig | 2008 | 3 | | | | | | | | | 4.4 | 80.9 | 11.8 | | | | 1.5 | 1.5 |
| | Pork | | 0 | | | | | | | | 5.9 | 58.8 | 35.3 | | | | | | |
| | Sheep | 2006-09 | 0 | | | | | | | | | 8.3 | 75.0 | 16.7 | | | | | |
| Linezolid | Pig | 2008 | 0 | | | | 2.9 | 69.1 | 27.9 | | | | | | | | | | |
| | Pork | | 0 | | | | | 76.5 | 23.5 | | | | | | | | | | |
| | Sheep | 2006-09 | 0 | | | | | 95.8 | 4.2 | | | | | | | | | | |
| Narasin | Pig | 2008 | 0 | | 48.5 | 42.6 | 8.8 | | | | | | | | | | | | |
| | Pork | | 0 | | 29.4 | 64.7 | 5.9 | | | | | | | | | | | | |
| | Pig | 2000-05 | 2 | 2.8 | 13.6 | 62.8 | 18.4 | 0.8 | 0.4 | 0.4 | 0.4 | 0.4 | | | | | | | |
| | Sheep | 2006-09 | 0 | | 66.7 | 33.3 | | | | | | | | | | | | | |
| Streptomycin | Pig | 2008 | 13 | | | | | | | | | | 11.8 | 75.0 | | | | 13.2 | |
| | Pork | | 0 | | | | | | | | 11.8 | 76.5 | 11.8 | | | | | | |
| | Pig | 2000-03[c] | - | | | | | | | | | 4.1 | 20.5 | 51.8 | 23.6 | | | | |
| | Sheep | 2006-09 | 4 | | | | | | | | 4.2 | | 4.2 | 83.3 | 4.2 | | | 4.2 | |
| Tetracycline | Pig | 2008 | 62 | | | 22.1 | 14.7 | 1.5 | | | | 20.6 | 38.2 | 2.9 | | | | | |
| | Pork | | 24 | | | 17.6 | 58.8 | | | | | | 23.5 | | | | | | |
| | Pig | 2000-05 | 65 | | | 7.2 | 18.0 | 9.6 | 0.8 | 0.4 | 7.2 | 25.2 | 31.6 | | | | | | |
| | Sheep | 2006-09 | 8 | | | 70.8 | 20.8 | | | | | 4.2 | 4.2 | | | | | | |
| Vancomycin | Pig | 2008 | 0 | | | | 20.6 | 63.2 | 16.2 | | | | | | | | | | |
| | Pork | | 0 | | | | 11.8 | 41.2 | 47.1 | | | | | | | | | | |
| | Pig | 2000-05 | <1 | | | | 11.6 | 70.0 | 18.0 | 0.4 | | | | | | | | | |
| | Sheep | 2006-09 | 0 | | | | | 70.8 | 29.2 | | | | | | | | | | |
| Virginiamycin | Pig | 2008 | 0 | | | | | 2.9 | | 8.8 | 79.4 | 8.8 | | | | | | | |
| | Pork | | 0 | | | | 5.9 | | | 23.5 | 64.7 | 5.9 | | | | | | | |
| | Pig | 2000-05 | 0 | | | 0.8 | 0.8 | 3.6 | 1.6 | 9.2 | 67.6 | 16.4 | | | | | | | |
| | Sheep | 2006-09 | 0 | | | | | | 8.3 | 37.5 | 45.8 | 8.3 | | | | | | | |
| | | | | **≤0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **64** | **128** | **256** | **512** | **1024** | **2048** | **>2048** |

[a] White 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. Bold vertical lines indicate cut-off values for resistance; [b]MIC in U/mL, see Appendix 3 for details; [c]Not tested 2000-01, n = 142; [d]Not tested 2005 n=195.

**TABLE ENT VIII.** Distribution of MICs for *Enterococcus faecium* from pigs (n=39) year 2008 and from sheep (n=15) 2006-09. Composite data for pigs from SVARM 2000, 2001, 2003 and 2005 (n=272) given for comparison.

| | | | Resis- | Distribution (%) of MICs[a] (mg/L) | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **Sample** | **Year** | **tance (%)** | **≤0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **64** | **128** | **256** | **512** | **1024** | **2048** | **>2048** |
| Ampicillin | Pig | 2008 | 0 | | | 20.5 | 64.1 | 12.8 | 2.6 | | | | | | | | | | |
| | | 2000-05 | <1 | | 12.1 | 11.8 | 34.2 | 36.4 | 4.8 | 0.4 | 0.4 | | | | | | | | |
| | Sheep | 2006-09 | 0 | | 20.0 | 40.0 | 33.3 | 6.7 | | | | | | | | | | | |
| Bacitracin[b] | Pig | 2008 | 10 | | | | | 7.7 | 5.1 | 5.1 | 61.5 | 10.3 | 5.1 | | 5.1 | | | | |
| | | 2000-05 | 6 | | | | 10.3 | 5.1 | 3 .7 | 10.7 | 32.7 | 32.0 | 5.5 | | | | | | |
| | Sheep | 2006-09 | 0 | | | | 6.7 | | | 20.0 | 60.0 | 13.3 | | | | | | | |
| Chloramph. | Pig | 2008 | 0 | | | | | | 20.5 | 79.5 | | | | | | | | | |
| | | 2003-05[c] | <1 | | | | | | 33.9 | 61.9 | 3.4 | 0.8 | | | | | | | |
| | Sheep | 2006-09 | 0 | | | | | | 13.3 | 86.7 | | | | | | | | | |
| Erythromycin | Pig | 2008 | 13 | | | 33.3 | 10.3 | 10.3 | 33.3 | 10.3 | 2.6 | | | | | | | | |
| | | 2000-05 | 13 | | | 29.0 | 6.3 | 19.9 | 31.6 | 8.5 | 2.6 | | 2.2 | | | | | | |
| | Sheep | 2006-09 | 0 | | | 66.7 | 26.7 | 6.7 | | | | | | | | | | | |
| Gentamicin | Pig | 2008 | 0 | | | | | | 23.1 | 66.7 | 10.3 | | | | | | | | |
| | | 2000-03[d] | <1 | | | | 0.4 | 5.3 | 26.2 | 44.9 | 19.6 | 3.1 | 0.4 | | | | | | |
| | Sheep | 2006-09 | 0 | | | | | | 6.7 | 73.3 | 20.0 | | | | | | | | |
| Kanamycin | Pig | 2008 | 0 | | | | | | | | | 5.1 | 30.8 | 33.3 | 25.6 | 5.1 | | | |
| | Sheep | 2006-09 | 0 | | | | | | | | | 66.7 | 20.0 | 6.7 | 6.7 | | | | |
| Linezolid | Pig | 2008 | 0 | | | | | 28.2 | 71.8 | | | | | | | | | | |
| | Sheep | 2006-09 | 0 | | | 6.7 | | 26.7 | 66.7 | | | | | | | | | | |
| Narasin | Pig | 2008 | 0 | | | 53.8 | 46.2 | | | | | | | | | | | | |
| | | 2000-05 | <1 | 1.5 | 5.9 | 31.6 | 51.8 | 6.6 | 2.2 | 0.4 | | | | | | | | | |
| | Sheep | 2006-09 | 0 | | 13.3 | 53.3 | 33.3 | | | | | | | | | | | | |
| Streptomycin | Pig | 2008 | 3 | | | | | | | | | 25.6 | 71.8 | | | | 2.6 | | |
| | | 2000-03[d] | 3 | | | | | | | | | 52.4 | 41.8 | 2.7 | 3.1 | | | | |
| | Sheep | 2006-09 | 7 | | | | | | | | 6.7 | 13.3 | 66.7 | 6.7 | 6.7 | | | | |
| Tetracycline | Pig | 2008 | 15 | | | 79.5 | 5.1 | | | | | 2.6 | 12.8 | | | | | | |
| | | 2000-05 | 12 | | | 23.9 | 49.6 | 14.3 | 1.5 | | 1.1 | 4.0 | 5.5 | | | | | | |
| | Sheep | 2006-09 | 7 | | | 40.0 | 53.3 | | | | 6.7 | | | | | | | | |
| Vancomycin | Pig | 2008 | 0 | | | | 87.2 | 10.3 | 2.6 | | | | | | | | | | |
| | | 2000-05 | 0 | | | | 77.6 | 19.1 | 3.3 | | | | | | | | | | |
| | Sheep | 2006-09 | 0 | | | | 66.7 | 6.7 | 26.7 | | | | | | | | | | |
| Virginiamycin | Pig | 2008 | 0 | | | 43.6 | 5.1 | 35.9 | 15.4 | | | | | | | | | | |
| | | 2000-05 | 12 | | | 19.5 | 23.5 | 24.3 | 21.0 | 8.1 | 2.6 | 1.1 | | | | | | | |
| | Sheep | 2006-09 | 0 | | | 6.7 | 13.3 | 53.3 | 26.7 | | | | | | | | | | |
| | | | | **≤0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **64** | **128** | **256** | **512** | **1024** | **2048** | **>2048** |

[a]White 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. Bold vertical lines indicate cut-off values for resistance; [b]MIC in U/mL; [c]Not tested 2000-01, n =118; [d]Not tested 2005 n=225.

**TABLE ENT IX.** Distribution of MICs for *Enterococcus hirae* from pigs (n=111) year 2008 and from sheep (n=33) 2006-09. Composite data for pigs from SVARM 2000, 2001, 2003 and 2005 (n=419) given for comparison.

| | | | Resis- | Distribution (%) of MICs[a] (mg/L) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **Sample** | **Year** | tance (%) | **≤0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **64** | **128** | **256** | **512** | **1024** | **2048** | **>2048** |
| Ampicillin | Pig | 2008 | 0 | | 53.2 | 9.0 | 27.0 | 9.0 | 1.8 | | | | | | | | | | |
| | | 2000-05 | <1 | | 48.2 | 19.6 | 17.2 | 13.4 | 1.4 | | 0.2 | | | | | | | | |
| | Sheep | 2006-09 | 0 | | 3.0 | 3.0 | 51.5 | 39.4 | 3.0 | | | | | | | | | | |
| Bacitracin[b] | Pig | 2008 | 0 | | | | 57.7 | 34.2 | | 0.9 | 5.4 | 1.8 | | | | | | | |
| | | 2000-05 | 0 | | | | 33.9 | 53.0 | 9.1 | 1.0 | 2.6 | 0.5 | | | | | | | |
| | Sheep | 2006-09 | 0 | | | | 45.5 | 51.5 | | | 3.0 | | | | | | | | |
| Chloramph. | Pig | 2008 | 0 | | | | 0.9 | 3.6 | 73.9 | 21.6 | | | | | | | | | |
| | | 2003-05[c] | 0 | | | | | 4.2 | 75.8 | 19.9 | | | | | | | | | |
| | Sheep | 2006-09 | 0 | | | | | | 69.7 | 30.3 | | | | | | | | | |
| Erythromycin | Pig | 2008 | 9 | | | 89.2 | | 1.8 | 1.8 | 0.9 | | | | 6.3 | | | | | |
| | | 2000-05 | 2 | | | 94.0 | 1.7 | 1.9 | 0.2 | 0.7 | | | 1.4 | | | | | | |
| | Sheep | 2006-09 | 0 | | | 97.0 | 3.0 | | | | | | | | | | | | |
| Gentamicin | Pig | 2008 | 0 | | | | | | 15.3 | 30.6 | 50.5 | 3.6 | | | | | | | |
| | | 2000-03[d] | <1 | | | 0.3 | | 0.3 | 10.7 | 50.2 | 32.9 | 4.9 | 0.7 | | | | | | |
| | Sheep | 2006-09 | 0 | | | | | 3.0 | 3.0 | 39.4 | 42.4 | 12.1 | | | | | | | |
| Kanamycin | Pig | 2008 | 4 | | | | | | | | 0.9 | 32.4 | 56.8 | 4.5 | 0.9 | 0.9 | | | 3.6 |
| | Sheep | 2006-09 | 0 | | | | | | | | 3.0 | 18.2 | 60.6 | 15.2 | 3.0 | | | | |
| Linezolid | Pig | 2008 | 0 | | | | 5.4 | 64.9 | 29.7 | | | | | | | | | | |
| | Sheep | 2006-09 | 0 | | | 3.0 | 6.1 | 72.7 | 18.2 | | | | | | | | | | |
| Narasin | Pig | 2008 | 0 | 0.9 | 12.6 | 61.3 | 20.7 | 4.5 | | | | | | | | | | | |
| | | 2000-05 | 0 | 6.9 | 22.0 | 27.7 | 35.6 | 4.8 | 3.1 | | | | | | | | | | |
| | Sheep | 2006-09 | 0 | 3.0 | 48.5 | 27.3 | 21.2 | | | | | | | | | | | | |
| Streptomycin | Pig | 2008 | 5 | | | | | | | | | 3.6 | 68.5 | 23.4 | | | 0.9 | 3.6 | |
| | | 2000-03[d] | 1 | | | | | | | | | 14.7 | 69.1 | 15.0 | 1.3 | | | | |
| | Sheep | 2006-09 | 3 | | | | | | | 3.0 | | | 60.6 | 33.3 | 3.0 | | | | |
| Tetracycline | Pig | 2008 | 14 | | | 79.3 | 7.2 | | | | | 3.6 | 9.0 | 0.9 | | | | | |
| | | 2000-05 | 13 | | | 36.3 | 40.3 | 10.3 | 0.7 | 0.2 | | 2.6 | 9.5 | | | | | | |
| | Sheep | 2006-09 | 0 | | | 81.8 | 18.2 | | | | | | | | | | | | |
| Vancomycin | Pig | 2008 | 0 | | | | 81.1 | 18.9 | | | | | | | | | | | |
| | | 2000-05 | 0 | | | | 82.1 | 17.4 | 0.5 | | | | | | | | | | |
| | Sheep | 2006-09 | 0 | | | | 75.8 | 24.2 | | | | | | | | | | | |
| Virginiamycin | Pig | 2008 | <1 | | | 49.5 | 5.4 | 40.5 | 3.6 | 0.9 | | | | | | | | | |
| | | 2000-05 | 4 | | | 42.7 | 14.1 | 27.2 | 12.2 | 3.8 | | | | | | | | | |
| | Sheep | 2006-09 | 0 | | | 18.2 | 6.1 | 60.6 | 15.2 | | | | | | | | | | |
| | | | | **≤0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **64** | **128** | **256** | **512** | **1024** | **2048** | **>2048** |

[a]White 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. Bold vertical lines indicate cut-off values for resistance; [b]MIC in U/mL; [c]Not tested 2000-01, n =236; [d]Not tested 2005 n=307.

# Animal pathogens

**ISOLATES TESTED** are from clinical submission of samples to SVA if not otherwise stated. For these samples, information on the indications for sampling is not available but the vast majority of submissions are likely from diseased animals. Therefore, data are probably biased towards samples from treated animals or from herds where antimicrobial treatments are common. Any assessment of trends is based on the assumption that this bias is inherent throughout the observation period.

In SVARM, isolates are, when possible, classified as susceptible or resistant by epidemiological cut-off values issued by EUCAST (see Appendix 3 for details). This classifies isolates with acquired reduced susceptibility as resistant, which is relevant for monitoring purposes, but it should be understood that this not always implies clinical resistance. Some cut-off values defining resistance (breakpoints) previously used in SVARM have been changed. To facilitate comparisons, resistance data from earlier reports have been recalculated using current cut-off values when possible.

## Pig

### *Escherichia coli*

Isolates of *Escherichia coli* from years 1992–2008 are from clinical submissions of samples from the gastro-intestinal tract (intestinal content, faecal samples or mesenteric lymph nodes), while data from 1989–1991 include all *E. coli* isolated from pigs, irrespective of material type.

Before the first of October, 2007, all *E. coli* isolated from the gastro-intestinal tract were susceptibility tested. After that date, the criteria for susceptibility testing were changed and only *E. coli* that harbour genes coding for virulence factors are tested for susceptibility. The following genes are analysed by PCR: enterotoxin (LT), heat-stabile enterotoxin a and b (STa and STb), verocytotoxin (VT2e) and adhesionsfactors F4, F5, F6, F18 and F41. Isolates with at least one of these genes were susceptibility tested. The gene for STb alone was common and also a combination of STb, LT and F4. The distribution of genes coding for virulence factors is shown in Table Pig I.

As in previous years, resistance to ampicillin, streptomycin, tetracycline or trimethoprim-sulphonamides in *E. coli* was common in 2008 (Table Pig II). In the 70s and 80s, prevalence of *E. coli* resistant to ampicillin was only around seven percent (Franklin, 1976; Franklin, 1984). From the early 90s to year 2004, prevalence of ampicillin resistance rose gradually to 22%. In 2007, the figure increased further but this year it is at the same level as before 2007.

In 2008, only one isolate was resistant to ampicillin alone. Thus, 93%, of the ampicillin resistant isolates were resistant to at least one other antimicrobial. Resistance to ampicillin and trimethoprim-sulphonamides was the most common combination of traits. Of the ampicillin resistant isolates, 80% were also resistant to trimethoprim-sulphonamides and two-thirds of isolates resistant to trimethoprim-sulphonamides, were also resistant to ampicillin. This indicates that the genes coding for resistance to ampicillin and trimethoprim-sulphonamides are linked. This association is also shown for indicator *E. coli* in Table EC III, where a majority of ampicillin resistant *E. coli* is resistant to trimethoprim or, especially, to sulphonamides.

Multiresistance (i.e. resistance to three or more antimicrobials) occurred in 14% of the isolates. This figure is considerably lower than last year when 25% of the *E. coli* was multiresistant. The most frequent combination, found in 67% of the multiresistant isolates, was resistance to ampicillin, trimethoprim-sulphonamides and streptomycin. Four percent of the isolates were resistant to five or more antimicrobials.

In Sweden, data on use of antimicrobials are not yet fully available per animal species. Therefore, the extent of use of aminopenicillins or trimethoprim-sulphonamides for Swedish pigs during the last years is not known and it is not possible to make any inference on the association between resistance and use.

### *Brachyspira hyodysenteriae*

Isolates of *Brachyspira hyodysenteriae* are from clinical submissions of faecal samples from pigs.

All isolates were susceptible to tiamulin (Table Pig III).

**TABLE PIG I.** Combinations of genes coding for virulence factors in *Escherichia coli* from clinical submissions of faecal samples or samples taken post mortem from the gastro-intestinal tract in 2008.

| Genes coding for virulence factors[a] | Number of isolates |
|---|---|
| F4 with STb and LT[b] | 25 |
| F5 with STa and or STb[c] | 5 |
| F6 with STa | 2 |
| F18 with STa and or STb[c] | 12 |
| No adhesins demonstrated, STa STb and LT alone or combined | 29 |
| Adhesins without demonstrated toxins | 2 |
| VT2e[d] | 8 |

[a] The following genes are analysed by PCR: enterotoxin (LT), heat-stabile enterotoxin a and b (STa and STb), verocytotoxin (VT2e) and adhesionsfactors F4, F5, F6, F18 and F41; [b] including five isolates also with STa, of which one also had F5; [c] including one isolate also with F41; [d] including two isolates with F18

**TABLE PIG II.** Resistance (%) in *Escherichia coli* from pigs 1989-2008 and distribution of MICs for isolates from 2008. Isolates are from clinical submissions of faecal samples or samples taken post mortem from the gastro-intestinal tract.

| | Resistance (%) | | | | | | | | | Distribution (%) of MICs[a] (mg/L) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Antimicrobial | 1989-1991 n=248 | 1992-1994 n=431 | 1995-1997 n=1244 | 1998-2000 n=1074 | 2001-2003 n=935 | 2004-2005 n=711 | 2006 n=298 | 2007 n=93 | 2008 n=83 | ≤0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | >32 |
| Ampicillin | 6 | 10 | 9 | 11 | 17 | 22 | 21 | 30 | 18 | | | | 18.1 | 55.4 | 8.4 | | 18.1 | | |
| Ceftiofur | - | - | - | - | <1[h] | <1 | <1 | 0 | 0 | | 43.4 | 53.0 | 3.6 | | | | | | |
| Enrofloxacin[b] | 1[g] | 7 | 5 | 6 | 8 | 9 | 8 | 4 | 6 | 94.0 | 3.6 | | 1.2 | 1.2 | | | | | |
| Florfenicol | - | - | - | - | <1[h] | 0 | <1 | 0 | 0 | | | | | 6.0 | 38.6 | 48.2 | 7.2 | | |
| Gentamicin[c] | 1 | 1 | <1 | 1 | 4 | 1 | 1 | 2 | 0 | | | | | 95.2 | 4.8 | | | | |
| Neomycin | 17 | 14 | 9 | 6 | 5[i] | 4 | 3 | 3 | 6 | | | | | | 89.2 | 4.8 | | | 6.0 |
| Streptomycin[d] | 44 | 44 | 32 | 30 | 36 | 37 | 32 | 40 | 40 | | | | | | 12.0 | 26.5 | 21.7 | 12.0 | 27.7 |
| Tetracycline | 28 | 35 | 31 | 33 | 30 | 26 | 26 | 27 | 25 | | | | 31.3 | 33.7 | 9.6 | | 25.3 | | |
| Trim/Sulph.[e,f] | 17 | 15 | 13 | 14 | 19 | 26 | 21 | 27 | 22 | | | 77.1 | 1.2 | | | 21.7 | | | |

[a] White 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. Bold vertical lines indicate cut-off values defining resistance; [b] Cut-off value >0.25 mg/L until 2001; [c] Cut-off value >8 mg/L until 2002; [d] Cut-off value >32 mg/L until 2001; [e] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [f] Cut-off value >4 mg/L until year 2001; [g] 227 isolates tested; 9 688 isolates tested; [i] 926 isolates tested.

**TABLE PIG III.** Resistance (%) in *Brachyspira hyodysenteriae* from pigs 2001-08 and distribution of MICs for isolates from 2008. Isolates are from clinical submissions of faecal samples.

| | Resistance (%) | | | | | | | Distribution (%) of MICs[a] (mg/L) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Antimicrobial | 2001 n=75 | 2002 n=109 | 2003 n=100 | 2005 n=31 | 2006 n=26 | 2007 n=23 | 2008 n=15 | ≤0.06 | 0.125 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | 64 | 128 | >128 |
| Tiamulin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 20.0 | 46.7 | 6.7 | 13.3 | 13.3 | | | | | | | | |
| Tylosin | 83 | 73 | 89 | 81 | 85 | 65 | 93 | | | | | | | | 6.7 | | | | | 93.3 |
| Tylvalosin | - | - | - | - | - | - | ND[b] | | | | | 6.7 | 6.7 | 33.3 | 33.3 | 13.3 | 6.7 | | | |

[a] White 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; [b] ND=not determined because no cut-off value is available.

In the late 80s, susceptibility of *B. hyodysenteriae* was tested with an agar dilution technique, and 20% of the isolates were resistant to tylosin (Gunnarsson et al., 1991). In year 2001, the figure had increased dramatically to around 80% (Table Pig III). This year´s figure is even higher but the small number of isolates precludes valid conclusions on trends.

This year isolates were susceptibility tested also for tylvalosin, a macrolide authorised for treatment of swine dysentery in the European Union. No cut-off value for resistance to tylvalosin is available and due to the small number of *B. hyodysenteriae* tested this year a value cannot be determined from the distribution of MICs. However, Karlsson et al. (2004) showed a correlation between the MICs of tylosin and tylvalosin indicating that macrolide resistance caused by structural changes of ribosomal RNA also affects the binding of tylvalosin.

Sweden has a programme for controlling swine dysentery by three strategies; testing of nucleus and multiplying herds for *B. hyodysenteriae* twice a year, eradication of the bacteria in infected herds and tracing the source of infection. Nevertheless, it is imperative that all herds where treatment failure is suspected are thoroughly investigated. Since only macrolides and tiamulin are authorised for treatment of swine dysentery in pigs it is important to monitor resistance development in *B. hyodysenteriae*.

### *Brachyspira pilosicoli*

Isolates of *Brachyspira pilosicoli* are from clinical submissions of faecal samples from pigs. In 2001, the first isolates of *B. pilosicoli* resistant to tiamulin were confirmed in Sweden. These isolates were associated with treatment failure in a Swedish pig herd with spirochaetal diarrhoea (see SVARM 2003). Since then, tiamulin resistant strains have been isolated every year but there is no apparent increasing trend in prevalence of resistance (Table Pig IV). The frequency of resistance to tylosin has during the last two years been stable, around 60% of the isolates being resistant to this antimicrobial (Table Pig IV).

This year's isolates are susceptibility tested also for tylvalosin. Tylvalosin is a macrolide authorised for treatment of swine dysentery in the European Union, however, not for treatment of spirochaetal diarrhoea. The MICs of tylosin and tylvalosin for *B. pilosicoli* correlate well in this year's data (data not shown), which was shown also by Karlsson et al. (2004) for *B. hyodysenteriae*. This indicates that macrolide resistance caused by structural changes of ribosomal RNA also affects the binding of tylvalosin. With this background, together with the distribution of the MICs in this material a cut-off value for tylvalosin of >4 mg/L is suggested.

In 2008, 16% of the isolates were resistant to all three substances tested, i.e. five isolates. Although such isolates may be susceptible to other antimicrobials, only tiamulin and tylosin are currently licensed for treatment of spirochaetal diarrhoea in pigs in Sweden. The findings stress the need for susceptibility testing of *B. pilosicoli* from herds where tiamulin is to be used.

**TABLE PIG IV.** Resistance (%) in *Brachyspira pilosicoli* from pigs 2002-08 and distribution of MICs for isolates from 2008. Isolates are from clinical submissions of faecal samples.

| | **Resistance** (%) | | | | | **Distribution** (%) **of MICs**[a] (mg/L) | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **2002-03** n=93 | **2005** n=57 | **2006** n=72 | **2007** n=44 | **2008** n=31 | **≤0.06** | **0.125** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **64** | **128** | **>128** |
| Tiamulin | 14 | 16 | 12 | 9 | 16 | 38.7 | 25.8 | 6.4 | 9.7 | 3.2 | | | 3.2 | 12.9 | | | | |
| Tylosin | 50[b] | 63 | 67 | 61 | 55 | | | | | | 3.2 | 19.4 | 16.1 | 6.4 | 16.1. | 3.2 | 3.2 | 32.3 |
| Tylvalosin | - | - | - | - | 39 | | | | 6.4 | 19.4 | 29.0 | 6.4 | | 6.4 | 19.4 | 12.9 | | |

[a] White 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; [b] 86 isolates tested.

### *Actinobacillus pleuropneumoniae*

*Actinobacillus pleuropneumoniae* from years 1992–2000 were isolated from the respiratory tract (nasal swabs and lung, including regional lymph nodes) but from years 2005–2008 all isolates are from lungs sampled post mortem.

In 2008, *A. pleuropneumoniae* were susceptible to all antimicrobials tested (Table Pig V). The comparatively high prevalence of tetracycline resistance observed in the 90s did not appear in this year's data.

In years 2005 to 2008 around 30 strains of *A. pleuropneumoniae* were isolated and susceptibility tested each year. This is a considerable increase compared to the situation in the 90s when only 18 isolates were tested for antimicrobial susceptibility. Nonetheless, the number of isolates tested is low and a higher frequency of sampling and susceptibility testing is desirable if emerging resistance is to be detected early. Especially, since pneumonia caused by *A. pleuropneumoniae* is an increasing problem in Swedish pig production.

**TABLE PIG V.** Resistance (%) in *Actinobacillus pleuropneumoniae* from pigs the years 1992-2000, 2005-07 and 2008. Distribution of MICs for isolates from 2008. Isolates are from clinical submissions of samples from the respiratory tract or from post mortem investigations of lungs.

| | **Resistance** (%) | | | **Distribution** (%) **of MICs**[a] (mg/L) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **1992-00** n=18 | **2005-07** n=84 | **2008** n=39 | **≤0.03** | **0.06** | **0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **64** | **128** | **256** | **512** | **>512** |
| Ampicillin | 6 | 0 | 0 | | | 28.2 | 71.8 | | | | | | | | | | | | |
| Cefotaxime | - | 0 | 0 | | 100.0 | | | | | | | | | | | | | | |
| Ceftiofur | - | 0 | 0 | | | 100 | | | | | | | | | | | | | |
| Chloramphenicol | 11 | 0 | 0 | | | | | | 100.0 | | | | | | | | | | |
| Ciprofloxacin | 6[b] | 0 | 0 | 94.9 | 5.1 | | | | | | | | | | | | | | |
| Florfenicol | - | 0 | 0 | | | | | | | | 100.0 | | | | | | | | |
| Gentamicin | - | 0 | 0 | | | | | | 2.6 | 12.8 | 84.6 | | | | | | | | |
| Nalidixic acid | - | 0 | 0 | | | | | | | 5.1 | 94.9 | | | | | | | | |
| Penicillin | 6 | 0 | 0[d] | | | 2.5 | 64.1 | 33.4 | | | | | | | | | | | |
| Streptomycin | - | 0 | 0 | | | | | | | | | 2.6 | 87.2 | 10.3 | | | | | |
| Sulphonamide | - | 0 | 0 | | | | | | | | | | | 5.1 | 53.8 | 38.5 | 2.6 | | |
| Tetracycline | 11[c] | 1 | 0 | | | | | 92.3 | 7.7 | | | | | | | | | | |
| Trimethoprim | - | 0 | 0 | | | | 94.9 | 5.1 | | | | | | | | | | | |

[a] White 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. Bold vertical lines indicate cut-off values defining resistance; [b] enrofloxacin tested, cut-off value 2 mg/l.; [c] cut-off value >8 mg/l; [d] a shorter range is used compared to previous years.

### *Pasteurella* spp.

*Pasteurella* spp. are from nasal swabs collected within a control programme for atrophic rhinitis in nucleus and multiplying herds. In 2008, all *Pasteurella* spp were susceptible to all antimicrobials tested as in the beginning of the current decade (Table Pig VI). However, since isolates tested are collected in a control programme and not from clinical submissions they are likely from healthy pigs and the antimicrobial resistance might be different in *Pasteurella* spp. from production herds with respiratory problems.

# SVARMpat – studies in progress

**THE PURPOSE** of SVARMpat is to increase the knowledge on resistance in animal pathogens from Swedish farm animals and the programme has been running since 2005 (for more information See SVARM 2005). SVARMpat is a co-operation between the National Veterinary Institute (SVA) and the Swedish Animal Health Service and is financed by the Swedish Board of Agriculture. Results are reported yearly in the SVARM report, and in addition three times yearly in newsletters directly to veterinary practitioners. The purpose of the newsletters is to continuously inform practitioners on activities and results but also to deepen their knowledge on antimicrobials, antimicrobial treatment and resistance.

An important activity in SVARMpat has been to encourage practitioners and pathologists to submit samples for microbiological culture and susceptibility testing. In this year´s SVARM report some results from this work are presented, e.g. susceptibility data on *Actinobacillus pleuropneumoniae* from pigs and on *Pasteuerella* spp. from both cattle and pigs. Also the data on *Staphylococcus aureus* isolated from milk from dairy cows with sub-clinical mastitis were collected in the SVARMpat programme. Results of susceptibility testing of *Fusobacterium necrophorum* isolated from cattle and sheep are presented in a highlight. Moreover, results from a study on antimicrobial resistance in indicator bacteria (*Escherichia coli* and *Enterococcus* spp.) of healthy sheep are presented in "Indicator bacteria".

### Other activities in SVARMpat

During 2008, the following activities have been ongoing:

- A workshop on antimicrobial treatment of cattle was held for bovine practitioners in October 2008 in collaboration with Strama VL and Swedish Animal Health Services.
- A full-time PhD-student working on genotyping of resistance genes in *E. coli* from faecal samples from diseased pigs is financed by the programme. A major part of the research will be based on a microarray technique.
- Another PhD project – Vancomycin resistant enterococci in Swedish broilers –is partly financed by SVARMpat. In the project, started 2007, the apparent spread of vancomycin resistant enterococci (VRE) in Swedish broilers since 2000 is investigated. The aim is to elucidate the epidemiology of VRE in broilers and, if possible, to mitigate further spread and reduce the prevalence on farms where VRE already occur. See also Highlight "Vancomycin resistant enterococci (VRE) in broilers".

During 2009, other specific studies will be initiated:

- Screening for production of extended spectrum betalactamase (ESBL) in *E. coli* from pigs with diarrhoea.
- Investigations on correlations between antimicrobial resistance, genes coding for virulence factors and serotypes in *E. coli* from pigs with diarrhoea.
- Screening of causative agents of arthritis in piglets and the antimicrobial susceptibility of these bacteria.
- Screening of causative agents of chronic mastitis in sows and the antimicrobial susceptibility of these bacteria.
- Screening for MRSA in pigs in finishing herds.

**TABLE PIG VI.** Resistance (%) in *Pasteurella* spp. from pigs 2000-01, 2005-07 and 2008. Distribution of MICs for isolates from 2008. Isolates are from the respiratory tract, isolated from nasal swabs.

| | **Resistance** (%) | | | **Distribution** (%) **of MICs**[a] (mg/L) | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **2000-01** n=75 | **2005-07** n=38 | **2008** n=25 | **≤0.03** | **0.06** | **0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **64** | **128** | **256** | **512** | **>512** |
| Ampicillin | 0 | 0 | 0 | | | | | 84.0 | 16.0 | | | | | | | | | | |
| Cefotaxime | - | 0 | 0 | | 100.0 | | | | | | | | | | | | | | |
| Ceftiofur | - | 0 | 0 | | | 96.0 | 4.0 | | | | | | | | | | | | |
| Chloramphenicol | 1 | 0 | 0 | | | | | | 100.0 | | | | | | | | | | |
| Ciprofloxacin | 1[b] | 0 | 0 | 100.0 | | | | | | | | | | | | | | | |
| Florfenicol | - | 0 | 0 | | | | | | | | 100.0 | | | | | | | | |
| Gentamicin | 4 | 0 | 0 | | | | | | 8.0 | 76.0 | 16.0 | | | | | | | | |
| Nalidixic acid | - | 0 | 0 | | | | | | | 44.0 | 44.0 | 12.0 | | | | | | | |
| Penicillin | 0 | 0 | 0[d] | | | | 88.0 | 12.0 | | | | | | | | | | | |
| Streptomycin | 4 | 0 | 0 | | | | | | | | 8.0 | 48.0 | 32.0 | 12.0 | | | | | |
| Sulphonamide | - | 0 | 0 | | | | | | | | | | 4.0 | 40.0 | 24.0 | 28.0 | 4.0 | | |
| Tetracycline | 1 | 0 | 0 | | | | | 72.0 | 24.0 | 4.0 | | | | | | | | | |
| Trimethoprim | - | 0 | 0 | | | | 68.0 | 28.0 | 4.0 | | | | | | | | | | |

[a] White 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. Bold vertical lines indicate cut-off values defining resistance; [b] enrofloxacin tested, cut-off value 2 mg/l; [d] a shorter range is used compared to previous years.

## Cattle

### *Pasteurella* spp.

The *Pasteurella* spp. from 2005 to 2008 were isolated from clinical submissions of samples from calves with respiratory disease or from post-mortem investigations of lungs. The isolates from years 1997–2000 are from a field study on respiratory pathogens in calves presented in SVARM 2000.

Antimicrobial resistance among isolates of *Pasteurella* spp. is rare (Table Cattle I). In year 2003, the first Swedish isolates of beta-lactamase producing *Pasteurella* spp. were confirmed. Resistance to penicillin and tetracycline, the substances commonly used for therapy of respiratory disease in calves, was not detected in this year's material. The number of isolates is low and more frequent sampling of calves with respiratory disorders and subsequent susceptibility testing is desirable if emerging resistance is to be detected early.

**TABLE CATTLE I.** Resistance (%) in *Pasteurella* spp. from calves 1997-2000, 2005-07 and 2008. Distribution of MICs for isolates from 2008. Isolates are from the respiratory tract of calves.

| | **Resistance** (%) | | | **Distribution** (%) **of MICs** [a] (mg/L) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **1997-00** n=254 | **2005-07** n=27 | **2008** n=32 | **≤0.06** | **0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **>32** |
| Ampicillin | 1 | 0 | 0 | | | | | 100.0 | | | | | | |
| Ceftiofur | - | 0 | 0 | | | 100.0 | | | | | | | | |
| Ciprofloxacin | - | - | 0 | 100.0 | | | | | | | | | | |
| Enrofloxacin | 2 | 0 | 0 | | 100.0 | | | | | | | | | |
| Florfenicol | - | 0 | 0 | | | | | | 100.0 | | | | | |
| Penicillin | 0 | 0 | 0 | | 21.9 | 65.6 | 12.5 | | | | | | | |
| Tetracycline | 3 | 0 | 0 | | | | | 100.0 | | | | | | |
| Trim/Sulph.[b] | 2 | 0 | 0 | | | | 100.0 | | | | | | | |

[a] White 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. Bold vertical lines indicate cut-off values defining resistance; [b] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole).

### *Staphylococcus aureus*

Isolates of *Staphylococcus aureus* are from milk samples from dairy cows with subclinical mastitis. Each isolate represented a unique herd.

Antimicrobial resistance among tested isolates was rare (Table Cattle II). Only two isolates were positive for beta-lactamase production, i.e. resistant to penicillin. Three isolates were resistant to clindamycin, tetracycline and fusidic acid. In addition, one isolate was resistant to fusidic acid and kanamycin. None of the isolates were resistant to oxacillin and therefore no methicillin resistant *S. aureus* was suspected.

In Sweden, parenteral penicillin is the drug of choice in treatment of clinical mastitis in cows and most practitioners adhere to this recommendation. Accordingly, penicillin is commonly used in dairy cows but despite this, penicillin resistant *S. aureus* are rare. This could possibly be explained by different control measures maintained by Swedish veterinarians, for example cows with mastitis caused by *S. aureus* with beta-lactamase production are segregated from healthy cows and recommended for culling.

**TABLE CATTLE II.** Resistance (%) and distribution of MICs in *Staphylococcus aureus* from cows, 2008. Isolates are from milk samples from dairy cows with subclinical mastitis.

| | **Resistance** (%) | **Distribution** (%) **of MICs** [a] (mg/L) | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **2008** n=87 | **≤0.03** | **0.06** | **0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **64** | **>64** |
| Cephalothin | 0 | | | 51.7 | 44.8 | 3.4 | | | | | | | | |
| Chloramphenicol | 0 | | | | | | | 2.3 | 21.8 | 71.2 | 4.6 | | | |
| Ciprofloxacin | 0 | | 2.3 | 17.2 | 56.3 | 23.0 | 1.1 | | | | | | | |
| Clindamycin | 7 | | | | 93.1 | 6.9 | | | | | | | | |
| Erythromycin | 0 | | | | 14.9 | 75.9 | 9.2 | | | | | | | |
| Fusidic acid | 6 | | 2.3 | 4.6 | 48.3 | 41.4 | 1.1 | 3.4 | | | 1.1 | | | |
| Gentamicin | 0 | | | | | 67.8 | 28.7 | 3.4 | | | | | | |
| Kanamycin | 1 | | | | 1.1 | 1.1 | 14.9 | 56.3 | 21.8 | 3.4 | 1.1 | | | |
| Oxacillin[b] | 0 | | | | 49.4 | 40.2 | 9.2 | 1.1 | | | | | | |
| Penicillin | 2[c] | 37.9 | 41.3 | 18.4 | | | 1.1 | | | 1.1 | | | | |
| Tetracycline | 3 | | | | | 94.2 | 2.3 | 3.4 | | | | | | |
| Trimethoprim | 5 | | | | | 4.6 | 11.4 | 64.4 | 14.9 | 4.6 | | | | |

[a] White 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. Bold vertical lines indicate cut-off values defining resistance; [b] tested with 2% NaCl; [c] denotes β-lactamase production.

# *Fusobacterium necrophorum* from cattle and sheep

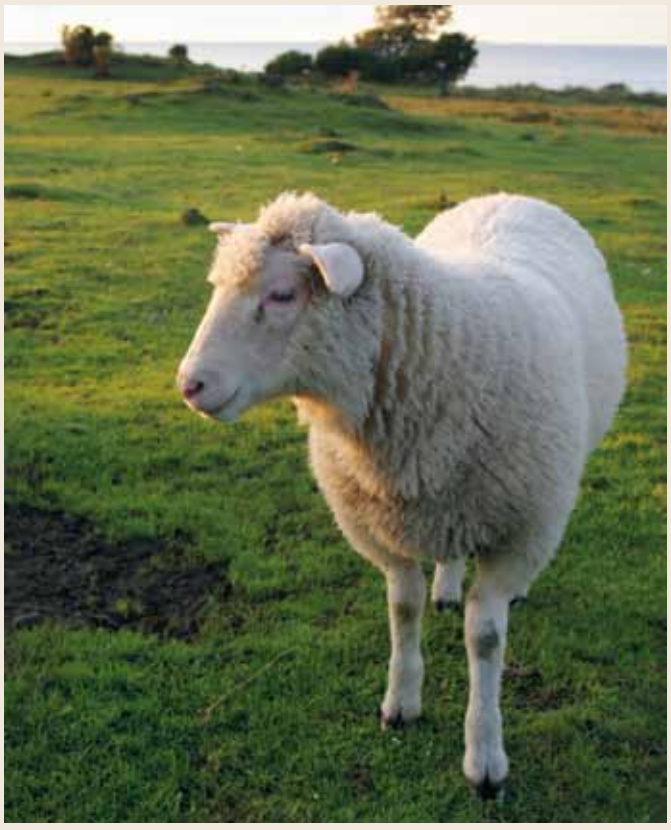
**INTERDIGITAL PHLEGMONE** and foot-root are common diseases in cattle and sheep, respectively. These diseases are often treated with antimicrobials. Interdigital phlegmone in cattle is caused by *Fusobacterium necrophorum* while *Dichelobacter nodosus* is the major causative agent for foot-root in sheep and *F. necrophorum* plays a minor role. In Sweden, these diseases are usually treated with penicillin or tetracycline.

*Fusobacterium necrophorum* is comprised of two subspecies where ssp. *necrophorum* is virulent and ssp. funduliforme is less pathogenic. It is difficult to distinguish between these two subspecies phenotypically. Moreover, there are few publications on antimicrobial susceptibility of *Fusobacterium necrophorum*. To improve knowledge in this field a PCR to facilitate subtyping of *F. necrophorum* (Narongwanichgarn et al., 2003), and a broth dilution method for susceptibility testing, were developed within SVARMpat during 2007.

In 2008, 50 samples from interdigital phlegmone in cattle were cultured at SVA, and from these, 21 *F. necrophorum* were isolated. All of these were identified as *F. necrophorum* ssp. *necrophorum* by PCR. The susceptibility of these isolates is shown in the table below. To our knowledge there are no accepted cut-off values for resistance for *F. necrophorum* and from this small data set it is not possible to propose a cut-off value. Anyhow, *F. necrophorum* ssp. *necrophorum* had low MICs for both penicillin and tetracycline and the MICs for these antimicrobials are concordant with those presented by Lechtenberg et al. (1998). For both substances the MICs were below the lower end of the range tested. The MICs for penicillin and tetracycline are on a level with those of β-hemolytic streptococci. Isolates of β-hemolytic streptococci with MIC of ≤0.03 for penicillin and of ≤0.5 for tetracycline are regarded as susceptible according to CLSI (2008). Therefore *F. necrophorum* ssp. *necrophorum* with these MICs are most likely also susceptible on treatment with penicillin or tetracyclines. On the other hand, fluoroquinolones seem not to be suitable to treat interdigital phlegmone because *F. necrophorum* ssp. necrophorum has high MICs compared clinically susceptible bacteria such as e.g. *Escherichia coli* (EUCAST).

In 2008, 53 samples from foot-root in sheep were cultured at SVA, and from these only seven *F. necrophorum* were isolated, where six were *F. necrophorum* ssp *necrophorum* and one ssp. *funduliforme*. These isolates have not been susceptibility tested yet.

Analyses of *F. necrophorum* regarding both subtyping and susceptibility testing will continue during 2009 within the SVARMpat programme.



Distribution of MICs among *Fusobacterium necrophorum* ssp. *necrophorum* from cows, 2008 (n=19). Isolates are from samples from interdigital phlegmone.

| | Distribution (%) of MICs[a] (mg/L) | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **≤0.03** | **0.06** | **0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **64** | **>64** |
| Cephalothin | | | 10.5 | 89.5 | | | | | | | | | |
| Ciprofloxacin | | | 5.3 | | 47.4 | 47.4 | | | | | | | |
| Erythromycin | | | | | | | 5.3 | 47.3 | 47.3 | | | | |
| Penicillin | 100 | | | | | | | | | | | | |
| Tetracycline | | | | | 100 | | | | | | | | |
| Trimethoprim | | | | | | | | | | 42.1 | 42.1 | 15.7 | |

[a] White 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

## Farmed fish

Isolates of *Aeromonas salmonicida* subsp. *achromogenes*, *Flavobacter columnare* and *Flavobacter psychrophilum* are from clinical submissions of farmed fish. Most isolates represent a unique batch of fish but occasional isolates are duplicates within the same batch. In 2008, the majority of *A. salmonicida* subsp. *achromogenes* and *F. columnare* are from brown trout, 75 and 68%, respectively, whereas the majority of *F. psychrophilum* are from rainbow trout, 85%. A similar distribution among fish species applies for isolates from 2005–2007, previously presented in SVARM 2007.

Until recently there have been no accepted standard reference methods for testing antimicrobial susceptibility of bacteria from fish. In 2005, the VetMIC™ microdilution system for testing bacteria from warm-blooded animals used at SVA was adapted to bacteria from fish according to recommendations by Alderman & Smith (2001). The methodology has since been used for routine testing of isolates from clinical submissions of fish.

At present there are no accepted interpretative criteria for MIC data of bacteria from aquaculture. Evaluation of the distributions of MICs however indicates the presence of isolates with reduced susceptibility, i.e. deviating high MICs, (Table Fish I). For example, MIC distributions for the quinolone nalidixic acid are bimodal in all three bacterial species. This indicates the presence of acquired resistance to quinolones. Likewise deviating high MICs for tetracycline in Flavobacter, and for florfenicol among *A. salmonicida* and *F. columnare*, indicate acquired resistance to these antimicrobials.

Occurrence of quinolone resistance is conceivable since the quinolone oxolinic acid is used therapeutically in aquaculture in Sweden. Also resistance to tetracycline or florfenicol is in agreement with the use of these antimicrobials in farmed fish. The amounts of antimicrobial prescribed for use in farmed fish was presented in SVARM 2007. The small number of isolates tested and the limited time period covered however preclude conclusions on trends in susceptibility.

**TABLE FISH I.** Distribution of MICs for *Aeromonas salmonicida* subsp. *achromogenes, Flavobacter columnare* and *Flavobacter psychrophilum*. Isolates from 2005-2007 and 2008.

| Species | Antimicrobial | Year | Number of isolates | Distribution (%) of MICs[a] (mg/L) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | ≤0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | 64 | >64 |
| *Aeromonas salmonicida* subsp. *achromogenes* | Florfenicol | 2008 | 20 | | | | 95.0 | | 5.0 | | | | |
| | | 2005-07 | 67 | | | | 97.0 | 3.0 | | | | | |
| | Nalidixic acid | 2008 | 20 | | 75.0 | 5.0 | | | | 5.0 | 5.0 | 5.0 | 5.0 |
| | | 2005-07 | 67 | | 82.1 | 4.5 | | | | | 3.0 | 6.0 | 4.5 |
| | Tetracycline | 2008 | 20 | 95.0 | | | | 5.0 | | | | | |
| | | 2005-07 | 67 | 89.6 | 10.4 | | | | | | | | |
| *Flavobacter columnare* | Florfenicol | 2008 | 16 | | | | 93.8 | | | | 6.3 | | |
| | | 2005-07 | 30 | | | | 96.7 | 3.3 | | | | | |
| | Nalidixic acid | 2008 | 16 | | 68.8 | 25.0 | 6.3 | | | | | | |
| | | 2005-07 | 30 | | 76.7 | 6.7 | 3.3 | | | | 3.3 | 3.3 | 6.7 |
| | Tetracycline | 2008 | 16 | 75.0 | 6.3 | 12.5 | | | | | 6.3 | | |
| | | 2005-07 | 30 | 90.0 | 6.7 | | | 3.3 | | | | | |
| *Flavobacter psychrophilum* | Florfenicol | 2008 | 27 | | | | 96.3 | 3.7 | | | | | |
| | | 2005-07 | 42 | | | | 100.0 | | | | | | |
| | Nalidixic acid | 2008 | 27 | | | | 25.9 | 59.3 | | | | | 14.8 |
| | | 2005-07 | 42 | | 11.9 | | 45.2 | 26.2 | | 2.4 | 2.4 | | 11.9 |
| | Tetracycline | 2008 | 27 | 66.7 | 3.7 | 11.1 | 11.1 | | 3.7 | 3.7 | | | |
| | | 2005-07 | 42 | 76.2 | 7.1 | 2.4 | 4.8 | 9.5 | | | | | |

[a] White 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.

Horse

## Horse

### *Escherichia coli*

The isolates of *Escherichia coli* included are from the genital tract of mares. As in previous years, resistance to trimethoprim-sulphonamides or streptomycin are the most common resistance traits in *E. coli* from horses (Table Horse I). Trimethoprim-sulphonamide resistance is probably a consequence of the frequent use of this antimicrobial combination in horses. Moreover, this usage probably co-selects for streptomycin resistance, since 71% of isolates resistant to trimethoprim-sulphonamides were also resistant to streptomycin. Since the introduction of trimethoprim-sulphonamides on the Swedish market as an oral formulation for horses in the late 80s, the prevalence of resistance in *E. coli* quickly increased from only 2% in years 1992–1994 to the current level of about 20% in the beginning of year 2000.

Resistance to gentamicin occurred only in the three isolates

that were resistant to five antimicrobials, and it is possible that gynaecological use of gentamicin selects for multiresistant *E. coli*. However, the prevalence of gentamicin resistance is still low despite the use of gentamicin in extenders for semen and in solutions for uterine douching in equine stud practice (Table Horse I).

Multiresistance (i.e. resistance to three or more antimicrobials) occurred in 5% of the isolates. One isolate resistant to ceftiofur was positive for production of extended-spectrum beta-lactamases (ESBL) when tested according to CLSI (see Appendix 3). The isolate was resistant also to gentamicin, neomycin, streptomycin and trimethoprim-sulphonamides. Although ceftiofur is not authorised for treatment in horses in Sweden, it is used for instances to treat mares with gynaecological disorders at stud farms. This usage will select for ESBL and the number of infections with ESBL producing *E. coli* will increase. In addition, ceftiofur should only be used to treat life-threatening infections for instance in foals.

**TABLE HORSE I.** Resistance (%) in *Escherichia coli* from horses 1992-2008 and distribution of MICs for isolates from 2008. Isolates are from clinical submissions of samples from the female genital tract.

| | **Resistance** (%) | | | | | | | **Distribution** (%) **of MICs**[a] (mg/L) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **1992-94** n=48 | **1995-97** n=216 | **1998-00** n=222 | **2001-03** n=457 | **2004-06** n=473 | **2007** n=273 | **2008** n=174 | **≤0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **>32** |
| Ampicillin | 15 | 17 | 10 | 9 | 7 | 8 | 6 | | | | 2.9 | 53.8 | 35.8 | 1.7 | 5.8 | | |
| Ceftiofur | - | - | - | <1[g] | <1 | <1 | 1 | | 18.4 | 6.5 | 10.9 | 0.6 | 0.6 | | | | |
| Enrofloxacin[b] | 8 | 3 | 3 | 2 | 4 | 1 | 3 | 96.6 | 1.1 | | 1.1 | 1.1 | | | | | |
| Florfenicol | - | - | - | 0 | 0 | <1 | <1 | | | | | 3.4 | 17.2 | 74.1 | 4.6 | 0.6 | |
| Gentamicin[c] | 0 | 3 | 6 | 6 | 2 | 3 | 2 | | | | | 92.0 | 6.3 | | | 1.7 | |
| Neomycin | 4 | 5 | 5 | 3 | 4 | 1 | 2 | | | | | | 95.4 | 2.9 | 0.6 | | 1.1 |
| Streptomycin[d] | 31 | 24 | 21 | 23 | 21 | 19 | 22 | | | | | | 2.3 | 43.7 | 32.2 | 2.9 | 19.0 |
| Tetracycline | 6 | 5 | 9 | 6 | 8 | 7 | 5 | | | | 49.4 | 36.8 | 8.1 | 1.1 | 4.6 | | |
| Trim/Sulph.[e, f] | 2, | 15 | 17 | 18 | 21 | 16 | 20 | | | 78.7 | 1.1 | 1.1 | 0.6 | 18.4 | | | |

[a] White 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. Bold vertical lines indicate cut-off values defining resistance; [b] Cut-off value >0.25 mg/L until 2002; [c] Cut-off value >8 mg/L until 2002; [d] Cut-off value >16 mg/L until 2001, [e] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [f] Cut-off value >4 mg/L until 2001; [g] 353 isolates tested.

### *Streptococcus zooepidemicus*

The isolates included are from the respiratory tract of the horse. As in previous years, *Streptococcus zooepidemicus* are susceptible to penicillin (Table Horse II). Occurrence of resistance to trimethoprim-sulphonamides has been high during the last years, probably due to a concurrent increase in use of oral trimethoprim-sulphonamides in horses. However, in 2007 and 2008, the prevalence of isolates resistant to trimethoprim-sulphonamides was numerically lower compared to previous years. Resistance to antimicrobials other than trimethoprim-sulphonamides is rare. *Streptococcus zooepidemicus* has a low inherent susceptibility to aminoglycosides (i.e. gentamicin, neomycin and streptomycin) and it can be observed that MIC ranges are above the concentrations that can be obtained during systemic therapy with these antimicrobials.

**TABLE HORSE II.** Resistance (%) in *Streptococcus zooepidemicus* from horses 1992-2008 and distribution of MICs for isolates from 2008. Isolates are from clinical submissions of samples from the respiratory tract.

| | **Resistance** (%) | | | | | | | **Distribution** (%) **of MICs**[a] (mg/L) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **1992-94** n=218 | **1995-97** n=402 | **1998-00** n=409 | **2001-03** n=505 | **2004-06** n=534 | **2007** n=180 | **2008** n=159 | **≤0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **>32** |
| Ampicillin | 0 | <1 | 0 | 0 | 0 | 0 | 0 | | | | 99.4 | 0.6 | | | | | |
| Enrofloxacin | NR[c] | NR | NR | NR | NR | NR | NR | 0.6 | | 1.9 | 61.0 | 36.5 | | | | | |
| Florfenicol | - | - | - | 1[d] | <1 | 0 | 0 | | | | | 97.5 | 2.5 | | | | |
| Gentamicin | NR | NR | NR | NR | NR | NR | NR | | | | | 1.3 | 1.3 | 25.8 | 64.2 | 7.5 | |
| Neomycin | NR | NR | NR | NR | NR | NR | NR | | | | | | 1.3 | 0.6 | 3.1 | 25.9 | 69.2 |
| Penicillin | 0 | <1 | 0 | 0 | 0 | 0 | 0 | 98.7 | 0.6 | 0.6 | | | | | | | |
| Spiramycin | <1 | 1 | 0 | 1 | <1 | 0 | 0 | | | | | | 100.0 | | | | |
| Streptomycin | NR | NR | NR | NR | NR | NR | NR | | | | | | 0.6 | 0.6 | 3.8 | 66.0 | 28.9 |
| Tetracycline | 4 | 3 | 4 | 5 | 3 | 3 | 2 | | | | 62.2 | 32.1 | 1.9 | 1.9 | 1.9 | | |
| Trim/Sulph.[b] | 1 | 11 | 57 | 36 | 42 | 17 | 21 | | | 58.5 | 12.6 | 5.7 | 2.5 | 20.8 | | | |

[a] White 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. Bold vertical lines indicate cut-off values defining resistance; [b] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [c] NR= Not relevant as the inherent susceptibility is such that the MIC range is above concentrations that can be obtained during therapy; [d] 370 isolates tested.

## Dog

### *Escherichia coli*

Isolates of *Escherichia coli* are from urine samples, submitted either as urine or as dip-slide cultures. The proportions of resistant *E. coli* have remained stable during the years studied (Table Dog I). Resistance to ampicillin is around 20% and the prevalence of resistance to enrofloxacin, streptomycin, tetracycline or trimethoprim-sulphonamides are all around 10%. However, resistance to gentamicin or nitrofurantoin is rare.

The high proportion of *E. coli* resistant to enrofloxacin throughout the study period is partly explained by the use of a low cut-off value for resistance (>0.12 mg/L), compared to the clinical break-point recommended by CLSI (2008), which is >1 mg/L. Nevertheless, isolates with MIC >0.12 mg/L have decreased susceptibility. Such phenotypes are likely to be explained by at least one mutation in one of the genes encoding the target enzymes of this class of drugs. If an infection caused by such a strain is treated with any fluoroquinolone, there is a risk of further mutations resulting in decreased susceptibility (Drlica, 2003).

In 2008, multiresistance (i.e. resistance to three or more antimicrobials) occurred in 9% of the isolates which is numerically lower than last year. Of the multiresistant isolates, 19% were resistant to five or more antimicrobials i.e. 2% of all isolates. Of the multiresistant isolates, 72% were resistant to ampicillin, streptomycin and trimethoprim-sulphonamides, and 26% were resistant to these antimicrobials and to tetracycline.

Uncomplicated cystitis in dogs is frequently treated with aminopenicillins, which are by far the most commonly prescribed antimicrobials for dogs (Pettersson, 2007). This could explain the high proportion of *E. coli* resistant to ampicillin. However, streptomycin is rarely prescribed for outpatient use for dogs (unpublished data 2006) and only 2% of all antimicrobial prescriptions for systemic treatment of dogs are for trimethoprim-sulphonamides (Pettersson, 2007). Yet, resistance to these substances has been above 10% most years. This could probably be explained by co-resistance between ampicillin, streptomycin and trimethoprim-sulphonamides. Of those isolates resistant to streptomycin, 74% were also resistant to ampicillin, and for isolates resistant to trimethoprim-sulphonamides, 95% were resistant to ampicillin. The excessive use of aminopenicillins therefore probably selects for resistance to the other two substances.

Besides aminopenicillins, urinary tract infections are often treated with fluoroquinolones, and occasionally with trimethoprim-sulphonamides. Three percent of all isolates were resistant to these three antimicrobial groups and of the multiresistant isolates, 30% were resistant to ampicillin, enrofloxacin and trimethoprim-sulphonamides.

**TABLE DOG I.** Resistance (%) in *Escherichia coli* from dogs 1992-2008 and distribution of MICs for isolates from 2008. Isolates are from clinical submissions of urinary tract samples.

| | **Resistance** (%) | | | | | | | **Distribution** (%) **of MICs**[a] (mg/L) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **1992-94** n=245 | **1995-97** n=296 | **1998-00** n=418 | **2001-03** n=621 | **2004-06** n=917 | **2007** n=425 | **2008** n=503 | **≤0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **>32** |
| Ampicillin | 18 | 18 | 18 | 18 | 19 | 18 | 17 | | | | 2.4 | 64.4 | 15.7 | 0.4 | 17.1 | | |
| Enrofloxacin[b] | 9 | 9 | 10 | 9 | 10 | 7 | 10 | 90.4 | 1.2 | 3.8 | 1.8 | 2.8 | | | | | |
| Gentamicin[c] | 2 | 1 | 2 | 2 | 1 | <1 | 1 | | | | | 87.7 | 9.9 | 0.4 | 0.8 | 0.2 | |
| Nitrofurantoin | 3 | 3 | 1 | 2 | 2 | <1 | 3 | | | | | | | | 96.6 | 0.8 | 2.6 |
| Streptomycin[d] | 16 | 18 | 15 | 19 | 16 | 17 | 13 | | | | | | 3.6 | 46.9 | 36.6 | 0.8 | 12.1 |
| Tetracycline | 16 | 14 | 12 | 11 | 10 | 9 | 7 | | | | 39.6 | 48.1 | 5.4 | 0.4 | 6.6 | | |
| Trim/Sulph[e, f] | 9 | 8 | 11 | 13 | 15 | 12 | 8 | | | 91.3 | 0.4 | | | 8.3 | | | |

[a] White 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. Bold vertical lines indicate cut-off values defining resistance; [b] Cut-off value >0.25 mg/L until 2002; [c] Cut-off value >8 mg/L until 2001; [d] Cut-off value >32 mg/L until 2001; [e] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [f] Cut-off value >4 mg/L until 2001; [g] 417 isolates tested.

### *Staphylococcus pseudintermedius*

*Staphylococcus pseudintermedius* are from skin samples. In 2005, *S. pseudintermedius*, a novel staphylococcal species was described (Devriese et al., 2005). Further on Sasaki et al. (2007) and Bannoehr et al. (2007) reported that canine isolates of *S. intermedius* were classified as *S. pseudintermedius*. Therefore, it was proposed to report isolates from dogs as *S. pseudintermedius*, unless genomic investigations prove that the isolate belongs to another related species (Devriese et al., 2008). Consequently, resistance data on *S. intermedius* from previous SVARM reports should be regarded as resistance data on *S. pseudintermedius*.

As in previous years, the prevalence of resistance to penicillin due to production of β-lactamases (penicillinase) in *S. pseudintermedius* is high, 86% (Table Dog II). Already in the late 70s, 70% of *S. pseudintermedius* were resistant to penicillin (Franklin, 1978) and during the last decade, the resistance rate has been around 80%. Besides penicillin, resistance to clindamycin, erythromycin, fusidic acid, streptomycin or tetracycline was common in 2008. Noteworthy, resistance to trimethoprim-sulphonamides was low, possibly because this combination is seldom prescribed to dogs (Pettersson, 2007) and consequently the selective pressure is low. The prescription of tetracycline to dogs is also low (Pettersson, 2007) but

resistance to tetracycline was common (28%) in 2008. This can probably be explained by co-selection through clindamycin use (see discussion below).

Multiresistance (i.e. resistance to three or more antimicrobials) occurred in 29% of the isolates. Resistance to penicillin, clindamycin and erythromycin was the most common phenotype, occurring in 74% of multiresistant isolates. Of these, 23 isolates (9% of the total) were resistant also to streptomycin and tetracycline. Macrolide resistance in *S. pseudintermedius* is commonly mediated by *erm*-genes, and if these genes are constitutively expressed, the bacteria will be resistant also to lincosamides (clindamycin) and streptogramin B. In this material, 87% of isolates resistant to erythromycin were also resistant to clindamycin.

Half of the multiresistant isolates, i.e. 14% of all isolates in this year´s material, were resistant to five or more antimicrobials. This figure has doubled since 2007. Out of these 35 isolates, six were confirmed methicillin resistant *S. pseudintermedius* (MRSP) i.e. harbouring the *mecA* gene. For further information on MRSP see Highlight on "Methicillin resistant *S. pseudintermedius* – an update". At SVA, all isolates of *S. pseudintermedius* with high MIC of oxacillin (>0.5 mg/L) are examined for *mecA* gene with PCR (see Appendix 3 for details).

Since the tested isolates are from clinical submissions of samples from skin, there is a high probability of bias towards dogs with recurrent skin infections, previously treated with antimicrobials. A prospective study by Holm et al., (2002) showed higher levels of multiresistance among isolates from recurrent compared to those from first-time pyoderma. This probably explains the high levels of resistance in this material. Clindamycin and cephalosporins are commonly used to treat pyoderma in dogs. With the high proportion of multiresistant isolates, treatment with e.g. clindamycin will co-select for resistance to erythromycin, streptomycin, and tetracycline, despite the fact that the two latter substances are rarely used in treatment of pyoderma. Interestingly, resistance to enrofloxacin occurred only in multiresistant phenotypes. In year 2006, 13% of the antimicrobial prescriptions to dogs were fluoroquinolones, and the figure has increased since the 90s (Pettersson, 2007). Fortunately, the number of fluoroquinolone prescriptions has declined during 2007 and 2008 (See Highlight on "Decreased sales of antimicrobials for dogs).

**TABLE DOG II.** Resistance (%) in *Staphylococcus pseudintermedius* from dogs 1992-2008 and distribution of MICs for isolates from 2008. Isolates are from clinical submissions of samples from skin.

| | **Resistance** (%) | | | | | | | **Distribution** (%) **of MICs**[a] (mg/L) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **1992-94** n=304 | **1995-97** n=322 | **1998-00** n=433 | **2001-03** n=382 | **2004-06** n=374 | **2007** n=220 | **2008** n=258 | **≤0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **>32** |
| Cephalothin | <1 | <1 | 0 | 1 | 1 | <1 | 3 | | | | | 96.5 | 1.2 | | 0.8 | 1.6 | |
| Clindamycin | 12 | 20 | 21 | 18 | 19 | 18 | 22 | | | | 74.4 | | 3.9 | 21.7 | | | |
| Enrofloxacin | - | - | - | 2[e] | 2 | 4[h] | 4 | 75.2 | 18.2 | 1.9 | 1.6 | 2.7 | | | | | |
| Erythromycin | 21[i] | 28[i] | 27[i] | 24 | 26 | 25 | 25 | | | 75.2 | | | 0.4 | 24.4 | | | |
| Fusidic acid | 9 | 14 | 20[d] | 20[f] | 25 | 24 | 24 | | | | | 71.7 | 4.3 | 24.0 | | | |
| Gentamicin | <1 | <1 | <1 | 0 | 1 | 2 | 2 | | | | | 96.9 | 0.8 | | 1.6 | 0.8 | |
| Nitrofurantoin | 1 | 1 | <1 | 1 | <1 | <1 | <1 | | | | | | | | 98.1 | 1.2 | 0.8 |
| Oxacillin | 1 | 2 | 1 | 2 | 1 | 1 | 2 | | | 96.5 | 1.2 | 2.3 | | | | | |
| Penicillin[b] | 79 | 80 | 80 | 80 | 84 | 84 | 86 | | | | | | | | | | |
| Streptomycin | - | - | - | 22[e] | 30 | 29 | 25 | | | | | | 69.8 | 4.3 | | 0.8 | 25.2 |
| Tetracycline | 24 | 12 | 28 | 25[g] | 32 | 32 | 28 | | | | 71.3 | 0.4 | | | 28.3 | | |
| Trim/Sulph[c] | 1 | 2 | 1 | 3 | 6 | 5 | 5 | | | 80.6 | 13.2 | 1.2 | 0.8 | 4.3 | | | |

[a] White 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. Bold vertical lines indicate cut-off values defining resistance; [b] Denotes β-lactamase production; [c] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [d] 421 isolates tested; [e] 273 isolates tested; [f] 346 isolates tested; [g] 381 isolates tested; [h] 212 isolates tested; [i] Cut-off value >4 mg/L until 2001.

## Cat

### *Escherichia coli*

Isolates of *Escherichia coli* are from urine samples, submitted either as urine or as dip-slide cultures. As in previous years, resistance to ampicillin, streptomycin or tetracycline were the most common resistance traits (Table Cat I). Only two isolates were resistant to nitrofurantoin.

As for dogs, the high proportion of *E. coli* resistant to enrofloxacin throughout the study period is partly explained by the low cut-off value for resistance (>0.12 mg/L), chosen for fluoroquinolones in SVARM, compared to the break-point recommended by e.g. CLSI (2008), which is >1 mg/L. As mentioned above, strains with MIC >0.12 mg/L are less susceptible and there is a risk for further mutations during fluoroquinolone treatment.

In 2008, 8% of the isolates were multiresistant (i.e. resistant to three or more substances), and that is on the same level as last year (6%). Of the multiresistant isolates, six (43%) were resistant to ampicillin, streptomycin and tetracycline. Two isolates were resistant to ampicillin, enrofloxacin, gentamicin, streptomycin, tetracycline and trimethoprim-sulphonamides. Cats with symptoms from the urinary tract are often treated with aminopenicillins or fluoroquinolones. This year, six isolates were resistant to both these antimicrobials, i.e. about 4% of all isolates.

# Methicillin resistant *Staphylococcus pseudintermedius* (MRSP) – an update

**A CONTINUED** increase of methicillin resistant *Staphylococcus pseudintermedius* (MRSP) isolated from Swedish dogs was seen during 2008. Although antibiotic treatment and nosocomial transmission are thought to be key factors in promoting this increase, the epidemiology is far from fully understood. A further increase in the number of infected dogs can however be expected, since the possibilities of introducing strict, truly effective control measures into private veterinary practices, kennels and other privately owned environments where groups of dogs gather are limited.

Data on resistance in *Staphylococcus pseudintermedius* (previously *S. intermedius*) back to 1992 have been reported in SVARM. The first methicillin resistant *S. pseudintermedius* from a Swedish dog was isolated 2006 in a survey screening for MRSP in healthy dogs. Later the same year clinical isolates were confirmed from postoperative wounds, and mainly from dogs sampled at two referral small animal hospitals. The number of confirmed cases rose rapidly from 13 isolates in 2006 to 77 in 2007. A majority of these isolates were apparently clonally related. Most isolates had the same antibiogram, being susceptible only to fusidic acid and tetracyclines (SVARM 2007). In 2008, the first isolates with resistance to tetracycline emerged. During the year 2008 over 100 methicillin-resistant isolates of *S. pseudintermedius* were confirmed to carry the *mecA* gene by PCR at the National Veterinary Institute (SVA). Additionally four cats were found to be infected with MRSP.

Whether the figures from 2008 represent a true increase of infections with MRSP among dogs is uncertain. An increased awareness amongst clinically active veterinarians might contribute to increasing numbers of bacterial infections on dogs being reported as caused by MRSP. On the other hand, although findings of MRSP in animals are notifiable in Sweden sending isolates for confirmation to SVA is only a general recommendation. Therefore, and also in view of the infection being made notifiable only quite recently (January 2008), it is quite possible that not all isolates have been reported, or recognised. The infection has now been found in various geographical areas of Sweden. The samples submitted include swabs from dermatological infections, infected wounds, postoperative infections and urinary samples.

Continuous education and an increased awareness in all clinically active veterinarians of the risk of infection with MRSP in any dog is necessary if the problem is to be controlled. Heightened attention to hygiene routines in combination with restricted use of antimicrobials and routine bacteriological sampling are well known key features in effective control programs for nosocomial infections. The risk of spread to healthy dogs in direct or indirect contact with infected individuals remains to be investigated, including the risk of spread from asymptomatic carriers. Until further knowledge is obtained, restrictions regarding close contact between infected dogs and others should be applied. Owners must be given extensive information on the infection and its implications, including hygienic precautions and the not yet explored possibility of the infection recurring if the dog is treated with antibiotics.

SVA is looking into possible further research regarding epidemiology of MRSP. Currently running projects include carriage of MRSP in dogs. SVA also participates in a larger international study on genomic characterisation on MRSP regarding antimicrobial resistance and relatedness between isolates.

**TABLE CAT I.** Resistance (%) in *Escherichia coli* from cats 1992-2008 and distribution of MICs for isolates from 2008. Isolates are from clinical submissions of urine samples.

| | **Resistance** (%) | | | | | | **Distribution** (%) **of MICs**[a] (mg/L) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **1992-97** n=61 | **1998-00** n=74 | **2001-03** n=135 | **2004-06** n=224 | **2007** n=131 | **2008** n=170 | **≤0.12** | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **16** | **32** | **>32** |
| Ampicillin | 26 | 34 | 27 | 22 | 16 | 19 | | | | 1.8 | 69.4 | 9.4 | | 19.4 | | |
| Enrofloxacin[b] | 5 | 8 | 13 | 7 | 4 | 7 | 92.9 | 2.4 | 1.2 | | 3.5 | | | | | |
| Gentamicin | 0 | 3 | 5 | 0 | <1 | 2 | | | | | 92.4 | 5.9 | 0.6 | | 1.2 | |
| Nitrofurantoin | 2 | 2 | 1 | 3 | <1 | 1 | | | | | | | | 97.1 | 1.8 | 1.2 |
| Streptomycin[d] | 25 | 18 | 21 | 17 | 12 | 15 | | | | | | 3.5 | 51.2 | 30.6 | 2.9 | 11.8 |
| Tetracycline | 28 | 16 | 16 | 14 | 8 | 9 | | | | 44.1 | 43.5 | 2.9 | 5.9 | 8.8 | | |
| Trim-Sulph.[e, f] | 7 | 10 | 15 | 7 | 5 | 6 | | | 92.4 | 1.8 | 0.6 | | 5.3 | | | |

[a] White fields denote the 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. Bold vertical lines indicate microbiological cut-off values defining resistance; [b] Cut-off value >0.25 (mg/L) until 2002; [c] Cut-off value >8 mg/L until 2001; [d] Cut-off value >32 mg/L until 2001; [e] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [f] Cut-off value >4 mg/L until 2001.

# Appendix 1: Demographic data

**AGRICULTURAL** statistics are provided by Statistics Sweden in collaboration with the Board of Agriculture and published annually as a Yearbook of Agricultural Statistics and continuously as Statistical Messages (SM). The Yearbook and Statistical Messages are is available on the Internet via the websites for Statistics Sweden (www.scb.se) or the Board of Agriculture (www.sjv.se).

Annual figures on number of animals and holdings are given in Table AP1 I & II, and on numbers and volumes of animals slaughtered in Table AP1 III & IV. For details on methodology, see the respective sources of the statistics.

Over the last two decades, the total number of dairy cows, pigs, and laying hens has decreased notably concomitantly with an increase in herd size. In the same period, the number of beef cows and sheep as well as the number of broilers slaughtered has increased.

**TABLE AP1 I.** Number of livestock and horses (in thousands) 1980-2008 (Yearbook of Agricultural Statistics, Sweden 2001 & 2008 and Statistical Message JO 20 SM 0802).

| Animal Species | 1980[a] | 1985[a] | 1990 | 1995 | 2000 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|
| **Cattle** | | | | | | | | | |
| Dairy cows | 656 | 646 | 576 | 482 | 428 | 393 | 388 | 370 | 357 |
| Beef cows | 71 | 59 | 75 | 157 | 167 | 177 | 178 | 186 | 196 |
| Other cattle >1 year | 614 | 570 | 544 | 596 | 589 | 527 | 530 | 516 | 513 |
| Calves <1 year | 595 | 563 | 524 | 542 | 500 | 508 | 496 | 489 | 492 |
| Total, cattle | 1 935 | 1 837 | 1 718 | 1 777 | 1 684 | 1 605 | 1 590 | 1560 | 1 558 |
| **Pigs** | | | | | | | | | |
| Boars & sows | 290 | 260 | 230 | 245 | 206 | 188 | 187 | 181 | 170 |
| Fattening pigs >20 kg [b] | 1 254 | 1 127 | 1 025 | 1 300 | 1 146 | 1 085 | 1 002 | 1015 | 974 |
| Piglets <20kg [c] | 1 170 | 1 113 | 1 009 | 769 | 566 | 539 | 492 | 480 | 465 |
| Total, swine | 2 714 | 2 500 | 2 264 | 2 313 | 1 918 | 1 811 | 1 680 | 1 676 | 1 609 |
| **Sheep** | | | | | | | | | |
| Ewes and rams | 161 | 173 | 162 | 195 | 198 | 222 | 244 | 242 | 252 |
| Lambs | 231 | 252 | 244 | 266 | 234 | 249 | 262 | 267 | 273 |
| Total, sheep | 392 | 425 | 406 | 462 | 432 | 471 | 505 | 509 | 525 |
| **Laying hens** | | | | | | | | | |
| Hens | 5 937 | 6 548 | 6 392 | 6 100 | 5 670 | 5 065 | 4 524 | 5 328 | 5 546 |
| Chickens reared for laying | 2 636 | 2 159 | 2 176 | 1 812 | 1 654 | 1 697 | 1 646 | 1 753 | 1 649 |
| Total, hens | 8 573 | 8 708 | 8 568 | 7 912 | 7 324 | 6 762 | 6 170 | 7 080 | 7 195 |
| **Turkeys** | | | | | | | | | |
| Total, turkeys | - | - | - | - | - | 122 | - | 101 | - |
| **Horses** | | | | | | | | | |
| Total, horses | - | - | - | - | - | 283[d] | - | - | - |

[a] For 1980 and 1985 only cattle and sheep at premises with more than 2 ha counted; [b] Before 1995, the figure denotes pigs above 3 months of age; [c] Before 1995, the figure denotes pigs below 3 months of age; [d] Data from 2004.

**TABLE AP1 II.** Number of holdings with animals of different types, 1980-2008 (Yearbook of Agricultural Statistics, Sweden 2001 & 2008 and Statistical Message JO 20 SM 0802).

| Animal Species | 1980 | 1985 | 1990 | 1995 | 2000 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|
| **Cattle** | | | | | | | | | |
| Dairy cows | 44 143 | 35 063 | 25 921 | 17 743 | 12 676 | 8 548 | 8 027 | 7 096 | 6 474 |
| Beef cows | 12 436 | 10 310 | 10 883 | 17 069 | 13 861 | 12 821 | 12 447 | 12 494 | 12 345 |
| Other cattle >1 year | 63 179 | 52 652 | 42 696 | 39 160 | 30 457 | 24 808 | 23 700 | 22 501 | 21 536 |
| Calves <1 year | 62 314 | 52 001 | 41 986 | 36 542 | 27 733 | 22 888 | 21 752 | 20 780 | 19 911 |
| Total holdings with cattle | 70 503 | 58 872 | 47 292 | 41 990 | 32 063 | 26 179 | 25 054 | 23 878 | 22 844 |
| **Sheep** | 10 238 | 10 595 | 9 749 | 10 037 | 8 089 | 7 653 | 9 152 | 8 014 | 8 186 |
| **Pigs** | 26 122 | 19 937 | 14 301 | 10 753 | 4 809 | 2 794 | 2 414 | 2 277 | 2 380 |
| **Laying hens** | 23 603 | 17 531 | 12 900 | 9 593 | 5 678 | 4 916 | 4 877 | 4 245 | 4 643 |
| **Chickens reared for laying** | 5 093 | 2 714 | 1 875 | 1 405 | 715 | 634 | 528 | 496 | 854 |
| **Broilers** | - | - | - | - | - | 234 | 192 | 212 | 198 |
| **Turkeys** | - | - | - | - | - | 383 | - | 130 | - |
| **Horses** | - | - | - | - | - | 56 000[a] | - | - | - |

[a] Data from 2004.

**TABLE AP1 III.** Number of animals slaughtered (in thousands) at slaughterhouses, 1980-2008. (Yearbook of Agricultural Statistics, Sweden 1981, 1986, 1991 & 2008 and Statistical Message JO 48 SM 0903).

| Animal Species | 1980 | 1985 | 1990 | 1995 | 2000 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|
| **Cattle** | | | | | | | | | |
| Cattle >1 year | 574 | 584 | 523 | 502 | 490 | 433 | 434 | 420 | 395 |
| Calves < 1 year | 130 | 152 | 70 | 30 | 39 | 33 | 32 | 30 | 28 |
| Total, cattle | 704 | 736 | 593 | 532 | 529 | 466 | 466 | 450 | 423 |
| **Pigs** | 4 153 | 4 283 | 3 653 | 3 743 | 3 251 | 3 160 | 3 022 | 3 004 | 3 034 |
| **Sheep** | 302 | 328 | 280 | 189 | 202 | 206 | 213 | 231 | 227 |
| **Broilers** | 40 466[a] | 36 410[a] | 38 577[a] | 61 313 | 68 617 | 73 458 | 72 906 | 74 666 | 76 109 |

[a] Data supplied by the National Food Administration.

**TABLE AP1 IV.** Quantity of livestock slaughtered (in 1000 tonnes) at slaughterhouses, 1990-2006 (Yearbook of Agricultural Statistics, Sweden 1991 & 2007 and Statistical Message JO 48 SM 0903).

| Animal Species | 1990 | 1995 | 2000 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|
| **Cattle** | | | | | | | | |
| Cattle >1 year | 139.5 | 140.1 | 145.4 | 137.8 | 131.4 | 132.9 | 129.2 | 122.5 |
| Calves < 1 year | 6.8 | 3.2 | 4.4 | 4.6 | 4.5 | 4.5 | 4.3 | 4.2 |
| Total, cattle | 146.3 | 143.3 | 149.8 | 142.4 | 135.9 | 137.4 | 133.9 | 126.7 |
| **Pigs** | 293.1 | 308.8 | 277.0 | 294.5 | 275.1 | 264.5 | 264.9 | 266.8 |
| **Sheep** | 5.0 | 3.5 | 3.9 | 3.8 | 4.1 | 4.2 | 4.6 | 4.5 |
| **Broilers** | 44.0[a] | 73.6[a] | 89.9 | 91.2 | 96.2 | 95.5 | 105.3 | 107.3 |

[a] Data supplied by the National Food Administration.

# Appendix 2: Materials and methods, use of antimicrobials

### Source for the statistics

The antimicrobial drugs used in veterinary medicine in Sweden are only available on veterinary prescription. Furthermore, antimicrobial drugs are dispensed through pharmacies only. Sales statistics are available from Apoteket AB (The National Corporation of Swedish Pharmacies). From year 2003, statistics on drug sales is based on electronic records of amount of drugs dispensed at or from pharmacies, i.e. sales statistics. Data for previous years are the amount of antimicrobial products sold from the wholesalers to the pharmacies.

Sweden has a long tradition in drug consumption statistics. Apoteket AB, former Apoteksbolaget AB, has since 1976 monitored the consumption of drugs for use in humans mainly by using wholesalers´ statistics. In the case of drugs for animal use, 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. For a review of the figures from 1980–2000 as well as references to publications on which that review is based, see SVARM 2000.

### Classification of drugs

Veterinary medicinal drugs are classified according to the Anatomical Therapeutic Chemical veterinary classification system (ATCvet) (WHO, Guidelines for ATCvet classification). 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 system for human drugs), 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) and QS (sensory organs) depending on the therapeutic use.

### Inclusion criteria

All veterinary antibacterial drugs authorised for use in animals except dermatologicals, ophtalmologicals and otologicals (i.e., ATCvet codes QA, QG and QJ) were included. Veterinary drugs are preparations authorised for use in animals. 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.

Drugs with antibacterial activity can also be found in other groups, notably among the antiprotozoals (QP51). Of these, the nitroimidazoles were included earlier but no such substances are presently authorised for use in animals. Sulfaclozine is licensed for treatment of coccidiosis only and has therefore not been included. The ionophoric antibiotics are presently regulated as feed additives and not sold through pharmacies and are therefore not included in the wholesalers' statistics. However, the Board of Agriculture collects figures on sales of ionophores from the feed mills as a part of the feed control system. As the source differs, data on ionophores are given only in Table AC III.

### Prescriptions for dogs

From the spring of 2004, animal species is recorded for all prescriptions dispensed to animal care-takers. Data on all prescriptions for dogs, i.e. drugs authorised for use in animals (ATC vet code QJ01) as well as for humans (ATC code J01) were retrieved and are presented in a highlight in this year's report. The data-set corresponds to out-patient use in human medicine.

### 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. In case there are no authorised veterinary medicinal products for a certain condition, the MPA can also permit special license prescription for a drug.

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 drugs. 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

#### *Salmonella*

Salmonellosis in animals is a notifiable disease in Sweden and one isolate from each notified incident must be confirmed at SVA. Data presented in SVARM include one isolate of each serovar, and when appropriate phage-type, from each warm-blooded animal species in each incident notified 2008 and in incidents previously notified and still under restrictions 2008. Also included are isolates obtained 2008 in the salmonella surveillance programme from samples collected at slaughter (carcass swabs, neck skins and lymph nodes). However, in 2008 *Salmonella* was isolated from 47 cats but of these 10 representative isolates were selected for testing.

#### *Campylobacter*

*Campylobacter* from pigs were cultured from samples of colon content collected at abattoirs for isolation of indicator bacteria (see below). From the total number of samples collected about one fourth (n=129) was selected for culture. The selection was made sequential but ensuring that cultured samples were distributed between abattoirs according to annual slaughter volume and evenly distributed over the four sampling periods. Each isolate of *Campylobacter coli* or *C. jejuni* is from a unique herd.

Isolates from broilers were from the 2008 survey on prevalence of *Campylobacter* in broilers initiated by a decision of the European Commission (2007/516/EC). The protocol of the survey is given in the directive. Briefly, samples of caeca from healthy broilers were collected at slaughter and cultured for *Campylobacter*. Samples were collected all year.

### Indicator bacteria

#### Pigs

Indicator bacteria, i.e. *Escherichia coli* and *Enterococcus* spp., from pigs were isolated from colon content of healthy pigs sampled at slaughter. Nine geographically separated abattoirs participated in collection of samples. The abattoirs accounted for 92% of the total volume of pigs slaughtered in Sweden 2007.

At each abattoir, an equal number of samples were collected during each of four periods (February-March, April-May, August–September and October-November). The number of samples collected at each abattoir was proportional to the annual volume of pigs slaughtered at an abattoir and each sample represents a unique herd. By these measures, bacterial isolates included are from randomly selected healthy pigs of Swedish herds. Each isolate of *Escherichia coli*, *Enterococcus faecalis*, *E, Faecium* or *E. hirae* is from a unique herd.

#### Pork

Indicator bacteria from pork were isolatad from samples of raw pork of Swedish origin collected at retail in the county of Stockholm. In total 50 samples of pre packed pork (i.e. loin of pork, pork chops, minced pork) were collected in October 2008. To avoid duplicates, only one sample from a package day from each meat cutting-plant was collected.

#### Sheep

Indicator bacteria from sheep were isolated from rectal swabs collected from healthy ewes, suckling lambs and newborn lambs sampled on farms. To avoid duplicates within farms, one sample from each of the three age categories was collected on each farm.

#### Broilers

The rate of colonisation by VRE among broilers in 2008 was investigated in a separate study on samples of caeca obtained through the Swedish *Campylobacter* programme. From these samples, 51 and 56 caeca collected at slaughter were selected in order of arrival at SVA in May and September, respectively. Samples selected for culture were from unique flocks but not necessarily from unique production sites.

### Animal pathogens

Isolates of animal pathogens included are from routine bacteriological examinations of clinical submissions or post-mortem examinations at SVA. *Actinobacillus pleuropneumoniae* from pigs and *Staphylococcus aureus* from cows were however isolated from samples collected in surveys initiated within SVARMpat.

*Escherichia coli* from pigs are from the gastro-intestinal tract (gut content, faecal samples or mesenteric lymph nodes). *Escherichia coli* from horses are from the genital tract of mares and *E. coli* from dogs and cats from samples of urine. *Brachyspira* spp. from pigs are from faecal samples. *Pasteurella* spp. from cattle are from the respiratory tract and *Pasteurella* spp. from pigs from nasal swabs collected within a control programme for atrophic rhinitis in nucleus and multiplying herds. *Streptococcus zooepidemicus* from horses and *Actinobacillus pleuropneumoniae* from pigs are from the respiratory tract. *Staphylococcus pseudintermedius* from dogs were isolated from skin samples. *Staphylococcus aureus* were isolated from milk samples from cows with sub-clinical mastitis. *Aeromonas salmonicida* subsp. *achromogenes*, *Flavobacter columnare* and *Flavobacter psychrophilum* are from post mortem examination of farmed fish.

## Isolation and identification of bacteria

### Zoonotic bacteria

#### Salmonella

*Salmonella* were isolated and identified at the Dept. of Bacteriology, SVA or at regional laboratories in accordance with standard procedures. All samples within official control programmes are cultured according to the procedures detailed by the Nordic Committee on Food Analysis (NMKL Nr 71 5th ed., 1999). Confirmatory identification and serotyping of isolates was performed at the Dept. of Bacteriology, SVA according to the standard procedures of Kaufmann and White. The Dept. of Bacteriology, SVA is accredited for isolation, identification and serotyping of *Salmonella*.

Isolates of *Salmonella* Typhimurium and *S.* Enteritidis were phage-typed by the Swedish Institute for Infectious Disease Control (SMI), Stockholm using the Colindale scheme.

#### Campylobacter

*Campylobacter* spp. from pigs were isolated and identified at Dept. of Animal Health and Antibiotic Strategies. Briefly, samples were cultured directly on Preston selective agar for thermophilic *Campylobacter* spp. and incubation at 42°C for 48h. Samples from broilers were isolated at Dept. of Bacteriology according to ISO 10272:1, 2006 and ISO 10272:2, 2006.

Identification was based on colony morphology, microscopic appearance including motility and the following phenotypic characteristics: production of oxidase, catalase, hippurate hydrolysis reaction and indoxyl-actetate reaction (Nachamkin, 1999). With these tests, hippurate-positive *C. jejuni* can be identified whereas other isolates are described as hippurate-negative thermophilic *Campylobacter* spp.

### Indicator bacteria

#### *Escherichia coli*

Approximately 0.5 g of colon content from pig was diluted in 4.5 mL saline. After thorough mixing, 0.1 mL of this suspension was spread on MacConkey agar and MacConkey agar with cefotaxime 1mg/L and incubated overnight at 37°C. A similar procedure was followed for culture of rectal swabs from sheep. Approximately100 g of pork was thoroughly shaken 1–2 min with 50 mL saline. Ten mL was thereafter transferred to 90 mL MacConkey broth and incubated at 44°C for 18–24 h. From the pre-enrichment 0.1 mL of was spread on MacConkey agar and MacConkey agar with cefotaxime 1mg/L and incubated overnight at 44°C.

One lactose positive colony with morphology typical for *E. coli* was sub-cultured onto horse-blood agar (5% v/v), after which the isolate was tested for production of tryptophanase (indole) and β-glucuronidase (p-nitrophenyl-β-D-glucopyranosiduronic acid, PGUA). Only lactose-positive isolates with typical morphology and positive reactions in both tests were selected for susceptibility tests. Colonies growing on MacConkey agar with cefotaxime were sub-cultured on horse-blood agar (5% v/v) and further tested for ESBL detection.

#### Enterococci

Colon content from pigs was diluted as described for *E. coli* and cultured on solid media without antibiotics. A similar procedure was followed for culture of rectal swabs of sheep. Twenty-five mL of the saline from shaken pork (above) was mixed with 25 mL double concentrated Enterococcosel broth and incubated at 44°C over night. Caecal content from broilers was diluted in the same way as the colon content from pigs but cultured only on selective plates with vancomycin (16 mg/L).

*Culture without selective antibiotics:* Diluted colon content (0.1 mL) was spread onto Slanetz-Bartley (SlaBa) agar. The plates were incubated for 48 h at 37°C. For pork, from the Enterococcosel broth 0.1 mL was cultured on SlaBa agar and incubated at 44°C for 48 h. One colony, randomly chosen, was sub-cultured on bile-esculin agar and blood agar (37°C, 24 h). Colonies with morphology consistent with enterococci, and with a positive reaction on bile-esculin agar were tested for antimicrobial susceptibility and identified to species level according to Devriese et al. (1993) by use of the following biochemical tests: mannitol, sorbitol, arabinose, saccharose, ribose, raffinose and methyl-α-D-glucopyranoside.

*Selective culture for vancomycin resistant enterococci:* Diluted caecal content (0.1 mL) was cultured on SlaBa with vancomycin (16 mg/L). From plates showing growth of colonies typical for enterococci, at least one colony of each morphological type was sub-cultivated on bile-esculin agar and blood agar (37°C, for 24 h). Identification of presumptive enterococci was performed as above.

### Animal pathogens

Animal pathogens were isolated and identified with accredited methodology, following standard procedures at SVA. Bacteria from terrestrial animals were isolated at the Dept. of Bacteriology, and bacteria from fish at the Dept. of Animal Health and Antibiotic Strategies.

## Susceptibility testing

#### Microdilution

The Dept. of Animal Health and Antimicrobial Strategies or the Dept. of Bacteriology performed antimicrobial susceptibility tests on bacteria from terrestrial animal, with accredited methodology, using dilution methods in cation adjusted Mueller-Hinton broth (CAMBH). Tests were performed following the standards for microdilution of the Clinical and Laboratory Standards Institute (CLSI, 2007). The microdilution panels used, VetMIC™, are produced at the Dept. of Animal health and antimicrobial Strategies, SVA. Different panels were used depending on the bacterial species tested and the original purpose of the investigation (monitoring or clin-

ical diagnostics). Minimum inhibitory concentration (MIC) was recorded as the lowest concentration of the antimicrobial that inhibits bacterial growth.

The Dept. of Animal Health and Antibiotic Strategies performed antimicrobial susceptibility tests on bacteria from fish, using the same methodology as described above but adapted for aquatic bacteria according to Alderman & Smith (2001), which e.g. implies incubation at 20°C for two days.

For susceptibility testing of *Brachyspira hyodysenteriae*, a broth dilution method was used (Karlsson et al., 2001). The antimicrobials were dried in serial twofold dilutions in the tissue culture trays with 48 wells per plate. The wells were filled with 0.5 mL of a suspension of bacteria in brain heart infusion broth with 10% foetal calf serum ($1x10^6$–$5x10^6$ CFU/ml). The trays were incubated in an anaerobic atmosphere at 37°C for four days on a shaker.

Screening for methicillin resistance was performed with microdilution according to CLSI (2007), testing oxacillin with 2% NaCl added to the broth, and in addition oxacillin without added NaCl and cefoxitin.

Phenotypic confirmatory test for production of extended spectrum beta-lactamases (ESBLs) in *Escherichia coli* was performed by the standard disc diffusion test recommended by CLSI (2007).

### Genotyping

Presence of the *mecA* gene in *Staphylococcus aureus* and *S. pseudintermedius* was tested by polymerase chain reaction (PCR) according to Smyth et al. (2001) in isolates with a phenotype indicating methicillin resistance.

Genotypic screening of ESBL positive *Escherichia coli* was performed by using Identibact Array Tube test according to the manufacturer (www.identibact.com). The test allows detection of the most common resistance genes of gram-negative isolates (Anjum et al., 2007).

In ten randomly selected enterococcal isolate with MICs of vancomycin above >128 mg/L, the resistance genotype was confirmed with PCR for the *vanA* gene according to Dutka-Malen et al. (1995).

PCR was used to subtype *Fusobacterium necrophorum* into subsp. *necrophorum* and subsp. *funduliforme* (Narongwanichgarn et al., 2003).

### Cut-off values

Epidemiological cut-off values issued by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) (http://www.escmid.org) were used for interpretation of results of susceptibility testing of zoonotic bacteria (*Salmonella* and *Campylobacter*) and indicator bacteria (*E. coli* and enterococci). When no cut-off value was available a value was defined on basis of the actual MIC distributions obtained in the SVARM programme. This approach was also used for ciprofloxacin in *E. coli* because the recommended cut-off value (>0.03 mg/L) cuts through distributions of MICs in SVARM in a manner not in agreement with the concept of wild-type distributions, causing an erroneously high frequency of resistance.

Also for animal pathogens epidemiological cut-off values issued by EUCAST were used when available. When no cut-off value was available, or the range of concentrations tested was inappropriate for the recommended value, a cut-off value was defined on basis of the actual MIC distributions obtained in SVARM. The clinical breakpoints recommended for animal pathogens by CLSI (2008) were also taken into consideration. It should be understood that epidemiological cut-off values classifies isolates with acquired reduced susceptibility as resistant, which is relevant for monitoring purposes, but that this not always implies clinical resistance.

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 15 µg. 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 Animal Health and Antimicrobial Strategies and Dept. of Bacteriology are accredited according to SS-EN ISO/IEC 17025 by the Swedish Board for Accreditation and Conformity Assessment (SWEDAC) to perform antimicrobial susceptibility tests with microdilution methods. The Dept. of Bacteriology is also accredited for isolation and identification of animal pathogens and *Salmonella* according to the same standard.

For susceptibility tests of zoonotic and indicator bacteria, *Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212 and *Campylobacter jejuni* CCUG 11284 (analogue to *Campylobacter jejuni* ATCC 33560) were included as quality controls. Relevant control strains were also included and evaluated at least once weekly for animal pathogens. For testing of *Brachyspira*, the *B. hyodysenteriae* type strain B78T ATCC 27164T was used for quality control.

In the Fusobacterium subtyping PCR *Fusobacterium necrophorum* subsp. *necrophorum* CCUG 9994 and *Fusobacterium necrophorum* subsp. *funduliforme* CCUG 42162 were used as positive controls.

The Dept. of Animal Health and Antimicrobial Strategies participates in several proficiency tests for antimicrobial susceptibility testing. These are arranged either by the Community Reference Laboratory (CRL) or as national studies. Likewise, the Dept. of Bacteriology participates in proficiency tests concerning isolation and identification of *Salmonella* spp. and general clinical veterinary bacteriology and susceptibility tests.

### Data handling

Records on *Salmonella* and animal pathogens such as source of cultured sample, identification results, antimicrobial suscep-

tibility etc. are routinely registered in an Oracle database at SVA. From this, relevant data were extracted to a Microsoft Access database for evaluation and compilation.

For indicator bacteria, data on animal species, date of sampling, abattoir and herd of origin were together with results of culture identification and susceptibility tests recorded in an Access database at the Dept. of Animal Health and Antimicrobial Strategies.

Calculations and analysis of data were performed in the computer programs Microsoft Access, Microsoft Excel, or EpiInfo.

### Concerning confidence limits

When the prevalence of antimicrobial resistance is close to zero, e.g. when one out of 120 isolates is 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.

One way out of the dilemma 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, the beta-distribution and the binomial distribution can be used. This gives the formulae that enable calculations of the confidence interval (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.

**TABLE AP3 I.** Cut-off values (mg/L) defining resistance. Values in red lettering are current (April 2009) epidemiological cut-off values presented by EUCAST, values in blue italic lettering deviate from values presented by EUCAST and for values in normal lettering EUCAST epidemiological cut-off values are not available (See "Susceptibility testing" above for details).

| Antimicrobial | *Actinobacillus pleuropneumoniae* | *Brachyspira* spp. | *Campylobacter jejuni* | *Campylobacter coli* | *Enterococcus faecalis* | *Enterococcus faecium* | *Enterococcus hirae* | *Escherichia* coli (indicator) | *Escherichia* coli (pathogen) | *Pasteurella* spp. | *Salmonella enterica* | *Staphylococcus pseudintermedius* | *Staphylococcus aureus* | *Streptococcus zooepidemicus* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ampicillin | >1 | | **>8** | **>16** | **>4** | **>4** | >4 | **>8** | **>8** | >1 | **>4** | | | >8 |
| Bacitracin[a] | | | | | **>32** | **>32** | >32 | | | | | | | |
| Cefotaxime | >0.06 | | | | | | | **>0.25** | | >0.06 | **>0.5** | | | |
| Cefoxitin | | | | | | | | | | | | >4 | | |
| Ceftiofur | >0.25 | | | | | | | **>1** | **>1** | >0.25 | **>2** | | | |
| Cephalothin | | | | | | | | | | | | >2 | **>1** | |
| Chloramphenicol | >2 | | | | **>32** | **>32** | **>8** | **>16** | | >2 | **>16** | | **>16** | |
| Ciprofloxacin | >0.06 | | **>1** | **>1** | | | | ***>0.06*** | | >0.06 | **>0.06** | | **>1** | |
| Clindamycin | | | | | | | | | | | | ***>4*** | **>0.25** | |
| Enrofloxacin | | | >0.5 | >0.5 | | | | **>0.12** | **>0.12** | >0.25 | >0.25 | >0.5 | | |
| Erythromycin | | | **>4** | **>16** | **>4** | **>4** | **>2** | | | | | **>1** | **>1** | |
| Florfenicol | >16 | | | | | | | **>16** | **>16** | >16 | **>16** | | | >8 |
| Fusidic acid | | | | | | | | | | | | >4 | **>0.5** | |
| Gentamicin | >8 | | **>1** | **>2** | **>32** | **>32** | >32 | **>2** | ***>4*** | >8 | **>2** | >4 | **>2** | |
| Kanamycin | | | | | >1024 | >1024 | >1024 | **>8** | | | >16 | | **>8** | |
| Linezolid | | | | | **>4** | **>4** | >4 | | | | | | | |
| Nalidixic acid | >16 | | **>16** | **>32** | | | | **>16** | | >16 | **>16** | | | |
| Narasin | | | | | **>2** | **>4** | >2 | | | | | | | |
| Neomycin | | | | | | | | | **>8** | | **>4** | | | |
| Nitrofurantoin | | | | | | | | | ***>32*** | | | >32 | | |
| Oxacillin | | | | | | | | | | | | **>1** | **>2** | |
| Penicillin | >1 | | | | | | | | | >1 | | [c] | [c] | >1 |
| Spiramycin | | | | | | | | | | | | | | >16 |
| Streptomycin | >32 | | **>2** | **>4** | **>512** | **>128** | **>128** | **>16** | **>16** | >32 | >32 | >32 | | |
| Sulphametoxazole | >256 | | | | | | | >256 | | >256 | >256 | | | |
| Tetracycline | >2 | | **>2** | **>2** | **>2** | **>2** | **>2** | **>8** | **>8** | >2 | **>8** | >8 | **>1** | >8 |
| Tiamulin | | >2 | | | | | | | | | | | | |
| Trimethoprim | >4 | | | | | | | **>2** | **>2** | >4 | **>2** | | **>4** | |
| Trim & sulpha[b] | | | | | | | | | **>1** | >4 | ***>0.5*** | >2 | | >4 |
| Tylosin | | >16 | | | | | | | | | | | | |
| Vancomycin | | | | | **>4** | **>4** | >4 | | | | | | | |
| Virginiamycin | | | | | **>32** | **>4** | >4 | | | | | | | |

[a] MIC in U/mL; [b] Concentration of trimethoprim given, tested with sulphamethoxazole in concentration ration 1/20; [c] ß-lactamase production.

# Appendix 4: Antimicrobial agents licensed

**ANTIMICROBIAL AGENTS** licensed for therapy in veterinary medicine in Sweden year 2008 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. 2008. For explanation of ATCvet code, see Appendix 2.

TABLE AP4 I. Antimicrobial agents authorised for therapeutic use in cattle, sheep, pigs, poultry, horses, dogs and cats in Sweden, 2008. Products authorised during 2008 in bold underlined lettering. Routes of administration are indicated[a].

| | | Animal species | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Antimicrobial agent** | **ATCvet code** | **Cattle** | **Sheep** | **Pigs** | **Poultry** | **Horses** | **Dogs** | **Cats** |
| **Tetracyclines** | | | | | | | | |
| Doxycycline | QJ01A A02 | | | O | | | O | O |
| Oxytetracycline | QJ01A A06, QG01A A07 | I O U | I U | I O U | O | | | |
| **Beta-lactams, penicillins** | | | | | | | | |
| Ampicillin | QJ01C A01 | O | | O | | O | O | O |
| Amoxicillin | QJ01C A04 | I | | I | | | I O | O |
| Amoxicillin/Clavulanic acid | QJ01C R02 | | | I | | | I O | I O |
| Penicillin G, sodium | QJ01C E01 | I | | I | | I | | |
| Penicillin G, procaine | QJ01C E09/QJ51C E09 | IM | I | I | | I | I | I |
| Penicillin G, penetamathydroiodide | QJ01C E90 | I | | | | | | |
| **Beta-lactams, cephalosporins** | | | | | | | | |
| Cephalexin | QJ01D B01 | | | | | | O | |
| Cefadroxil | QJ01D B05 | | | | | | O | O |
| Ceftiofur | QJ01D D90 | I | | | | | | |
| **Cefovecin** | QJ01D D91 | | | | | | I | I |
| **Sulphonamides /Trimethoprim** | | | | | | | | |
| Sulphadiazine/Trimethoprim | QJ01E W10 | I | I | I | | I O | O | |
| Sulphadoxine/Trimethoprim | QJ01E W13 | I | | I | | I | | |
| **Sulphonamides** | | | | | | | | |
| Sulphaclozin | QP51A G04 | | | | O | | | |
| **Macrolides** | | | | | | | | |
| Spiramycin | QJ01F A02 | I | | | | | | |
| Tulathromycin | QJ01FA94 | I | | I | | | | |
| Tylosin | QJ01F A90 | I | | I O | O | | I | I |
| **Acetylisovaleryltylosin** (tylvalosin) | QJ01F A92 | | | O | | | | |
| **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 U | O | O |
| **Fluoroquinolones** | | | | | | | | |
| Danofloxacin | QJ01M A92 | I | | | | | | |
| Difloxacin | QJ01M A94 | | | | | | O | |
| Enrofloxacin | QJ01M A90 | I | | I | O | | I O | I O |
| Marbofloxacin | QJ01M A93 | | | | | | O | O |
| **Orbafloxacin** | QJ01M A95 | | | | | | O | |
| Ibafloxacin | QJ01M A96 | | | | | | O | O |
| **Pleuromutilins** | | | | | | | | |
| Tiamulin | QJ01X X92 | | | I O | | | | |
| Valnemulin | QJ01X X94 | | | O | | | | |
| **Combinations** | | | | | | | | |
| Penicillin G, procaine/DHS | QJ01R A01, QJ51R C23 | I M | I | 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 | | | | | | |

[a] O = oral; I = injection; U = intrauterine; M = intramammary.

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# Appendix 6: SVARM 2000-2008 – an overview

**SINCE 2000,** data on antimicrobial susceptibility of over 20 000 isolates of bacteria form the categories; zoonotic, indicator or animal pathogens have been presented in SVARM. In the tables below the number of isolates of the different categories is presented by animal species and year of presentation.

**TABLE AP6 I.** Number of isolates of zoonotic bacteria presented per year in SVARM 2000-2008.

| | Source | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|---|
| ***Salmonella*** | Warm blooded animals | 67 | 52 | 49 | 101 | 68 | 105 | 101 | 112 | 122 |
| ***Campylobacter*** | Cattle | | 67 | | | | | 68 | | |
| | Pig | | 98 | | 105 | | 100 | 46 | | 97 |
| | Broiler | | 50 | 100 | | 100 | | | | 38 |
| | Raw meat | | 74 | | | | | | | |
| | Water | | 19 | | | | | | | |

**TABLE AP6 II.** Number of isolates of indicator bacteria presented per year in SVARM 2000-2008.

| Bacterial species | Source | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|---|
| ***Escherichia coli*** | Cattle | 293 | | | | | | 314 | | |
| | Pig | 260 | 308 | | 303 | | 390 | | 342 | 349 |
| | Pork | | | | | | | | | 19 |
| | Broiler | 274 | 296 | 306 | | 300 | | | 296 | |
| | Dog | | | | | | | 257 | | |
| | Willow grouse | | | | | | 19 | | | |
| | Wild boar | | | 87 | | | | | | |
| | Sheep | | | | | | | | | 115 |
| ***Entreococcus*** *(faecium/faecalis/ hirae)* | Cattle | 71/22/127 | | | | | | 98/13/147 | | |
| | Pig | 48/56/106 | 106/52/77 | | 71/87/124 | | 47/55/124 | | | 39/68/111 |
| | Pork | | | | | | | | | 17/3/- |
| | Broiler | 151/47/28 | 204/49/27 | 189/57/45 | | 163/48/34 | | | 197/36/51 | |
| | Dog | | | | | | | 29/135/22 | | |
| | Wild boar | | | 35/12/9 | | | | | | |
| | Sheep | | | | | | | | | 25/18/34 |

**TABLE AP6 III.** Number of isolates of animal pathogens presented per year in SVARM 2000-2008.

| Animal species & bacterial species | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|
| **Cattle** | | | | | | | | | |
| *Pasteurella* spp. | 254 | | | 100 | | | | 27 | 32 |
| *Staphylococcus aureus* (udder) | | 100 | 100 | | | 96 | | | 87 |
| *Streptococcus uberis* (udder) | | | 100 | | | | | | |
| *Streptococcus dysgalactiae* (udder) | | | 100 | | | | | | |
| *Escherichia coli* (udder) | | | | 169 | | | | | |
| *Klebsiella* spp. (udder) | | | | 44 | | | 24 | | |
| *Escherichia coli* (enteric) | | | 220 | | 87 | 39 | 24 | | |
| **Pig** | | | | | | | | | |
| *Escherichia coli* (enteric) | 399 | 82 | 340 | 340 | 386 | 325 | 298 | 93 | 83 |
| *Actinobacillus pleuropneumoniae* | 18 | | | | | | | 84 | 39 |
| *Brachyspira hyodysenteriae* | 50 | 75 | 109 | 100 | | 31 | 26 | 23 | 15 |
| *Brachyspira pilosicoli* | | | | 93 | | 57 | 72 | 44 | 31 |
| *Pasteurella* spp. | | 75 | | | | | | 38 | 25 |
| *Staphylococcus hyicus* | | | | | 20 | | | | |
| **Poultry (laying hens)** | | | | | | | | | |
| *Escherichia coli* (infection) | | | | | | | | 70 | |
| **Sheep** | | | | | | | | | |
| *Staphylococcus aureus* (udder) | | | | | | | | 25 | 87 |
| **Fish** | | | | | | | | | |
| *Aeromonas salmonicida* subsp.*achromogenes* | | | | | | | | 67 | 20 |
| *Flavobacter columnare* | | | | | | | | 30 | 16 |
| *Flavobacter psychrophilum* | | | | | | | | 42 | 27 |
| **Horse** | | | | | | | | | |
| *Streptococcus zooepidemicus* | 301 | 174 | 163 | 150 | 185 | 175 | 174 | 180 | 159 |
| *Rhodococcus equi* | 73 | 20 | | | 187 | | | | |
| *Escherichia coli* (genital) | 323 | 103 | 166 | 188 | 188 | 161 | 124 | 273 | 174 |
| *Actinobacillus* spp. | | 40 | | | | | | | |
| **Dog** | | | | | | | | | |
| *Staphylococcus pseudintermedius* | 145 | 156 | 133 | 102 | 159 | 126 | 89 | 220 | 258 |
| *Escherichia coli* (urinary) | 185 | 183 | 204 | 234 | 247 | 304 | 366 | 425 | 503 |
| *Pseudomonas aeruginosa* | | | | 234 | | | | | |
| *Pasteurella multocida* | | | | | 231 | | | | |
| **Cat** | | | | | | | | | |
| *Escherichia coli* (urinary) | | | 46 | 52 | 55 | 74 | 95 | 131 | 170 |

NATIONAL
VETERINARY
INSTITUTE

**Department of Animal Health and Antimicrobial Strategies**
**mail:** SE-751 89 Uppsala, Sweden, **phone:** +46 18 67 42 12 **fax:** +46 18 30 91
**e-mail:** e-post.sva@sva.se **web:** www.sva.se

# SWEDRES | 2008

## A Report on Swedish Antimicrobial Utilisation and Resistance in Human Medicine

Strama
Swedish Strategic Programme against Antibiotic Resistance

SMITTSKYDDSINSTITUTET
*Swedish Institute for Infectious Disease Control*

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*Swedish Institute for Infectious Disease Control*

**SMI,** The Swedish Institute for Infectious Disease Control (SMI) is a government expert authority with a mission to monitor the epidemiology of infectious diseases among Swedish citizens and promote control and prevention of these diseases.

Strama

**Strama,** The Swedish Strategic Programme against Antibiotic Resistance was founded in 1995. The remit from the Government is to collaborate interdisciplinary on issues aiming to preserve the effectiveness of antibiotics.

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**Editors:**
Johan Struwe and Barbro Olsson-Liljequist

**Address:**
Swedish Institute for Infectious Disease Control
SE 171 82 Solna, Sweden
Phone: +46 8 457 23 00
Fax: +46 8 30 06 26
E-mail: smi@smi.ki.se
www.smittskyddsinstitutet.se
www.strama.se

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# Content

# 1. Preface

# 2.1 Summary

### Use of antibiotics

Sales of antibiotics in Sweden 2008 were 1.6% lower than the previous year. This decrease follows a series of years with rising use. In 2008, media attention has been drawn towards health-care issues related to the use of antibiotics in both primary health care and hospital care.

Together with tetracyclines, different kinds of penicillins are the most common classes of antibiotics in primary health care. The prescribing of penicillins shows great variance within Sweden, both in terms of number of prescriptions and in choice of drug. Penicillins with an extended spectrum constitute 20% of the prescriptions to children aged 0 to 6 years in the counties with the lowest use and 40% in the high-prescribing counties. One third of all children aged 0 to 6 years were treated with at least one course of antibiotics in 2008. This is 5% lower than in 2007.

The treatment of lower urinry tract infections in women has been the subject of information campaigns for several years. This is clearly reflected in the sales of antibiotics commonly used against this condition in women aged 18 to 79 years: Pivmecillinam and nitrofurantoin, the recommended first-line antibiotics, represent more than 60% of the prescriptions. However, the use of fluoroquinolones is still high in the elderly.

The use of antibiotics in hospital care has continuously increased since the end of the 1990s. A difficulty in the interpretation of these data is that the way nursing homes buy their antibiotics has changed over the years and also differ between the counties. The change in nursing homes from personal prescriptions to dispensing antibiotics from store rooms can probably explain some of the increase within hospital care. When measuring the use of antibiotics only in hospitals, in relation to patient admissions and patient-days, there is no increase at all during the last three years. This analysis has been possible this year by collecting local data from each county.

The distribution of antibiotics used within hospital care has changed in a desirable way, less broad spectrum and more narrow spectrum antibiotics. Various types of penicillin have increased and the use of cephalosporins and fluoroquinolones is decreasing. When analysing data per quarter, beta-lactamase sensitive penicillins increase and cephalosporins decrease to the same levelby the end of 2008 (DDD/1000/year). This is a remarkable shift since Sweden has a long tradition of an extensive use of cephalosporins. Stramas point prevalence studies, performed in 2003, 2004, 2006 and 2008, confirm that the use of cephalosporins for the treatment of uncomplicated community acquired pneumonia has decreased considerably.

### Use of antifungals in Sweden 2008

While the total use of systemic antifungals in hospital care remained constant, a significant increase in the utilization of amphotericin B and a decrease in the use of fluconazole stands out during 2008. Amphotericin B, a macrolide with excellent activity against most fungi that cause human disease, has many serious side effects. The development and marketing in recent years of lipid-based formulations of amphotericin B have made a safer administration of this drug possible. The in-patient use of fluconazole, a triazol compound widely indicated for the prophylaxis and treatment of Candida and Cryptococcus infections, declined during 2008 after several years of steep increases. Fluconazole still represents 80% of the total antifungal used in hospitalized patients. Fluconazole shows reduced or lack of activity against Candida species that account for every fifth episode of candidemia in Sweden. Equinocandin antifungals such as caspofungin and the newly introduced anidulafungin and micafungin, have good activity against azole-resistant Candida species and are increasingly being used for the treatment of invasive candidiasis. As in previous years, more than 95% of all antifungal prescriptions took place in community care.

### Antibiotic resistance

While a few forms of antibiotic resistance is notifiable under the Communicable Disease Act the vast amount of data on antibiotic resistance in Sweden is gathered by the voluntary reporting by Swedish clinical microbiology laboratories. All laboratories take part in the annual resistance surveillance and quality control (RSQC) programme, and three fourths of the laboratories also contribute with data on defined invasive isolates to the European Antimicrobial Resistance Surveillance System, EARSS, network database. For some microorganisms data are produced and presented by laboratories with referral functions and/or with special interest in certain species (e.g. *Neisseria* spp.). In this report the most recent data on antibiotic resistance is presented and analysed together with data from previous years.

*Staphylococcus aureus:* A total of 1307 cases of MRSA were notified in 2008, a 16% increase compared with 1128 cases in 2007. More than half of the reported cases (665 cases) had acquired MRSA in Sweden, and one-third (450 cases) had acquired the infection abroad. Six of the Swedish counties had an incidence of notified MRSA cases above the average country incidence of 14.1 cases/100 000 inhabitants, and four of them had the highest incidences also in 2006 or 2007.

Invasive isolates of MRSA were as few in 2008 (n=16, 0.7%) as in previous years and thus Sweden is still one of the few countries having less than 1% of MRSA among invasive *Staphylococcus aureus*, as reported in the European surveillance network EARSS.

Epidemiological typing of all MRSA isolates has been performed by spa-typing since 2006. The five most commonly encountered spa-types in 2008 were t002 (n=132), t008 (n=113), t044 (n=107), t019 (n=54), t032 (n=51). The prevalence of MRSA with PVL toxin was slowly increasing and was

present in all or a majority of isolates with the common spa-types t008, t044, and t019.

*Staphylococcus aureus* from wound infections (RSQC programme) were susceptible to antibiotics in > 95% of the cases, the only exception being fusidic acid resistance which was decreasing but still above 5%.

*Streptococcus pneumoniae:* In 2008 there were 565 notifications of PNSP (*Streptococcus pneumoniae* with MIC of penicillin > 0.5 mg/L) in Sweden. PNSP have decreased in annual incidence rate per 100 000 population from around 10 in 1997 to values between 6 and 8 since 2000. Most cases were identified through nasopharyngeal culture. The majority of PNSP cases, independent of year observed, were found in the age group 0–4 years. In 19 cases (3.4%) the PNSP isolates came from invasive sites, i.e. blood and/or spinal fluid. Multiresistance (resistance to penicillin and at least two more antibiotics) was common among PNSP. The most common serotypes/groups found were 19F, 9V, 14, 6B, and 23F.

For all four antibiotics tested on *Streptococcus pneumoniae* in the RSQC programme 2008 the rates of resistance were back to the levels noted in 2006, and the decrease in 2007 was probably only temporary.

Rates of non-susceptibility to penicillins in *Streptococcus pneumoniae* (=PNSP) were lower among invasive isolates than in the nasopharyngeal isolates from the RSQC programme. Resistance to macrolide antibiotics was 5–6% in both types of isolates.

*Enterococcus faecalis* and *Enterococcus faecium*: Enterococci, and more specifically vancomycin resistant enterococci (VRE), have been important causes of nosocomial outbreaks in many parts of the world, but have up til now been rare in Sweden. The 53 notified cases of VRE during 2007, which was the highest number since the mandatory notifications begun, indicated a shift. In 2008 there were 618 notified cases of VRE, almost 12 times more cases than 2007. This high notification rate was attributable to the spread of *vanB*-carrying *Enterococcus faecium* not only in the Stockholm county, but also in the counties of Halland and Västmanland, which led to intensive infection control efforts of screening and contact tracing. The strain of *Enterococcus faecium* with the *vanB* gene, affecting all three counties, was new according to epidemiological typing using PFGE.

This new epidemic strain also appeared in blood cultures, giving a rate of vancomycin resistance of 1.5% as reported to EARSS. A more common feature among invasive isolates of both *Enterococcus faecalis* and *Enterococcus faecium* was high-level aminoglycoside resistance (HLAGR) with 20% and 25%, respectively.

*Streptococcus pyogenes:* Data were obtained on 196 invasive isolates in 2008 (data derived from eleven laboratories using ADBact laboratory information system). Only one of the isolates (0.5%) was resistant to erythromycin and none was resistant to clindamycin. Twenty-six isolates (15%) were resistant to tetracycline, and this was a marked increase compared with 2007 when 8% of the isolates were resistant.

*Streptococcus agalactiae*: Data were obtained on 107 invasive isolates in 2008 (data derived from eleven laboratories). Seven isolates (6.5%) were resistant to erythromycin and clindamycin, a figure that was similar to those from 2006 and 2007.

*Haemophilus influenzae:* Data were obtained in the RSQC programme in 2008 after three years without reporting. A marked increase in rates of penicillin-resistant and trimethoprim-sulfamethoxazole-resistant isolates was seen. Against both types of antibiotics the resistance rates were > 20%, compared with stable results for many years of 10–13% resistance. indicated that One third of the patients with beta-lactamase-producing isolates was children 0–9 years, and the remaining isolates were evenly distributed among all other age groups.

*Haemophilus influenzae* was rarely found among blood isolates, only 63 cases in 2008 according to data derived from eleven laboratories. Sixteen of these (25%) were beta-lactamase producing, a marked increase compared with 2007 when only three resistant isolates were found in the corresponding small material.

*Enterobacteriaceae* producing extended spectrum beta-lactamases (ESBL) were made notifiable by the laboratories from February 2007. A total of 2957 cases were notified during 2008. Reports came from all 21 counties of Sweden, corresponding to an average national incidence of 32 cases per 100,000 inhabitants. When comparing the second halfs of 2007 and 2008, respectively, a 28% increase of ESBL cases was noted for 2008. Most ESBLs were found in urine samples (70%) and the most commonly reported species was *E. coli* (84%). Isolates with ESBLs, most often of CTX-M-type, were often multiresistant, i.e. resistant to several other antibiotics, seriously limiting the options for treatment.

*Escherichia coli*, mainly derived from urinary tract infections, has been included in the national surveillance program (RSQC) since 1996, and invasive isolates have been included in the EARSS network since 2001. Ampicillin resistance, caused by production of plasmid-mediated beta-lactamase (most often of TEM-type) was increasingly found in both blood isolates and urine isolates (32% and 29%) in 2008. The level of resistance to third generation cefalosporins had increased to 2.2% among blood isolates, and in the majority of these cases the resistance was caused by plasmid-mediated ESBLs of CTX-M type. This resistance was often accompanied by resistance to many other antibiotics, e.g. aminoglycosides and fluoroquinolones. Resistance to fluoroquinolones has increased every year and was almost the same in urine as in blood isolates (13 vs. 14%) in 2008.

Other gram-negative bacteria that have been monitored in the RSQC programme and also through the EARSS network are *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. The levels of resistance for the antibiotics tested were comparable between the two surveillance programmes for each of the microorganisms. Approximately 2% of *Klebsiella pneumoniae* were cephalosporin resistant and ESBL-producing. In 2007 the first

isolate of *Klebsiella pneumoniae* with KPC-2 was detected in Sweden. In 2008 at least one more isolate with a KPC beta-lactamase has been identified, and also one isolate with a metallo-betalactamase of VIM-type. In all these cases hospital care in the south of Europe were reported.

In *Pseudomonas aeruginosa*, the prevalence of carbapenem resistance was approximately 5% and of fluoroquinolone resistance 10%.

*Helicobacter pylori* has been monitored locally by a few laboratories. Resistance to clarithromycin (and erythromycin) has been steadily increasing but a marked decrease was noted since 2007 according to tests performed in one laboratory. In *Campylobacter jejuni/coli* high levels of resistance were seen against fluoroquinolones (> 60%), tetracyclines (> 30%) and lower but increasing levels against erythromycin (7%) in 2008.

*Neisseria gonorrhoeae*. Gonorrhoeae is a notifiable disease, and in 2008 724 clinical cases of the disease were reported. Isolates from 447 of the notified clinical cases were completely characterised at the Swedish Reference Laboratory for Pathogenic Neisseria, Örebro University Hospital, and at the Division of Clinical Bacteriology, Karolinska University Hospital Huddinge, Stockholm, representing 62% of the notified cases. In 2008 28% of these isolates were beta-lactamase producing and ampicillin resistant, and 63% were resistant to ciprofloxacin.

*Mycobacterium tuberculosis*. The total number of new cases of TB diagnosed in Sweden 2008 was 554. Resistance against at least isoniazid and rifampicin (MDR-TB) was diagnosed in 3.2% of all foreign born patients with culture confirmed TB (14/359), 6.4% of those coming from Somalia (7/110) and 2.8% from other countries (7/249).

Genetic typing with RFLP (restriction fragment length polymorphism) was performed in 49 of the 57 resistant strains of *Mycobacterium tuberculosis* or *M. africanum*. Twentynine of the 49 examined isolates were identified to belong to 16 different clusters with two or more patients in each cluster.

# 2.2 Sammanfattning

**Antibiotikaförbrukning**

Efter flera år med ökande användning av antibiotika sjönk försäljningen något år 2008. Den minskade försäljningen omfattar de flesta preparat, län och åldersgrupper. Flera hälso- och sjukvårdsfrågor med anknytning till antibiotikaanvändning har fått uppmärksamhet i media under året. Som exempel kan nämnas vårdvalsmodeller i primärvården och utbrott av resistenta bakterier på flera sjukhus.

Tillsammans med tetracykliner är olika slags penicilliner de preparat som oftast förskrivs på recept. Användningen av penicilliner varierar mycket inom Sverige, både vad gäller antalet recept och val av preparat. Penicilliner med brett spektrum utgör 20 procent av recepten till barn mellan 0 och 6 år i de län som har lägst totalförskrivning av penicilliner till denna åldersgrupp. I län med hög förskrivning är motsvarande siffra 40 procent. En tredjedel av barnen mellan 0 och 6 år fick minst en antibiotikakur under 2008. Detta var fem procent lägre än 2007.

Behandlingen av nedre urinvägsinfektioner hos kvinnor har varit föremål för informationsinsatser under flera år. Detta märks tydligt i förskrivningen av preparat mot detta tillstånd till kvinnor mellan 18 och 79 år: Pivmecillinam och nitrofurantoin, de rekommenderade förstahandspreparaten, utgör tillsammans mer än 60 procent av förskrivningen.

Antibiotikaanvändningen inom slutenvård har ökat stadigt sedan slutet av 1990-talet. En svårighet i analysen av data är att sjukhem och särskilda boenden i varierande utsträckning har börjat beställa läkemedel på rekvisition istället för att använda recept till enskilda patienter. Läkemedel som rekvireras blir därmed en del av slutenvårdsstatistiken. Andelen antibiotika som köps på detta vis varierar över tid och mellan länen. Till årets rapport har data över försäljningen av antibiotika till enbart sjukhus beställts. Dessa data visar inte någon ökning av antibiotikaförsäljningen till svenska sjukhus under de senaste tre åren.

Fördelningen mellan olika antibiotikaklasser i slutenvården har förändrats i önskvärd riktning. Användningen av preparat med smalt antibakteriellt spektrum, såsom penicilliner, ökar medan preparaten med brett spektrum, exempelvis fluorokinoloner, minskar. Under det sista kvartalet2008 passerar penicilliner med smalt spektrum cefalosporinerna som största grupp. Detta är anmärkningsvärt, eftersom Sverige har haft en tradition av utbredd använding av cefalosporiner. Stramas punktprevalensstudier som genomförts 2003, 2004, 2006 och 2008 bekräftar att användningen av cefalosporiner i behandlingen av okomplicerad samhällsförvärvad pneumoni har minskat kraftigt.

Förhållandet mellan cefalosporiner och penicilliner med smalt spektrum varierar mycket mellan länen. Karbapenemer och piperacillin/tazobactam är preparatgrupper som fortfarande utgör en liten del av den totala användningen i slutenvård, men som ökat stadigt under de senaste åren. Även här är användningen mycket varierande mellan länen.

### Förbrukning av antimykotika i Sverige 2008

I jämförelse med föregående år förblev den sammanlagda användningen av antimykotika för systemisk bruk oförändrad. Som märkbara företeelser konstaterades under 2008 en avsevärd ökning i förbrukningen av amphotericin B och en minskning av medlet flukonazol. Amphotericin B är en antimykotikum med hög aktivitet mot de flesta svamparter av klinisk betydelse. Alvarliga biverkningar är emellertid vanliga vid amphotericin B-behandling. Utvecklingen och marknadsföringen av nya lipidbaserade sammansättningar av amphotericin B har under senare år möjliggjort en säkrare användning av läkemedlet. Förbrukningen av flukonazol, en triazol som indikeras för profylax och behandling av Candida- och Cryptococcusinfektioner, sjönk under 2008 efter flera år av kraftiga ökningar. Trots nedgången utgör flukonazol 80% av den totala antimykotikakonsumtion i landets slutenvård. Medlet har nedsatt effekt, eller saknar aktivitet, mot Candidaarter som ger upphov till 20-25% av candidemifallen i Sverige. Caspofungin såsom de nyligen godkända anidulafungin och micafungin tillhör echinocandinerna, en ny klass av svampmedel. Equinocandiner har hög aktivitet mot azolresistenta Candidaarter och används i ökad utsträckning för behandlingen av invasiv candidos. Liksom tidigare år utfördes drygt 95% av alla ordinationer av svampmedel i öppenvården.

### Antibiotikaresistens

Vissa former av antibiotikaresistens anmäls enligt smittskyddslagen men den frivilliga rapporteringen av resistensdata från de svenska kliniskt mikrobiologiska laboratorierna utgör basen för resistensövervakningen. Alla laboratorier deltar i den årliga insamlingen av data till ResNet, och tre fjärdedelar av laboratorierna bidrar också med data avseende de invasiva isolat som definierats av EARSS. För vissa mikroorganismer sammanställs data av laboratorier med referensfunktion och/eller med speciellt intresse för dessa arter (till exempel Neisseriaarter). I denna rapport presenteras resistensdata från 2008 och analyseras tillsammans med föregående års data.

*Staphylococcus aureus:* Totalt 1307 fall av MRSA anmäldes 2008, en ökning med 16 procent från 2007 då 1128 fall noterades. Mer än hälften av fallen hade blivit smittade i Sverige (665 fall), och en tredjedel (450 fall) hade blivit smittade utomlands. Jämfört med övriga länder i Europa är förekomsten av MRSA låg i Sverige. I sex län/regioner var incidensen av MRSA-fall högre än riksgenomsnittet (14.1 fall per 100 000 invånare). Fyra av dessa hade också haft högre incidens än genomsnittet under 2006 eller 2007. Antalet invasiva isolat av MRSA var lika få 2008 (n=16) som föregående år, vilket innebär att Sverige fortfarande är ett av de få länder i Europa som ännu ej nått nivån 1 procent av alla invasiva *Staphylococcus aureus* enligt rapportering till den europeiska resistensövervakningen EARSS.

Från och med 2006 har spa-typning utgjort den primära typningsmetoden. De fem vanligast förekommande spa-typerna var t002 (n=132), t008 (n=113), t044 (n=107), t019 (n=54) och t032 (n=51). Förekomsten av MRSA med PVL-toxin ökade långsamt och toxinet förekom hos alla eller hos majoriteten av de vanliga spa-typerna t008, t044 och t019, men dessutom hos ett flertal andra spa-typer. *Staphylococcus aureus* i sårinfektioner (data från ResNet) var i mer än 95 procent av fallen känsliga för antibiotika med undantag för fusidinsyra. Nivån var lägre än föregående år, men fortfarande var mer än 5 procent av isolaten resistenta.

*Streptococcus pneumoniae*: Under 2008 noterades 565 fall med nedsatt känslighet för penicillin (MIC av penicillin > 0.5 mg/L, definierade som PNSP). Incidensen PNSP/ 100 000 invånare har minskat från 10,1 1997 till 6–8 sedan år 2000. De flesta fallen identifierades genom nasofarynxodling. Majoriteten av PNSP-fallen var i åldersgruppen 0–4 år. I 19 fall (3,4 procent) påvisades PNSP från blod och/eller spinalvätska. Multiresistens (resistens mot penicillin och minst två ytterligare antibiotika) var vanlig hos PNSP. De vanligast förekommande serotyperna/grupperna var 19F, 9V, 14, 6B och 23F. Enligt data rapporterade i ResNet var resistens mot testade antibiotika åter tillbaka till 2006 års nivå, och den minskning som sågs 2007 var sannolikt tillfällig. Frekvensen PNSP var lägre hos invasiva isolat än hos nasofarynx-isolat medan däremot frekvensen av makrolidresistens var densamma i båda kategorierna (5–6 procent).

*Enterococcus faecalis* och *Enterococcus faecium*: Enterokocker, särskilt de med resistens mot vankomycin (VRE), har varit frekvent förekommande vid sjukvårdsrelaterade utbrott i många delar av världen och har ofta drabbat riskpatienter. De har hittills varit ovanliga i Sverige, men den ökning av anmälda fall som noterades 2007 indikerade ett skifte. Under 2008 rapporterades 618 fall vilket var nästan tolv gånger så många som 2007. Det stora antalet fall kunde tillskrivas förekomst och spridning av en *vanB*-innehållande *Enterococcus faecium* som uppträdde inte enbart i Stockholm utan också i Halland och Västmanland. Intensiva vårdhygieniska åtgärder, kontaktspårning och screening har vidtagits. Genom epidemiologisk typning med PFGE framkom att den aktuella VRE-stammen sannolikt inte hade förekommit i Sverige före 2007. Bland invasiva enterokock-isolat rapporterade till EARSS 2008 förekom den nya stammen i ett par fall vilket gav 1,5 procent resistens. Hos invasiva isolat av både *Enterococcus faecalis* och *Enterococcus faecium* förekom också höggradig aminoglykosidresistens (HLAGR), i 20 respektive 25 procent av isolaten.

*Streptococcus pyogenes:* Data för 196 invasiva isolat, erhållna från elva laboratorier under 2008, visade minskad förekomst av makrolid-resistens, 0.,5 procent jämfört med 2,5 procent 2007, men högre frekvens tetracyklin-resistens, 15 procent jämfört med 8 procent 2007.

*Streptococcus agalactiae:* Data för 107 invasiva isolat, erhållna från elva laboratorier under 2008, visade att 6,5 procent var makrolid-resistenta, vilket var en liten minskning jämfört med 2007.

*Haemophilus influenzae:* Data från övervakningen i ResNet, som genomfördes 2008 efter ett uppehåll på tre år, visade på en kraftigt ökad förekomst av betalaktamas-producerande (ampicillin-resistenta) isolat och också av trimetoprim-sulfa-

resistenta isolat. Siffrorna var nu > 20 procent jämfört med tidigare års genomsnitt på 10–13 procent. En tredjedel var 0–9 år, medan övriga var jämnt fördelade mellan åldersgrupperna. *Haemophilus influenzae* var ett sällsynt fynd bland invasiva isolat, och endast 63 fall fanns registrerade från de elva ADBakt-laboratorierna 2008. Sexton av dessa var betalaktamas-producerande (25 procent), vilket var en kraftig ökning jämfört med 2007 då endast tre sådana isolat fanns.

*Enterobacteriaceae* som producerar betalaktamaser med utvidgat spektrum, så kallade ESBL, blev anmälningspliktiga i februari 2007. Totalt 2057 fall rapporterades under 2008. Samtliga landsting rapporterade, och den genomsnittliga incidensen i Sverige var 32 fall per 100 000 invånare. Vid jämförelse mellan andra halvåret 2008 och samma period 2007 noterades en 28-procentig ökning av fallen 2008. De flesta isolaten återfanns i urinprover (70 procent) och var *Escherichia coli* (84 procent), och de hade oftast ESBL av CTX-M-typ. Multiresistens var vanlig hos dessa isolat.

*Escherichia coli* huvudsakligen från urinvägsinfektioner, har övervakats enligt det nationella programmet (ResNet) sedan 1996, och blodisolat har inkluderats i EARSS sedan 2001. Ampicillinresistens, oftast orsakad av plasmidmedierad beta-laktamasproduktion av TEM-typ, återfanns i ökande utsträckning både hos blodisolat och urinisolat 2008 (32 procent och 29 procent). Frekvensen blodisolat med resistens mot 3:e generationens cefalosporiner var 2,2 procent, och hos majoriteten av dessa var resistensen orsakad av plasmidmedierade ESBL av CTX-M-typ. De cefalosporin-resistenta stammarna var ofta resistenta mot andra antibiotikagrupper som aminoglykosider och kinoloner. Resistens mot kinoloner har ökat årligen och var hos både blodisolat och urinisolat 13–14 procent 2008.

Andra gram-negativa bakterier som övervakats nationellt och/eller internationellt är *Klebsiella pneumoniae* och *Pseudomonas aeruginosa*. Resistensnivåerna hos respektive patogen var oförändrade oberoende av övervakningsprogram och typ av prov. Hos *K. pneumoniae* var cirka 2 procent resistenta mot cefalosporiner genom ESBL-produktion. Under 2007 identifierades det första isolatet med KPC-2 i Sverige, och under 2008 har ytterligare ett KPC-producerande isolat påträffats, och även ett isolat med metallo-betalaktamas av VIM-typ. I samtliga dessa fall fanns en bakomliggande historia med sjukvård i södra Europa. Hos *P. aeruginosa* var karbapenemresistensen 5 procent och kinolonresistensen 10 procent.

*Helicobacter pylori* har övervakats regelbundet vid ett laboratorium. Resistens mot klaritromycin har ökat stadigt under flera år men från 2007 har en kraftig minskning skett.

Hos *Campylobacter jejuni/coli* var kinolonresistensen >60 procent och tetracyklinresistensen >30 procent, medan erytromycinresistensen var mycket lägre men ändå ökande upp till 7 procent 2008.

*Neisseria gonorrhoeae:* Gonorré är en anmälningspliktig sjukdom och 2008 rapporterades 724 kliniska fall. Isolat från 447 (62 procent) av dessa har undersökts. Tjugoåtta procent av isolaten var beta-laktamasproducerande och därmed ampicillinresistenta, och 63 procent var resistenta mot kinoloner (ciprofloxacin testat).

*Mycobacterium tuberculosis* Antalet anmälda nya fall av tuberkulos var 554 under 2008. *Mycobacterium tuberculosis* med resistens mot minst två antibiotika (MDR-TB) rapporterades hos 3,2 procent av alla utlandsfödda patienter med odlingsverifierad TB (14/359 fall). Epidemiologisk typning med RFLP av alla resistenta TB-isolat visade att de tillhörde 16 olika kluster med två eller fler patienter i varje.

# 2.3 Contributors to chapters 3 and 4

**Otto Cars,** Strama
*otto.cars@strama.se*

**Ulrica Dohnhammar,** Strama
*ulrica.dohnhammar@strama.se*

**Charlotta Edlund,** Medical Products Agency
*charlotta.edlund@mpa.se*

**Victor Fernandez,** Department of Parasitology, Mycologoy and Environmental Microbiology, Swedish Institute for Infectious Disease Control
*victor.fernandez@smi.se*

**Hans Fredlund,** Communicable Disease Control, National Reference Laboratory for Pathogenic Neisseria, Department of Laboratory Medicine, Clinical Microbiology, Örebro University Hospital
*hans.fredlund@orebroll.se*

**Birgitta Henriques Normark,** Department of Bacteriology, Swedish Institute for Infectious Disease Control
*birgitta.henriques@smi.se*

**Sven Hoffner,** Department of Bacteriology, Swedish Institute for Infectious Disease Control
*sven.hoffner@smi.se*

**Sara Hæggman,** Department of Bacteriology, Swedish Institute for Infectious Disease Control
*sara.haeggman@smi.se*

**Gunnar Kahlmeter,** Department of Clinical Microbiology, Växjö Hospital
*gunnar.kahlmeter@ltkronoberg.se*

**Bengt Lindeskog,** Medical Products Agency
*bengt.lindeskog@mpa.se*

**Christer Norman,** Strama
*christer.norman@strama.se*

**Per Olcén,** National Reference Laboratory for Pathogenic Neisseria, Department of Laboratory Medicine, Clinical Microbiology, University Hospital
*per.olcen@orebroll.se*

**Barbro Olsson-Liljequist,** Department of Bacteriology, Swedish Institute for Infectious Disease Control,
*barbro.liljequist@smi.se*

**Victoria Romanus,** Department of Epidemiology, Swedish Institute for Infectious Disease Control
*victoria.romanus@smi.se*

**Gunilla Skoog,** Strama
*gunilla.skoog@strama.se*

**Johan Struwe,** Department of Epidemiology, Swedish Institute for Infectious Disease Control and Strama
*johan.struwe@smi.se*

**Tomas Söderblom,** Department of Epidemiology, Swedish Institute for Infectious Disease Control
*tomas.soderblom@smi.se*

**Karin Tegmark Wisell,** Department of Bacteriology, Swedish Institute for Infectious Disease Control
*karin.tegmark-wisell@smi.se*

**Michael Toepfer,** Department of Clinical Microbiology, Ryhov's Hospital Jönköping
*michael.toepfer@lj.se*

**Magnus Unemo,** National Reference Laboratory for Pathogenic Neisseria, Department of Laboratory Medicine, Clinical Microbiology, Örebro University Hospital
*magnus.unemo@orebroll.se*

**Mats Walder,** Department of Clinical Microbiology, Malmö University Hospital,
*mats.walder@mikrobiol.mas.lu.se*

**Thomas Åkerlund,** Department of Bacteriology, Swedish Institute for Infectious Disease Control
*thomas.akerlund@smi.se*

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# 3. Use of antimicrobials

## 3.1. Use of antibiotics

Statistics on antibiotic sales have been obtained from The National Corporation of Swedish Pharmacies. Sales data are expressed either as defined daily doses per 1000 inhabitants and day (DDD/1000 inhabitants/day) or as prescriptions per 1000 inhabitants and year (prescriptions/1000 inhabitants/year).

Data on all drugs prescribed in primary health care are also included in the Swedish Prescribed Drug Register, which is administered by the Swedish National Board of Health and Welfare. Since this register is based upon individuals rather than products, it is possible to investigate the actual number of people treated during a certain period of time. The number of individuals treated with at least one course of antibiotics is expressed as users per 1000 inhabitants and year.

Sales of antibiotics in hospital care are related to either inhabitants, number of admissions to hospitals or number of patient-days. The latter are obtained from the Swedish Association for Local Authorities and Regions.

Denominator data are found in Appendix 2.

### Total sales of antibiotics

Sales of antibiotics in Sweden 2008 were 1.6% lower than the previous year, Table 3.1.1. This decrease follows a series of years with rising use. In 2008, some media attention has been drawn towards healthcare issues related to the use of antibiotics in both primary health care and hospital care. Several outbreaks of resistant bacteria in hospitals and patients' free choice of caregiver in primary healthcare are examples of debated topics.

**TABLE 3.1.1.** Total sales of antibacterial drugs for systemic use in Sweden 2000-2008, DDD/1000 inhabitants/day. Methenamine is an antiseptic and therefore of no interest regarding antibiotic resistance.

| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|
| Methenamine | 1,6 | 1,5 | 1,6 | 1,7 | 1,9 | 1,9 | 1,9 | 1,8 | 1,6 |
| J01 excl methenamine | 15,2 | 15,3 | 14,8 | 14,6 | 14,3 | 14,8 | 15,2 | 15,6 | 15,4 |
| Total J01 | 16,8 | 16,8 | 16,4 | 16,3 | 16,2 | 16,6 | 17,1 | 17,4 | 17,0 |

### Primary health care

After three years of increase, the sales of antibiotics in primary health care decreased in 2008. Moreover, the seasonal variation seems to be less pronounced than in the years before. This could be seen as an indicator of good quality in prescribing, Figure 3.1.1. The decrease in sales encompasses almost all classes of antibiotics, all age groups and all counties, as will be shown in the further analysis.

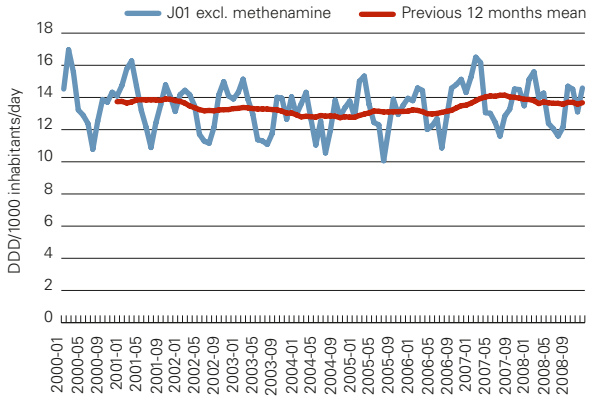


**FIGURE 3.1.1.** Antibiotics in primary health care 2000–2008, DDD/1000 inhabitants/day. Monthly sales and 12 months mean.

Beta-lactamase sensitive penicillins and tetracyclines are still the largest classes of antibiotics in primary health care in Sweden but these classes, as well as the vast majority of other antibiotics are decreasing in sales. Pivmecillinam, an antibiotic used in treatment of lower urinary tract infections in women, and the beta-lactamase resistant penicillins are the only classes showing a slight increase, Figure 3.1.2.

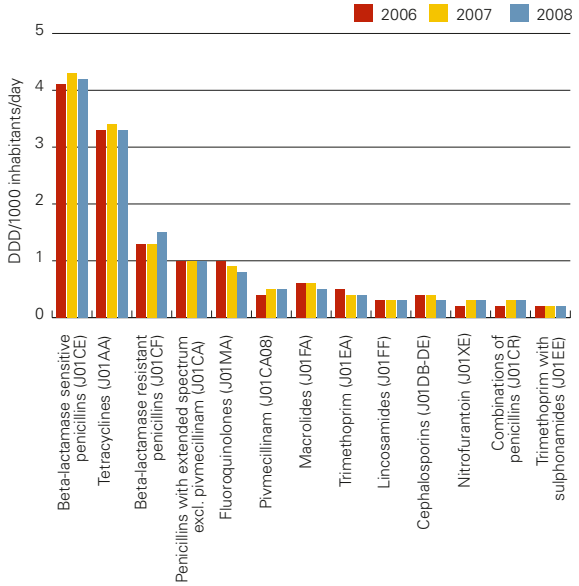


**FIGURE 3.1.2.** Antibiotics in primary health care 2006–2008, DDD/1000 inhabitants/day.

A shift towards higher doses of beta-lactamase sensitive penicillins is evident, since the number of DDDs increase by around 15% in all age groups except young children, while the number of prescriptions remains stable, Table 3.1.2. This change is expected and desirable since the Swedish Reference Group for Antibiotics has promoted the dosing of penicillins

**TABLE 3.1.2.** Antibiotics in primary health care, classes of antibiotics and age groups. DDD/1000 inhabitants/day and prescriptions/1000 inhabitants/year. 2004-2008. Users/1000 inhabitants/year. 2006-2008.

| Age group (years) | DDD/1000 inhabitants/day | | | | | Prescriptions/1000 inhabitants/year | | | | | Users/1000 inhabitants/year | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2004 | 2005 | 2006 | 2007 | 2008 | 2004 | 2005 | 2006 | 2007 | 2008 | 2006 | 2007 | 2008 |
| Tetracyclines (J01AA) | | | | | | | | | | | | | |
| 0-6 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.1 | 0.1 | 0.1 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 |
| 7-19 | 2.36 | 2.71 | 3.12 | 3.23 | 3.26 | 25.4 | 28.9 | 32.7 | 33.9 | 32.0 | 20.4 | 21.5 | 19.6 |
| 20-59 | 3.36 | 3.52 | 3.56 | 3.68 | 3.50 | 62.9 | 67.2 | 66.3 | 68.3 | 61.3 | 51.8 | 53.4 | 47.6 |
| 60-79 | 3.90 | 4.15 | 4.11 | 4.29 | 4.05 | 91.7 | 99.7 | 96.3 | 99.3 | 90.1 | 71.6 | 74.4 | 67.2 |
| 80 - | 2.83 | 3.04 | 2.89 | 2.93 | 2.78 | 75.8 | 82.6 | 76.4 | 77.8 | 71.7 | 60.1 | 62.0 | 56.8 |
| All age groups | 3.06 | 3.26 | 3.33 | 3.44 | 3.29 | 58.6 | 63.2 | 62.6 | 64.3 | 58.3 | 46.9 | 48.6 | 43.7 |
| Penicillins with extended spectrum (J01CA) excl. pivmecillinam | | | | | | | | | | | | | |
| 0-6 | 1.25 | 1.41 | 1.59 | 1.74 | 1.71 | 84.7 | 85.0 | 86.9 | 95.2 | 90.8 | 64.6 | 70.5 | 66.7 |
| 7-19 | 0.32 | 0.38 | 0.45 | 0.46 | 0.43 | 10.8 | 12.5 | 14.1 | 14.5 | 13.6 | 12.4 | 12.8 | 11.5 |
| 20-59 | 0.64 | 0.72 | 0.72 | 0.77 | 0.75 | 16.8 | 18.3 | 18.4 | 19.4 | 18.7 | 16.0 | 16.7 | 15.1 |
| 60-79 | 1.43 | 1.56 | 1.59 | 1.62 | 1.63 | 39.3 | 41.2 | 41.4 | 42.0 | 41.3 | 32.3 | 32.9 | 29.9 |
| 80 - | 1.65 | 1.80 | 1.81 | 1.79 | 1.83 | 45.3 | 47.5 | 47.3 | 46.8 | 46.5 | 38.3 | 38.0 | 32.9 |
| All age groups | 0.84 | 0.94 | 0.98 | 1.02 | 1.02 | 27.4 | 29.0 | 29.6 | 31.0 | 30.5 | 23.4 | 24.5 | 22.5 |
| Pivmecillinam (J01CA08) | | | | | | | | | | | | | |
| 0-6 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.3 | 0.4 | 0.5 | 0.5 | 0.7 | 0.4 | 0.5 | 0.6 |
| 7-19 | 0.14 | 0.15 | 0.17 | 0.19 | 0.24 | 7.4 | 8.7 | 10.7 | 12.4 | 15.5 | 9.6 | 11.0 | 13.6 |
| 20-59 | 0.32 | 0.31 | 0.34 | 0.36 | 0.43 | 15.4 | 16.9 | 20.1 | 22.2 | 26.9 | 17.3 | 19.0 | 22.5 |
| 60-79 | 0.72 | 0.70 | 0.71 | 0.74 | 0.84 | 33.4 | 36.2 | 40.3 | 43.0 | 49.5 | 31.2 | 33.1 | 37.3 |
| 80 - | 2.05 | 1.90 | 1.84 | 1.84 | 1.95 | 97.4 | 100.0 | 106.7 | 109.3 | 116.6 | 80.1 | 81.8 | 85.1 |
| All age groups | 0.43 | 0.42 | 0.43 | 0.46 | 0.53 | 20.5 | 22.3 | 25.5 | 27.6 | 32.2 | 20.7 | 22.3 | 25.6 |
| Beta-lactamase sensitive penicillins (J01CE) | | | | | | | | | | | | | |
| 0-6 | 3.32 | 3.35 | 3.59 | 4.03 | 4.14 | 307.9 | 310.5 | 327.3 | 350.7 | 343.7 | 230.8 | 244.3 | 235.9 |
| 7-19 | 2.92 | 3.01 | 3.38 | 3.68 | 3.64 | 120.6 | 121.5 | 135.0 | 142.5 | 135.0 | 113.1 | 117.3 | 110.2 |
| 20-59 | 4.16 | 4.18 | 4.28 | 4.49 | 4.42 | 105.5 | 105.2 | 107.9 | 112.8 | 108.4 | 91.6 | 95.2 | 90.9 |
| 60-79 | 4.33 | 4.27 | 4.46 | 4.57 | 4.51 | 104.8 | 102.9 | 107.0 | 109.0 | 106.1 | 88.0 | 89.4 | 87.0 |
| 80 - | 3.32 | 3.39 | 3.33 | 3.36 | 3.51 | 86.8 | 87.1 | 84.2 | 84.2 | 85.7 | 71.4 | 72.2 | 72.4 |
| All age groups | 3.90 | 3.92 | 4.09 | 4.30 | 4.26 | 122.6 | 122.5 | 128.1 | 134.3 | 130.0 | 104.0 | 108.1 | 103.7 |
| Beta-lactamase resistant penicillins (J01CF) | | | | | | | | | | | | | |
| 0-6 | 0.33 | 0.31 | 0.35 | 0.33 | 0.33 | 34.3 | 32.2 | 35.6 | 32.9 | 32.8 | 26.7 | 25.2 | 24.8 |
| 7-19 | 0.67 | 0.65 | 0.70 | 0.69 | 0.80 | 32.0 | 30.7 | 33.6 | 31.9 | 31.9 | 27.5 | 26.4 | 26.2 |
| 20-59 | 0.88 | 0.88 | 0.95 | 0.96 | 1.14 | 31.7 | 31.7 | 33.5 | 33.3 | 33.2 | 26.9 | 26.7 | 26.5 |
| 60-79 | 1.94 | 1.91 | 2.04 | 2.04 | 2.37 | 54.5 | 54.4 | 57.4 | 56.3 | 56.9 | 37.7 | 37.1 | 37.3 |
| 80 - | 4.47 | 4.38 | 4.44 | 4.40 | 5.01 | 124.2 | 122.0 | 123.4 | 122.6 | 122.1 | 68.7 | 67.9 | 66.8 |
| All age groups | 1.18 | 1.18 | 1.25 | 1.25 | 1.46 | 40.9 | 40.5 | 42.9 | 42.2 | 42.3 | 31.2 | 30.7 | 30.5 |
| Combinations of penicillins (J01CR) | | | | | | | | | | | | | |
| 0-6 | 0.68 | 0.73 | 0.73 | 0.75 | 0.67 | 48.5 | 51.8 | 51.2 | 52.7 | 46.4 | 34.4 | 35.2 | 30.9 |
| 7-19 | 0.17 | 0.20 | 0.22 | 0.21 | 0.20 | 5.1 | 6.0 | 6.4 | 6.4 | 6.0 | 5.1 | 4.9 | 4.5 |
| 20-59 | 0.15 | 0.17 | 0.18 | 0.20 | 0.21 | 3.3 | 3.8 | 3.9 | 4.4 | 4.6 | 3.5 | 3.9 | 4.0 |
| 60-79 | 0.17 | 0.20 | 0.22 | 0.25 | 0.27 | 3.5 | 4.2 | 4.5 | 5.1 | 5.5 | 3.6 | 4.1 | 4.4 |
| 80 - | 0.11 | 0.15 | 0.15 | 0.17 | 0.20 | 2.4 | 3.0 | 3.0 | 3.4 | 4.1 | 2.3 | 2.7 | 3.2 |
| All age groups | 0.19 | 0.22 | 0.24 | 0.26 | 0.26 | 6.9 | 7.8 | 8.0 | 8.5 | 8.3 | 6.1 | 6.5 | 6.3 |
| Cephalosporins (J01DB-DE) | | | | | | | | | | | | | |
| 0-6 | 0.53 | 0.50 | 0.52 | 0.52 | 0.46 | 49.7 | 46.4 | 49.0 | 49.7 | 43.6 | 37.6 | 38.0 | 33.9 |
| 7-19 | 0.30 | 0.29 | 0.30 | 0.29 | 0.27 | 20.9 | 19.6 | 20.6 | 20.2 | 18.4 | 17.4 | 17.2 | 15.7 |
| 20-59 | 0.30 | 0.30 | 0.29 | 0.28 | 0.25 | 16.9 | 16.6 | 16.8 | 16.2 | 14.5 | 14.2 | 13.7 | 12.2 |
| 60-79 | 0.48 | 0.47 | 0.46 | 0.40 | 0.36 | 23.6 | 23.1 | 22.6 | 20.2 | 17.7 | 17.1 | 15.5 | 13.5 |
| 80 - | 0.79 | 0.77 | 0.73 | 0.65 | 0.54 | 42.6 | 42.3 | 40.5 | 35.4 | 29.4 | 30.9 | 27.4 | 22.9 |
| All age groups | 0.40 | 0.38 | 0.37 | 0.35 | 0.31 | 23.4 | 22.5 | 22.5 | 21.5 | 19.0 | 17.9 | 17.2 | 15.3 |

| Age group (years) | DDD/1000 inhabitants/day | | | | | Prescriptions/1000 inhabitants/year | | | | | Users/1000 inhabitants/year | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2004 | 2005 | 2006 | 2007 | 2008 | 2004 | 2005 | 2006 | 2007 | 2008 | 2006 | 2007 | 2008 |
| Trimethoprim (J01EA) | | | | | | | | | | | | | |
| 0-6 | 0.12 | 0.11 | 0.12 | 0.12 | 0.10 | 15.6 | 14.8 | 16.0 | 15.4 | 14.0 | 11.1 | 10.6 | 9.8 |
| 7-19 | 0.21 | 0.20 | 0.21 | 0.18 | 0.15 | 12.4 | 11.9 | 12.4 | 10.9 | 8.9 | 10.8 | 9.5 | 7.8 |
| 20-59 | 0.36 | 0.33 | 0.33 | 0.29 | 0.24 | 18.7 | 17.3 | 17.4 | 14.6 | 11.8 | 14.7 | 12.4 | 9.9 |
| 60-79 | 0.92 | 0.86 | 0.84 | 0.76 | 0.64 | 44.6 | 41.7 | 40.7 | 35.2 | 29.2 | 29.7 | 25.6 | 21.0 |
| 80 - | 2.48 | 2.28 | 2.19 | 1.91 | 1.58 | 136.0 | 125.6 | 120.1 | 104.5 | 84.7 | 73.3 | 61.6 | 49.1 |
| All age groups | 0.53 | 0.49 | 0.49 | 0.43 | 0.36 | 28.2 | 26.4 | 26.3 | 22.8 | 18.8 | 19.8 | 16.9 | 13.8 |
| Trimethoprim with sulphonamides (J01EE) | | | | | | | | | | | | | |
| 0-6 | 0.15 | 0.15 | 0.16 | 0.16 | 0.14 | 18.4 | 18.1 | 18.1 | 18.8 | 16.7 | 13.2 | 13.5 | 12.0 |
| 7-19 | 0.09 | 0.10 | 0.10 | 0.10 | 0.11 | 4.0 | 4.1 | 4.0 | 4.1 | 4.2 | 2.7 | 2.6 | 2.7 |
| 20-59 | 0.12 | 0.12 | 0.13 | 0.14 | 0.14 | 2.7 | 2.8 | 2.9 | 3.0 | 3.1 | 1.9 | 1.9 | 2.0 |
| 60-79 | 0.33 | 0.34 | 0.36 | 0.39 | 0.44 | 8.2 | 8.4 | 8.8 | 9.2 | 10.1 | 5.8 | 6.1 | 6.8 |
| 80 - | 0.35 | 0.34 | 0.36 | 0.39 | 0.43 | 11.8 | 11.5 | 11.7 | 12.2 | 13.1 | 8.8 | 9.1 | 9.9 |
| All age groups | 0.18 | 0.18 | 0.19 | 0.20 | 0.21 | 6.2 | 6.2 | 6.3 | 6.4 | 6.5 | 4.0 | 4.1 | 4.3 |
| Macrolides (J01FA) | | | | | | | | | | | | | |
| 0-6 | 0.73 | 0.80 | 0.80 | 0.85 | 0.68 | 34.5 | 37.4 | 37.3 | 38.1 | 29.9 | 29.6 | 30.4 | 23.3 |
| 7-19 | 0.62 | 0.72 | 0.76 | 0.74 | 0.54 | 18.1 | 21.0 | 22.1 | 21.7 | 15.4 | 17.9 | 17.2 | 11.8 |
| 20-59 | 0.54 | 0.56 | 0.54 | 0.55 | 0.49 | 16.3 | 16.8 | 16.3 | 16.5 | 14.3 | 13.0 | 13.2 | 11.3 |
| 60-79 | 0.49 | 0.51 | 0.50 | 0.50 | 0.47 | 14.1 | 14.8 | 14.5 | 14.6 | 13.0 | 11.0 | 11.0 | 9.6 |
| 80 - | 0.31 | 0.34 | 0.34 | 0.32 | 0.30 | 9.7 | 9.8 | 9.3 | 8.7 | 8.4 | 7.2 | 6.8 | 6.4 |
| All age groups | 0.55 | 0.59 | 0.58 | 0.59 | 0.50 | 17.3 | 18.4 | 18.2 | 18.4 | 15.3 | 14.4 | 14.4 | 11.7 |
| Lincosamides (J01FF) | | | | | | | | | | | | | |
| 0-6 | 0.02 | 0.02 | 0.02 | 0.03 | 0.02 | 4.1 | 4.5 | 5.0 | 5.3 | 5.0 | 3.6 | 3.9 | 3.7 |
| 7-19 | 0.09 | 0.10 | 0.11 | 0.12 | 0.12 | 6.5 | 6.9 | 7.8 | 8.3 | 8.4 | 6.2 | 6.7 | 6.9 |
| 20-59 | 0.24 | 0.25 | 0.28 | 0.29 | 0.30 | 12.6 | 13.0 | 14.3 | 15.6 | 15.6 | 11.1 | 12.2 | 12.2 |
| 60-79 | 0.51 | 0.53 | 0.55 | 0.55 | 0.57 | 21.1 | 22.1 | 23.7 | 24.4 | 24.6 | 15.3 | 15.9 | 16.3 |
| 80 - | 0.71 | 0.77 | 0.75 | 0.74 | 0.76 | 30.0 | 32.2 | 32.6 | 32.8 | 33.2 | 18.1 | 18.6 | 19.2 |
| All age groups | 0.27 | 0.29 | 0.31 | 0.32 | 0.33 | 13.5 | 14.1 | 15.4 | 16.3 | 16.4 | 10.9 | 11.7 | 11.9 |
| Fluoroquinolones (J01MA) | | | | | | | | | | | | | |
| 0-6 | 0.01 | 0.02 | 0.01 | 0.01 | 0.01 | 0.4 | 0.8 | 0.8 | 0.8 | 0.7 | 0.4 | 0.4 | 0.4 |
| 7-19 | 0.12 | 0.12 | 0.12 | 0.13 | 0.12 | 5.5 | 5.5 | 5.5 | 5.5 | 4.8 | 4.7 | 4.4 | 3.9 |
| 20-59 | 0.81 | 0.81 | 0.80 | 0.76 | 0.69 | 33.1 | 31.9 | 30.2 | 27.8 | 23.8 | 22.0 | 20.3 | 17.3 |
| 60-79 | 2.07 | 2.08 | 2.05 | 1.93 | 1.75 | 88.0 | 84.6 | 80.2 | 73.7 | 63.9 | 52.7 | 48.7 | 42.7 |
| 80 - | 3.14 | 3.13 | 3.00 | 2.74 | 2.41 | 158.4 | 149.4 | 136.8 | 119.7 | 98.5 | 92.5 | 81.5 | 68.1 |
| All age groups | 0.98 | 0.99 | 0.98 | 0.93 | 0.84 | 42.5 | 41.0 | 39.0 | 35.7 | 30.6 | 27.0 | 24.9 | 21.5 |
| Nitrofurantoin (J01XE) | | | | | | | | | | | | | |
| 0-6 | 0.07 | 0.07 | 0.07 | 0.07 | 0.06 | 6.9 | 6.4 | 6.3 | 6.3 | 6.2 | 4.2 | 4.2 | 4.2 |
| 7-19 | 0.11 | 0.12 | 0.12 | 0.14 | 0.13 | 4.9 | 5.3 | 5.2 | 6.7 | 6.6 | 4.4 | 5.8 | 5.8 |
| 20-59 | 0.17 | 0.19 | 0.20 | 0.24 | 0.23 | 7.4 | 8.5 | 8.5 | 11.0 | 10.6 | 7.0 | 9.1 | 8.8 |
| 60-79 | 0.29 | 0.34 | 0.36 | 0.46 | 0.47 | 11.7 | 14.1 | 14.6 | 19.4 | 20.6 | 10.7 | 14.3 | 15.2 |
| 80 - | 0.68 | 0.78 | 0.78 | 0.97 | 0.95 | 31.0 | 36.5 | 37.2 | 46.7 | 47.7 | 24.0 | 30.3 | 31.2 |
| All age groups | 0.20 | 0.23 | 0.24 | 0.30 | 0.29 | 9.0 | 10.3 | 10.5 | 13.5 | 13.6 | 8.0 | 10.3 | 10.4 |
| All agents (J01 excl. methenamine) | | | | | | | | | | | | | |
| 0-6 | 7.23 | 7.49 | 7.98 | 8.62 | 8.34 | 605.9 | 608.8 | 634.7 | 666.8 | 630.8 | 335.6 | 348.5 | 330.3 |
| 7-19 | 8.13 | 8.76 | 9.79 | 10.18 | 10.02 | 274.1 | 283.4 | 311.1 | 319.8 | 301.4 | 204.5 | 208.1 | 195.8 |
| 20-59 | 12.09 | 12.37 | 12.63 | 13.04 | 12.82 | 344.2 | 350.9 | 357.6 | 366.1 | 348.0 | 223.9 | 228.7 | 217.8 |
| 60-79 | 17.66 | 18.02 | 18.34 | 18.58 | 18.46 | 541.0 | 550.0 | 554.5 | 553.7 | 531.0 | 288.8 | 289.6 | 279.0 |
| 80 - | 23.01 | 23.20 | 22.74 | 22.33 | 22.37 | 856.3 | 854.2 | 833.3 | 807.9 | 765.1 | 379.4 | 372.5 | 356.2 |
| All age groups | 12.77 | 13.13 | 13.51 | 13.87 | 13.70 | 418.2 | 425.6 | 436.1 | 443.8 | 423.1 | 249.8 | 254.1 | 242.5 |

three instead of two times daily in the treatment of several common infections in primary care. Notably, the number of macrolide prescriptions to the age groups 0–6 years and 7–19 years was 25% lower in 2008 than in 2007. Young children and the elderly have the highest consumption of antibiotics and variation in sales is often most evident in these groups.

The shift in sales of antibiotics commonly used in the treatment of lower urinary tract infections in women continues and is even more pronounced in 2008, Figure 3.1.3. Pivmecillinam is the most common substance and accounts with nitrofurantoin, the other recommended first-line drug, for over 60% in women aged 10–79 years. Unfortunately, there was a shortage of nitrofurantoin in the summer of 2008.

Treatment of lower urinary tract infections in women has been the subject of campaigns and educational activities for several years. The new recommendations launched by Strama and The Swedish Medicinal Products Agency in 2007 seem to have added to the shift. Pivmecillinam and nitrofurantoin are recommended over trimethoprim, and prescribers are encouraged to minimize the use of fluoroquiolones.

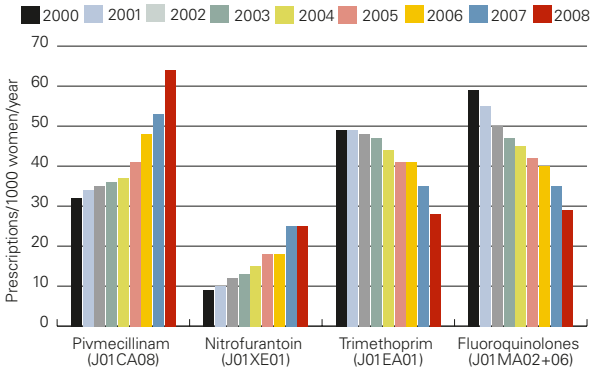


**FIGURE 3.1.3.** Antibiotics commonly used to treat lower urinary tract infections in women, 2000–2008, prescriptions/1000 women/year.

The fraction of people treated with any kind of antibiotic (users per 1000 inhabitants) is about the same as in previous years. However, antibiotic use varies within Sweden. A comparison of age and gender standardized sales data from the counties shows that the use is highest in the big cities and their surroundings.

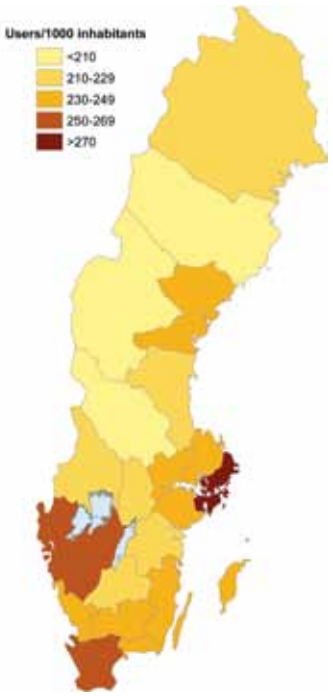


**FIGURE 3.1.4.** Fraction of people treated with at least one course of antibiotics (J01 excl. methenamine) in 2008, users/1000 inhabitants. Age and gender standardized data.

Concerning the fraction of children that had at least one course of antibiotics in 2008, Stockholm county was again the highest with 384 users per 1000 children whereas Västerbotten county was the lowest with 249 users per 1000 children, Figure 3.1.5. Taken together, the fraction of children treated with antibiotics was 330 users per 1000 children, which is 5% lower than in 2007.

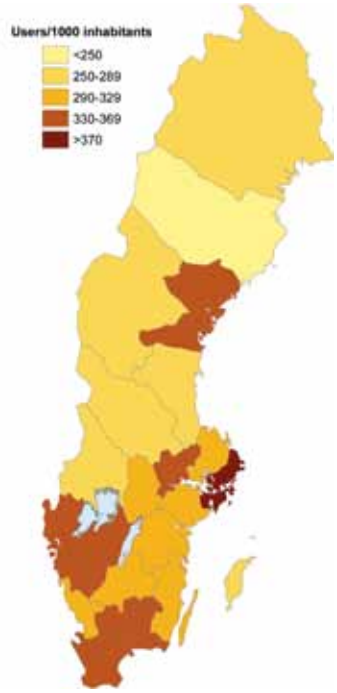


**FIGURE 3.1.5.** Fraction of children aged 0 to 6 years treated with at least one course of antibiotics (J01 excl. methenamine) in 2008, users /1000 children.

As seen in Table 3.1.2., different kinds of penicillins are the most commonly prescribed antibiotics to children in Sweden. However, there are large differences between the counties. The number of prescriptions range from nearly 600 per 1000 children in Stockholm county to 300 in Västerbotten county, Figure 3.1.6. The diversity seems mostly relate to the use of penicillins with an extended spectrum, i.e. amoxicillin and amoxicillin with clavulanate. The use of these substances varies from over 200 prescriptions per 1000 children to less than 80 per 1000 children. Penicillins with an extended spectrum are prescribed to a much greater extent in counties that also have a high level of prescription of narrow spectrum penicillins, hence the big difference between counties.

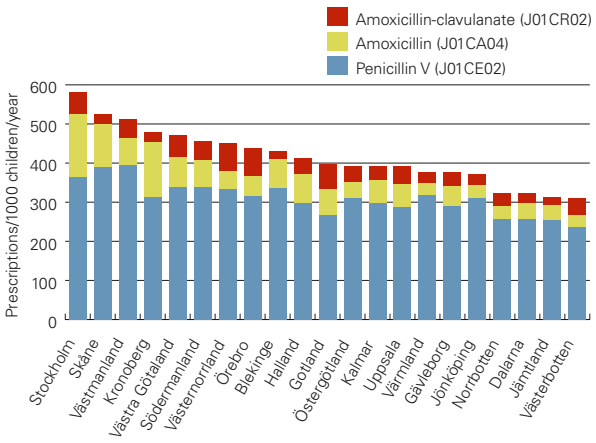


**FIGURE 3.1.6.** Penicillins to children aged 0–6 years, per county. Prescriptions/1000 children/year.

**Ulrica Dohnhammar, Gunilla Skoog**

### Hospital care

Hospital care includes data from all Swedish hospitals as well as data from those nursing homes that order their antibiotics through requisitions. Patients in some nursing homes get their antibiotics through prescriptions and in those cases data are included in primary health care data, presented in the previous section. The analysis of hospital care data is thus complicated as the number of nursing homes using requisitions vary over the years and between counties.

In this section we also present data from local data sources of antibiotic treatment in hospitals, i.e. nursing homes excluded.

The use of antibiotics in hospital care has continuously increased since the end of the 1990s. This trend was broken 2008. About 10% of the total antibiotic use is within hospital care. In Table 3.1.3. the antibiotic use within hospital care, with and without methenamine, is listed.

**TABLE 3.1.3.** Antibiotic use in hospital care 2000-2008, DDD/1000/inhabitants/day.

| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|
| J01 excl methenamine | 1.26 | 1.26 | 1.27 | 1.33 | 1.37 | 1.43 | 1.50 | 1.55 | 1.52 |
| Methenamine | 0.03 | 0.03 | 0.03 | 0.05 | 0.07 | 0.07 | 0.07 | 0.07 | 0.05 |
| Total J01 | 1.30 | 1.29 | 1.30 | 1.38 | 1.44 | 1.50 | 1.57 | 1.62 | 1.57 |

Figure 3.1.7. shows all classes of antibiotics used in hospital care during the last three years. The most pronounced increases are seen in the various types of penicillin. Broad spectrum antibiotics, such as cephalosporins and fluoroquinolones are decreasing. This change towards less broad spectrum and more narrow spectrum antibiotics is desirable and has been promoted by the Strama hospital care group.

Moreover, new recommendations for the treatment of uncomplicated community acquired pneumonia were published by the Swedish Society of Infectious Diseases a few years ago. Beta-lactamase sensitive penicillins were suggested as first choice and the use of cephalosporins should be reduced. These are possible explanations of the decrease in cephalosporins and increase in beta-lactamase sensitive penicillins. Stramas point prevalence studies, performed in 2003, 2004, 2006 and 2008, confirm that the use of cephalosporins for the treatment of uncomplicated community acquired pneumonia has decreased considerably.

Cephalosporins have traditionally been used extensively within Swedish hospital care, in particular cefuroxime. In 2007 cephalosporins represented 15% of total DDD per 1000 inhabitants and in 2008 this proportion had decreased to 13%. The decrease in DDD is partially a result of the shift from cefuroxime to cefotaxime since the prescribed daily doses, PDD, in Sweden do not correspond to the WHO definition of DDD. The most commonly used PDD in Sweden for cefuroxime is 4.5g (WHO 3g) and for cefotaxime 3g (WHO 4g).

The increased use of tetracyclines was commented in Swedres 2007. The high use in 2007 seems to have diminished but the reason for this is unclear.

The increase in sales of beta-lactamase resistant penicillins could be a result of changed dosage recommendations, from twice to three times daily.

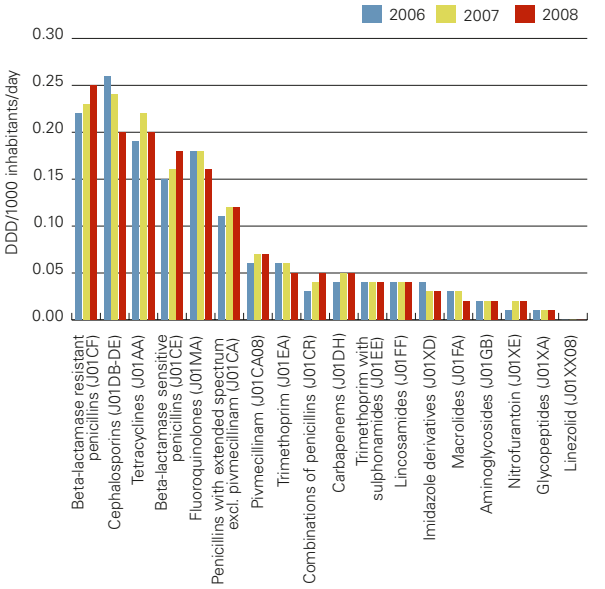


**FIGURE 3.1.7.** Antibiotics in hospital care 2006–2008, DDD/1000/day.

An increasing number of infections involving ESBL-producing bacteria may be another reason for the lower use of cephalosporins. Stramas proposed action plan "ESBL resistance in enteric bacteria" recommends a reduction in cephalosporins in favour of penicillins (http://en.strama.se/dyn//,95,15.html). Figure 3.1.8. shows the use of cephalosporins and the possible alternatives such as narrow spectrum penicillin, carbapenems, piperacillin/tazobactam and aminoglycosides. There has been an obvious reduction in the use of cephalosporins during the last two years. Meanwhile the use of beta-lactamase sensitive penicillins and piperacillin/tazobactam has increased. Part of the increase of the former may be a result of changed dosage recommendations. Also the use of carbapenems seems to increase over the last years.

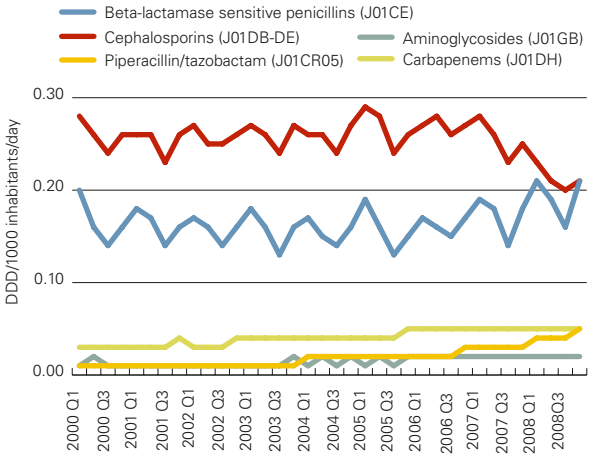


**FIGURE 3.1.8.** The use of some antibiotic groups within hospital care, per quarter 2000–2008, DDD/1000/day.

The use in all counties of cephalosporins and possible alternatives is shown in Figure 3.1.9. These data represent only hospital use, nursing homes are excluded. The proportion between cephalosporins and beta-lactamase sensitive penicillins varies considerably within Sweden. Perhaps this is an effect of campaigns and activities in certain counties, conducted by local Strama-groups and drug committees. Carbapenems and piperacillin/tazobactam still comprise a small portion of the total antibiotic use in hospital care in most counties.

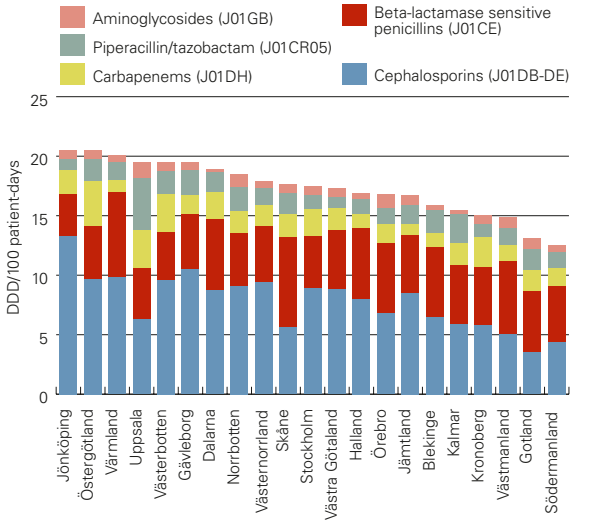


**FIGURE 3.1.9.**. The use of some antibiotic groups within Swedish hospitals, all counties 2008 (denominator data from 2007), DDD/100-patient days.

Table 3.1.4. and 3.1.5. show antibiotic use in relation to number of admissions and number of patient days in hospital somatic care during 2006–2008. Please pay attention to that comparable tables in previous Swedres reports also partly include data from nursing homes.

**TABLE 3.1.4.** Antibiotics in Swedish hospitals 2006-2008, DDD/100 admissions within somatic care.

| | 2006 | 2007 | 2008* |
|---|---|---|---|
| Tetracyclines (J01AA) | 28.8 | 29.9 | 26.5 |
| Penicillins with extended spectrum (J01CA) | 26.2 | 27.1 | 28.3 |
| Beta-lactamase sensitive penicillins (J01CE) | 24.2 | 25.2 | 30.1 |
| Beta-lactamase resistant penicillins (J01CF) | 40.3 | 41.8 | 46.5 |
| Combinations of penicillins (J01CR) | 6.7 | 8.2 | 11.0 |
| Cephalosporins (J01DB-DE) | 57.2 | 53.9 | 45.9 |
| Carbapenems (J01DH) | 10.6 | 10.8 | 11.3 |
| Trimethoprim (J01EA) | 6.7 | 6.3 | 5.8 |
| Trimethoprim with sulphonamides (J01EE) | 7.7 | 8.3 | 9.1 |
| Macrolides (J01FA) | 5.4 | 5.3 | 4.7 |
| Lincosamides (J01FF) | 7.8 | 8.0 | 8.2 |
| Aminoglycosides (J01GB) | 3.8 | 3.8 | 4.3 |
| Fluoroquinolones (J01MA) | 33.9 | 32.5 | 29.5 |
| Glycopeptides (J01XA) | 3.4 | 3.4 | 3.4 |
| Imidazole derivatives (J01XD) | 8.4 | 7.9 | 7.5 |
| Methenamine (J01XX05) | 4.7 | 4.5 | 3.8 |
| Linezolid (J01XX08) | 0.3 | 0.3 | 0.3 |
| All agents (J01) | 278.4 | 279.8 | 278.9 |

*Denominator data from 2007.

**TABLE 3.1.5.** Antibiotics in Swedish hospitals 2006-2008, DDD/100 patient-days within somatic care.

| | 2006 | 2007 | 2008* |
|---|---|---|---|
| Tetracyclines (J01AA) | 5.5 | 5.7 | 5.1 |
| Penicillins with extended spectrum (J01CA) | 5.0 | 5.2 | 5.4 |
| Beta-lactamase sensitive penicillins (J01CE) | 4.6 | 4.8 | 5.8 |
| Beta-lactamase resistant penicillins (J01CF) | 7.7 | 8.0 | 8.9 |
| Combinations of penicillins (J01CR) | 1.3 | 1.6 | 2.1 |
| Cephalosporins (J01DB-DE) | 10.9 | 10.4 | 8.8 |
| Carbapenems (J01DH) | 2.0 | 2.1 | 2.2 |
| Trimethoprim (J01EA) | 1.3 | 1.2 | 1.1 |
| Trimethoprim with sulphonamides (J01EE) | 1.5 | 1.6 | 1.8 |
| Macrolides (J01FA) | 1.0 | 1.0 | 0.9 |
| Lincosamides (J01FF) | 1.5 | 1.5 | 1.6 |
| Aminoglycosides (J01GB) | 0.7 | 0.7 | 0.8 |
| Fluoroquinolones (J01MA) | 6.5 | 6.3 | 5.7 |
| Glycopeptides (J01XA) | 0.6 | 0.6 | 0.7 |
| Imidazole derivatives (J01XD) | 1.6 | 1.5 | 1.4 |
| Methenamine (J01XX05) | 0.9 | 0.9 | 0.7 |
| Linezolid (J01XX08) | 0.1 | 0.1 | 0.1 |
| All agents (J01) | 53.2 | 53.8 | 53.6 |

*Denominator data from 2007.

**Gunilla Skoog, Ulrica Dohnhammar**

### Adverse reactions related to antibiotic use

Spontaneously reported drug-related adverse reactions are continuously entered into SWEDIS, a national database administered by the Swedish Medical Products Agency (Läkemedelsverket). The reports originate from health care professionals. The antibiotic related adverse reactions in the last five years (2004–2008) were analysed for various groups of agents. The following organ system groups received most reports related to the use of systemic antibiotic drugs (J01): skin- and subcutaneous tissue disorders (n=485), hepatobiliary disorders (n=204), gastrointestinal disorders (n=200), general disorders (n=151), musculoskeletal disorders (n=143), blood disorders (n=129), and neurological reactions (n=125). The majority of the reports (62%) concern female patients.

The 10 antibiotic substances most commonly associated with adverse reactions, in the last 5 years unadjusted for consumption and regardless of the cause of the report are presented in Table 3.1.6. A newcomer in this top-ten-list is cefuroxime.

TABLE 3.1.6. Most reported antibiotic agents to the Swedish Medical Products Agency 2004–2008

| Antibiotic | Total number of ADR reports 2004 to 2008 | Number of 'serious' reports | Number of fatal cases (causal relationship possible) |
|---|---|---|---|
| Ciprofloxacin | 210 | 111 | 3 |
| Flucloxacillin | 114 | 76 | 3 |
| Nitrofurantoin | 105 | 53 | 1 |
| Clindamycin | 86 | 36 | 1 |
| Fenoxymethylpenicillin | 82 | 37 | 0 |
| Trimethoprim | 81 | 35 | 0 |
| Doxycylin | 71 | 26 | 3 |
| Sulphamethoxaxol + trimethoprim | 66 | 41 | 2 |
| Cefuroxime | 55 | 30 | 1 |
| Norfloxacin | 45 | 20 | 2 |

We have previously reported that amended treatment recommendations resulted in changed prescription patterns for uncomplicated urinary tract infections. There was a decreased consumption of fluoroquinolones which was reflected in a decrease in reported adverse events. In recent years the reporting rate has been stable. For nitrofurantoin which was increasingly prescribed a slight corresponding increase in the reporting of adverse reactions was noted. Due to the low number of reports and to the fact that the data are based on spontaneous reporting, no clear conclusions can be made regarding these trends, Table 3.1.7.

TABLE 3.1.7. Number of most frequently spontaneously reported adverse events for fluoroquinolones and nitrofurantoin, during the period 2004–2008

| | 2004 | 2005 | 2006 | 2007 | 2008 | 2004-2008 |
|---|---|---|---|---|---|---|
| **Fluoroquinolones** | | | | | | |
| Total no of reports | 69 | 56 | 45 | 55 | 35 | 260 |
| Number of reactions | | | | | | |
| Musculoskeletal | 34 | 24 | 19 | 22 | 9 | 108 |
| endinitis | 15 | 13 | 11 | 10 | 2 | 51 |
| tendon rupture | 12 | 5 | 3 | 6 | 5 | 31 |
| Skin- and subcutaneous tissue | 7 | 11 | 6 | 17 | 4 | 45 |
| Psychiatric disorders | 4 | 10 | 8 | 4 | 2 | 28 |
| **Nitrofurantoin** | | | | | | |
| Total no of reports | 24 | 15 | 20 | 22 | 24 | 105 |
| Number of reactions | | | | | | |
| Respiratory system | 10 | 8 | 12 | 3 | 7 | 40 |
| dyspnoea | 3 | 2 | 4 | 0 | 1 | 10 |
| interstitial pneumonia | 2 | 2 | 2 | 2 | 2 | 10 |
| pulmonary fibrosis | 1 | 0 | 2 | 0 | 0 | 3 |
| Skin- and subcutaneous tissue | 7 | 1 | 7 | 8 | 7 | 30 |
| General disorders | 11 | 7 | 8 | 7 | 6 | 39 |
| Fever | 6 | 6 | 4 | 3 | 4 | 23 |

**Charlotta Edlund, Bengt Lindeskog**

## 3.2. Use of antifungals

### Hospital care

The total use of antifungals administered systemically in hospital care remained basically unchanged from 2007 to 2008 (from 52.2 to 52.8 DDD/106/day). However, two developments representing somewhat of a trend shift in the use of systemic antimycotics in Sweden, namely an increase in the utilization of amphotericin B and a decrease in fluconazole, stand out during 2008, Figure 3.2.1. The use of amphotericin B, that steadily decreased from 8.3 to 2.2 DDD/106/day in the period 2001–2007, showed a 35% increase in 2008. Amphotericin B is a macrolide polyene with excellent antifungal activity against most fungi that cause human disease. It is primarily indicated for the treatment of aspergillosis and other invasive mold infections, cryptococcal meningitis, and infections caused by endemic dimorphic fungi. Adverse effects of amphotericin B are many and often severe. Nephrotoxicity, electrolyte imbalance and hepatotoxicity are most common. Lipid-based formulations of amphotericin B such as liposome conjugates have been developed to reduce systemic toxicity and improve tolerability to higher doses. With a superior safety profile, the second-generation triazole voriconazole has increasingly being used as the first choice drug for the treatment of invasive aspergillosis since 2002, when its efficacy was established. Other approved indications for voriconazole include severe infections caused by *Scedosporium* spp., *Fusarium* spp. and fluconazole-resistant *Candida* spp. Recent recognition of frequent clinical *Candida glabrata* isolates with decreased susceptibility to voriconazole and the widespread occurrence of cross-resistance between triazoles nevertheless argue against the use of voriconazole for the treatment of infections caused by *Candida* species with innate resistance to azole compounds. After peaking in 2005–2006, the total use of voriconazole has decreased by 23% in the last two years.

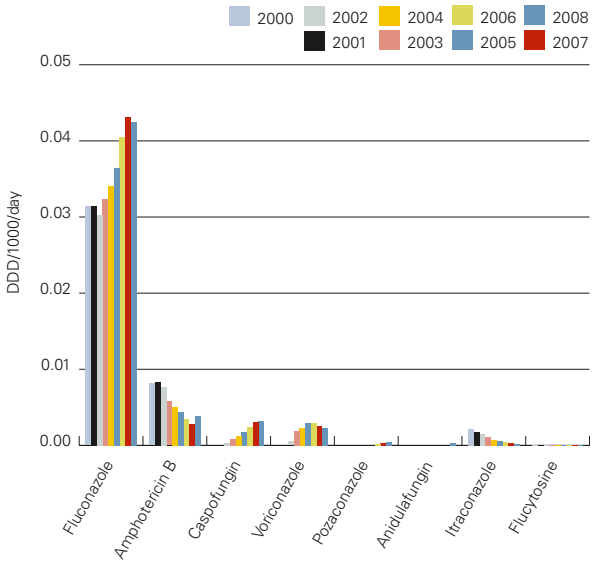


FIGURE 3.2.1. Use of antifungals in hospital care, 2000–2008.

The reduction of the in-patient use of fluconazole during 2008 was fairly small (2%) but stands in contrast to the steep increase observed in the period 2002–2007, Figure 3.2.1. Despite this trend shift, fluconazole still accounted for 80% of the total use of antifungals in hospitalized patients during 2008. Fluconazole is a fungistatic agent indicated for the treatment of candidosis in non-neutropenic patients as well as cryptococcal meningitis, and prophylactically against invasive Candida infections. In later years, awareness has increased in regards to the risks associated with the use of fluconazole to treat C. non-albicans infections, in particular those caused by azole-resistant species such as *C. glabrata* and *C. krusei* that in Sweden represent 20–25% of all candidemia episodes. The echinocandin antifungal caspofungin is increasingly being used, since its introduction in 2002, for the treatment of invasive candidiasis and as salvage therapy for invasive aspergillosis. Caspofungin, as other echinocandins, disrupt glucan synthesis in the fungal cell wall by inhibiting the enzyme β(1,3)-D-glucan synthase. It has a well demonstrated activity against azole-resistant Candida species and a relatively benign safety profile. Two new echinocandin drugs, anidulafungin and micafungin, have been recently licensed in Sweden. These developments underscore the need for continued surveillance of antifungal resistance and for diagnostic methods that make possible the early application of pathogen-specific antifungal therapy.

### Primary health care

In 2008, as in previous years, more than 95% of all antifungal prescriptions took place in primary health care. Formulations of two agents, miconazole and fluconazole, accounted for nearly half of the total. The imidazole miconazole combined with hydrocortisone is indicated for topical use against dermatophyte infections, Trychophyton-, Epidermophyton- and Microsporum-species, and for application on mucosal membranes against oral and vaginal thrush caused by Candida spp. Fluconazole, administered orally, is indicated against vaginal and other mucocutaneal Candida infections. Measured as DDD/1000/day, the antifungal most sold over-the-counter was ketoconazole, an imidazol available in shampoo formulations used for body wash against seborrhoeic dermatitis caused by Malassezia yeasts. Azole agents for gynecological use constitute the antifungal group most commonly sold (46% of total sales) over-the-counter.

**Victor Fernandez**

# 4. Antimicrobial resistance

**IN SWEDEN**, testing of clinical isolates for antibiotic susceptibility is routinely performed using standardized methods (Appendix 4). The first finding of a methicillin resistant *Staphylococcus aureus* (MRSA), a pneumococcus with decreased susceptibility to penicillin G (PNSP, MIC >0,5 mg/L), a vancomycin resistant *Enterococcus faecalis* or *faecium* (VRE) or an ESBL-producing *Enterobacteriaceae* are notifiable according to the Communicable Disease Act, regardless of whether it was judged to be a clinical infection or colonisation without infection. MRSA, PNSP and VRE require laboratory as well as clinical notification, whereas ESBL require laboratory notification only.

In addition to these mandatory notifications a national programme for the surveillance of resistance was initiated in 1994 (Appendix 5). Well-characterised data on resistance in many bacterial pathogens are available since several years both at regional and national level.

Twenty-one of the Swedish laboratories, covering approximately 75% of the population, report susceptibility data on invasive isolates of seven defined bacterial species to the European Antimicrobial Resistance Surveillance system, EARSS. Eleven of these laboratories also deliver data from all positive blood cultures, in total 11.115 isolates in 2008. (Appendix 5).

One of the cornerstones in the battle against antibacterial resistance in Sweden has been the early identification of cases via screening programmes and contact-tracing around cases with notifiable resistance. The annual numbers of samples specifically registered to be analysed for screening for (multi-) resistant bacteria, MRB, is shown in Figure 4.1. Even if the screening programmes and criteria for registering analyses under this heading may vary between laboratories, they are fairly constant within each laboratory. In 2008 27 of 31 laboratories provided data on MRB-screening.

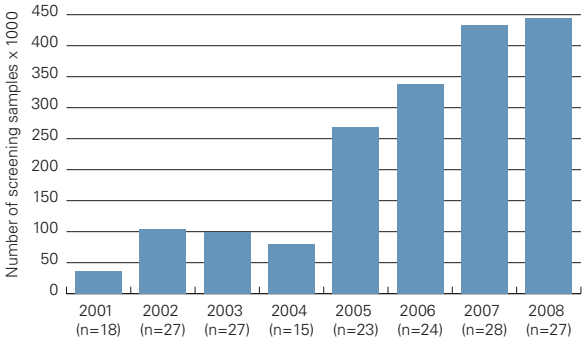


FIGURE 4.1. Annual number of recorded screening samples for multiresistant bacteria, 2001–2008. n refers to the number of participating laboratories

## *Staphylococcus aureus*

### Background

Following an extensive outbreak in Western Sweden and increasing alertness responding to the situation seen in other European countries MRSA was made mandatory notifiable in the year 2000. Compared to many other European countries, where the proportion of MRSA exceeds 25% of invasive *S. aureus* isolates, the prevalence of MRSA among such isolates is still below 1% in Sweden (see details on EARSS data in the following text). Infection control programmes have been developed and implemented locally under supervision by the County Department for Communicable Disease Control (CDCDC) and infection control teams. These programmes are based on early case-finding through extensive screening of patients with risk factors and contact tracing combined with infection control measures such as isolation of MRSA positive cases and intensive campaigns on basic hygiene precautions.

### Notifications of MRSA according to the Communicable Disease Act

The following presentation is based on data collected in the web-based notification system "SmiNet 2" as recorded at the county level. During the last three years an active effort has been made to improve the quality of the data and to collect missing data. The notifications have been reviewed and complemented with available relevant epidemiologic information from investigations around each case, in collaboration with the CDCDCs. A total of 1307 cases of MRSA were notified in 2008, an increase with 16% compared with the 1128 cases 2007, Figure 4.2.

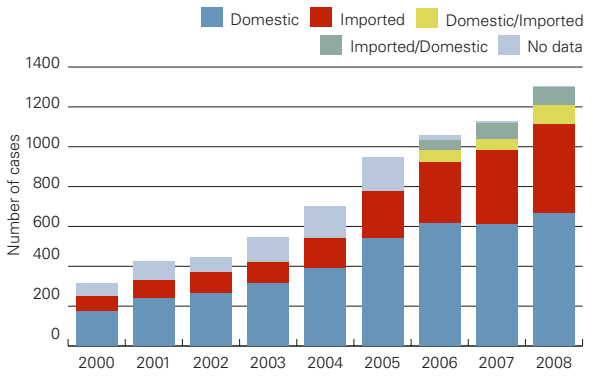


FIGURE 4.2. Number of MRSA notified annually by country of infection, Sweden 2000–2008. "Domestic/Imported" and "Imported/Domestic" indicate several mentioned countries of infection with the most likely mentioned first.

In 2008, six of the Swedish counties had a higher incidence than the total national incidence of 14.1 cases/100 000 inhabitants, Table 4.1.

**TABLE 4.1.** MRSA notified in 2000-2008 by county according to the Communicable Disease Act

| | 2000 | | 2001 | | 2002 | | 2003 | | 2004 | | 2005 | | 2006 | | 2007 | | 2008 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **County** | **No** | **Inc*** | **No** | **Inc*** | **No** | **Inc*** | **No** | **Inc*** | **No** | **Inc*** | **No** | **Inc*** | **No** | **Inc*** | **No** | **Inc*** | **No** | **Inc*** |
| Stockholm | 97 | 5.3 | 166 | 9.0 | 205 | 11.1 | 228 | 12.3 | 277 | 14.8 | 315 | 17.1 | 356 | 18.9 | 351 | 18.0 | 342 | 17.3 |
| Uppsala | 19 | 6.5 | 17 | 5.7 | 10 | 3.3 | 12 | 4.0 | 26 | 8.6 | 28 | 9.2 | 24 | 7.9 | 33 | 10.2 | 40 | 12.2 |
| Södermanland | 2 | 0.8 | 1 | 0.4 | 4 | 1.5 | 2 | 0.8 | 8 | 3.1 | 11 | 3.8 | 9 | 3.4 | 26 | 9.8 | 20 | 7.5 |
| Östergötland | 2 | 0.5 | 7 | 1.7 | 7 | 1.7 | 14 | 3.4 | 14 | 3.4 | 101 | 24.3 | 48 | 11.5 | 49 | 11.6 | 43 | 10.2 |
| Jönköping | 7 | 2.1 | 6 | 1.5 | 5 | 1.5 | 24 | 7.3 | 14 | 4.3 | 40 | 12.1 | 44 | 13.0 | 17 | 5.1 | 20 | 6.0 |
| Kronoberg | 1 | 0.6 | 0 | 0.0 | 4 | 2.3 | 5 | 2.8 | 17 | 9.5 | 11 | 6.1 | 14 | 7.8 | 13 | 7.2 | 19 | 10.4 |
| Kalmar | 3 | 1.3 | 5 | 0.9 | 5 | 2.1 | 6 | 2.6 | 16 | 6.8 | 23 | 9.7 | 26 | 11.1 | 36 | 15.4 | 29 | 12.4 |
| Gotland | 1 | 1.8 | 10 | 17.5 | 3 | 5.3 | 2 | 3.5 | 1 | 1.7 | 10 | 17.3 | 4 | 6.9 | 8 | 14.0 | 6 | 10.5 |
| Blekinge | 7 | 4.7 | 1 | 0.7 | 3 | 2.0 | 2 | 1.3 | 3 | 2.0 | 9 | 5.9 | 4 | 2.7 | 16 | 10.5 | 10 | 6.6 |
| Skåne | 22 | 1.9 | 76 | 6.7 | 68 | 5.9 | 104 | 9.1 | 128 | 11.3 | 162 | 13.9 | 179 | 15.5 | 166 | 13.8 | 273 | 22.5 |
| Halland | 10 | 3.6 | 26 | 9.4 | 13 | 4.7 | 13 | 4.6 | 9 | 3.2 | 21 | 7.4 | 23 | 8.1 | 18 | 6.2 | 16 | 5.5 |
| Västra Götaland | 114 | 7.6 | 56 | 3.7 | 48 | 3.2 | 63 | 4.2 | 118 | 7.8 | 125 | 8.1 | 177 | 11.6 | 178 | 11.5 | 245 | 15.7 |
| Värmland | 9 | 3.3 | 7 | 2.6 | 6 | 2.2 | 11 | 4.0 | 18 | 6.6 | 9 | 3.2 | 13 | 4.8 | 32 | 11.7 | 22 | 8.0 |
| Örebro | 8 | 2.9 | 7 | 2.6 | 16 | 5.9 | 8 | 2.9 | 11 | 4.0 | 16 | 5.8 | 35 | 12.8 | 25 | 9.1 | 46 | 16.6 |
| Västmanland | 3 | 1.2 | 8 | 3.1 | 6 | 2.3 | 11 | 4.2 | 12 | 4.6 | 35 | 13.4 | 48 | 18.4 | 54 | 21.7 | 23 | 9.2 |
| Dalarna | 0 | 0.0 | 5 | 1.8 | 1 | 0.4 | 2 | 0.7 | 3 | 1.1 | 6 | 2.1 | 11 | 4.0 | 15 | 5.4 | 23 | 8.3 |
| Gävleborg | 2 | 0.7 | 1 | 0.4 | 12 | 4.3 | 5 | 1.8 | 5 | 1.8 | 24 | 8.6 | 17 | 6.1 | 12 | 4.4 | 26 | 9.4 |
| Västernorrland | 14 | 5.7 | 12 | 4.9 | 7 | 2.9 | 10 | 4.1 | 5 | 2.0 | 4 | 1.6 | 9 | 3.7 | 22 | 9.0 | 35 | 14.4 |
| Jämtland | 0 | 0.0 | 0 | 0.0 | 2 | 1.6 | 5 | 3.9 | 1 | 0.8 | 8 | 6.2 | 4 | 3.1 | 24 | 18.9 | 31 | 24.4 |
| Västerbotten | 3 | 1.2 | 17 | 6.7 | 10 | 3.9 | 13 | 5.1 | 16 | 6.2 | 10 | 3.8 | 7 | 2.7 | 23 | 8.9 | 22 | 8.5 |
| Norrbotten | 3 | 1.2 | 5 | 2.0 | 7 | 2.8 | 9 | 3.6 | 7 | 2.8 | 8 | 3.1 | 5 | 2.0 | 10 | 4.4 | 16 | 6.4 |
| Total | 327 | 3.7 | 429 | 4.8 | 442 | 4.9 | 549 | 6.1 | 709 | 7.8 | 975 | 10.8 | 1057 | 11.7 | 1128 | 12.3 | 1307 | 14.1 |

* = Incidence (cases/100 000 inhabitants)

During 2008, 51% (n=665) of all reported MRSA cases were domestically acquired and 34% (n=450) were acquired abroad. Thailand (39 cases), Iraq (31 cases), the Philippines (29 cases), India (28 cases) and USA (20 cases) made up the five most common countries for imported MRSA infection during 2008. In 14% Sweden and at least one more country was mentioned as possible countries for acquisition of MRSA. These cases were divided between "domestic/imported or "imported/domestic" depending on the order of listing the countries in the clinical notification. The country for acquisition was reported as "unknown" in seven cases and in three cases no country of acquisition was listed.

The increase in the number of domestic cases in recent years has mainly occurred in the age groups below 50 years of age. Since mandatory reporting of MRSA started, the proportion of cases below the age of 50 has almost doubled, Figure 4.3.

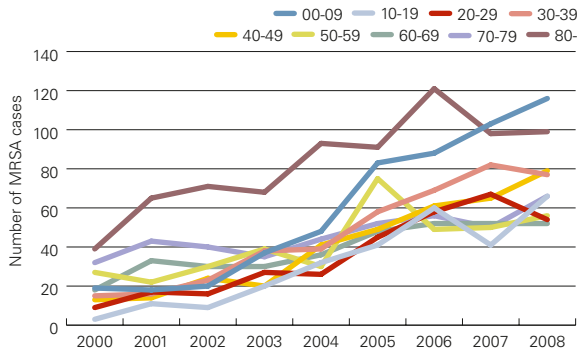


**FIGURE 4.3.** Age distribution of notified domestic cases of MRSA, Sweden 2000–2008.

Figure 4.4. shows that in 2008, 54% of the domestic and 64% of the imported cases were identified in targeted screening or contact tracing and 46% of the domestic and 35% of the imported cases presented with clinical symptoms. Fifteen newly discovered cases had invasive MRSA infection.

Even if aggregated data on the total number of clinical cultures are not available at present, it is reasonable to assume that the number of cultures have increased as culturing even of furuncula and minor blisters is widely encouraged in community care. Thus, wider indications for culturing in combination with spread of PVL (Panton-Valentine Leucocidin)-positive MRSA in the community may explain the increase in the proportion of clinical isolates during recent years.

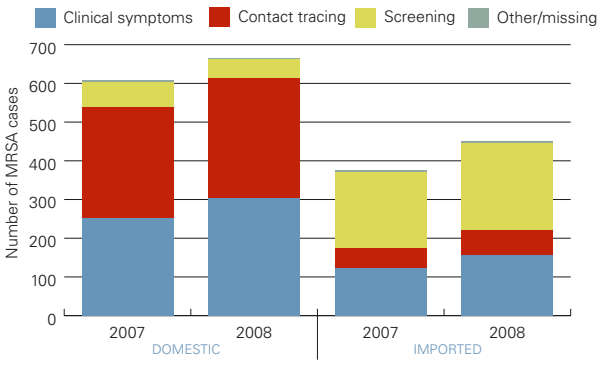


**FIGURE 4.4.** The reason for detection of domestic and imported MRSA cases in Sweden 2007–2008.

Epidemiological classification of the acquisition of MRSA is based on information in the clinical notifications and subsequent investigations at the local level, Figure 4.5.

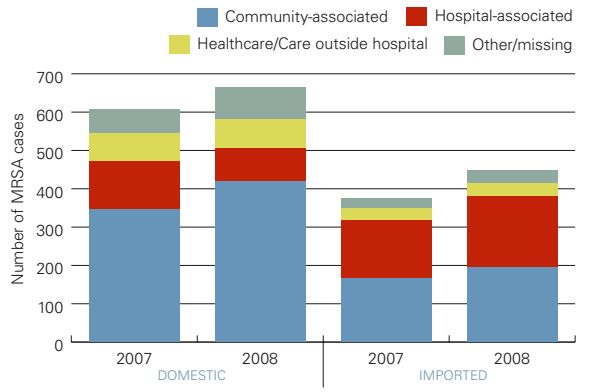


**FIGURE 4.5.** Epidemiological classification of the acquisition of domestic and imported MRSA, Sweden 2007–2008

Community associated infections dominated among domestic cases 2008 and comprised 63% (n=420) of all cases. This is an increase from 2007 and shows that MRSA in Sweden today is acquired primarily in the community. Also among the imported MRSA cases the proportion of community associated infections increased during 2008, representing 43% (n=194) of all cases.

Hospital associated MRSA was relatively more common in imported cases, 41% (n=186) as compared with 13% (n=85) among domestic cases. Among imported cases a similar proportion of hospital association was seen in 2007 and 2008, but for domestic cases the proportion of hospital associated MRSA in 2008 was lower than the 20% registered during 2006–2007.

In 14% of all 1307 notified MRSA cases several countries were mentioned (2–7 countries), and acquisition of MRSA in the community was stated for 70% of these cases.

During 2008 only minor outbreaks were reported from the Swedish healthcare system or from long-term care facilities for the elderly. These small outbreaks were reported from several counties. Despite the steady increase in domestic MRSA cases and reports of patients identified during hospitalisation, there is presently no Swedish region reporting secondary spread of MRSA in the hospitals. The diversity in MRSA types reported (see below) and the low numbers of multiresistant MRSA further suggest primarily community acquisition of MRSA in Sweden.

### Typing of MRSA

DNA-based methods have been used for typing of all MRSA isolates in Sweden since the year 2000. During 2000–2005 pulsed field gel electrophoresis (PFGE) was the standard method. It was replaced by spa-typing during 2006 which is now the primary typing method. spa-typing is based on sequencing of the polymorphic X-region of the *S. aureus* species-specific protein A gene, spa, and the Ridom StaphType® software is used for analysis.

The ten most common spa-types during 2008 were t002 (n=132), t008 (n=113), t044 (n=107), t019 (n=54), t032 (n=51), t127 (n=38), t437 (n=37), t024 (n=32), t015 (n=31), and t037 (n=30). Nine of these ten types were also found among the top-ten in 2007, the only change being that t690 had been replaced by t127 in 2008. The five most common of these types comprised more than one third, and all ten most common types comprised 50% of all cases. Spa-types found in connection with small hospital outbreaks were t002, t015 and t172.

In 2008 focus was on the zoonotic potential of MRSA and especially occurrence of the livestock associated MRSA belonging to clonal complex CC398 as reported from several European countries (see also SVARM 2008). In humans in Sweden 2008 only two cases of MRSA with spa-type t011 and one with t034 were found, both spa-types belonging to CC398.

As in 2007, isolates with spa-types t032, t037 and t015 were always negative for the PVL-toxin, whereas isolates with spa-type t044 were always positive. Among isolates of the other common spa-types both PVL-positive and –negative ones were found. In total, 445 (35%) of all tested isolates from 2008 were PVL-positive. This was in line with results from the last couple of years, when PVL-positive isolates have represented more than 30% of all MRSA cases. Among the PVL-positive isolates, those of spa type t044 were still most frequently found, followed in decreasing order by t008, t019, t437, t024, t002, t355 and t657.

### Antibiotic resistance in MRSA

All MRSA isolates were investigated with regard to resistance to antibiotics other than betalactam antibiotics, Table 4.2. In 2008 concomitant resistance to erythromycin, clin-

**TABLE 4.2.** Numbers and rates of resistance to indicated antibiotics among MRSA isolates 2000-2008

| Year/Antibiotic | Erythromycin | Clindamycin | Ciprofloxacin | Fusidic acid | Gentamicin | Mupirocin | Rifampicin |
|---|---|---|---|---|---|---|---|
| 2000 | 179 (55.9) | nt | 187 (58.4) | 74 (23.1) | 76 (23.8) | 8 (2.5) | 42 (13.1) |
| 2001 | 208 (50.5) | nt | 252 (61.2) | 89 (21.6) | 87 (21.1) | 30 (7.3) | 44 (10.7) |
| 2002 | 220 (50.3) | nt | 280 (64.1) | 128 (29.3) | 80 (18.3) | 48 (11) | 27 (6.2) |
| 2003 | 220 (40.4) | nt | 278 (51.1) | 156 (28.7) | 91 (16.7) | 47 (8.6) | 25 (4.6) |
| 2004 | 229 (33.3) | nt | 270 (39.3) | 135 (19.7) | 97 (14.1) | 24 (3.5) | 24 (3.5) |
| 2005 | 374 (39.2) | 326 (34.1) | 318 (33.3) | 155 (16.2) | 183 (19.2) | 21 (2.2) | 34 (3.6) |
| 2006 | 371 (37.1) | 308 (30.8) | 322 (32.2) | 162 (16.2) | 140 (14.0) | 20 (2.0) | 40 (4.0) |
| 2007 | 433 (39.6) | 343 (31.4) | 401 (36.7) | 159 (14.6) | 207 (19.0) | 20 (1.8) | 47 (4.3) |
| 2008 | 425 (33.7) | 317 (25.2) | 338 (26.8) | 155 (12.3) | 152 (12.1) | 18 (1.4) | 20 (1.6) |

damycin and ciprofloxaxin was still most frequently found, but the frequencies have slowly been decreasing since 2004. Approximately 75% of the macrolide resistant isolates had the $MLS_B$ type of resistance, indicated by simultaneous resistance to clindamycin (inducibly or constitutively expressed *erm* genes). Resistance to fusidic acid, which is typical for t044 isolates but also found in other types, became less frequent (<20%) since 2004. Aminoglycoside resistance (gentamicin tested) was found in 15–20% of isolates through the years but was less frequent in 2008. Resistance to mupirocin or rifampicin was found in less than 4% of isolates during the last five years.

The decrease in the proportion of concomitant antibiotic resistance in MRSA probably reflects the transition from hospital-acquired to community acquired strains.

### Annual Resistance Surveillance and Quality Control (RSQC) programme

*Staphylococcus aureus* from wound infections was included in the annual RSQC programme 2001 (Appendix 5). Twenty-nine laboratories regularly provide data on consecutive isolates using the disk diffusion method for cefoxitin (from 2004 used as screening disk for detection of MRSA), clindamycin, fusidic acid, aminoglycoside (gentamicin or tobramycin) and vancomycin. Erythromycin (group representative for macrolide antibiotics) and a fluoroquinolone (ciprofloxacin or norfloxacin) have also been tested since 2004. The average resistance rates, as retrieved from ResNet, are shown in Figure 4.6.

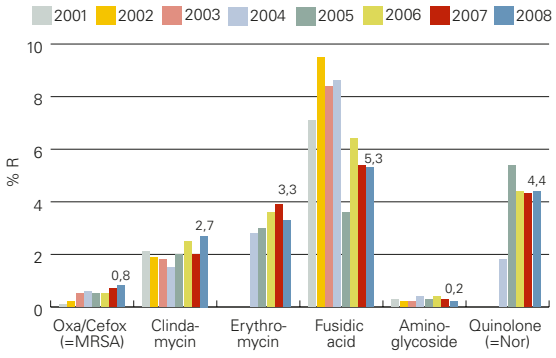


**FIGURE 4.6.** Resistance rates for *Staphylococcus aureus* 2001–2008 (data from the annual RSQC programme, approximately 3000 isolates per year). In 2005 resistance rates were recorded in *S.aureus* isolated from wounds and secretions from elderly (> 65 years) people only,

The frequency of MRSA in wound infections (cefoxitin used as test compound) increased in 2008 but the level remained below 1%. The resistance rate for erythromycin (3.3%) was only slightly higher than that for clindamycin (2.7%). This situation was different from previous years and indicated a shift with an increased prevalence of *erm* genes (constitutively or inducibly expressed) among the clinical isolates. The level of fusidic acid resistance was stable around 5%. The lower level of resistance in 2005 indicates that the epidemic fusidic acid resistant strain causing impetigo in children was not as prevalent in the elderly population. Almost no resistance to aminoglycosides was seen in bacteria from wound infections. Fluoroquinolone resistance was stable at 4–5%.

### Data on invasive isolates reported to EARSS

In 2008, only 0.7% of the invasive *S. aureus* isolates were MRSA (identified by the cefoxitin screen disk test and confirmed by detection of the *mecA* gene). This low level has remained during the eight years of mandatory reporting, indicating that infection control measures to prevent MRSA from spreading in the hospital environment have been successful. Twelve spa-types were identified among the 16 newly discovered invasive MRSA isolates in 2008.

**TABLE 4.3.** *Staphylococcus aureus* susceptibility results (number of strains and percentage) in blood isolates by the disk diffusion method and by confirmation of the *mecA* gene. Data reported from SMI to EARSS.

| Year | S | I | R |
|---|---|---|---|
| 2001 | 1618 (99.1%) | 0 | 14 (0.9%) |
| 2002 | 1830 (99.4%) | 0 | 12 (0.6%) |
| 2003 | 1839 (99.1%) | 0 | 16 (0.9%) |
| 2004 | 1891 (99.3%) | 0 | 14 (0.7%) |
| 2005 | 1756 (99%) | 0 | 18 (1.0%) |
| 2006 | 1849 (99.1%) | 0 | 16 (0.9%) |
| 2007 | 2162 (99.5%) | 0 | 11 (0.5%) |
| 2008 | 2408 (99.3%) | 0 | 16 (0.7%) |

**Tomas Söderblom, Johan Struwe, Sara Hæggman, Gunnar Kahlmeter, Barbro Olsson-Liljequist**

## *Streptococcus pneumoniae*

### Background

*S. pneumoniae* with reduced susceptibility to penicillin, MIC ≥0.5 mg/L (PNSP) became notifiable according to the Communicable Disease Act in 1996 after reports of increasing resistance in southern Sweden. In addition invasive infections with *S. pneumoniae*, regardless of resistance, became notifiable in 2004.

### Notifications according to the Communicable Disease Act

In 2008 there were 565 notifications of PNSP in Sweden, Figure 4.7, a decrease with 16% compared with 2007. Sixty-four percent of the cases were reported to be infected domestically and 12% in a foreign country. In the remaining 135 cases no country for acquisition was given.

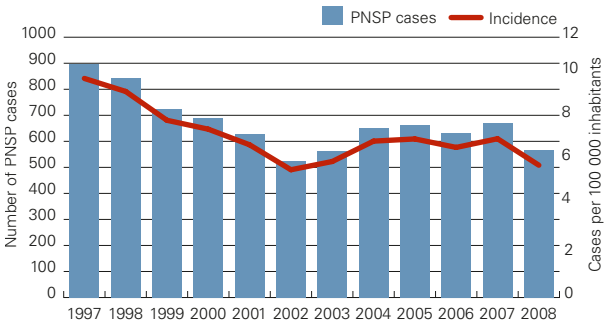


**FIGURE 4.7.** Number of cases of *S. pneumoniae* with reduced susceptibility to penicillin, MIC ≥0.5 mg/L (PNSP in Sweden 1997–2008.

The PNSP incidence in Sweden was 6.1 cases per 100 000 inhabitants 2008. Previous analysis has indicated that the declining incidence from 1997 to 2002 was related to a concurrent decrease in nasopharyngeal culturing propensity. The majority of PNSP cases, independent of year observed, are found in the age group 0–4 years, Figure 4.8. Compared with 2007 the decrease in number of reported cases primarily is in this age-group. There is no difference in the proportion of the reported cases with regard to sex.

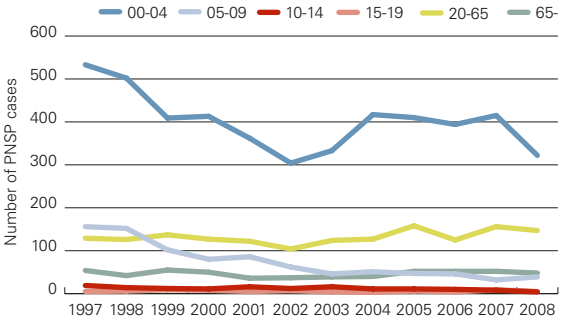


FIGURE 4.8. Age-group distribution among all cases reported with PNSP in Sweden 1997–2008.

PNSP were reported from all 21 counties with Stockholm (184 cases) and Skåne (216 cases) accounting for 71% of all notifications. Remaining counties report 1–32 cases each. Due to regional differences in general culturing propensity, case finding intensity as well as presence of targeted screening programme comparison of regional incidence rates is difficult.

The majority, 82% of all notifications of the PNSP, are found in cultures from nasopharynx. 19 cases in 2008 were reported to have invasive PNSP infections, 18 cases in blood and one in cerebrospinal fluid. For four of these cases the serotype were reported, two had serotype 19, one serotype 14 and one serotype 9. The most commonly found serotypes among all PNSP were, in decreasing order, 19F, 9V, 14, 6B, and 23F.

### Annual Resistance Surveillance and Quality Control (RSQC) programme

Pneumococci have been included since 1994 in the surveys by Swedish laboratories. These isolates are mainly derived from nasopharyngeal cultures. Approximately 3000 consecutive isolates per year from all the clinical laboratories have been tested for susceptibility to penicillin (by means of oxacillin 1 ug screen disk), erythromycin, tetracycline, and trimethoprim-sulfamethoxazol, using the disk diffusion method. The national summary of the results is shown in Figure 4.9. For all four tested antibiotics the rates of resistance are back to the levels noted in 2006, and the decrease seen in 2007 seems to have been only temporary.

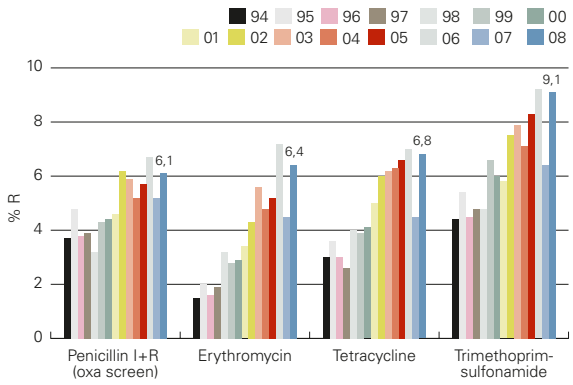


FIGURE 4.9. Resistance rates for *Streptococcus pneumoniae* 1994–2008 (data from the annual RSQC programme, approximately 3000 isolates per year).

### Data on invasive isolates reported to EARSS

The Swedish data on susceptibility to penicillin and erythromycin for 2001–2008 are given in Table 4.4. Levels of resistance are lower among invasive isolates than in the nasopharyngeal isolates from the RSQC programme. Also, there has been no trend of increasing resistance among invasive isolates, neither for penicillin nor erythromycin, contrary to the nasopharyngeal isolates.

TABLE 4.4. Invasive isolates of *Streptococcus pneumoniae* reported to EARSS.

| Penicillin * (I+R = PNSP) | | | | |
|---|---|---|---|---|
| **Year** | **S%** | **I%** | **R%** | **Total** |
| 2001 | 97.2 | 2.3 | 0.5 | 788 |
| 2002 | 97.5 | 2.4 | 0.1 | 783 |
| 2003 | 95.0 | 5.0 | 0 | 920 |
| 2004 | 96.8 | 2.8 | 0.4 | 955 |
| 2005 | 96.4 | 3.1 | 0.5 | 1017 |
| 2006 | 97.9 | 2.1 | 0 | 936 |
| 2007 | 97.1 | 2.9 | 0.1 | 1029 |
| **2008** | 98.0 | 1.6 | 0.4 | 1213 |
| **Erythromycin** | | | | |
| **Year** | **S%** | **I%** | **R%** | **Total** |
| 2001 | 95.4 | 0.2 | 4.4 | 653 |
| 2002 | 94.7 | 0.1 | 5.2 | 700 |
| 2003 | 94.9 | 0.1 | 5.0 | 736 |
| 2004 | 94.7 | 0.1 | 5.2 | 869 |
| 2005 | 94.3 | 0.3 | 5.4 | 924 |
| 2006 | 94.8 | 0.4 | 4.8 | 813 |
| 2007 | 94.9 | 0.1 | 5.2 | 926 |
| 2008 | 94.4 | 0.4 | 5.2 | 1123 |

* S <0.12 mg/L; I 0.12-1.0 mg/L; R > 1.0 mg/L

**Tomas Söderblom, Johan Struwe, , Birgitta Henriques Normark, Gunnar Kahlmeter, Barbro Olsson-Liljequist**

## *Enterococcus faecalis* and *Enterococcus faecium*

### Background

Vancomycin resistant enterococci (VRE) have become important causes of nosocomial infections in many parts of the world, usually involving high-risk populations such as immunosuppressed and intensive care patients. Like MRSA, VRE were made notifiable according to the Swedish Communicable Disease Act in the year 2000 and since 2004 contact tracing is also mandatory.

### Notifications of VRE according to the Communicable Disease Act

There were 618 notified cases of VRE during 2008, almost 12 times more cases compared with 2007. From 2000 to 2007 the numbers of reported cases of VRE have been 20, 18, 19, 47, 21, 35, 24 and 53 respectively. Reports on VRE came from 12 out of 21 Swedish counties but the majority of cases were from Stockholm (n=418), Halland (n=86), Västmanland (n=83), and Uppsala (n=13). Another 18 cases were reported from eight other counties. The national incidence for VRE was 6.7 cases per 100 000 inhabitants whereas the incidence figures in the affected counties were 21.1 in Stockholm, 29.3 in Halland, 33.2 in Västmanland, and 4.0 in Uppsala. The average age for all cases was 70 years, and there was an even distribution between the sexes.

In 13 cases the VRE was acquired abroad and 10 different countries were stated. For eight of the cases the acquisition was health-care related and for the remaining five cases information was missing.

During 2008, 610 notified cases had *Enterococcus faecium*. Of these 505 carried the *vanB* gene and 96 the *vanA* gene. Information was missing for four cases. In five cases a double infection was reported with *Enterococcus faecium -vanA* and *Enterococcus faecium -vanB*. *Enterococcus faecalis* was reported in only four cases. One isolate was reported as *vanA*-positive, information was missing for the other three. Two cases were reported with both *Enterococcus faecalis* and *Enterococcus faecium*.

According to the first laboratory notification for each case the majority were isolated from faeces (84%), whereas 5% each of the isolates were from wounds and urine. Invasive VRE infections were reported for 11 cases, all in blood.

A more detailed description is presented in Highlighted areas, section 5.4.

### Annual Resistance Surveillance and Quality Control (RSQC) programme

*Enterococcus faecalis* was not included in the RSQC programme on antibiotic resistance 2008.

### Data on invasive isolates reported to EARSS

*Enterococcus faecalis* and *Enterococcus faecium* have been reported to EARSS since 2001, (Appendix 5). The main focus has been on vancomycin resistance, but also on high-level resistance to aminoglycoside antibiotics.

In 2003 the first four Swedish vancomycin-resistant invasive isolates of *Enterococcus faecium* were reported (2.2% of all), and in 2004 three isolates were found (1.2%), Tables 4.5 and 4.6. Molecular typing of these vancomycin-resistant isolates indicated relatedness only between two of them from the same hospital. In 2006 two resistant blood isolates were found, in 2007 none, and in 2008 six isolates of *Enterococcus faecium* with *vanB*. These latter isolates all showed the same PFGE pattern as the epidemic strain.

High-level aminoglycoside resistance (HLAGR) was more prevalent in *Enterococcus faecium* (25%) than in *Enterococcus faecalis* (20%) in 2008. From 2006 and onwards all laboratories who reported HLAGR used gentamicin (GEN) as test disk for detection.

**TABLE 4.5.** Resistance among invasive isolates of *Enterococcus faecalis* reported to EARSS 2001-2008

| Year | Vancomycin-R (%) | HLAGR (%) | Total number (number tested for HLAGR by GEN) |
|---|---|---|---|
| 2001 | 0 | 12.7 | 395 (212) |
| 2002 | 0 | 17 | 430 (235) |
| 2003 | 0 | 17.5 | 593 (440) |
| 2004 | 0 | 15.4 | 592 (533) |
| 2005 | 0 | 18.7 | 567 (492) |
| 2006 | 0.4 | 19.9 | 579 (563) |
| 2007 | 0 | 16.1 | 651 (632) |
| 2008 | 0 | 20.1 | 720 (703) |

**TABLE 4.6.** Resistance among invasive isolates of *Enterococcus faecium* reported to EARSS 2001-2008

| Year | Vancomycin-R (%) | HLAGR (%) | Total number (number tested for HLAGR by GEN) |
|---|---|---|---|
| 2001 | 0 | 9.1 | 169 (99) |
| 2002 | 0 | 6.3 | 181 (96) |
| 2003 | 2.2 | 11.2 | 231 (170) |
| 2004 | 1.2 | 7 | 260 (227) |
| 2005 | 0 | 4.3 | 253 (211) |
| 2006 | 0.3 | 14 | 286 (286) |
| 2007 | 1.1 | 14.4 | 279 (263) |
| 2008 | 1.5 | 24.8 | 333 (331) |

**Johan Struwe, Tomas Söderblom, Karin Tegmark Wisell, Gunnar Kahlmeter, Barbro Olsson-Liljequist**

## *Streptococcus pyogenes*

### Annual Resistance Surveillance and Quality Control (RSQC) programme

*Streptococcus pyogenes* was not included in the RSQC programme in 2008.

### Surveillance of invasive isolates in addition to EARSS

Of data on consecutive blood isolates from the participating 11 laboratories 196/11.115 (1.8%) were *Streptococcus pyogenes* (GAS). This represented a small increase compared with 2007 when 1.2% of the blood isolates were identified as GAS.

Only one of the isolates (0.5%) was resistant to erythromycin and none was resistant to clindamycin. Twenty-six isolates (14.6%) were resistant to tetracycline, and this was an increase compared with 2007 when 8% of the isolates were resistant. A majority of the isolates were retrieved from adults (> 50 years), and only 5% were from children 0–9 years.

## *Streptococcus agalactiae*

### Surveillance on invasive isolates additional to EARSS data

107/11.115 (1.0%) of the blood isolates collected from the 11 laboratories were *Streptococcus agalactiae* (GBS), which was in the same order as in 2007 when 1.3% were GBS. Seven of the isolates (6.5%) were resistant to erythromycin and clindamycin, which is comparable to 2007 (8.8%) and 2006 (4.4%). A majority of the isolates were retrieved from adults (> 50 years), but 16 (15%) were isolated from children less than 2 months. A seasonal tendency was observed with peaks in December-January and June-July. Five (30%) of the 16 infant findings occurred in June.

## *Haemophilus influenzae*

### Annual Resistance Surveillance and Quality Control (RSQC) programme

*Haemophilus influenzae* was re-entered in the RSQC programme in 2008 after a period of three years. A marked increase in rates of penicillin-resistant and trimethoprim-sulfamethoxazole-resistant isolates was seen, which is further discussed in section 5.5. For both types of antibiotics the rates were > 20%, compared with stable results for many years of 10–13% resistance as a national average. The increased rates of resistance were seen in all counties. Also the rate of chromosomally mediated (BLNAR = betalactamase-negative ampicillin-resistant) had increased from 2 to 3%. The shift in 2008 from loracarbef back to cefaclor as screening disk might account for some of this increase and this needs to be confirmed by comparative testing. Tetracycline resistance in *H. influenzae* was still rare (approximately 1%).

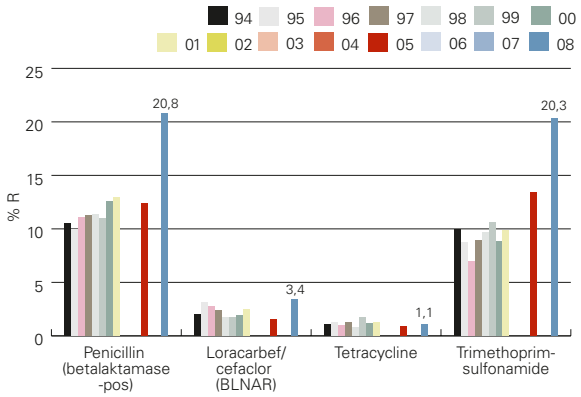


**FIGURE 4.10.** Resistance rates (resistant isolates in percent of all *Haemophilus influenzae* isolates) for four groups of antibiotics 1994–2008. No data available for 2002–2004 and 2006–2007.

### Surveillance on invasive isolates additional to EARSS data

Only 63 of the 11.115 blood isolates (0.6%) were *Haemophilus influenzae*. Three of the isolates were from CSF and were obtained during late summer and early autumn.

Sixteen isolates (25%) were betalactamase-producing and ampicillin-resistant. This was a marked increase compared with 2007 when only three ampicillin-resistant isolates were found, and the increase corresponded to the increase seen in respiratory tract isolates (RSQC survey, see above). One isolate with chromosomally mediated beta-lactam resistance (BLNAR) was detected. Nine isolates were resistant to trimethoprim-sulfamethoxazole in 2008, also an increase as compared with one isolate in 2007. A majority of the isolates were retrieved from adults (> 50 years), but 4 were from children 0–9 years.

**Barbro Olsson-Liljequist, Michael Toepfer, Gunnar Kahlmeter**

## Extended spectrum beta-lactamase-producing *Enterobacteriaceae* (ESBL)

### Background

Increasing numbers of findings at Swedish clinical laboratories and increasing numbers of reported outbreaks with bacteria producing beta-lactamases with an extended spectrum (ESBL), both nationally and internationally, were the reasons for ESBL-producing *Enterobacteriaceae* being notifiable according to the Communicable disease act from February 1st 2007. Notifications of ESBL are limited to clinical laboratories. As a result, information on ESBL is restricted to data on age, gender and cultured material while information on reasons for sampling or place of acquisition is not available.

### Notifications according to the Communicable Disease Act

A total of 2957 cases were notified during 2008. Reports came from all 21 counties of Sweden, corresponding to an average national incidence of 32 cases per 100,000 inhabitants, see Figure 4.11.

In Uppsala county the incidence decreased from 73 cases per 100 00 inhabitants (during 11 months of mandatory notification 2007) to 57 cases per 100 00 inhabitants for 2008. This was a result of an extensive infection control and screening program launched to control a large ESBL outbreak that was discovered in 2005. This shows that an outbreak situation with ESBL-producing *Klebsiella* may be reversed with an intensive effort and a combination of control measures.

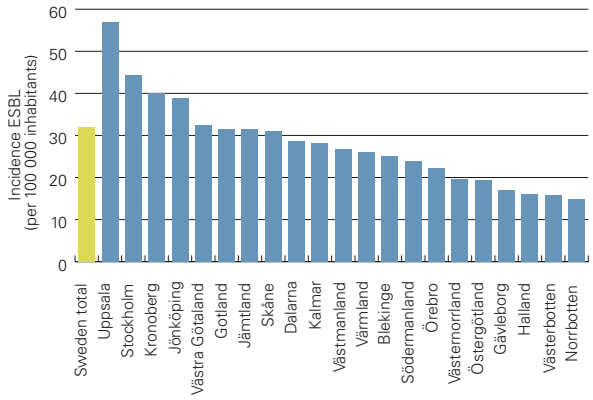


**FIGURE 4.11.** The incidence of ESBL in Swedish counties 2008.

When comparing the second half of the two years, a 28% increase of ESBL cases was noted for 2008, Figure 4.12. During the first month of 2007 the routine for notification system was under development which may have resulted in underreporting of cases. In May and June 2008 a strike in the health-care sector may have affected the sampling frequency and the number of reported cases, thus comparisons of these periods or the entire years are difficult to make.

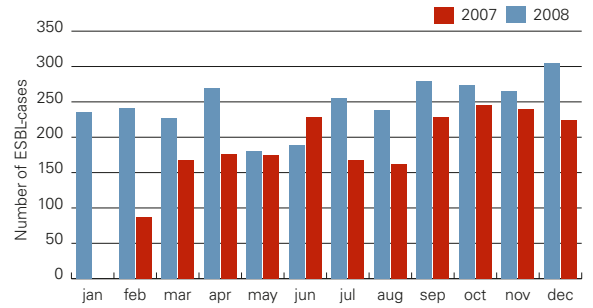


**FIGURE 4.12.** The number of reported ESBL cases per month, for 2007 and 2008.

The most commonly reported species were *Escherichia coli*, accounting for 83% of all cases, followed by *Klebsiella pneumoniae* with 9%, Table 4.7.

**TABLE 4.7.** Distribution of species among cases with ESBL-producing bacteria 2008.

| | |
|---|---|
| *Escherichia coli* | 2 512 |
| *Klebsiella pneumoniae* | 269 |
| *Proteus mirabilis* | 16 |
| *Citrobacter* species | 16 |
| *Salmonella* species | 5 |
| Other *Enterobacteriaceae* | 57 |
| Species not reported | 161 |
| Total number of reported species | 3 036* |

* In 65 cases two different ESBL-producing species were reported and 7 cases had notifications with three different species resulting in a higher number of isolates than number of cases reported.

Bacteria were cultured from urine in 70% of the cases according to the first laboratory notification. The second most common source for ESBL-producing *Enterobacteriaceae* was faecal samples with 13%. Samplings from blood and wounds constituted 4% each of the first notifications. One-hundred and fifty cases with invasive ESBL infections were notified during 2008, all in blood. Among these, 138 were new cases for 2008 and 12 were known carriers of ESBL notified the previous year.

The distribution of gender and age differed between species. The incidence in age groups and gender for the ESBL-cases with *E. coli* and *K. pneumoniae* is shown in Figure 4.13 and 4.14. Of ESBL-producing *E. coli* 69% were derived from women with an average age of 53 years. This was six years less than the average age for men. The *K. pneumoniae* ESBL cases were almost equally distributed between sexes (48% women), with mean ages of 56 years for women and 59 years for men. Compared with 2007 the mean age had decreased with 12 years for women and eight years for men. The reason for this was an increased number of cases of *K. pneumoniae* which were isolated from young patients during outbreaks in paediatric surgery and neonatal care.

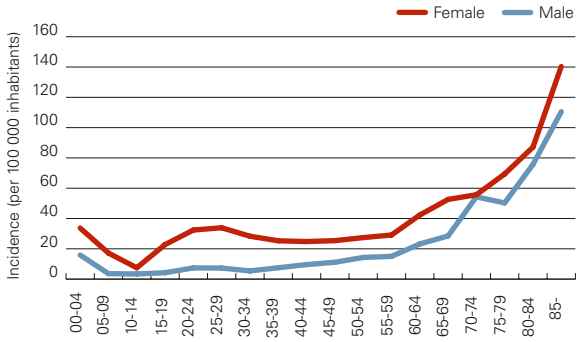


**FIGURE 4.13.** Age and gender distribution of *E. coli* ESBL cases 2008.

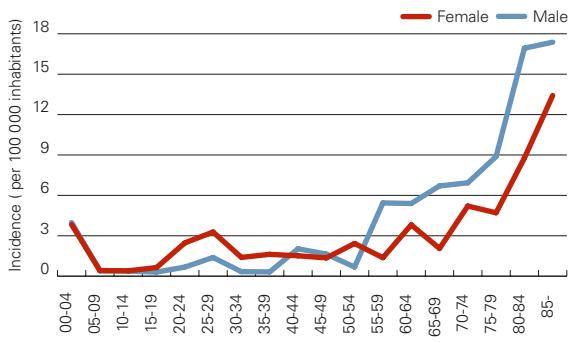


**FIGURE 4.14.** Age- and gender distribution of *K. pneumoniae* ESBL cases 2008.

The first full year of mandatory notification showed that the nation-wide problem with ESBL-producing bacteria in Sweden has proven to be a larger problem than MRSA, both in numbers of cases and severity of infections. Concomitant resistance to several other antibiotics in many isolates (data not shown) limits the options for treatment.

## *Escherichia coli*

### Annual Resistance Surveillance and Quality Control (RSQC) programme

*Escherichia coli*, mainly derived from urinary tract infections, has been included in the national surveillance program several times since 1996 and every year since 2001. Resistance to commonly prescribed oral antibiotics for treatment of urinary tract infections (UTI) has been tested each year. The average resistance rates to ampicillin have increased yearly, from 17 up to 29%, Figure 4.15. A similar trend has been seen for trimethoprim with an increase from 10 to 18%. Fluoroquinolone resistance, detected by the nalidixic acid screening disk since 2002, has also increased during this period and reached an average of almost 13% in 2008. Resistance to cephalosporins (cefadroxil tested), although much less prevalent than ampicillin resistance, has doubled during the last two years and reached 2.5%. This mirrored the increasing incidence of ESBL-producing bacteria as seen from the notified cases and reports to EARSS (below).

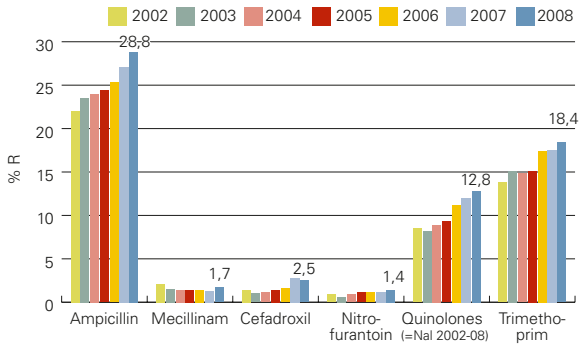


**FIGURE 4.15.** Resistance rates (resistant isolates in percent of all *Escherichia coli* isolates) for six antibiotics 2002–2008. Fluoroquinolone resistance was detected with nalidixic acid.

In 2007 the RSQC programme was extended to last for three months, February – April, and included not only urine isolates but *Escherichia coli* from all types of samples. Apart from the regular UTI antibiotics, the isolates were also tested for susceptibility to cefotaxime, ceftazidime, and a carbapenem. Resistance rates to cefotaxime, ceftazidime, and carbapenem were 2.4%, 2.2% and 0%, respectively. Isolates with verified ESBL-activity were collected and analysed further (n=240). In the collection 74% of the isolates harbored ESBL-genes belonging to the CTX-M-1 subgroup and 22% the CTX-M-9 subgroup. In two isolates genes belonging to both subgroup CTX-M-1 and CTX-M-9 were detected. The remaining 4% were CTX-M-negative but harboured ESBL-genes of SHV-type. A majority of these ESBL-producing isolates were multiresistant.

### Data on invasive isolates reported to EARSS

*Escherichia coli* derived from invasive infections (blood isolates) have been part of the European Antimicrobial Resistance Surveillance System (EARSS) since 2001. The surveillance system has focused on resistance to beta-lactam antibiotics, especially ESBL, and on resistance to aminoglycosides and fluoroquinolones. Results for 2001–2008 are presented in Table 4.8.

Ampicillin resistance, caused by production of plasmid-mediated beta-lactamase (most often of TEM-type) was slightly higher in blood isolates than in the urine isolates tested in the RSQC programme, 32% VS. 29%. However, data on blood isolates were incomplete since one third of participating laboratories do not include ampicillin in susceptibility testing of invasive isolates. The ampicillin resistance rates in Sweden are still much lower than in most other European countries where ampicillin resistance often exceeds 50%.

The level of resistance to third generation cefalosporins among blood isolates was 2.3% in 2008. In the majority of the cefotaxime-R isolates (1.9%) resistance was attributed to the presence of ESBLs of CTX-M type.

Aminoglycoside resistance in *Escherichia coli* has shown an increasing trend for the last couple of years but remained at 2.2% in 2008.

Reduced susceptibility and resistance to fluoroquinolones (I+R) has varied between 5.5% and 13% since 2001 but reached 14% in 2008. These increasing trends of resistance in blood isolates were the same as those in urine isolates from the RSQC programme, as can be seen in Figure 4.16.

**TABLE 4.8.** *Escherichia coli* from blood cultures in Sweden 2001-2008, reported to EARSS.

| Year | Ampi-cillin-R (%) * | Cefotaxi-me-R (%; ESBL / other mecha-nism) | Amin-oglyco-side-R (%) ** | Fluoro-quinolo-ne-I/R (%) *** | Total number of iso-lates |
|---|---|---|---|---|---|
| 2001 | 26.5 | 0.5 | 1 | 5.5 | 2 627 |
| 2002 | 24.9 | 0.5 | 0.6 | 7.1 | 3 062 |
| 2003 | 28.5 | 0.4 | 1 | 8.3 | 3 300 |
| 2004 | 23 | 0.5 / 0.6 | 1.5 | 11.1 | 3 336 |
| 2005 | 26 | 0.9 / 0.4 | 1.5 | 8.9 | 3 212 |
| 2006 | 28.1 | 1.3 / 0.1 | 1.7 | 8.7 | 3 514 |
| 2007 | 32.9 | 1.6 / 0.6 | 2.3 | 13.3 | 3 745 |
| 2008 | 31.9 | 1.9 / 0.4 | 2.2 | 14.3 | 4 028 |

*Only 55–60% of isolates were tested against ampicillin; **gentamicin or tobramycin, *** ciprofloxacin

**Tomas Söderblom, Johan Struwe, Karin Tegmark Wisell, Gunnar Kahlmeter, Barbro Olsson-Liljequist**

## *Klebsiella pneumoniae*

### Annual Resistance Surveillance and Quality Control (RSQC) programme

*Klebsiella pneumoniae* is one of the most important bacterial species from a hospital infection control point of view. It has been included in the RSQC programme and EARSS since 2005.

As for *Escherichia coli*, the RSQC 2008 programme for *Klebsiella pneumoniae* was mainly focused on urine samples,

Figure 4.16. Resistance to commonly prescribed oral antibiotics for treatment of UTI was tested in 2008. Data for 2008 indicated an increase in resistance only to trimethoprim, whereas the rates of resistance to both cefadroxil and fluoroquinolones were slightly lower than in 2007.

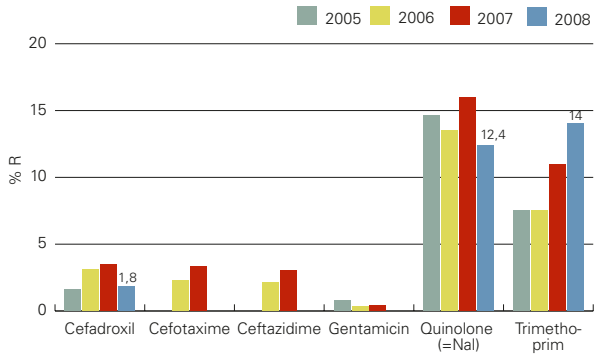


FIGURE 4.16. Resistance rates (resistant isolates in percent of all *Klebsiella pneumoniae* Isolates) for four groups of antibiotics 2005–2008.

In 2007 the RSQC programme was extended to last for three months, February – April, and included not only urine isolates but *Klebsiella pneumoniae* from all sample types. Apart from the regular UTI antibiotics, the isolates were also tested for susceptibility to cefotaxime, ceftazidime, and a carbapenem. From the results in Figure 4.16 it can be seen that cefadroxil resistance had more than doubled between 2005 and 2007 and reached 3.5% (> 3 500 isolates tested). Resistance rates to cefotaxime, ceftazidime, and carbapenem were 3.3%, 3% and 0%, respectively. Isolates with verified ESBL-activity were collected and analysed further (n=48). In the collection 73% of the isolates harbored ESBL-genes belonging to the CTX-M-1 subgroup and 10% the CTX-M-9 subgroup. Among the remaining there were ESBL-genes of SHV-type. A majority of these ESBL-producing isolates were multiresistant.

### Data on invasive isolates reported to EARSS

From 1 July 2005, participants in the EARSS network have contributed with data on blood isolates of *Klebsiella pneumoniae*. In 2008 the number of isolates had increased to 826 as shown in Table 4.9. All cephalosporin resistance was caused by ESBLs of CTX-M type. The rate of fluoroquinolone resistance is slowly increasing.

TABLE 4.9. *Klebsiella pneumoniae* from blood cultures in Sweden 2005-2008, reported to EARSS.

| Year | Cefotaxime-R (%; ESBL/other mechanism) | Aminoglycoside-R (%) * | Fluoro-quinolone-I/R (%) ** | Total number of isolates |
|---|---|---|---|---|
| 2005 | 0.7 / 0.7 | 1.4 | 9.8 | 281 |
| 2006 | 1.0 / 0.5 | 0.3 | 8.5 | 610 |
| 2007 | 1.1 / 0.3 | 1.1 | 10.8 | 649 |
| 2008 | 2.3 / 0 | 1.1 | 12.9 | 826 |

*gentamicin or tobramycin, ** ciprofloxacin

The data for 2005 represent six months from 20 laboratories. From 2006 and onwards the data represent the whole years from 20 laboratories.

### Isolates with new resistance mechanisms

In 2007 the first isolate of *Klebsiella pneumoniae* with KPC-2 (*K.pneumoniae* carbapenemase) was detected in Sweden. In 2008 at least one more isolate with a KPC betalactamase has been identified, and also one isolate with a metallo-betalactamase of VIM-type. In all these cases hospital care in the south of Europe were reported.

**Tomas Söderblom, Johan Struwe, Karin Tegmark Wisell, Gunnar Kahlmeter, Barbro Olsson-Liljequist**

## *Pseudomonas aeruginosa*

### Annual Resistance Surveillance and Quality Control (RSQC) programme

*Pseudomonas aeruginosa* was not included in the RSQC programme in 2008 but will be re-entered in 2009.

### Data on invasive isolates reported to EARSS

From 1 July 2005, participants in the EARSS network have been asked to contribute with data on blood isolates of *Pseudomonas aeruginosa*. From Sweden a total of 149 isolates from 20 laboratories were tested during the second half of 2005, and these data are compared with complete data sets for 2006, 2007 and 2008 in Table 4.10. The levels of resistance to beta-lactam antibiotics (ceftazidime and carbapenems) were in the range 3–7% for all three years. No change in resistance rates had occurred for either aminoglycosides or fluoroquinolones .

TABLE 4.10. *Pseudomonas aeruginosa* from blood cultures in Sweden 2005–2008, reported to EARSS.

| Year | Ceftazi-dime-R (%) | Carba-penem-R (%) * | Amino-glycoside-R (%) ** | Fluoroqui-nolone-I/R (%) *** | Total number of isolates |
|---|---|---|---|---|---|
| 2005 (half year) | 4.7 | Insuf-ficient data | 0 | 9.0 | 149 |
| 2006 | 2.6 | 4.4 | 0.5 | 10.4 | 296 |
| 2007 | 4.5 | 7.0 | 0 | 10.4 | 342 |
| 2008 | 5.2 | 4.0 | 0.3 | 7.6 | 315 |

* imipenem, meropenem, ** gentamicin, tobramycin, *** ciprofloxacin

**Barbro Olsson-Liljequist, Gunnar Kahlmeter**

## *Clostridium difficile*

A screening study aimed at identifying the internationally well established strain of moxifloxacin-resistant *C. difficile* correlated with high morbidity and mortality (PCR ribotype 027) was conducted in cooperation with 20 of the 29 Swedish microbiological laboratories. In total 581 strains were analysed with PCR ribotyping. One isolate was confirmed as PCR ribotype 027.

The frequency of moxifloxacin-resistant *C. difficile* varied geographically, from 2% to 34%. Among the resistant strains two types dominated, designated SE17 and SE37, Figure 4.17. Type SE17 (PCR ribotype 012 according to the international nomenclature), was common in the counties of Södermanland, Västra Götaland, Örebro and Östergötland, Figure 4.18. Type SE19c was frequent in counties of

Jönköping and Östergötland. In Gävleborg county all but one isolate belonged to type SE28 (international nomenclature PCR ribotype 017). SE37 dominated among the moxifloxacinresistant isolates analysed from Stockholm county. This type has until this study been reported only rarely and the international nomenclature is not known. Only one case of the international well established PCR ribotype 027 was identified. We therefore conclude that Sweden, contrary to many other European countries, does not have this strain established yet.

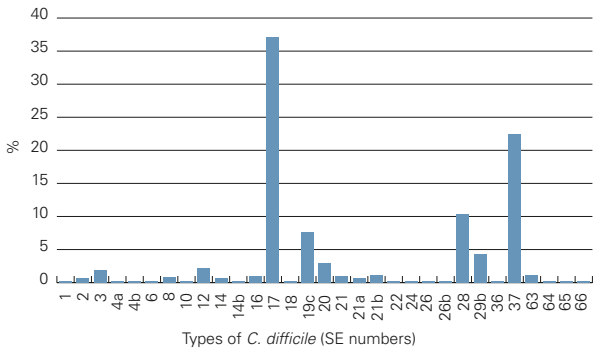


**FIGURE 4.17.** Moxifloxacinresistant *C. difficile* according to PCR ribotype.

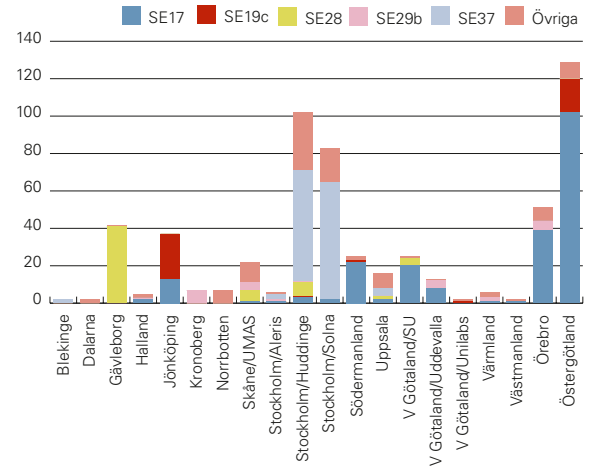


**FIGURE 4.18.** Distribution per county of the most common PCR ribotypes.

**Tomas Åkerlund, Karin Tegmark-Wisell, Johan Struwe**

## *Helicobacter pylori*

### Annual Resistance Surveillance and Quality Control (QCRS) programme

*Helicobacter pylori* derived from gastric biopsies has not until 2001 been included in the annual RSQC programme but has been monitored locally at a few laboratories. In vitro resistance to metronidazole has been reported in 10–40% of Scandinavian isolates. Resistance to clarithromycin was less common but has increased and has locally, at one laboratory, reached up to 16% in 2006, but then again during the last two years decreased dramatically. Frequencies of resistance to clarithromycin and metronidazole in clinical isolates from southwest of Sweden are presented, representing a population of approximately 300 000.

**TABLE 4.11.** *Helicobacter pylori* University Hospital MAS, Malmö, Sweden1996-2008, %R

| Year | Total number | Clarithromycin %R | Metronidazole %R |
|---|---|---|---|
| 1994 | 536 | 1.0 | 29.0 |
| 1995 | 588 | 2.9 | 32.1 |
| 1996 | 381 | 3.9 | 35.2 |
| 1997 | 331 | 7.7 | 39.8 |
| 1998 | 116 | 6.7 | 34.3 |
| 1999 | 149 | 6.1 | 33.1 |
| 2000 | 216 | 7.8 | 30.5 |
| 2001 | 188 | 8.8 | 40.2 |
| 2002 | 124 | 9.0 | 44.1 |
| 2003 | 112 | 7.2 | 42.6 |
| 2004 | 151 | 11.6 | 41.0 |
| 2005* | 217 | 11.2 | nt |
| 2006 | 257 | 16.0 | nt |
| 2007 | 375 | 9.8 | nt |
| 2008 | 156 | 5.2 | nt |

* Molecular biology technique from 2005

**Mats Walder**

## *Salmonella* and *Shigella* spp.

### Annual Resistance Surveillance and Quality Control (QCRS) programme

*Salmonella* spp. and *Shigella* spp. derived from faecal cultures was included in the annual RSQC programme from 2002 but have been monitored only by a few laboratories. Since most of the salmonella and more than 90% of the shigella strains isolated in Sweden originate from tourists returning home, the resistance patterns reflect their geographical origin. Too few strains are included in the Swedish survey to obtain conclusive results. However fluoroquinolone resistance is high, between 20–25%, among *Salmonella* strains, and among *Shigella* spp isolates producing ESBL have been detected.

**Mats Walder**

## *Campylobacter* spp

### Annual Resistance Surveillance and Quality Control (QCRS) programme

*Campylobacter* spp. derived from patients with diarrhoea was included in the annual RSQC programme from 2001 but has been monitored only by a few laboratories. Approximately 50% of *Campylobacter* strains are imported. Since resistance to fluoroquinolones is of major concern worldwide it is interesting to notice that the small decline in quinolone resistance among *Campylobacter* isolates noticed a few years ago has now regained the former level of about 50%. When screening for fluoroquinolone resistance using nalidixic acid disks was introduced in Sweden in 2001, it was expected to influence the resistance rates dramatically. The data for nalidixic acid and ciprofloxacin in parallel show, however, that the two disks are equally able to detect quinolone resistance in *Campylobacter* spp.

**TABLE 4.12.** *Campylobacter jejuni/coli* University Hospital MAS, Malmö, Sweden1995-2008

| Year | Nalidixic acid %R | Ciproflox-acin %R | Tetra-cycline %R | Erythro-mycin %R |
|---|---|---|---|---|
| 1995 | | 22 | 27 | 4 |
| 1997 | | 23 | 30 | 3 |
| 1998 | | 34 | 33 | 2 |
| 1999 | | 45 | 35 | 1 |
| 2000 | | 55 | 45 | 1 |
| 2001 | 32 | 30 | 28 | 1 |
| 2002 | 29 | 28 | 30 | 0,5 |
| 2003 | 48 | 46 | 22 | 0 |
| 2004 | 50 | 47 | 29 | 2 |
| 2005 | 57 | 52 | 18 | 1 |
| 2006 | 50 | 44 | 21 | 4 |
| 2007 | 49 | 45 | 31 | 7 |
| 2008 | 65 | 69 | 36 | 7 |

**Mats Walder**

## *Neisseria gonorrhoeae*

### Notifications according to the Swedish Communicable Diseases Act

Gonorrhoea is a notifiable disease/infection and in 2008, 725 cases were reported. Most of the cases were identified in the three largest counties of Sweden, which comprise the cities Stockholm, Gothenburg, and Malmö, respectively. Clinical isolates were characterised at the Swedish Reference Laboratory for Pathogenic Neisseria (an external body of the Swedish Institute for Infectious Disease Control), Department of Laboratory Medicine, Clinical Microbiology, Örebro University Hospital and at the Division of Clinical Bacteriology, Department of Laboratory Medicine, Karolinska University Hospital Huddinge.

In 2008, isolates from 447 of the notified clinical cases were completely characterised at these laboratories, representing 62% of the notified cases. In total, 447 different N. gonorrhoeae strains were cultured from these cases (n=447). Susceptibility testing was performed according to standardized methodology using Etest for MIC determination of ampicillin, cefixime, ceftriaxone, azithromycin, ciprofloxacin, and spectinomycin. SIR-breakpoints have been determined by the Swedish Reference Group for Antibiotics, SRGA. Production of ß-lactamase was examined by Nitrocefin discs.

Results for 2008 are compared with those from 2002 to 2007 in Table 4.12. Notable, even if the levels of resistance to azithromycin (3%) and especially cefixime (0%) remain low, the proportions of intermediate susceptibility to these antimicrobials have rapidly increased, i.e. to 10% and 4%, respectively.

**Magnus Unemo, Hans Fredlund**

**TABLE 4.13.** Antibiotic resistance rates (%) and ß-lactamase production of Swedish *Neisseria gonorrhoeae* strains from 2002 to 2008.

| | 2002 (n=120) | 2003 (n=130) | 2004 (n=149) | 2005 (n=497)* | 2006 (n=352)* | 2007 (n=406)* | 2008 (n=447)* |
|---|---|---|---|---|---|---|---|
| ß-lactamase pos. | 39 | 22 | 26 | 23 | 30 | 30 | 28 |
| Penicillin G | 48 | - | - | - | - | - | - |
| Ampicillin | 39 | 22 | 26 | 23 | 30 | 30 | 28 |
| Cefuroxime | 4 | - | - | - | - | - | - |
| Cefixime | 0 | 0 | 0** | 0 | 0 | 0 | 0 |
| Ceftriaxone | 0 | 0 | 0 | 0 | 0 | 0 | <1 |
| Azithromycin | 0 | <1 | 0** | 0 | 1 | 1 | 3 |
| Tetracycline | 54 | - | - | - | - | - | - |
| Ciprofloxacin | 58 | 56 | 51 | 49 | 61 | 70 | 63 |
| Spectinomycin | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(- = not analysed)

* Data from the Swedish Reference Laboratory for Pathogenic Neisseria, Department of Laboratory Medicine, Clinical Microbiology, Örebro University Hospital and the Division of Clinical Bacteriology, Department of Laboratory Medicine, Karolinska University Hospital Huddinge. From 2001 to 2004, only data from the Swedish Reference Laboratory were reported.

** *N. gonorrhoeae* strains resistant to azithromycin (n=14) and to cefixime (n=2) were identified in Stockholm, Sweden during 2004 (Personal communication, Bengt Wretlind, Karolinska University Hospital Huddinge).

TABLE 4.14. Drug resistant tuberculosis in Sweden. Resistance among initial isolates of *Mycobacterium tuberculosis* or *africanum* against at least one of the four drugs: isoniazid. rifampicin, ethambutol or pyrazinamid.

| Year of diagnosis | 2000 | | 2001 | | 2002 | | 2003 | | 2004 | | 2005 | | 2006 | | 2007 | | 2008 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Culture confirmed *M. tuberculosis* or *M.africanum* (N=) | 366 | | 354 | | 346 | | 345 | | 368 | | 448 | | 395 | | 361 | | 434 | |
| | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No | % | No | % |
| Any resistance Total (% ) | 45 | 12.3 | 38 | 10.7 | 36 | 10.4 | 32 | 9.3 | 43 | 11.7 | 52 | 11.6 | 43 | 10.9 | 49 | 13.6 | 57 | 13.1 |
| Isoniazid | 37 | 10.1 | 31 | 8.8 | 34 | 9.8 | 26 | 7.5 | 35 | 9.5 | 46 | 10.3 | 38 | 9.6 | 46 | 12.7 | 51 | 11.8 |
| Rifampicin | 5 | 1.4 | 6 | 1.7 | 4 | 1.2 | 10 | 2.9 | 6 | 1.6 | 5 | 1.1 | 6 | 1.5 | 15 | 4.2 | 15 | 3.5 |
| Ethambutol | 2 | 0.5 | 3 | 0.8 | 1 | 0.3 | 5 | 1.4 | 3 | 0.8 | 3 | 0.7 | 1 | 0.3 | 7 | 1.9 | 6 | 1.4 |
| Pyrazinamid | 11 | 3.0 | 6 | 1.7 | 4 | 1.2 | 7 | 2.0 | 12 | 3.3 | 6 | 1.3 | 6 | 1.5 | 11 | 3.0 | 18 | 4.1 |
| Isoniazid + rifampicin (MDR) | 5 | 1.4 | 4 | 1.1 | 4 | 1.2 | 8 | 2.3 | 5 | 1.4 | 4 | 0.9 | 3 | 0.8 | 15 | 4.2 | 14 | 3.2 |

## *Neisseria meningitidis*

### Notifications according to the Swedish Communicable Diseases Act

Invasive meningococcal disease is a notifiable disease. In 2008 49 clinical cases were reported. A total of 38 clinical isolates from blood or cerebrospinal fluid were analysed at the Swedish Reference Laboratory for pathogenic Neisseria (an external body of the Swedish Institute for Infectious Disease Control), Department of Laboratory Medicine, Clinical Microbiology, Örebro University Hospital.

Susceptibility testing was performed according to standardized methodology using Etest on Müller Hinton II agar medium with 5% defibrinated horse blood for determination of MIC for bensylpenicillin (pcG), fenoxymethylpenicillin (pcV), cefotaxime, ciprofloxacin, chloramphenicol and rifampicin. Production of beta-lactamase was examined by Nitrocefin discs.

None of the isolates produced beta-lactamase. Eleven isolates (29%) had reduced susceptibility to pcG (MIC>0.064 mg/L). The MIC for pcV is normally 5–10 times higher. All the isolates had cefotaxime-MIC ≤0.008, except three with MIC 0.012 and two with MIC 0.016, and ciprofloxacin-MIC ≤0.006 mg/L. Chloramphenicol-MIC varied between 0.19 and 1.0 and rifampicin was not higher than 0.023 mg/L. The intervals for MIC within the SIR-system, as determined by SRGA, are for pcG 0.06/0.25 (e.g. sensitive ≤0.06 mg/L and resistant >0.25 mg/L), cefotaxime 0.12/0.12, ciprofloxacin 0.03/0.06, chloramphenicol 2/4, and rifampicin 0.25/0.25.

**Per Olcén**

## *Mycobacterium tuberculosis*

### Drug resistant tuberculosis in Sweden during 2008

In 2008 a total number of 554 new cases of tuberculosis (TB) were diagnosed in Sweden compared with 491 in 2007, an increase of 13%. The number and proportion of culture confirmed cases increased from 365 (73%) in 2007 to 436 (79%) in 2008. *Mycobacterium tuberculosis* was identified in 432 cases, *Mycobacterium africanum* in two patients and Mycobacterium bovis in two patients. During 2008 the proportions of patients diagnosed with isoniazid resistant TB and MDR-TB were about the same as in 2007 and remaining on a higher level than the previous seven-year period.

Isolates of *M. tuberculosis* or *M. africanum* resistant against at least one of the four first line drugs (isoniazid, rifampicin, ethambutol or pyrazinamid) were identified in 57 patients (31 males and 26 females) corresponding to 13.1% of the 434 patients with culture confirmed TB, Table 4.14. Two patients with *M. bovis* isolates are not included since these strains are naturally resistant to pyrazinamid.

Resistant TB-bacteria were found in 4.0% of the Swedish born TB patients (3/75), in 18.2% of Somalian patients (20/110) and in 13.7% of those born abroad in other countries (34/249). Resistance against isoniazid was reported in isolates from 11.8% of all patients (4% of Swedish born patients, 16.4% of patients from Somalia and 12% of those born abroad in other countries). Resistance against rifampicin was shown in 3.5%, pyrazinamid in 4.1% and ethambutol in 1.4% of all culture confirmed cases.

Isolates resistant against at least isoniazid and rifampicin (MDR-TB) were found in 3.2% of all foreign born patients with culture confirmed TB (14/359), 6.4% of those coming from Somalia (7/110) and 2.8% from other countries (7/249). No MDR-TB was found in TB patients born in Sweden.

Thirty patients of the total 434 culture confirmed cases had a previous history of TB after 1949 (7%), thus they were classified as retreatment cases. Resistant TB was reported in 30% (9/30) including MDR-TB in 16.7% (5/30) of these cases. The corresponding figures for new or never treated cases were 12% for any resistance and 2.2% for MDR, respectively.

Genetic typing with RFLP (restriction fragment length polymorphism) was performed on 49 of the 57 resistant strains of *Mycobacterium tuberculosis* or *M. africanum*. Twentynine of the 49 examined isolates were identified to belong to 16 different clusters with two or more patients in each cluster. Genetic typing with RFLP indicates ongoing spread of resistant strains. However, a number of clusters include patients with different resistance patterns, either sensitive or resistant strains, thus making the interpretation of possible transmission difficult.

The proportion of patients with *M. tuberculosis* resistant against isoniazid has gradually increased from an annual average of 5% during the period 1991–1998 to 9% during the period 2000–2006 and further to 12.7% in 2007 and 11.8% in 2008. In parallel the annual proportions of MDR-TB increased from 1.1% to 1.3% and further to 4% in 2007 and 3.2% in 2008. The observed high proportions of resistance against isoniazid and also MDR-TB in Somalian TB patients claim for increased attention and action!

**Sven Hoffner, Victoria Romanus**

# 5. Highlighted areas

## 5.1. Antibiotic use in intensive care units (ICU)

The ICU-Strama programme was developed ten years ago and used for regular audit of antibiotic use, antibiotic resistance and infection control procedures in Swedish ICUs. It is a joint project between the Strama-ICU and Swedish Intensive Care Registry. A central component has been a web-based application which includes a system for automatic feed-back.

The median antibiotic consumption increased from 1256 defined daily doses per 1,000 occupied bed days ($DDD_{1000}$) 1999 to 1434 $DDD_{1000}$ 2008 ($p < 0.001$), Figure 5.1.1.

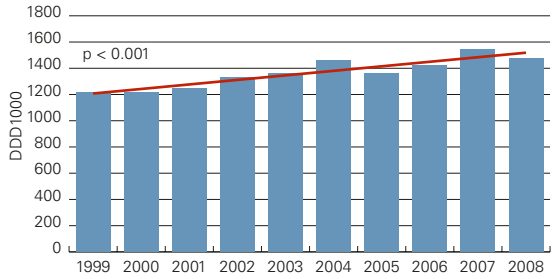


**FIGURE 5.1.1.** Trends in total antibiotic consumption in Swedish intensive care units, $DDD_{1000}$. Trend analysis performed by linear regression.

Although $DDD_{1000}$ is a highly standardised measure that allows comparison of antibiotic consumption between different settings and countries (http://www.whocc.no/atcddd/), a couple of factors complicate such comparisons. First, a common definition for length of stay must be used. Second, antibiotic use was based on the quantities of drugs delivered by each hospital pharmacy, despite that some drugs delivered might not be administered to patients in the ICU. A third source of error is that dosing in the critically ill is influenced by many factors other than the DDD (i.e. increased dosing due to life-threatening disease, reduced dosing due to renal impairment).

Antibiotic consumption varied widely between different units during 2008, ranging between 696 and 2722 $DDD_{1000}$ with a median of 1434 $DDD_{1000}$, Figure 5.1.2. This variation can be explained by different case mix, but there were also great variations between ICUs of the same type. The high antibiotic consumption concurs with figures from European and US ICUs in general, but like a few ICUs in our programme, relatively low antibiotic consumption has been reported from Switzerland. The lower antibiotic consumption suggests that it is possible to reduce antibiotic consumption in the critically ill, but it has to be accompanied with a quality control system to make sure that it does not compromise patient outcomes.

Trend analyses of usage of different classes of antibiotics were performed and showed increased carbapenem, triazole and piperacillin-tazobactam consumption ($p<0.001$), Figure 5.1.3, whereas there was no significant change in consumption of cephalosporins for the ten year period but a trend towards decreased consumption the last two years, Figure 5.1.4. Swedish guidelines for antibiotic treatment in severe infections are available from several sources including www.infektion.net, www.strama.se, www.srga.org. However, there is no agreement on a national antibiotic policy in intensive care. Strama (www.strama.se) has since 2007 recommended a reduction of cephalosporins for treatment of community acquired pneumonia and to avoid cephalosporins where there is an outbreak of ESBL producing *Enterobacteriaceae*. It is also advised to adapt the antibiotic policy to local hospital reports on antibiotic consumption and resistance. The compliance to these recommendations is measured every second year in the Point Prevalence Studies (PPS), but the number of observations is too low to evaluate the precision of antibiotic use in the individual ICU.

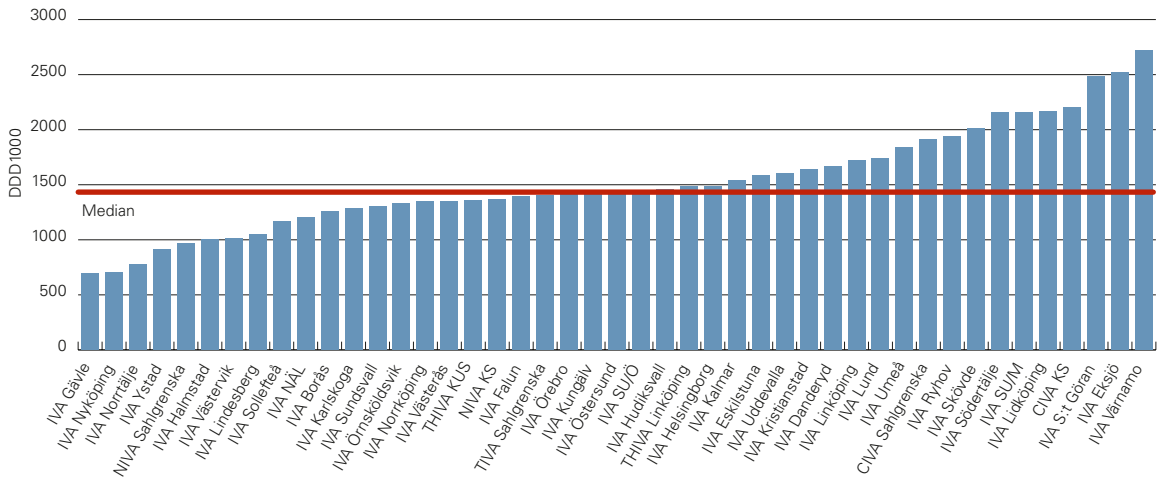


**FIGURE 5.1.2.** Median antibiotic consumption ($DDD_{1000}$) for individual ICUs during 2008.

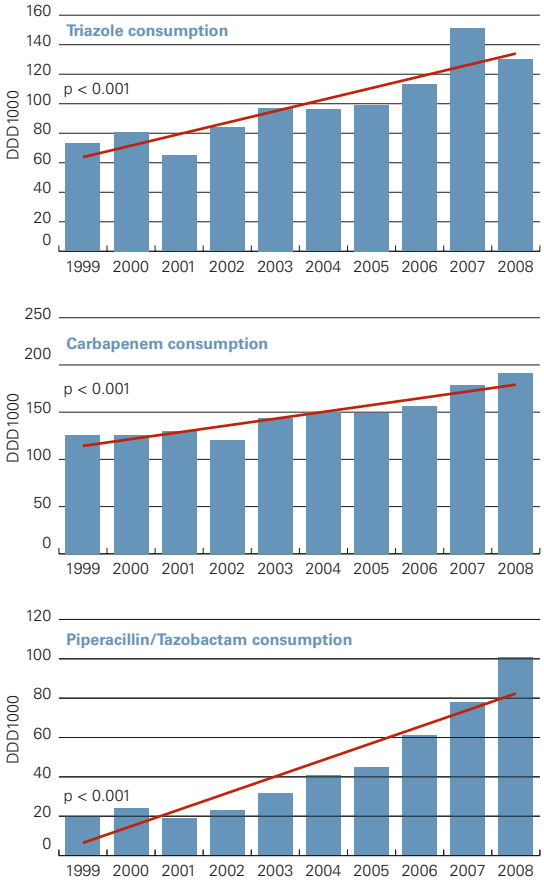


**FIGURE 5.1.3.** Trends in Triazole (a), Carbapenem (b) and Piperacillin-Tazobactam (c) consumption, $DDD_{1000}$. Trend analysis performed by linear regression.

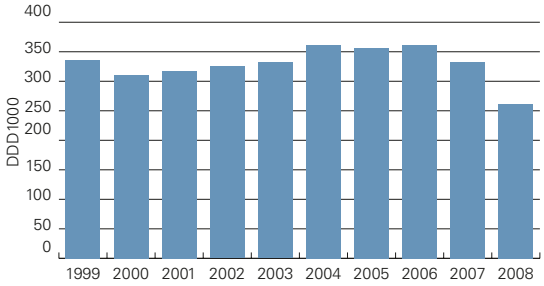


**FIGURE 5.1.4.** Yearly cephalosporin consumption, $DDD_{1000}$.

**Håkan Hanberger,** Faculty of Health Sciences Linköping University; **Morgan Edström,** Hospital Pharmacy Linköping University Hospital; **Hans Gill,** Department of Biomedical Engineering, Medical Informatics, Linköping University; **Sten Walther** Faculty Of Health Sciences Linköping University.

## 5.2. Antibiotic use and antibacterial resistance in the elderly

### Prescriptions to the elderly

Individually based data from the National Board of Health and Welfare reveals that 36% of people over 80 years took delivery of at least one antibiotic prescription during 2008, compared with 33% of children 0–6 years. In addition, the elderly receive more prescriptions of antibiotics per individual, 2.1 as compared with 1.8 per year. A problem in the analysis is that antibiotics given to the elderly in nursing homes may be dispensed instead of prescribed. The lack of a uniform basis for registering antibiotic use in nursing homes makes analysis and comparisons difficult. Another problem is that antibiotic consumption in hospitals, where many patients belong to the elderly, can not be analysed according to age. Thus, the antibiotic pressure among the geriatric segment of the population is likely even higher.

The number of prescriptions per 1000 inhabitants/year (age adjusted data) is shown for the age groups 65–79 (a) and 80+ (b) in Figure 5.2.1. The figure shows that the number of prescriptions is higher in the age group 80+ (b) than among those 65–79 years old (a).

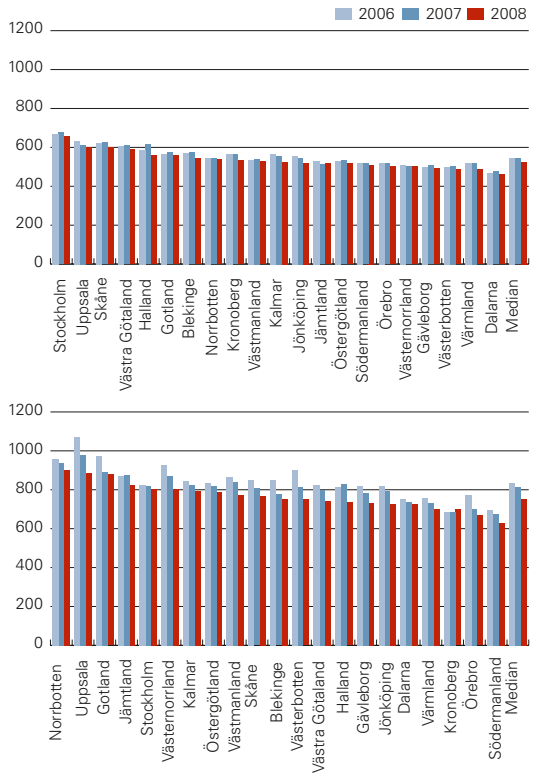


**FIGURE 5.2.1.** Number of prescriptions per 1000 inhabitants/ year (age adjusted data) is shown for the age groups 65–79 (a, top) and 80+ (b, bottom).

The high antibiotic pressure in the elderly has previously been documented in 2,752 residents (mean age 86 years) of 58 nursing homes, the SANT-study[1]. Among a total of 890 infection

[1] Pettersson E, Vernby Å, Mölstad S, Stålsby Lundborg C. Infections and antibiotic prescribing in Swedish nursing homes: A cross-sectional study. Scand J Infect Dis 2008;40:393-398.

episodes 84% were treated with antibiotics of which 38% without any direct physical examination. Among those receiving antibiotics 43% had received a previous course during the preceding 3-month period.

Among antibiotics predominantly used for lower urinary tract infections (UTI), the proportion of the not recommended alternative fluoroquionolones is shown for women in the age groups 65–79 and 80+, respectively, in Figure 5.2.2. It can be seen that there is quite a wide variation between Dalarna, Jämtland and Västerbotten having the best compliance to recommendations, and Kronoberg and Örebro counties with the poorest compliance.

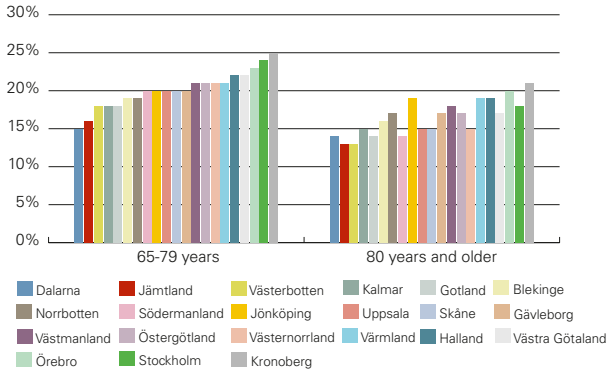


**FIGURE 5.2.2.** The proportion of fluoroquionolones among antibiotics predominantly used for lower urinary tract infections (UTI) is shown for women in the age groups 65–79 and 80+, respectively. Presciptions/1000/inhabitants and year, 2008.

Figure 5.2.3. illustrates that tetracyclines account for approximately 30% of all prescriptions of antibiotics predominantly used for respiratory tract infections. The reason why this proportion is so high is not known. Penicillin is the recommended alternative for community acquired pneumonia and antibiotic treatment in acute bronchitis is not recommended although it could be difficult to distinguish between pneumonia and acute bronchitis in the elderly.

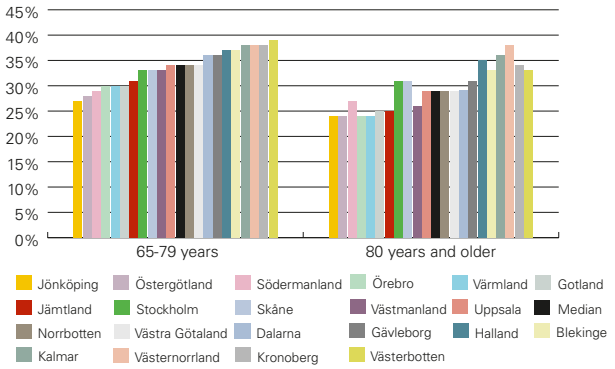


**FIGURE 5.2.3.** Proportion of tetracyclines among antibiotics most frequently prescribed for respiratory tract infections (penicillin V, amoxicillin and macrolides). Presciptions/1000/inhabitants and year, 2008.

### Antibiotic use in geriatric clinics

An increasing number of geriatric clinics and hospitals have enrolled for Stramas Point Prevalence Surveys. The total number of observed geriatric patients in the four studies have been 3571, of whom 825 (23%) received antibiotics on the day of the survey. Lower urinary tract infection was the most common diagnosis and accounted for 1/3 of the treatments. Second most common indication was skin and soft tissue infections (19%) followed by lower respiratory tract infections (13%). Figure 5.2.4. shows that fluoroquinolones, cephalosporines and penicillins with extended spectrum were the most commonly used antibiotics in the geriatric clinics.

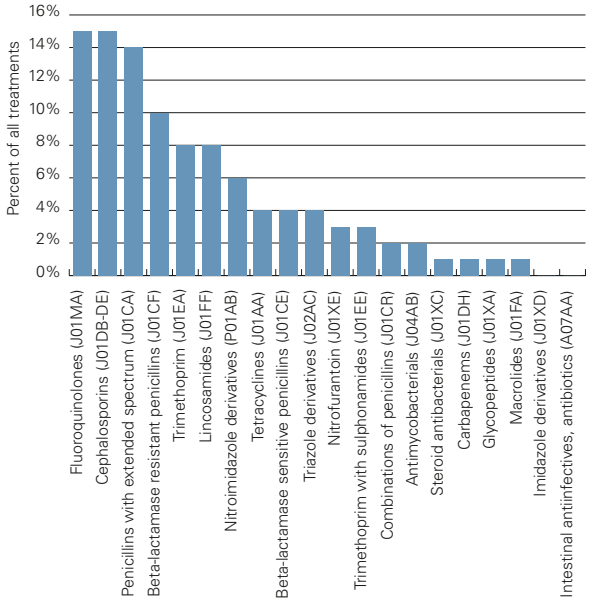


**FIGURE 5.2.4.** Distribution of antibiotic use in geriatric clinics during Stramas four Point Prevalence studies 2003–2008.

The treatment of community acquired lower UTI in women showed poor compliance to guidelines with quinolones and trimethoprim accounting for 55% of the courses. Likewise, the compliance to recommendations for the treatment of community acquired pneumonia was questionable; 60% received cephalosporins and only 20% penicillin V or G, which is recommended to mild and moderate cases. Data on disease severity (CRB 65 score) were not however, recorded in the studies.

The results of both the PPS and SANT suggest a lack of adherence to the guidelines for antibiotic choice for treatment of lower UTI in elderly women. This stands in contrast to the improvement seen in the latest years when analysing data on the treatment of this condition in younger women. In SANT it was also found that the prescribed courses were too long, only 6% received 5 days or shorter treatment. Even though neither PPS nor SANT was designed to evaluate the quality of the diagnostics as a basis for the prescription, the impression was that the high proportion of UVI-treatments probably partly was due to over-treatment of asymptomatic bacterieuria in women, a condition which does not need antibiotic treatment.

## Antibiotic resistance

### MRSA-meticillinresistant *Staphylococcus aureus*

The annual number, and the incidence, of reported MRSA-cases acquired domestically has slowly increased in the age groups above 70 years of age since reporting was introduced, Figure 5.2.5.), during the last years however, at a lower rate than in the younger population. Their relative proportion in relation to those younger than 70 years has steadily decreased due to an increase of community acquired cases in the younger population as shown in Figure 4.3.

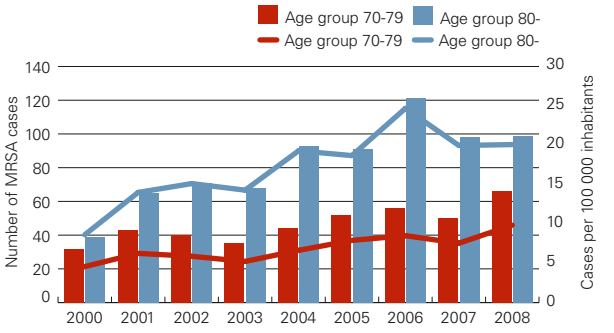


FIGURE 5.2.5. Number of reported domestic MRSA cases and incidence in age groups 70–79 and 80+.

### ESBL – *Enterobacteriaceae* producing extended spectrum beta-lactamases

The incidence of reported findings of ESBL is also increasing with age, Figure 5.2.6.

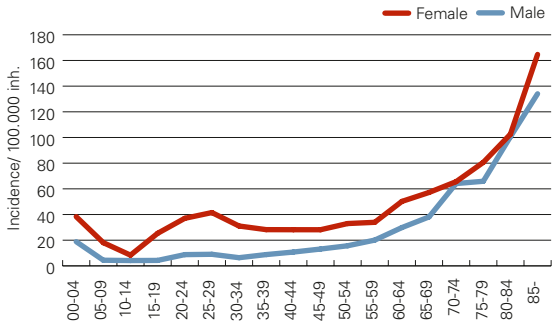


FIGURE 5.2.6. Age-adjusted incidence of notified cases 2008 of ESBL – Enterobacteriaceae producing extended spectrum beta-lactamases, in different age-groups.

### VRE – Vancomycinresistant *Enterococcus faecium* and *E. faecalis*

The hitherto largest outbreak of VRE, first recognised in 2007 (see section 5.4) has mainly affected hospitalised elderly people in Stockholm and Västmanland counties and in a nursing home in Halland county, Figure 5.2.7.

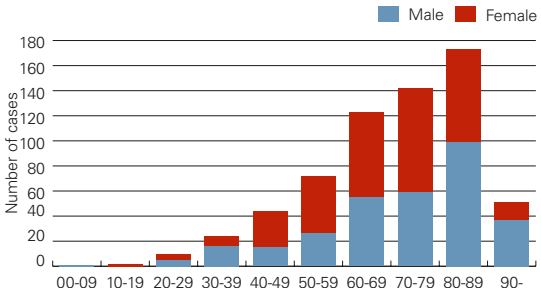


FIGURE 5.2.7. Age-distribution of all VRE-cases identified in Sweden after the detection of an outbreak of vancomycinresistant *Enterococcus faecium VanB* in the fall of 2007.

### Conclusions

Available data show that the antibiotic pressure is high in the elderly. The compliance to recommendations for treatment of lower urinary tract infections in elderly women may be improved. Information that there is no indication for treatment of asymptomatic bacteriuria with antibiotics should be spread. Resistance in bacteria spread via the oral-fecal route such as ESBL and VRE seem to be of increasing importance among the elderly, whereas the situation with regard to MRSA seem to be relatively stable.

**Ulrica Dohnhammar,** Strama; **Mats Erntell,** Communicable Disease Control, Halland County Council; **Gunilla Skoog,** Strama; **Tomas Söderblom,** Dep of Epidemiology, Swedish Institute for Infectious Disease Control; **Lars Kärvestedt,** Stockholms sjukhem; **Christer Norman,** Strama; **Johan Struwe,** Strama/Dep of Epidemiology, Swedish Institute for Infectious Disease Control.

## 5.3 Antibacterials prescribed in dentistry

Dentists account for approximately 7% of all recipes of antibiotics in community care. Around 80% of this is penicillin V and the rest is mainly divided between amoxicillin, clindamycin and metronidazole. Notably, there is great variance within Sweden, with more than twice as many prescriptions in Stockholm and Skåne as in Västerbotten county, Figure 5.3.1.

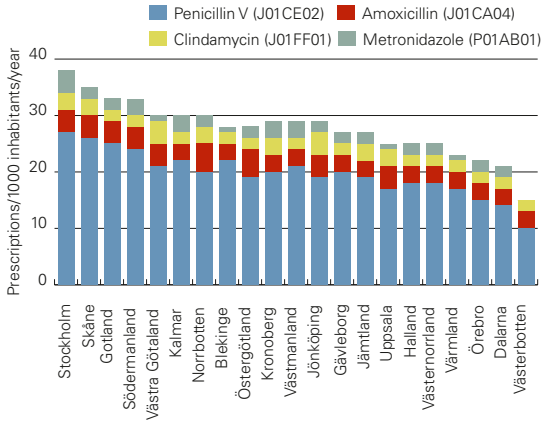


FIGURE 5.3.1. Antimicrobials prescribed by dentists, per county. Prescriptions/1000 inhabitants/year.

The number of prescriptions from dentists has increased during the last 10 years. The reason for this is unknown. Prescribing of both penicillin V and amoxicillin has increased by 25% each since 2000, Figure 5.3.2. The sizes of packages prescribed indicate that these substances are used in both prophylaxis and treatment (data not shown). During the same period the sale of clindamycin has almost tripled. This is of particular interest due to the high risk for severe side effects caused by *Clostridium difficile* attributed to clindamycin. The main recommended indication for clindamycin is as an alternative for patients with penicillin allergy. If this is the explanation to the increase or not, remains to be investigated.

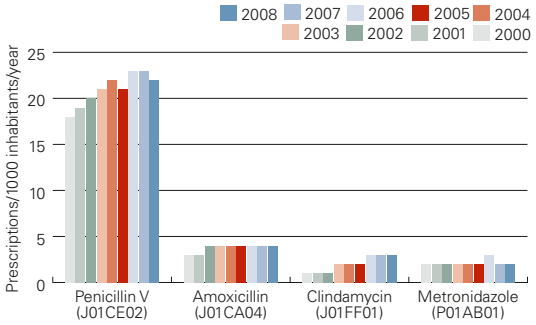


**FIGURE 5.3.2.** Antimicrobials prescribed by dentists. Prescriptions/1000 inhabitants/year, 2000–2008.

**Ulrica Dohnhammar,** Strama; **Johan Struwe,** Strama; **Johan Blomgren,** Dep of Oral Medicine Sahlgrenska University hospital, **Gunnar Dahlén,** Dep of Oral Microbiology Göteborg University; **Anders Heimdahl,** Dep of Oral Surgery Karolinska Institute; **Ylva Britt Wahlin,** Dep of Oral Diagnostics, Umeå University; **Mikael Zimmerman,** BZB CareSystems.

## 5.4 A nationwide outbreak of vancomycinresistant *Enterococcus faecium VanB*

Vancomycin-resistant *Enterococcus faecium* and *Enterococcus faecalis* (VRE), infection as well as colonisation, have been mandatory notifiable according to the Swedish Communicable Diseases Act since year 2000. Mandatory contact tracing was implemented 2004. During 2000–2006 the number of reported VRE-cases has varied from 18 to 47 annually. Previously in Sweden, only a few minor outbreaks with VRE have been recognised.

An increase of VRE was recognised in Stockholm county during the autumn 2007 and was reported in Swedres 2007. During 2008 the outbreak continued in Stockholm county and large outbreaks were subsequently reported from Västmanland and Halland counties. Due to the exchange of patients between regions, an increased number of VRE cases has also been reported from Uppsala County.

The recognition of the outbreak has led to intensive contact tracing, screening and other infection control measures.

Since the outbreak started in 2007 altogether 661 cases of VRE have been reported from 13 counties. 641 cases acquired VRE domestically and 18 cases abroad. 95% (n=612) of the domestic cases were health-care related. Among the domestic cases 66% were identified through contact tracing and 16% by screening. 9% had clinical symptoms and in another 9% the indication for sampling was unknown. According to the first laboratory confirmation 82% (n=549) were isolated from faeces, 5% (n=34) from wounds, 5% (n=31) from urine and 5 cases (0.75%) isolated in blood. The mean age for the domestic VRE cases was 70 years.

### Typing of epidemic VRE and antibiotic resistance

Verification of the resistance mechanism showed that 544 of the domestic cases were *E. faecium* with *vanB*-gene and 94 *E. faecium* with *vanA*-gene, Table 5.4.1. In another 10 cases either the species or the resistance gene was not reported.

**TABLE 5.4.1.** Species and genotype for the domestic VRE cases 2008? E.fm = *Enterococcus faecium*, E.fs = *Enterococcus faecalis*

| County | Number of cases | E.fm, *vanA* | E.fm, *vanB* | E.fs, *vanA* | E.fs, *vanB* |
|---|---|---|---|---|---|
| Stockholm | 450 | 93 | 356 | 1 | - |
| Västmanland | 83 | 1 | 82 | - | - |
| Halland | 86 | - | 86 | - | - |
| Uppsala | 13 | - | 12 | - | - |
| Others (n=6) | 9 | - | 8 | - | - |

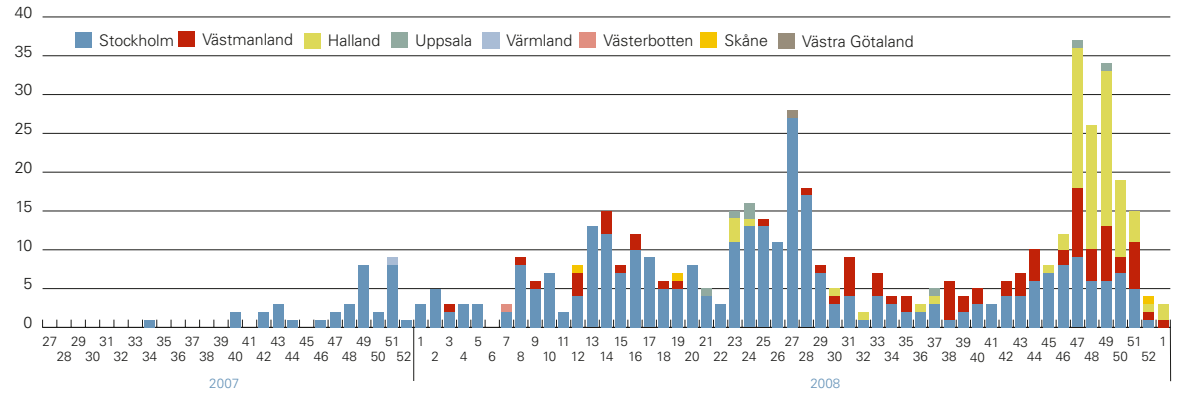


**FIGURE 5.4.1.** Epidemic curve for clonal spread of health-care related domestic *Enterococcus faecium* with *vanB*

Epidemiological typing of the *Enterococcus faecium* isolates with the *vanB* gene was performed by PFGE. The results showed that all examined isolates from Västmanland and Halland, as well as the majority of the isolates from Stockholm County, had closely related PFGE patterns, suggesting dissemination of related strains/alternatively clonal dissemination. Preliminary, and still incomplete, data indicate that this pattern has not been seen in VRE isolates reported before 2007 in Sweden. Moreover, this PFGE pattern could not be identified in a large collection of recent VRE isolates from Germany (G Werner, personal communication).

The isolates of the epidemic strain were typically resistant to vancomycin (MICs 8–64 mg/L) but susceptible to teicoplanin (MICs 0.125–1 mg/L), and also resistant to ampicillin, imipenem, ciprofloxacin and macrolides but showed only low-level resistance to gentamicin. The epidemic curve for isolates showing the same PFGE-pattern is shown in Figure 5.4.1.

The intensive sampling surprisingly yielded a high number of *E. faecium vanA* in Stockholm county. Epidemiological analysis and PFGE showed that these were related to other types of *E. faecium* strains than the epidemic strain.

### Conclusions

The reasons for the extensive dissemination in the country and in the affected counties, respectively, are still unclear but under investigation. Intensive efforts have been made in the respective region to control the outbreaks. In addition to standard infection control measures like isolation of the infected patient and broad screening whenever a new case was found, also an ambitious teaching programme in infection control for all staff, increased awareness of hand hygiene for patients and visitors, banning of food buffets from wards and probiotic treatment has been implemented in the affected hospitals.

At present there appears to be a decrease in the number of detected new cases, but it is too early to judge if this is permanent. A national working-group has been formed and a strategy for laboratory coordination of typing developed.

**Tomas Söderblom,** Dep of Epidemiology, Swedish Institute for Infectious Disease Control; **Olov Aspevall,** Infection Control, Karolinska University Hospital Huddinge; **Mats Erntell,** Communicable Disease Control, Halmstad Hospital; **Ingegerd Gustavsson,** Dep of Clinical Microbiology, Halmstad Hospital; **Göran Hedin,** Dep of Clinical Microbiology, Falun Hospital; **Daniel Heimer,** Dep of Clinical Microbiology and Infection Control, Västerås Hospital; **Ingegerd Hökeberg,** Communicable Disease Control, Karolinska University Hospital; **Karin Kidd-Ljunggren,** Infection Control, Halmstad Hospital; **Åsa Melhus,** Dep of Clinical Microbiology, Akademiska University Hospital; **Barbro Olsson-Liljequist,** Dep of Bacteriology, Swedish Institute for Infectious Disease Control; **Jan Smedjegård,** Communicable Disease Control, Västmanland County Council; **Staffan Sylvan,** Communicable Disease Control, Akademiska University Hospital; **Karin Tegmark-Wisell,** Dep of Bacteriology, Swedish Institute for Infectious Disease Control; **Magnus Thore,** Dep of Bacteriology, Swedish Institute for Infectious Disease Control; **Johan Struwe,** Strama/Dep of Epidemiology, Swedish Institute for Infectious Disease Control.

## 5.5 Increase of the proportion of *Haemophilus influenzae* with beta-lactamases

During the winter 2007–2008 the laboratory in Malmö noted an increase in the proportion of *Haemophilus influenzae* with beta-lactamases (6 mm penicillin V zone). This was later confirmed by other laboratories and in the results from ResNet, RSQC 2008, Figure 5.5.1.

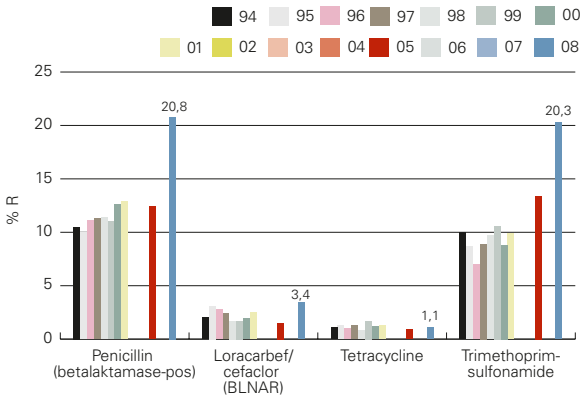


**FIGURE 5.5.1.** Resistance in *H influenzae* collected in the annual RSQC programme (approximately 3000 isolates per year). No data available for 2002–2004 and 2006–2007.

Figure 5.5.1 also shows that there was a concommittant increase in the trimethoprim-sulfamethoxazole resistance, suggesting that the increase might be clonally related. This has prompted further investigations to see whether this increase is due to the spread of one or several clones in Sweden.

In order to better understand the epidemiology of the resistant *Haemophilus influenzae* isolates we retrospectively collected data on the age distribution of patients being infected with betalactamase-producing isolates during the ResNet (RSQC) data collection period 2008. The age distribution among 487/517 (94%) of the patients with betalactamase-producing isolates for which information could be retrieved is shown in Figure 5.5.2.

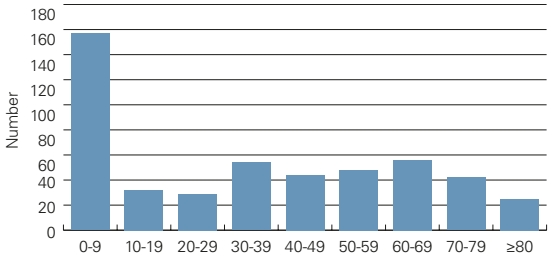


Figure 5.5.2. Age distribution of patients with betalactamase-producing *Haemophilus influenzae* in the RSQC survey 2008.

One third of the patients were children 0–9 years, and the remaining isolates were evenly distributed among all other age groups. This age distribution was comparable among patients with betalactamase-producing *Haemophilus influenzae* when looking into regional databases is Skåne and Västra Götaland regions and Kronoberg county.

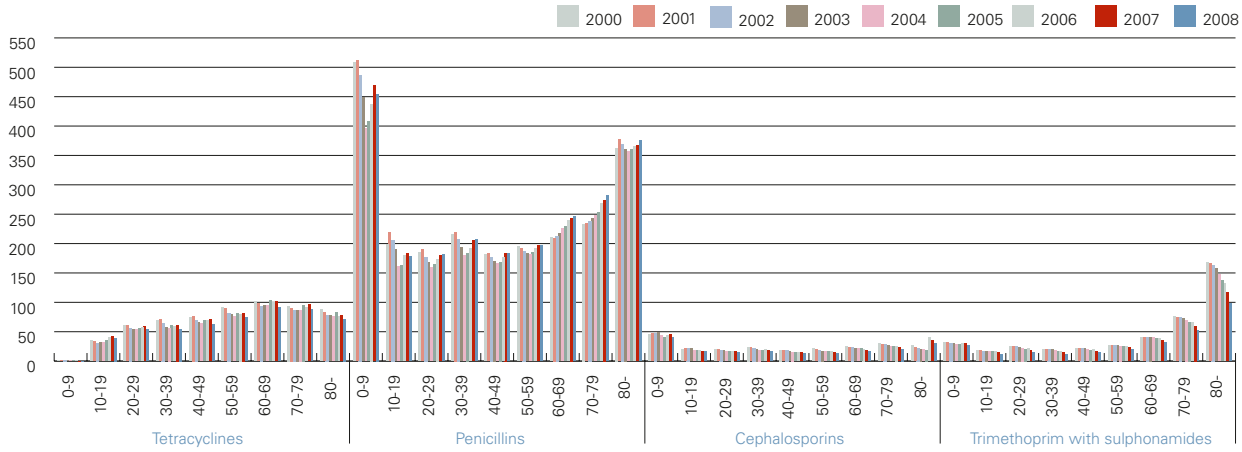


**FIGURE 5.5.3.** The use of antibiotics mainly used for respiratory tract infections in different age groups. Prescpitions/1000 inhabitants/year.

Figure 5.5.3 illustrates that there has not been any major shift in antibiotic use from narrow spectrum penicillin to antibiotics with broader spectrum during the last decade. This may speak in favour of a clonal spread rather than a shift in antibiotic use as the main driver for the change in resistance rates.

### Conclusion

The increased resistance in *Haemophilus influenzae* is worrisome, but should not lead to any change in the present recommendations in the treatment of benign upper respiratory infections in primary health care such as acute mediaotitis and rhinosinuitis, as most of them are self-limiting even without antibiotics. Epidemiological typing will be performed on representative isolates to investigate a possible clonal relationship.

**Eva Melander,** Laboratory medicine/Hospital hygiene, Malmö University Hospital; **Tinna Åhrén,** Infection Control unit and Clin Bacteriology, Sahlgrenska University Hospital; **Gunnar Kahlmeter,** Dep of Clin Microbiology, Växjö Central Hospital; **Jonatan Dahlkvist,** Drug Management and Informatics, Stockholm County Council; **Christer Norman,** Strama; **Barbro Olsson-Liljequist,** Dep of Bacteriology, Swedish Institute for Infectious Disease Control; **Johan Struwe,** Strama/Dep of Epidemiology, Swedish Institute for Infectious Disease Control.

## 5.6 Prevalence of wildtype clones among some common pathogens in Kronoberg County.

To further understand the impact of antibiotic resistance on empiric treatment and to understand development of antibiotic resistance it is important to analyse routine resistance data in several ways. Figure 5.6.1 shows the rate of isolates susceptible to all commonly used antibitotics rather than the commonly used techniques to show individual resistance rates over time.

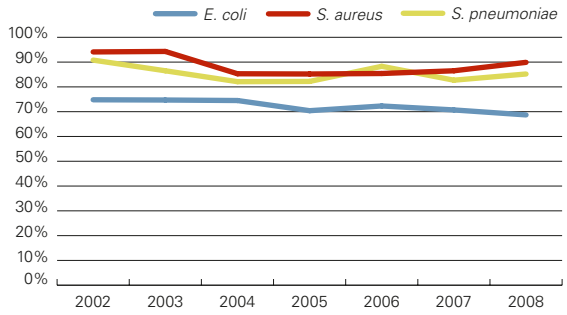


**FIGURE 5.6.1.** Prevalence of "wildtype" clones (% of isolates devoid of any resistance to a large number of antimicrobial agents) in Kronoberg County for some common pathogens.

The graph illustrates that antimicrobial resistance development primarily occurs in clones already resistant to one or several antimicrobials. Although the proportion of strains totally devoid of antimicrobial resistance is still high in Sweden (corresponding figures for *E. coli* in Spain and Portugal are 50%), the risk of failing with empirical therapy is increasing.

**Gunnar Kahlmeter,** Dep of Clin Microbiology, Växjö Central Hospital; **Martin Sundqvist,** Dep of Infectious Diseases, Växjö Central Hospital.

# Appendix 1. Abbreviations

| | |
|---|---|
| **ABU** | Asymptomatic bacteriuria |
| **AST** | Antibiotic susceptibility testing |
| **ATC** | The Anatomical Therapeutic Chemical classification system |
| **BLNAR** | Betalactamase negative ampicillin resistant |
| **CDCDC** | County Department for Communicable Disease Control |
| **DDD** | Defined daily dose |
| **DST** | Drug susceptibility testing |
| **EARSS** | European Antimicrobial Resistance Surveillance System |
| **ESBL** | Extended spectrum beta-lactamase |
| **GAS** | Group A streptococci or *Streptococcus pyogenes* |
| **GBS** | Group B streptococci or *Streptococcus agalactiae* |
| **ICU** | Intensive care unit |
| **KPC** | |
| **MDR** | Multidrug resistance |
| **MIC** | Minimal Inhibitory concentration |
| **MRB** | Multiresistant bacteria |
| **MRSA** | Methicillin resistant *Staphylococcus aureus* |
| **PFGE** | Pulsed field gel electrophoresis |
| **PNSP** | Penicillin non-susceptible pneumococci, MIC ≥ 0,5 mg/L |
| **PVL** | Panton-Valentine leukocidin |
| **RSQC** | Resistance Surveillance and Quality Control Programme |
| **RTI** | Respiratory tract infection |
| **SRGA-M** | The Swedish Reference Group of Antibiotics – subcommittee on Methodology |
| **ST** | Sequence type |
| **Strama** | Swedish strategic programme against antibiotic resistance |
| **TB** | Tuberculosis |
| **TEM** | |
| **UTI** | Urinary tract infection |
| **VIM** | |
| **VRE** | Vancomycin resistant enterococci |

# Appendix 2. Demographics and denominator data

**TABLE APP 2.1.** Population by county and age group December 31st, 2007.

| | 0-6 years | 7-19 years | 20-59 years | 60-79 years | 80 years | All ages |
|---|---|---|---|---|---|---|
| Stockholm | 176 065 | 299 593 | 1 075 518 | 313 612 | 84 728 | 1 949 516 |
| Uppsala | 26 053 | 52 720 | 173 328 | 56 394 | 14 775 | 323 270 |
| Södermanland | 20 121 | 43 450 | 130 581 | 55 907 | 15 131 | 265 190 |
| Östergötland | 31 464 | 68 240 | 216 893 | 80 542 | 23 670 | 420 809 |
| Jönköping | 26 269 | 56 915 | 166 701 | 63 956 | 19 769 | 333 610 |
| Kronoberg | 13 680 | 29 054 | 91 461 | 35 760 | 10 832 | 180 787 |
| Kalmar | 15 549 | 37 383 | 114 133 | 51 687 | 15 082 | 233 834 |
| Gotland | 3 681 | 9 488 | 28 524 | 12 162 | 3 267 | 57 122 |
| Blekinge | 11 040 | 23 229 | 75 213 | 33 206 | 9 212 | 151 900 |
| Skåne | 94 308 | 186 594 | 627 514 | 225 742 | 65 199 | 1 199 357 |
| Halland | 23 610 | 49 289 | 144 912 | 57 512 | 16 070 | 291 393 |
| Västra Götaland | 120 481 | 247 368 | 813 506 | 283 391 | 82 548 | 1 547 294 |
| Värmland | 18 513 | 43 356 | 135 967 | 58 943 | 17 047 | 273 826 |
| Örebro | 20 310 | 44 670 | 139 546 | 55 276 | 16 265 | 276 067 |
| Västmanland | 18 271 | 40 442 | 125 581 | 51 069 | 13 830 | 249 193 |
| Dalarna | 18 971 | 44 851 | 134 833 | 59 609 | 17 354 | 275 618 |
| Gävleborg | 19 136 | 43 499 | 135 876 | 60 215 | 16 830 | 275 556 |
| Västernorrland | 17 608 | 37 748 | 119 273 | 54 047 | 14 773 | 243 449 |
| Jämtland | 9 111 | 19 903 | 63 196 | 26 536 | 8 191 | 126 937 |
| Västerbotten | 18 652 | 41 278 | 134 155 | 50 005 | 13 503 | 257 593 |
| Norrbotten | 17 074 | 39 722 | 126 341 | 54 582 | 12 883 | 250 602 |
| Sweden | 719 967 | 1 458 792 | 4 773 052 | 1 740 153 | 490 959 | 9 182 923 |

**TABLE APP 2.2.** Population of Sweden 2000-2008 (the numbers represents the population on December 31st the previous year).

| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|
| Population | 8861265 | 8882831 | 8909322 | 8940744 | 8975669 | 9011391 | 9047803 | 9113297 | 9182923 |

**TABLE APP 2.3.** Number of admissions and patient-days in somatic medical care 2006-2007.

| | Patient-days | |
|---|---|---|
| | 2006 | 2007 |
| Stockholm | 1617616 | 1291013 |
| Uppsala | 290597 | 294355 |
| Södermanland | 258018 | 251242 |
| Östergötland | 300953 | 314572 |
| Jönköping | 330655 | 311519 |
| Kronoberg | 180039 | 148346 |
| Kalmar | 223035 | 212446 |
| Gotland | 53533 | 52340 |
| Blekinge | 156472 | 143853 |
| Skåne | 1179747 | 1133429 |
| Halland | 253933 | 235671 |
| Västra Götaland | 1571130 | 1498342 |
| Värmland | 242936 | 246473 |
| Örebro | 258861 | 252833 |
| Västmanland | 253676 | 240762 |
| Dalarna | 252806 | 223019 |
| Gävleborg | 229064 | 239620 |
| Västernorrland | 243998 | 234511 |
| Jämtland | 126414 | 122325 |
| Västerbotten | 297329 | 296568 |
| Norrbotten | 262023 | 236848 |

**TABLE APP 2.5.** Denominator data from the microbiological laboratories. NP = test not performed, NA = data not available

| | Number of analyses 2008 | | | | | | | Number of positive cultures 2008 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Laboratory** | **Blood (pair of bottles)** | **Cerebro-spinal fluid (CSF)** | **Nasopharynx** | **Throat** | **General culture** | **Screen MRB** | **Faeces SSYC** | **Faeces *Clostridium difficile* (toxin)** | ***Staphylococcus aureus*** | ***Streptococcus pneumoniae*** | ***Streptococcus pyogenes*** | ***Escherichia coli*** | ***Clostridium difficile* (toxinpositive)** |
| Borås | 14224 | 169 | 3277 | 5167 | 10930 | 1322 | 7439 | 1905 | 4557 | 910 | 1093 | 7404 | 201 |
| Eskilstuna (Unilabs) | 8246 | 164 | 6175 | 5002 | 8398 | 1055 | 4412 | 2181 | 3947 | 914 | 1007 | 7093 | 300 |
| Falun | 13726 | 353 | 2796 | 1967 | 10041 | 2411 | 4416 | 1742 | 4072 | 481 | 807 | 7304 | 361 |
| Gävle | 10027 | 182 | 1733 | 1344 | 8311 | 2934 | 3708 | 2100 | 3729 | 326 | 405 | 6602 | 394 |
| Göteborg | 20742 | 875 | 3194 | 3877 | 14829 | 36927 | 10901 | 3922 | 11952 | 888 | 1194 | 16926 | NA |
| Halmstad | 9925 | 146 | 2268 | 2577 | 8649 | 14671 | 6332 | 2086 | 3288 | 300 | 704 | 6837 | 325 |
| KS/HS Stockholm | 64611 | 2658 | 35181 | 13162 | 76801 | 170112 | 24351 | 12093 | 24315 | 4959 | 3727 | 39758 | 1593 |
| Jönköping | 14100 | 200 | 3770 | 4280 | 12880 | 7200 | 7770 | 2640 | 6040 | 650 | 1110 | 9610 | 530 |
| Kalmar | 9501 | 149 | 3698 | 2711 | 6691 | 4153 | 4754 | 1474 | 4177 | 619 | 606 | 6900 | 181 |
| Karlskrona | 5191 | 35 | 1285 | 2625 | 5478 | 1199 | 3983 | 1444 | 1947 | 253 | 382 | 4304 | 354 |
| Karlstad | 14269 | 211 | 1237 | 2606 | 12187 | 5555 | 4638 | 1941 | 5580 | 328 | 761 | 7505 | 273 |
| Kristianstad | 8196 | 94 | 5074 | 5074 | 11343 | 5713 | 5695 | 2104 | 4021 | 874 | 928 | 8643 | 282 |
| Linköping | 15751 | 750 | 5408 | 3570 | 19832 | 12894 | 8467 | 3652 | 4449 | 687 | 657 | 7428 | 555 |
| Lund | 24305 | 1326 | 11338 | 7659 | 25247 | 14207 | 14510 | 4056 | 11465 | 2815 | 3048 | 17527 | 511 |
| Malmö | 22081 | 324 | 5968 | 6663 | 18083 | 50120 | 11991 | 4291 | 8403 | 2056 | 1614 | 15700 | 589 |
| Aleris Medilab | NP | NP | 10458 | 5015 | 8637 | 11886 | 9496 | 1130 | 3871 | 1299 | 1176 | 8407 | 54 |
| St:Göran (Unilabs) | 6509 | 184 | 5449 | 5148 | 15458 | 27637 | 9202 | 1903 | 5247 | 952 | 1070 | 9870 | 494 |
| Skövde (Unilabs) | 11306 | 151 | 2419 | 3076 | 6556 | 6778 | 5532 | 1997 | 3990 | 452 | 605 | 8981 | 235 |
| Sunderby, Luleå | 8216 | 146 | 2548 | 3175 | 8145 | 2256 | 3856 | 1376 | 3182 | 352 | 638 | 7435 | 265 |
| Sundsvall | 9233 | 118 | 2635 | 2071 | 7574 | 12970 | 4105 | 1701 | 3437 | 510 | 537 | 7300 | 230 |
| Uddevalla | 16970 | 180 | 1900 | 3240 | 8650 | 5090 | 5640 | 1580 | 4460 | 490 | 685 | 9490 | 230 |
| Umeå | 12074 | 748 | 2670 | 2708 | 11833 | 5557 | 5014 | 1573 | 3994 | 499 | 762 | 9248 | 96 |
| Uppsala | 18418 | 788 | 5022 | 2629 | 14058 | 25350 | 5718 | 3006 | 5135 | 842 | 674 | 7998 | 582 |
| Visby | 3106 | 23 | 2363 | 738 | 2954 | NP | 1245 | 780 | 1354 | 339 | 193 | 2043 | 129 |
| Västerås | 9362 | 133 | 2609 | 2202 | 8843 | 8897 | 3165 | 1718 | 3508 | 489 | 448 | 7336 | 698 |
| Växjö | 5938 | 89 | 2186 | 2434 | 6162 | 1400 | 4086 | 1331 | 2659 | 366 | 521 | 5112 | 111 |
| Örebro | 14062 | 315 | 8479 | 1970 | 13715 | 5819 | 5221 | 2684 | 5543 | 1196 | 711 | 7708 | 344 |
| Östersund | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| Total | 370089 | 10511 | 141140 | 102690 | 362285 | 444113 | 185647 | 68410 | 148322 | 24846 | 26063 | 260469 | 9917 |

MRB = multiresistant bacteria

SSYC = *Salmonella, Shigella, Yersinia* and *Campylobacter* spp.

# Appendix 3 Surveillance of antibiotic consumption

## Statistical sources and units of measurement

### The ATC classification system and defined daily doses (DDD)

Since 1988, the Anatomical Therapeutic Chemical (ATC) classification system recommended by the WHO is used in Sweden for national drug statistics. To facilitate drug utilisation studies from a medical point of view, the concept of defined daily dose (DDD) is used as a unit of comparison in drug statistics. The DDD for a drug is established on the basis of the assumed average dose per day for the drug given to adults for its main indication. If possible, the DDD is given as the amount of active substance. The DDDs are usually equal for all dosage forms of a preparation. The statistical data systems of the National Corporation of Swedish Pharmacies (Apoteket AB) are upgraded yearly according to the recommendations made by the WHO Collaborating Centre for Drug Statistics methodology in Oslo, Norway. The sales of drugs are presented as number of DDDs per 1000 inhabitants and day (DDD/1000/day), which give an estimate of the proportion of the population daily exposed to a particular drug. This figure is a rough estimate and should be interpreted with caution.

### Swedish national statistics on drug utilisation

Since 1975, the National Corporation of Swedish Pharmacies regularly produces sales statistics on drugs, for the country as a whole and for individual counties. The sales are registered as number of DDDs, cash value and number of packages. Out-patient care data includes information on the sales of drugs dispensed on prescription by all Swedish pharmacies by the prescription survey, running since 1974. The statistical material was until 1995 built of samples of dispensed prescriptions. From 1996 all prescriptions dispensed by pharmacies are included. From 1999, ApoDos (individually packed doses of drugs often dispensed to elderly) is also included in the survey. Recorded data are trade name, quantity, patient fee, total cost, sex and year of birth of the patient. Data can be expressed as DDD/1000/day or number of prescriptions/1000 inhabitants. Hospital care data includes drugs delivered by all hospital pharmacies to the hospital departments. The system also produces sales statistics for each hospital department and on national and county sales to hospitals. The sales are expressed as cash value, number of packages and number of defined daily doses.

### The Swedish Prescribed Drug Register

Since July 2005, the Swedish National Board of Health and Welfare supplies an individually based register on all drugs prescribed and dispensed in primary health care. Among others this data gives information on the number of individuals treated with at least one course of antibiotics during a specific period of time, i.e. number of users per 1000 inhabitants and year (Users/1000/year). It is also possible to follow the number of purchases per person.

### Number of admissions and patient-days

Each of the 21 county councils in Sweden deliver once a year data to the National Patient Register kept by The National Board on Health ad Welfare. Administrative data within hospital care include, among others, date of admission, date of discharge and length of stay. Since data for 2007 is not available until August denominator data from 2006 and sales data from 2007 are used in some figures in this report. The number of admissions and patient-days in Swedish medical care 1997–2006 is shown in Appendix 2, Table App 2.3. The Swedish Association of Local Authorities and Regions keeps a searchable database at the web, http://www.skl.se/artikel.asp?A=3768&C=1801.

The present system for surveillance of antibiotic consumption has been investigated and analysed by order of the government. Together with suggestions for future improvements it was reported back to the government on the first European Antibiotic Awareness Day Nov 18th, 2008.

# Appendix 4. Antibiotic susceptibility testing

The **agar dilution method** is the reference method in Swedish susceptibility testing to which other methods are compared. Clinical microbiology in Sweden has a long tradition of using **paper disk diffusion** antibiotic susceptibility testing (AST). This method is quantitative (diameter of inhibition zones measured in mm) but results are normally interpreted to give a qualitative "recommendation": **S** (susceptible, sensitive), I (intermediate) and **R** (resistant).

The disk diffusion method has been successfully standardized by the Swedish clinical microbiology laboratories in collaboration with the SRGA-M. It is used as the routine method for susceptibility testing, and as a screening method which in some instances needs to be followed up by methods for gene detection (e.g. MRSA, VRE) and in other instances by MIC-determination using broth- or agar-dilution or with Etest (betalactam resistance in pneumococci, chromosomally mediated betalactam resistance in *Haemophilus influenzae*), and still in others by methods for enzyme detection (beta-lactamase detection in *Haemophilus influenzae*, *Neisseria gonorrhoeae* and others).

Phenotypic methods (disk diffusion or MIC) are performed on a basic medium for AST, ISA (IsoSensitest Agar) from Oxoid Ltd, UK. For this medium and the corresponding antibiotic paper disks, interpretive criteria for SIR-categorization are provided by the SRGA-M. The criteria are regularly updated and available through the web-site www.srga.org .

Internal and external quality assurance and quality control of susceptibility testing is performed by each laboratory. Internal quality control includes using international QC strains regularly (every day, once a week) and analysing data in relation to national guidelines. Validation of susceptibility testing can also be done by histogram analysis of consecutive clinical isolates (see www.srga.org) External quality control is often done by participation in UK-NEQAS and/or other international programs, whereas quality assurance is one of the features of the Swedish "100-strains or RSQC programme".

# Appendix 5. National surveillance of antibiotic resistance

### Surveillance regulated in the Communicable Disease Act

Statutory notifications of certain communicable diseases are regulated in the Communicable Disease Act (SFS 2004:168, SFS 2004:255). With the exception of certain sexually transmitted infection (STI), and from 2007 ESBL-producing *Enterobacteriaceae*, both the clinician caring for a patient with a notifiable disease (clinical notification) and the laboratory diagnosing the pathogen causing the disease (laboratory notification) are obliged to notify. This double notification significantly enhances the sensitivity of the surveillance system.

Notification shall be done within 24 hours, in duplicate to the County Medical Officer for Communicable Disease Control (smittskyddsläkare) and to the Swedish Institute for Infectious Disease Control (SMI). Notifications, with the exception of STI, are done with full person identification. The clinical notification shall also include information on the likely source and route of infection, as well as other information of epidemiological importance.

Infections (or carriage) with different antibiotic resistant pathogens are included in the list of notifiable diseases. *Streptococcus pneumoniae* with Penicillin G MIC > 0.5 mg/L (PNSP) have been notifiable since 1996. Methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecalis* and *Enterococcus faecium* (VRE) have been notifiable since 2000.

Since 1st February 2007 ESBL-producing *Enterobacteriaceae* were made notifiable by laboratory notifications. All notifications are entered into the national computerized surveillance system, SmiNet2. At the SMI, the clinical and laboratory notification for each case are merged and checked for errors. If data are missing, contact persons in the counties are asked to supplement the information. As an important complement to the notifications, the MRSA, VRE and PNSP strains are sent to SMI for epidemiological typing using pulsed-field gel electrophoresis (PFGE). For MRSA from 1 July 2006 spa-typing replaced PFGE as the primary typing method.

Tuberculosis (TB) is a notifiable disease, irrespective of drug resistance. On a voluntary basis the TB laboratories are reporting all drug-resistant isolates of *Mycobacterium tuberculosis* and bovis to SMI. All resistant isolates are sent to SMI for epidemiological typing, using restriction fragment length polymorphism (RFLP).

The feed back of notification data is done monthly on SMI internet homepage (http://www.smittskyddsinstitutet.se) and yearly in "Communicable Diseases in Sweden – the Yearly Report of the Department of Epidemiology" and in this report. Data on drug-resistant TB is also annually published in "the Swedish Tuberculosis Index".

Possible epidemiological links between patients from different counties, as identified from the epidemiological typing results and the notifications, are communicated to the persons in charge of the communicable disease control actions at the county level.

### Swedish combined surveillance and QC programme (RSQC surveys) further developed into ResNet since 2002

In 1994 a model for the concomitant surveillance of antimicrobial resistance and quality assurance of antimicrobial susceptibility testing was devised. In Sweden there are 29 clinical microbiology laboratories, each covering a county (or part of county) of Sweden. The demographics of the laboratories, their geographic areas and their corresponding populations are well characterized. The antimicrobial susceptibility testing methods of the laboratories are standardized through the combined work of the SRGA-M (Swedish Reference Group of Antibiotics – subcommittee on Methodology) and the microbiological laboratories (see also Appendix 4).

Each year the laboratories are asked to collect quantitative data (zone diameters) for defined antibiotics in 100–200 consecutive clinical isolates of a number of bacterial species. Since 1994, *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Haemophilus influenzae* have been part of this yearly program. On one or several occasions *Escherichia coli*, *Enterococcus faecalis/E.faecium*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Klebsiella* have been part of these surveys. The number of antibiotics tested for each pathogen has varied between 4 and 6.

From 2002 a web-based software (ResNet) will receive the data from the laboratories and, following approval of registered data by one of two web administrators, instantly displayed it in the form of resistance frequencies on the geographical areas on maps of Sweden. Behind each resistance frequency the distribution of zone diameters or MICs together with the relevant demographic data are directly accessible. The software will accept both MIC and zone distributions of well-characterized data sets. The graphs presenting the data are designed to include all necessary information in order for the graphs to be used on their own (in presentations etc). A recently introduced feature enables each laboratory to view all its own data and also to link this information to a website of its own local health care system. The Resnet software also has the feature of displaying aggregated, quantitative data of invasive isolates which form the Swedish part of the EARSS network (see below).

### EARSS

EARSS, funded by DG SANCO of the European Commission, is an international network of national surveillance systems, collecting comparable and validated antimicrobial susceptibility data for public health action. EARSS performs on-going surveillance of antimicrobial susceptibility of invasive infections of *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Escherichia coli*, and *Enterococcus faecalis/E. faecium*, and monitors variations in antimicrobial resistance over time and place. From 2005 invasive isolates of *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* are also part of the scheme.

Participation in EARSS was initially intended for member states of the European Union, also including Norway and Iceland, but in year 2000 six countries in eastern Europe were included, and by 2003 28 countries provide susceptibility data regularly. Information about EARSS, as well as a database yielding information about the susceptibility results for each country, year and pathogen, is available through a web-site (www.earss.rivm.nl).

Data collected by EARSS should be routinely generated quantitative data (MICs or inhibition zones), but the data presented are only in the format of susceptibility cathegories (SIR). External quality assurance exercises have so far been carried out by EARSS in cooperation with UK-NEQAS and the EARSS Advisory Board once every year. Results of those exercises showed that participating laboratories were capable of delivering good quality susceptibility data, indicating that the overall resistance rates as monitored through EARSS are accurate.

Although not perfect, the EARSS network of networks form a solid base for surveillance of resistance and is constantly extended and improved.

The participation from twentyone laboratories in Sweden is coordinated through the SMI, where electronic data collection, validation and verification of specific resistance mechanisms is performed. Sweden, because of its well organised network of clinical laboratories and high quality of routine susceptibility testing, is so far the largest contributor of national data to EARSS.

### Surveillance of invasive isolates additional to EARSS data

Data on invasive isolates on all positive blood cultures were obtained from eleven laboratories that are using the same laboratory information system (ADBakt). Their total catchment population is 3.7 millions, thus representing more than 40% of the Swedish population. From these laboratories data for the pathogens specified by the EARSS network are retrieved, but also data on all other bacterial pathogens consecutively isolated from blood cultures. In SWEDRES 2007 and 2088 report data for *Streptococcus pyogenes*, *Streptococcus agalactiae* and *Haemophilus influenzae* are presented.

### Sentinel surveillance

Susceptibility testing of gastrointestinal pathogens such as *Salmonella*, *Shigella*, *Campylobacter jejuni/coli* and *Helicobacter pylori* is not performed on a regular basis by clinical laboratories. Existing data are mainly derived from special investigations by devoted researchers / laboratories.

In order to get a national overview of the situation, the ResNet software developed by SMI (see above) is available also for data on these pathogens, as well as for national quantitative data on *Neisseria gonorrhoeae* and *N. meningitidis* performed by the reference centre in Örebro. Also collections of quantitative susceptibility data on other pathogens of general interest are suitable for entering and displaying in ResNet.

The present system for surveillance of antibiotic resistance has been investigated and analysed by order of the government. Together with suggestions for future improvements it was reported back to the government on the first European Antibiotic Awareness Day Nov 18th, 2008.

# Appendix 6. Recent publications (2006-2008)

## Use of antibiotics

**André M, Hedin K, Håkansson A, Mölstad S, Rodhe N, Petersson C.** More physician consultations and antibiotic prescriptions in families with high concern about infectious illness – adequate response to infection-prone child or self-fulfilling prophecy? Family Practice 2007;24:302-7.

**Dumpis U, Gulbinovic J, Struwe J, Lagergren L, Grishkevichus L, Bergman U.** Differences in antibiotic prescribing in three university hospitals in the Baltic region revealed by a simple protocol for quality assessment of therapeutic indications. Int J Clin Pharm Ther 2007;45:568-576 .

**Erlandsson M, Burman LG, Cars O, Gill H, Nilsson LE, Walther SM, Hanberger H,** the STRAMA ICU Study Group. Prescription of antibiotic agents in Swedish intensive care units is empiric and precise. Scand J Infect Dis 2007;39:63–69.

**Grigoryan L, Burgerhof J, Jaaijer-Ruskamp F, Degener J, Deschepper R, Monnet DL, Di Matteo A, Scicluna E, Bara AC, Stålsby Lundborg C, Birkin J.** Is self-medication with antibiotics in Europe driven by prescribed use? JAC 2007;59:152-6.

**Grigoryan L, Haaijer-Ruskamp FM, Johannes Burgerhof GM, Mechtler R, Deschepper R, Tambic-Andrasevic A, Andrajati R, Monnet DL, Cunney R, Di Matteo A, Edelstein Hm, Valinteliene R, Alkerwi A, Scicluna EA, Grzesiowski P, Bara AC, Tesar T, Cizman M, Campos J, Stålsby Lundborg C, Birkin J.** Self-medication with antibiotics in the general population: a survey in nineteen European countries. Emerg Inf Dis 2006;12:452-9.

**Hedin K, André M, Håkansson A, Mölstad S, Rodhe N, Petersson C.** A population-based study of different antibiotic prescribing in different areas. Br J Gen Pract. 2006 Sep;56(530):680-5

**Hedin K, André M, Mölstad S, Rodhe N, Peterson C.** Infections in families with small children – use of social insurance and health care. Scand J Prim Health Care 2006 Jun;24(2):98-103

**Hedin K, Petersson C, Cars H, Beckman A, Håkansson A.** Infection prevention at day-care centres: Feasibility and possible effects of intervention. Scand J of Prim Health Care 2006;24:44-49.

**Mölstad S, Erntell M, Hanberger H, Melander E, Norman C, Skoog G, Stålsby Lundborg C, Söderström A, Torell E, Cars O.** Sustained reduction of antibiotic use and low bacterial resistance: 10-year follow-up of the Swedish Strama programme. Lancet Infect Dis 2008;8:125-32.

**Pettersson E, Vernby Å, Mölstad S, Stålsby Lundborg C.** Infections and antibiotic prescribing in Swedish nursing homes: A cross-sectional study. Scand J Inf Dis 2008;40:5,393-398.

**André M, Vernby Å, Odenholt I, Stålsby Lundborg C, Axelsson I, Eriksson M, Runehagen A, Schwan Å and Mölstad S.** Diagnosis-prescribing surveys in 2000, 2002 and 2005 in Swedish general practice: Consultations, diagnosis, diagnostics and treatment choices. Scand J Inf Dis 2008;40:8,648-654.

**Vlahovic-Palevski V, Dumpis U, Mitt P, Struwe J, Palevska G, Stimac D, Lagergren Å, Bergman U.** Benchmaking antimicrobial drug use at university hospitals in five European countries. Clin Microbiol Infect 2007;13:277-283.

## Antimicrobial resistance

**Agvald Öhman C, Lund B, Hedin G, Hjelmqvist H, Struwe J, Edlund C.** ICU stay promotes enrichment and dissemination of multi-resistant coagulase-negative staphylococcal strains. Scand J Infect Dis 2006;38:441-447.

**Blahna MT, Zalewski CA, Reuer J, Kahlmeter G, Foxman B, Marrs CF.** The role of horizontal gene transfer in the spread of trimethoprim-sulfamethoxazole resistance among uropathogenic *Escherichia coli* in Europe and Canada. J Antimicrob Chemother 2006;57:666-672.

**Cars O, Olsson-Liljequist B,** Short summary of Swedres 2005, a report on Swedish antibiotic utilisation and resistance. Eurosurveillance 2007;12:225.

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## Workshop

Management of lower urinaty tract infections (in swedish), Medical Products Agency, www.lakemadelsverket.se (April 2007)

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