Eläinlääkintä- ja elintarviketutkimuslaitos
National Veterinary and Food Research Institute, Finland

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FINRES-Vet 2002-2003
FINNISH VETERINARY ANTIMICROBIAL RESISTANCE MONITORING AND CONSUMPTION OF ANTIMICROBIAL AGENTS

EELA

LÄÄKELAITOS
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KTTK
KASVINTUOTANNON
TARKASTUSKESKUS

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Kuvailulehti

Julkaisija Eläinlääkintä- ja elintarviketutkimuslaitos, EELA

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Julkaisun nimi Eläimistä eristettyjen bakteerien mikrobilääkeresistenssi sekä mikrobilääkkeiden ja rehun lisäaineiden kulutus Suomessa

Tiivistelmä

Tässä FINRES-Vet -raportissa esitellään vuosien 2002 ja 2003 resistenssituloksia. Resistenssilukujen lisäksi raportti sisältää vuodelta 2002 mikrobilääkkeiden ja vuosilta 2002 ja 2003 rehun lisäaineiden kulutustiedot.

Eläimistä eristettyjen bakteerien resistenssitilanne Suomessa on hyvä. Tämä johtunee tiukasta mikrobilääkepolitiikasta. Vain eläinlääkärit voivat määrätä mikrobilääkkeitä eläimille. Suomessa annettiin jo vuonna 1996 mikrobilääkkeiden käyttösuositukset eläinten tärkeimpiin tulehdus- ja tartuntatauteihin. Käyttösuositukset päivitettiin vuonna 2003. Suositusten tarkoituksena on edistää mikrobilääkkeiden hallittua käyttöä eläinlääkinnässä ja siten rajoittaa resistenssin kehittymistä.

Tiettyjen bakteerien resistenssitilanne on kuitenkin huolestuttava. Mikrobilääkkeiden hallittu käyttö on siksi tärkeää myös tulevaisuudessa. Infektioiden hoidon tulee jatkossakin olla mahdollisimman suunnattua.

Mikrobilääkkeiden ja rehun lisäaineiden kulutus

Mikrobilääkkeitä käytettiin eläinten lääkinnässä vuonna 2002 13 000 kg (aktiivista lääkeainetta). Mikrobilääkkeiden kulutus on laskenut tasaisesti viime vuosina; kulutus väheni 27 % vuodesta 1995 vuoteen 2002. Käytön väheneminen johtui osaksi eläinten määrän vähenemisestä, mutta myös parantuneista tuotanto-olosuhteista ja resistenssiriskin tiedostamisesta.

Vuonna 2002 kaikista eläimille käytetyistä mikrobilääkkeistä β-laktaamien osuus oli 60 %, sulfonamidi-trimetopriimi-valmisteiden 18 % ja tetrasykliinien 15 %. Kaikista penisilliinejä sisältävistä eläinlääkevalmisteista 85 % oli β-laktamaasille herkkiä penisilliinejä.

Kaikista eläimille käytetyistä mikrobilääkkeistä käytettiin lääkerehuissa vain 4 %; noin 40 % käytettiin turkiseläimille, 40 % kaloille ja 20 % sioille. Mikrobilääkkeitä annettiin injektiovalmisteissa vuonna 2002 noin 7000 kg. Injektioina annettujen mikrobilääkkeiden määrä pysyi suhteellisen tasaisena vuosina 1999-

2002. G-penisilliini on ollut vuosien mittaan käytetyin mikrobilääke, koska se on hyvin usein ensisijainen vaihtoehto monien tuotantoeläinten tautien hoidossa. Penisilliinin käyttö on resistenssitilanteen hallinnan kannalta hyvä vaihtoehto.

Vuonna 2002 mikrobilääkkeitä annettiin suun kautta noin 6000 kg. Tetrasykliinit ja sulfonamidit (yhdessä trimetopriimin kanssa) olivat tärkeimpiä suun kautta annettuja mikrobilääkkeitä: niiden osuus oli 64 % kaikista oraalisesti annetuista mikrobilääkkeistä.

Lypsykauden aikana käytettävien utareen sisäisten lääkkeiden (intramammaarien) käyttö väheni vuosina 1999-2002. Muutos ei johtunut vähentyneestä maidontuotannosta. Sen sijaan umpeenpanohoidoissa ei ole neljän vuoden aikana tapahtunut suuria muutoksia. Noin 20 % lypsylehmistä käsitellään mikrobilääkettä sisältävillä valmisteilla umpeenpantaessa.

Suomen rehuteollisuus luopui vapaaehtoisesti antimikrobisten kasvunedistäjien käytöstä 1990-luvulla. Virginiamysiinin käyttö loppui vuonna 1990, basitrasiinin vuonna 1992 sekä flavomysiinin ja avoparsiinin vuonna 1996. Esimerkiksi virginiamysiinin ja avoparsiinin käyttö loppui, ennen kuin EU kielsi niiden käytön.

Tällä hetkellä varsinaisia kasvunedistäjiä ei käytetä Suomessa lainkaan. Kokkidiostaatteja käytetään kokkidioosin ennaltaehkäisyyn broileri- ja kalkkunatuotannossa. Monensiini ja narasiini ovat yleisimmin käytettyjä kokkidiostaatteja.

Zoonoosia aiheuttavien bakteerien resistenssi

Salmonellan esiintyvyyttä seurataan kansallisen salmonellavalvontaohjelman puitteissa naudoissa, sioissa, siipikarjassa sekä lihassa ja kananmunissa. Salmonellojen resistenssiseuranta aloitettiin jo 1980-luvulla. Valvontaohjelman tulosten perusteella salmonellaa on tuotantoeläimissä ja eläimistä saatavissa elintarvikkeissa vähän.

Salmonelloja eristettiin vuosina 2002 ja 2003 kotimaisista elintarvikkeista, naudoista, sioista ja siipikarjasta. Eläimistä eristetyt salmonellakannat olivat mikrobilääkkeille hyvin herkkiä. Vuosina 2002-2003 vain 4 % eläimistä eristetyistä kannoista oli resistenttejä yhdelle tai kahdelle mikrobilääkkeelle. Kaikki kotimaisista elintarvikkeista eristetyt kannat olivat herkkiä kaikille testatuille mikrobilääkkeille.

Kampylobakteereita eristettiin vuonna 2003 projektissa, jossa seurattiin termofiilisten kampylobakteerien esiintyvyyttä suomalaisissa naudoissa. Resistenssiä todettiin naudoista eristetyillä *C. jejuni* -kannoilla vain vähän. Kannoista 7 % oli resistenttejä ainakin yhdelle tutkitulle mikrobilääkeaineelle. Multiresistenssiä ei havaittu. Tavallisinta oli resistenssi ampisilliinille. Resistenssiä todettiin myös oksitetrasykliinille, enrofloksasiinille ja nalidiksiinihapolle.

Indikaattoribakteerien resistenssi

Vuosina 2002 ja 2003 mikrobilääkeresistenssiä tutkittiin terveiden broilereiden ja nautojen suolinäytteistä eristetyistä *E. coli* - ja enterokokkikannoista.

Resistenssitutkimukseen otettiin mukaan broilereista ja naudoista eristetyt *E. faecium* -kannat sekä broilereista eristetyt *E. faecalis* -kannat. Kansainvälisesti vertailtuna enterokokkien mikrobilääkeresistenssi oli Suomessa harvinaista. Se oli yleisempää broilereista kuin naudoista eristetyillä enterokokeilla. Erot rehun lisäaine- ja kokkidiostaattiresistenssissä johtunevat siitä, että näitä aineita käytetään tai on käytetty eri tavoin eri eläinlajeilla. Narasiinia käytetään kokkidiostaattina broilerituotannossa. Broilereista eristetyistä *E. faecium* -kannoista 72 %, mutta naudoista eristetyistä kannoista vain 1 % oli resistenttejä narasiinille.

Kaiken kaikkiaan 85 % broilereista eristetyistä enterokokkikannoista ja 26 % naudoista eristetyistä *E. faecium* -kannoista oli resistenttejä ainakin yhdelle tutkitulle mikrobilääkkeelle. Broilereiden enterokokeilla todettiin eniten narasiini-, oksitetrasykliini- ja basitrasiiniresistenssiä. Nautojen *E. faecium* -kannoilla todettiin eniten erytromysiini-, basitrasiini- ja oksitetrasykliiniresistenssiä.

Mikrobilääkeresistenssi oli harvinaista sekä broilereista että naudoista eristetyillä *E. coli* -kannoilla. Kaikkiaan 23 % broilereista ja 7 % naudoista eristetyistä *E. coli*-kannoista oli resistenttejä ainakin yhdelle mikrobilääkkeelle. Broilereiden *E. coli* -kannoilla todettiin eniten ampisilliini-, oksitetrasykliini- ja sulfametoksatsoliresistenssiä, kun taas naudoista eristetyt kannat olivat resistenteimpiä streptomysiinille, ampisilliinille ja sulfametoksatsolille.

Todetut resistenssit selittyvät osittain mikrobilääkkeiden tämänhetkisellä ja aiemmalla käytöllä sekä resistenssitekijöiden samanaikaisella valikoitumisella.

Eläimille tautia aiheuttavien bakteerien resistenssi

Sikojen suolitulehduksista eristetyistä *E. coli* -kannoista 72 % oli resistenttejä ainakin yhdelle mikrobilääkkeelle. Peräti 42 % tutkituista kannoista oli multiresistenttejä eli resistenttejä vähintään kolmelle mikrobilääkkeelle. Tavallisimpia olivat oksitetrasykliini- ja streptomysiiniresistenssit, mutta myös sulfametoksatsoli- ja trimetopriimiresistenssi oli yleistä. Vaikka fluorokinoloneja käytetään sikojen lääkinnässä suhteellisen vähän, peräti 19 % *E. coli* -kannoista oli resistenttejä enrofloksasiinille.

Koirista eristetyistä *S. intermedius* -kannoista 79 % oli resistenttejä ainakin yhdelle mikrobilääkkeelle ja 32 % kannoista oli multiresistenttejä. Penisilliiniresistenssi oli *S. intermedius* -kantojen keskuudessa pikemminkin sääntö kuin poikkeus. Myös oksitetrasykliini-, neomysiini-, streptomysiini- sekä makrolidi- ja linkosamidiresistenssiä todettiin paljon.

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Beskrivning

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Publikation Kartläggning över resistens mot antiobiotika inom veterinärmedicin i Finland samt förbrukning av antibiotika och fodertillsatsämnen

Resumé

I FINRES-Vet rapporten presenteras resultaten av resistensundersökningar från åren 2002 och 2003. Ytterligare rapporteras mängden konsumerad antibiotika år 2002 samt fodertillsatsämnen åren 2002 och 2003.

I Finland är resistenssituationen bland bakterier från djur gynnsam. Detta torde bero på den strikta läkemedelspolitiken. Antibiotika används till djur endast ordinerat av veterinär. I Finland utarbetades redan år 1996 riktlinjer för användning av antibiotika till de viktigaste inflammations- och infektionssjukdomarna hos djur. Rekommendationen uppdaterades år 2003. Meningen är att främja behärskad användning av antibiotika inom veterinärmedicinen och därigenom begränsa resistensutvecklingen.

Hos vissa bakteriearter finns dock oroväckande tendenser. Det är beständigt viktigt att upprätthålla behärskad och riktad användning av antibiotika.

Förbrukning av antibiotika och fodertillsatsämnen

Den totala förbrukningen av antibiotika inom den veterinärmedicinska vårdbransche under år 2002 var 13 000 kg aktiv substans. Förbrukningen av antibiotika har minskat stadigt de sista åren; minskningen har varit 27 % från 1995 till 2002. Minskningen kan förklaras dels med en minskad djurmängd, men även med förbättrade produktionsomständigheter och ett bättre medvetande om resistensrisken.

År 2002 var andelen betalaktamer 60 %, andelen trimetoprim/sulfonamider 18 % och andelen tetracyklin 15 % av alla antibiotika som användes för behandling av djur. Av alla läkemedel inom veterinärmedicinen som innehöll penicillin var 85 % känsliga för betalaktamaser.

Av alla antibiotika som användes till djur användes endast 4 % i läkemedelsfoder, varav ca 40 % till pälsdjur, 40 % till fisk och 20 % till svin. Ca 7000 kg antibiotika gavs som injektionspreparat år 2002. Mängden av antibiotika som gavs som injektionspreparat var relativt konstant mellan åren 1999 och 2002. G-penicillin har under åren varit det mest använda antibiotika, eftersom det ofta är det främsta alternativet med tanke på vården av flera sjukdomar hos produktionsdjur. Användning av penicillin är ett bra alternativ med tanke på behärskning av resistensut-

vecklingen.

År 2002 gavs ca 6000 kg antibiotika peroralt, och av dessa var tetracykliner och trimetoprim/sulfonamider de viktigaste; deras andel var 64 % av den totala mängden perorala antibiotika.

Användning av intramammarer under mjölkningsperioden förminskade från år 1999 till 2002. Förändringen berodde inte på en förminskad mjölkproduktion. I sinläggningsterapin har det inte hänt stora förändringar. Ca 20 % av mjölkkorna behandlas med sinläggningspreparat som innehåller antibiotika.

Den finska foderindustrin avstod frivilligt från att använda växtbefrämjande antibiotika på 1990-talet. Man slutade med att använda virginiamycin 1990, bacitracin 1992 och flavomycin och avoparcin år 1996. Användning av t. ex. virginiamycin och avoparcin slutade innan deras användning förbjöds inom EU.

För tillfället används egentliga växtbefrämjande antibiotika inte alls i Finland. Koccidiostater används profylaktiskt i broiler- och kalkonproduktion. De mest använda koccidiostaterna är monensin och narasin.

Resistens hos zoonotiska bakterier

Förekomsten av salmonellabakterier följs upp inom ramen av det nationella kontrollprogrammet för salmonella hos nötkreatur, svin, fjäderfä samt i kött och ägg. Uppföljning av resistens hos salmonella påbörjades redan under 1980-talet. Enligt resultaten i övervakningsprogrammet är prevalensen av salmonella i produktionsdjur och i animala livsmedel i Finland mycket låg.

Under åren 2002 och 2003 påvisade man *Salmonella* i inhemska livsmedel, nöt, svin och fjäderfä. De isolerade stammarna var mycket känsliga för antibiotika. Bara 4 % av salmonellastammarna isolerade från djur var resistenta mot ett eller två antibiotika. Alla stammar från inhemska livsmedel var känsliga mot alla testade antibiotika.

Campylobacter isolerades inom ramen för ett projekt där man undersökte förekomsten av termofila *Campylobacter* hos finska nötkreatur år 2003. Förekomsten av resistens var låg hos *C. jejuni* stammar isolerade från nöt. 7 % av stammarna var resistenta åtminstone mot ett antibiotikum. Multiresistens förekom inte. Det vanligaste var resistens mot ampicillin, men resistens förekom även mot oxytetracyklin, enrofloxacin och nalidixinsyra.

Resistens hos indikatorbakterier

Åren 2002 och 2003 undersöktes antibiotikaresistens hos *E. coli* och *Enterococcus* spp. isolerade från den normala tarmfloran från friska broiler och kor.

I resistensundersökningen inkluderades *E. faecium* stammar påvisade hos broiler och ko, samt *E. faecalis* stammar från broiler. Ur ett internationellt perspektiv var resistens hos enterococker i Finland sällsynt. Hos isolat från broiler förekom resistens oftare än hos isolat från kor. Skillnaderna i resistens i fodrets tillsatsämnen och koccidiostater mellan broiler och nötkreatur torde bero på ämnenas olika användning till dessa djurarter. Narasin har använts som koccidiostat i broilerproduktionen. 72 % av *E. faecium* från broiler var resistenta mot narasin, emedan endast 1 % av *E. faecium* stammarna från kor var resistenta.

Resistens mot åtminstone ett undersökt antibiotikum förekom hos 85 % av enterococker från broiler och 26 % av *E. faecium* stammarna isolerade från kor. Enterococker från broiler visade sig vara oftast resistenta mot narasin, oxytetracyclin och bacitrasin. Hos enterococker från kor konstaterade man oftast resistens mot

erytromycin, bacitrasin och oxytetracyclin.

Förekomsten av resistens hos *E. coli* från broiler och ko var ovanlig. Resistens mot åtminstone ett antibiotikum förekom hos 23 % av *E. coli* stammarna påvisade hos broiler och 7 % av stammarna från kor. Hos *E. coli* från broiler konstaterade man oftast resistens mot ampicillin, oxytetracyklin och sulfa, och *E. coli* från kor var mest resistenta mot streptomycin, ampicillin och sulfa.

Den konstaterade resistenssituationen beror dels på tidigare och nutida användning av antibiotika, dels på co-selektion av resistensfaktorer.

Resistens hos sjukdomsframkallande bakterier

Av *E. coli* –stammar från enteriter hos gris var 72 % av isolaten resistenta mot åtminstone ett antibiotikum. Av de undersökta stammarna var 42 % multiresistenta, dvs. resistenta mot åtminstone tre antibiotika. Resistens mot oxytetracyklin och streptomycin var de mest prevalenta resistenstyperna, men även resistens mot trimetoprim/sulfametoksazol var vanlig. Trots att endast små mängder enrofloxacin används för behandling av svin, visade rentav 19 % av *E. coli*-stammar resistens mot enrofloxacin.

Av alla undersökta *S. intermedius*-stammar från hundar var 79 % resistenta mot åtminstone ett antibiotikum, och 32 % av stammarna var multiresistenta. Penicillinresistens var oftare en regel än ett undantag hos *S. intermedius* –stammarna. Även resistens mot oxytetracyklin, neomycin, streptomycin samt makrolider och linkosamider förekom ofta.

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Summary

This FINRES-Vet report presents resistance data for the years 2002 and 2003. The report also contains data on the consumption of antimicrobial agents for 2002 and feed additives in animals for 2002 and 2003.

Overall, the data in this report reveal a favourable resistance situation. This is probably the outcome of a strict antimicrobial policy. In Finland, antimicrobials for veterinary use, including medicated feed, are prescribed only by veterinarians. Recommendations for the prudent use of antimicrobial agents to treat the most important infectious diseases in animals were made in 1996, and updated in 2003. The objective of the recommendations was to promote the prudent use of antimicrobials in animal therapeutics in order to control the rise of antimicrobial resistance.

However, some of the resistance data are worrying, and indicate a persistent need for prudent use. The treatment of infections should continue to be as specific as possible.

Use of antimicrobial agents

The total amount of antimicrobial products used in Finland in 2002 for veterinary treatment was 13 000 kg of active substance. The volume of antimicrobial products used in veterinary medicine has declined consistently over recent years: by 27% from 1995 to 2002. Part of this decrease has been due to the declining numbers of animals, but also to improved management of domestic animals and growing awareness of risk of resistance.

β-lactams accounted for 60%, sulphonamide-trimethoprim for 18%, and tetracyclines for 15% of the total veterinary antimicrobial sales in 2002. Penicillins sensitive to β-lactamase accounted for 85% of the veterinary penicillin preparations sold.

The proportion of antimicrobial products used in medicated feed in 2002 was only 4%. About two-fifths were used for fur animals, two-fifts for fish, and one-

fifth for pigs. Antimicrobial medicines given in injectable form amounted to about 7000 kg in 2002. The volume remained relatively stable during the period of 1999 to 2002. Penicillin G remains the dominant antimicrobial substance, with little variation over the years, due to its position as the drug of choice in many diseases of production animals. This is a favourable pattern of use considering the risk of microbial resistance.

About 6000 kg oral antimicrobials were used in 2002. Tetracyclines and sulphonamides (together with trimethoprim) were dominant; together they accounted for 64% of all orally administered antimicrobials.

Intramammary treatment during lactation diminished during 1999 to 2002, but not as the result of declining milk production. In drycow treatment there were no great changes during four years of observation. Approximately 20% of the dairy cows were treated with antibiotic drycow preparations at drying-off.

The Finnish feed industry voluntarily quit the use of antimicrobial growth promoters in the 1990s. Virginiamycin was abandoned in 1990, bacitracin in 1992 and flavomycin and avoparcin in 1996. The use of e.g. virginiamycin and avoparcin was terminated before they were officially prohibited by the EU.

At present, no growth promoters are used in Finland. Coccidiostats are employed as prophylactic anti-parasitic agents in broiler and turkey production. Monensin and narasin are the most widely used coccidiostats.

Resistance in zoonotic bacteria

The prevalence of *Salmonella* in cattle, pigs and poultry, as well as in meat and eggs is monitored through the national *Salmonella* control programme. The monitoring of antimicrobial resistance in *Salmonella* began at early 80s. According to the results the occurrence of *Salmonella* is rare in production animals and foods of animal origin.

Salmonella isolates were collected from domestic food, cattle, pigs and poultry in 2002 and 2003. The strains isolated were very sensitive to antimicrobial agents. In 2002 to 2003, only 4% of the animal isolates were resistant to one or two antimicrobials. All strains found in domestic foodstuffs were sensitive to all antimicrobials tested.

Campylobacter isolates were collected in a survey of the prevalence of thermophilic *Campylobacter* in Finnish cattle in 2003. Resistance among *C. jejuni* from cattle was rare; only 7% of isolates were resistant to at least one antimicrobial. Multiresistance was not detected. Resistance to ampicillin was most prevalent, followed by resistance to oxytetracycline, enrofloxacin and nalidixic acid.

Resistance in indicator bacteria

Antimicrobial resistance in *E. coli* and *Enterococcus* spp. isolated from faecal samples of healthy broilers and cattle was monitored in 2002-2003.

Of the enterococci, *E. faecium* was monitored from broilers and cattle and *E. faecalis* from broilers. In the international perspective, resistance was rare. Isolates from broilers showed resistance more often than those from cattle. Differences in resistance against feed additives and coccidiostats may be due to the fact that the use pattern differs in poultry and cattle. The most obvious example was narasin, which is used as a coccidiostat in broiler production: 72% of the broiler *E. faecium* isolates were resistant to it, while only 1% of the cattle isolates were narasin resistant.

In total, 85% of the enterococcal isolates from broilers and 26% of *E. faecium* isolates from cattle were resistant to at least one antimicrobial. In broiler enterococci, narasin, oxytetracycline and bacitracin resistance were most common. In strains of cattle *E. faecium* erythromycin, bacitracin and oxytetracycline resistances were most common.

Overall resistance was rare among *E. coli* isolates isolated from broilers and cattle. In total, 23% of the isolates from broilers and 7% of those from cattle were resistant to at least one antimicrobial. The most common resistance traits in *E. coli* isolated from broilers were to ampicillin, oxytetracycline and sulphamethoxazole. In bovine isolates, resistance to streptomycin was most prevalent, followed by ampicillin and sulphamethoxazole.

Some cases of bacterial resistances can be explained by the current use of the respective antimicrobial, and some may reflect earlier antimicrobial use or concurrent selection for resistance.

Resistance in animal pathogens

Of the *E. coli* isolated from enteritis in pigs, 72% were resistant to at least one antimicrobial. As many as 42% of the strains were multiresistant, i.e. resistant to at least three antimicrobials. A high prevalence of both oxytetracycline and streptomycin resistance was detected. Resistance to both sulphamethoxazole and trimethoprim was also common. In spite of the apparently limited use of fluoroquinolones, resistance to them was observed in 19% of the isolates.

Of the *S. intermedius* isolates from dogs, 79% were resistant to at least one antimicrobial, and 32% were multiresistant. Penicillin resistance was the rule rather than the exception. Resistances to oxytetracycline, neomycin, streptomycin, macrolides and lincosamides were, after penicillin, most common.

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Johdanto

Mikrobilääkkeiden tehon säilyttäminen on yksi ihmisten ja eläinten lääkinnän suurimmista haasteista. Mikrobilääkeresistenssin aiheuttamia ongelmia ei pystytä ratkaisemaan uusia mikrobilääkkeitä kehittämällä, joten ainoita tehokkaita keinoja resistenssiongelman hallitsemiseksi ovat mikrobilääkkeiden hallittu käyttö sekä infektioiden ennaltaehkäisy. Resistenssiä ja mikrobilääkkeiden kulutusta tulee seurata säännöllisesti. Resistenssitilanteen säännöllinen seuranta mahdollistaa sen, että bakteerien resistenssissä tapahtuvat muutokset havaitaan mahdollisimman aikaisin ja tilanteeseen voidaan tarvittaessa puuttua. Resistenssiseurannan tuloksia hyödynnetään myös, kun kehitetään mikrobilääkepolitiikkaa ja annetaan mikrobilääkkeiden käyttösuosituksia.

Eläimistä eristettyjen bakteerien mikrobilääkeherkkyyttä on tutkittu Suomessa jo vuosikymmenien ajan. Esimerkiksi salmonellojen resistenssiä on seurattu 1980-luvun alusta asti. FINRES 1999-raportissa julkaistiin tietoja tärkeimpien eläimistä ja ihmisistä eristettyjen tautia aiheuttavien bakteerien sekä eläimistä eristettyjen indikaattoribakteerien resistenssitilanteesta.

Vuonna 2002 alkaneen resistenssin seurantaohjelman (FINRES-Vet) tavoitteena on seurata ja analysoida tärkeimmistä tuotantoeläinlajeista ja lemmikkieläimistä eristettyjen bakteerien mikrobilääkeaineresistenssissä tapahtuvia muutoksia, havaita uusien resistenttien kloonien ja fenotyyppien kehittyminen sekä seurata mikrobilääkkeiden kulutusta.

Ohjelmassa seurataan kolmen eri bakteeriryhmän, zoonoosia aiheuttavien bakteerien, eläimille tautia aiheuttavien bakteerien ja indikaattoribakteerien, mikrobilääkeherkkyyttä. Zoonoosit ovat tauteja, jotka voivat siirtyä eläimistä ihmisiin ja päinvastoin. Zoonoosia aiheuttavat bakteerit voivat tulla resistenteiksi eläimessä, minkä seurauksena sekä eläinten että ihmisten infektiotautien hoito saattaa vaikeutua. Eläimille tautia aiheuttavat bakteerit on usein eristetty vakavista ja uusiutuvista infektioista, minkä takia tieto niiden resistenssitilanteesta voi olla väärin painottunutta. Indikaattoribakteerit ovat terveiden eläinten suolistosta eristettyjä bakteereita. Niiden resistenssi kuvaa bakteeripopulaatioon kohdistunutta mikrobilääkkeiden käytön aiheuttamaa valintapainetta; normaaliflooran bakteerien resistenssin ajatellaan ennakoivan resistenssiä myös tautia aiheuttavilla bakteereilla.

Eläinlääkintä- ja elintarviketutkimuslaitos (EELA) koordinoi FINRES-Vet-ohjelmaa. Lääkelaitos seuraa eläimille käytettyjen mikrobilääkkeiden kulutusta ja Kasvintuotannon tarkastuskeskus (KTTK) rehun lisäaineiden kulutusta.

Kiitokset

FINRES-Vet-ohjelman koordinoijat kiittävät Elintarvikeviraston ja teurastamoiden lihantarkastushenkilökuntaa näytteiden keräämisestä. Suomen tarkastuseläinlääkäriyhdistystä kiitetään osallistumisesta ohjelman suunnitteluun.

Introduktion

En av de största utmaningarna inom human- och veterinärmedicin är att behålla antibiotika verksamma. Antibiotikaresistens medför problem som inte kan lösas genom att utveckla nya läkemedel, utan de enda effektiva medel för att behärska resistensproblemet är omdömesgillt bruk av antibiotika tillsammans med förebyggande åtgärder. Resistens och förbrukning av antibiotika skall uppföljas regelbundet för att kunna notera förändringar i resistens så tidigt som möjligt och att vid behov kunna ingripa i saken.

Antibiotikaresistens hos bakterier från djur har undersökts i Finland redan i årtionden. Resistens hos *Salmonella* har undersökts sedan 1980-talet. I rapporten FINRES 1999 publicerades information om resistenssituationen bland de viktigaste sjukdomsframkallande bakterier både hos människa och hos djur.

Det finska resistensprogrammet inom veterinärmedicinen FINRES-Vet påbörjades år 2002. Dess syfte är att följa och analysera förändringar i resistens hos bakterier från de viktigaste produktions- och sällskapsdjuren, bemärka utvecklingen av nya resistentkloner och fenotyper samt användningen av antibiotika.

I programmet följer man antibiotikaresistens hos zoonotiska bakterier, bakterier som förorsakar sjukdom hos djur och indikatorbakterier. Zoonoser är sjukdomar som kan smitta mellan människa och djur. Zoonotiska bakterier kan bli resistenta i djur, vilket medför att den terapeutiska arsenalen inom human- och veterinärmedicinen blir begränsad. Bakterier som förorsakar sjukdom hos djur har ofta isolerats från problematiska och återkommande infektioner, varför data om deras resistenssituation kan vara vinklade. Indikatorbakterier har isolerats från friska djurs tarmar. Resistens hos indikatorbakterier framställer det selektionstryck som användning av antibiotika mot en viss bakteriepopulation utgör; man tänker att resistens hos normalflorans bakterier förutsäger resistens även hos sjukdomsframkallande bakterier.

Forskningsanstalten för veterinärmedicin och livsmedel (EELA) koordinerar programmet FINRES-Vet. Läkemedelsverket följer användningen av antibiotika för djur och Kontrollcentralen för växtproduktion användningen av fodertillskottsämnen.

Tack!

Koordinatorer av programmet FINRES-Vet tackar köttbesiktningspersonalen från Livsmedelsverket och slakterier för insamlandet av prover. Finlands Besiktningsveterinärförening tackas för deltagandet i planeringen av programmet.

Introduction

Maintaining the efficacy of antimicrobial substances is one of the biggest challenges in human and veterinary medicine. Antimicrobial resistance cannot be overcome by developing new medicines, and thus the only effective means remaining is the prudent use of antimicrobials coupled with preventive measures. Resistance and consumption of antimicrobials should be monitored in order to provide a basis for policy adjustment and prudent use recommendations, and to identify the need for potential interventions.

Antimicrobial susceptibility testing of bacteria isolated from animals has been carried out in Finland for decades. Antimicrobial resistance monitoring of *Salmonella* from Finnish animals began in the early 1980s. Information on the resistance situation of the clinically most significant bacteria both in human and veterinary medicine, as well as indicator bacteria isolated from animals, was published in the FINRES 1999 report.

A regular resistance monitoring programme, The Finnish Veterinary Antimicrobial Resistance Monitoring Programme (FINRES-Vet), was established in 2002. The objectives of FINRES-Vet are to monitor and analyse trends in prevalence of resistance to antimicrobial agents in the major food producing animals and pets, and to monitor the emergence of resistant clones, the development of new resistance phenotypes and the use of antimicrobial agents.

The surveillance is targeted at zoonotic bacteria, animal pathogens and indicator bacteria. Zoonotic bacteria are bacteria isolated from animals but capable of causing human infections. They may become resistant to antimicrobials in an animal, and subsequently lead to treatment failures in animals and humans. Animal pathogens cause clinical infections in animals. Data on their resistance can be biased toward severe or recurrent clinical cases. Indicator bacteria are commensal bacteria isolated from healthy animals. Their resistance is a good indicator of the selection pressure caused by antimicrobial use in that population and of resistance problems in expected pathogens.

FINRES-Vet is coordinated by the National Veterinary and Food Research Institute (EELA). The consumption of antimicrobial agents for veterinary use is monitored by the National Agency for Medicines (NAM), and the consumption of feed additives by the Plant Production Inspection Centre (KTTK).

Acknowledgements

The coordinators of the FINRES-Vet programme would like to thank the meat inspection personnel of the National Food Agency and slaughterhouses for collecting the samples from animals at slaughter. Association for Official Veterinarians in slaughterhouses is also acknowledged for their contribution in the programme.

Use of therapeutic antimicrobials and feed additives for animals in Finland

Veterinary medicinal products

The National Agency for Medicines monitors the quantity of veterinary medicinal products, including antimicrobial, used in Finland. The following consumption figures were gathered from pharmaceutical wholesale companies. In addition, sales figures for antimicrobial premixes were collected by the Plant Production Inspection Centre of the Ministry of Agriculture and Forestry.

The figures include products that have marketing authorisation as well as those sold under special licence. Drugs authorised for human use but prescribed for animals are not included. It is unlikely that their absence skews the total markedly, as the proportion of such products used in canine practice is estimated to be about 10% and in feline practice about 5%.

Volume of use

The total yearly volumes of antimicrobial products used in veterinary treatment up to 2002 are given in Table 1, calculated as kg of the active substance. The volume has declined consistently over recent years - since 1995 by about 27% (Figure 1).

The proportion of antimicrobial products used in medicated feed was only 4% in 2002. About two-fifths were used for fur animals, the same amount for fish and one-fifth for pigs.

Table 1.
The total amount of antimicrobial products authorised for veterinary use expressed as kg active substance including imported medicated feed for fish (except for 1999).

ATCvet code	Substance class	1999	2000	2001	2002
QG01AA, QJ01AA, QD06AA,	Tetracyclines	2495	2228	1937	1980
QJ01CE, QJ01R, QJ51R	Penicillin G	6251	5499	6235	6054
QJ01CA, QJ01CR	Aminopenicillins	396	521	532	637
QJ01D,QJ51RD01, QJ51CF, QJ51CR	Other beta-lactam antimicrobials				
QJ51RD, QJ01DA	Cephalosporins	1178	1214	1153	1055
QJ51CR, QJ51CF	Cloxacillin	95	151	149	105
QA07AA, QJ01G, QJ01R, QJ51R	Aminoglycosides	727	610	632	385
QJ01E	Sulphonamides and trimethoprim	2121	2228	2490	2342
QJ01F	Macrolides and lincosamides	627	523	492	492
QJ01MA, QJ01MB	Fluoroquinolones, quinoxalines	126	116	101	95
QJ01XX, QJ01B	Other substances	116	156	103	97
Total		**14 132**	**13 247**	**13 824**	**13 242**

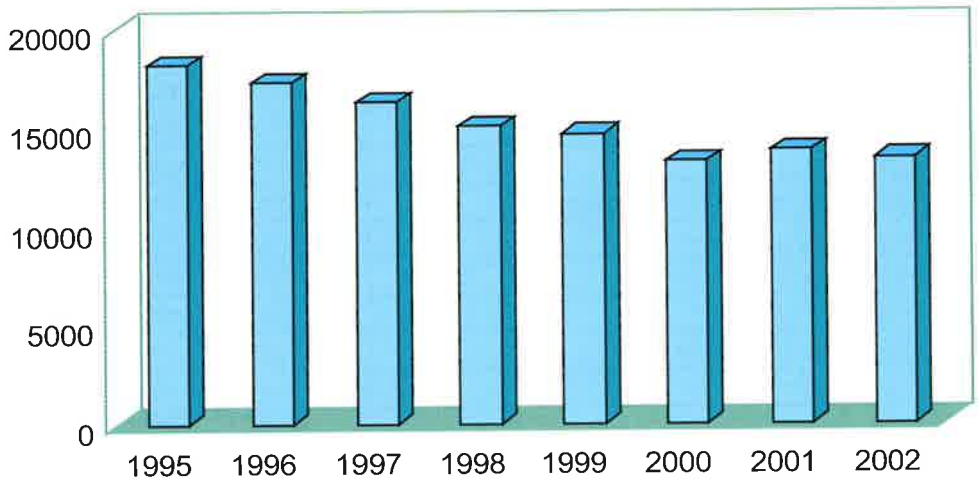

Figure 1.
Total sales of veterinary antimicrobial medicines in Finland, kg of active substance.

Injectable and orally used antimicrobial products

The amounts of antimicrobial medicines given in injectable form appear in Table 2. Overall, the volume has remained relatively stable. Penicillin G is still the dominant antimicrobial substance, with little variation over the years, due to its status as drug of choice in many diseases of production animals.

Table 3 lists the consumption of groups of antimicrobial products used orally for animals. Tetracyclines and sulphonamides (together with trimethoprim) remained the most important in the treatment of domestic animals. Together they accounted for 64% of all orally administered antimicrobials.

Table 2.
Antimicrobial substances used in injectables (kg of active substance) 1999-2002.

ATCvet code	Substance class	1999	2000	2001	2002
QG01AA, QJ01A	Tetracyclines	165	188	196	143
QJ01CE, QJ01R, QJ51R	Penicillin G	5988	5257	5981	5799
QJ01CA, QJ01CR	Aminopenicillins	43	59	76	115
QJ01E	Sulphonamides and trimethoprim	481	492	599	474
QJ01F	Macrolides and lincosamides	64	63	63	70
QJ01MA	Fluoroquinolones	68	69	70	70
QJ01BA,QJ01GA, QJ01DA	Other substances	1	1	2	0
Total		**6810**	**6129**	**6987**	**6671**

Table 3.
Total amount of oral antimicrobial products authorised for veterinary use (kg of active substance).

ATCvet code	Substance class	1999	2000	2001	2002
QJ01A, QD06AA, QS03CA	Tetracyclines	2177	2030	1672	1799
QJ01CA, QJ01CR	Aminopenicillins	333	440	424	508
QJ01DA	Other beta-lactam antimicrobials (Cephalosporins)	865	949	939	887
QA07AA, QJ01R	Aminoglycosides	170	166	150	142
QJ01E	Sulphonamides and trimethoprim	1640	2326	1892	1868
QJ01F	Macrolides and lincosamides	563	461	428	357
QJ01MA, QJ01MB	Fluoroquinolones, quinoxalines	58	59	31	44
QJ01XX, QJ01B	Other substances	104	156	101	87
Total		**5910**	**6587**	**5637**	**5692**

Intramammary antimicrobials

Table 4 presents the quantities of antimicrobials used for dry cow treatment of mastitis, expressed as kg of active substance. There were no great changes during four years of observation.

The quantity of antimicrobials used in intramammary treatment during lactation diminished over the years, as seen in Table 5. This change has not been caused by diminishing milk production. In 1998, 0.52 mg of intramammary antibiotics was used for each litre of milk produced. By 2002, this amount had fallen to 0.34 mg. The same trend can be seen in Table 6, which demonstrates the use of intramammary antimicrobials in defined daily doses (DDDs) per 1000 cows at risk.

Table 4.
Antimicrobials for intramammary use for dry cow period (kg of active substance).

ATCvet code	Substance class	1999	2000	2001	2002
QJ51CR, QJ51CF, QJ51RD	Aminopenicillins, cephalosporins, cloxacillins	112	125	125	112
QJ51RC	Penicillin G	30	29	29	32
QJ51RC	Aminoglycosides and other substances	86	75	70	53
Total		**228**	**229**	**224**	**197**

Table 5.
Antimicrobials for intramammary use during lactation period, expressed in kg.

ATCvet code	Substance class	1999	2000	2001	2002
QJ51CR, QJ51CF, QJ51RD	Cephalosporin and cloxacillin	297	295	245	207
QJ51CR	Aminopenicillins	20	24	25	25
QJ51RC	Penicillin G	233	217	225	223
QJ51RC	Aminoglycosides and other substances	478	373	414	194
Total		**1028**	**909**	**909**	**649**

General comments

The diminishing use of antimicrobial substances probably reflects improved management of domestic animals and growing awareness of the risk of resistance. A number of antimicrobial therapies can be identified, where further prudence could be exercised. These include intrauterine treatment of retained placenta in the cow. About 38 kg of oxytetracycline was used in total for this indication, despite no proven benefit. Another obsolete treatment is the oral use of dihydrostreptomycin for gastroenteritis in calves and pigs.

Table 6.
Antimicrobials for intramammary use calculated as number of single-dose applicators per 1000 cows per day.

Indication	1999	2000	2001	2002
Therapy during lactation[1]	3.9	3.77	3.73	3.64
Dry cow treatment[2]	0.55	0.57	0.59	0.58
Total	**4.45**	**4.34**	**4.32**	**4.22**

[1]DDD = two intramammary tubes/day/cow
[2]DDD = four intramammary tubes/day/cow

Antimicrobial feed additives

The Plant Production Inspection Centre monitors the consumption of feed additives annually by collecting data from feed manufacturers. The Finnish feed industry (producing feed for food producing animals) voluntarily terminated the use of antimicrobial growth promoters in the 1990s. The use of virginiamycin was ended in 1990, the use of bacitracin in 1992 and the use of flavomycin and avoparcin in 1996. E. g. virginiamycin and avoparcin were terminated before their use was officially prohibited by the EU in 1998 and 1997, respectively.

Table 7 presents the total sales of feed additives in Finland in 1993-2003. At present, no growth promoters are used in Finland. Coccidiostats are used as prophylactic anti-parasitic agents in broiler and turkey production. Monensin and narasin are the most widely used coccidiostats.

Table 7.
The use of antimicrobial feed additives, coccidiostats and growth promoters in Finland in 1993-2003 (kg active substance/year).

	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003
Amprolium (and ethopabate)					427 (27)	148 (9)	74 (5)	79	22	0	0
Avoparcin	3106	3389	1 294	47	0	0	0	0	0	0	0
Dimetridazole	214	228	231	204	63	42	0	0	0	0	0
Flavomycin	250	241	60	7	0	0	0	0	321[1]	31[1]	0
Lasalocid sodium	0	0	0	0	0	3024	3019	2 796	3624	3349	176
Carbadox	4465	4122	2 614	1 841	1 123	3286	1082	0	0	0	0
Olaquindox	3	15	1 576	2 882	2 883	730	0	0	0	0	0
Madmuramycin ammonium	144	103	0	0	0	0	0	0	0	8	43
Monensin	3292	5736	5 754	3 653	4 375	632	353	0	1475	1969	4422
Narasin	0	450	1 935	2 232	1 959	2866	2568	2 549	2101	5569	5769
Salinomycin	512	472	216	1 705	3 657	2320	3246	2 829	3272	28	3
Nifursol							188	0	0	0	0
Robenidine hydrochloride			0	0	0	0	0	67	0	0	0

[1]Used in exported feed mixtures

Resistance in zoonotic bacteria

Antimicrobial resistance in zoonotic bacteria represents a major public health problem worldwide. Isolates of *Salmonella* with resistance to antimicrobial drugs are widespread in both developed and developing countries. In developed countries it is now increasingly accepted that for the most part such isolates are of zoonotic origin and acquire their resistance in the food-animal host before onward transmission to humans through the food chain (Threlfall, 2002). Today, campylobacters are the most frequent cause for bacterial gastroenteritis around the world (Aarestrup and Engberg, 2001) including Finland (Huovinen et al., 2002). Recent data show a marked increase in resistance of *Campylobacter* especially to quinolones in developed countries (Coker et al., 2002). Data on trends and sources of zoonotic agents in animals, feed-stuffs, food and humans in Finland are published in a report (MAF, 2003a).

The FINRES-Vet programme includes *Salmonella* isolated from production animals and domestic food, as well as *Campylobacter* from domestic animals. In 2003, *Campylobacter* were collected from bovine cattle. *Salmonella* isolates were isolated from cattle, pigs and poultry in 2002 and 2003.

Salmonella in production animals and domestic food

The prevalence of *Salmonella* in cattle, pigs and poultry, as well as in meat and eggs, is monitored through the national *Salmonella* control programme. The objective of the programme is to maintain the annual incidence of *Salmonella* contamination among production animals, and in associated meat and eggs, at 1% or less (EELA, 2003a and b). The programme's results show that the occurrence of *Salmonella* in production animals and foods of animal origin is quite rare in Finland. Isolates from the national control programme and domestic food were included in the present report.

Results and comments

Of the 70 isolates from domestic animals included, 27 were *S.* Typhimurium, 9 *S.* Infantis, 6 *S.* Livingstone, 6 *S.* Tennessee, 5 *S.* Montevideo, 5 *S.* Brandenburg, 4 *S.* Konstanz, 3 *S.* Enteritidis and 5 isolates were other serovars. Nine isolates were from turkeys, 22 from cattle, 20 from pigs and 19 from poultry (*Gallus gallus*).

Resistance was rare (Table 8). Only three animal isolates (4%) were resistant to one or two antimicrobials. One bovine *S.* Tennessee isolate was resistant to streptomycin, one poultry *S.* Montevideo isolate to ampicillin and sulphamethoxazole, and one porcine *S.* Typhimurium isolate to enrofloxacin. No multiresistance was detected.

Of the food isolates, 14 were *S.* Typhimurium, 3 *S.* Enteritidis, 3 *S.* Infantis and three were other serovars. Of the food isolates (n=23) all were sensitive to every antimicrobial tested (Table 9).

Table 8.
Distribution of MICs for *Salmonella* in production animals (n=70).

Substance	% resistant	Distribution (%) of MICs (mg l^{-1})															
	(95 % CI)	≤ 0,03	0,06	0,12	0,25	0,5	1	2	4	8	16	32	64	128	256	512	>512
Ampicillin	1 (0.0-7.7)					7.1	70.0	18.6	2.9				1.4				
Ceftiofur	0 (0.0-5.1)					41.4	51.4	7.1									
Chloramphenicol	0 (0.0-5.1)								94.3	5.7							
Enrofloxacin	1 (0.0-7.7)		28.6	70.0	1.4												
Florfenicol	0 (0.0-5.1)								92.9	7.1							
Gentamicin	0 (0.0-5.1)					31.4	64.3	4.3									
Nalidixic acid	0 (0.0-5.1)							1.4	80.0	18.6							
Neomycin	0 (0.0-5.1)							94.3	5.7								
Oxytetracycline	0 (0.0-5.1)						17.1	57.1	25.7								
Streptomycin	1 (0.0-7.7)								5.7	40.0	42.9	10.0	1.4				
Sulphamethoxazole	1 (0.0-7.7)												97.1	1.4			1.4
Trimethoprim	0 (0.0-5.1)				42.9	45.7	10.0	1.4									

Bold vertical lines indicate microbiological cut-off values for resistance. Hatched fields denote range of dilutions tested for each substance. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration.

Table 9.
Distribution of MICs for *Salmonella* from domestic food (n=23)

Substance	% resistant	Distribution (%) of MICs (mg l^{-1})															
	(95 % CI)	≤ 0,03	0,06	0,12	0,25	0,5	1	2	4	8	16	32	64	128	256	512	>512
Ampicillin	0 (0.0-14.8)					4.3	87.0	8.7									
Ceftiofur	0 (0.0-14.8)					30.4	69.6										
Chloramphenicol	0 (0.0-14.8)								95.7	4.3							
Enrofloxacin	0 (0.0-14.8)		34.8	65.2													
Florfenicol	0 (0.0-14.8)								87.0	13.0							
Gentamicin	0 (0.0-14.8)					34.8	60.9	4.3									
Nalidixic acid	0 (0.0-14.8)							4.3	78.3	17.4							
Neomycin	0 (0.0-14.8)							100.0									
Oxytetracycline	0 (0.0-14.8)						17.4	60.9	21.7								
Streptomycin	0 (0.0-14.8)								8.7	21.7	65.2	4.3					
Sulphamethoxazole	0 (0.0-14.8)												100.0				
Trimethoprim	0 (0.0-14.8)				47.8	52.2											

Bold vertical lines indicate microbiological cut-off values for resistance. Hatched fields denote range of dilutions tested for each substance. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration.

Table 10.
Distribution of MICs for *Campylobacter jejuni* from cattle (n=90).

Substance	% resistant	Distribution (%) of MICs (mg l^{-1})													
	(95 % CI)	≤ 0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ampicillin	4 (1.2-11.0)					7.8	5.6	22.2	50.0	10.0		2.2	2.2		
Enrofloxacin	1 (0.0-6.0)	1.1	25.6	65.6	4.4	2.2				1.1					
Erythromycin	0 (0.0-4.0)			6.7	43.3	37.8	11.1	1.1							
Gentamicin	0 (0.0-4.0)				22.2	57.8	15.6	4.4							
Nalidixic acid	1 (0.0-6.0)							3.3	41.1	48.9	5.6				1.1
Oxytetracycline	1 (0.0-6.0)				78.9	15.6	2.2	2.2	1.1						

Bold vertical lines indicate microbiological cut-off values for resistance. Hatched fields denote range of dilutions tested for each substance. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration.

Campylobacter jejuni in cattle

Campylobacter isolates were isolated in a survey of the prevalence of thermophilic *Campylobacter* in Finnish cattle in 2003. Bovine faecal samples were collected at slaughter; the number of randomly taken samples from each plant was proportional to the annual slaughtering volume. Of the *C. jejuni* isolated, 90 were randomly selected for antimicrobial sensitivity testing.

Results and comments

According to the results, resistance among *C. jejuni* from cattle was rare. Of the isolates tested, 7% were resistant to at least one antimicrobial. No multiresistance was detected. Resistance to ampicillin was most prevalent (4%). One isolate (1%) was resistant to oxytetracycline and one to enrofloxacin and nalidixic acid. No resistance was detected to erythromycin or gentamicin.

The use of ampicillin, oxytetracycline and enrofloxacin for cattle in Finland is the probable cause of the cases of resistance detected. Erythromycin has been used for the treatment of cattle, whereas gentamicin has not been used for cattle in Finland.

Resistance in indicator bacteria

As a result of exposure to antimicrobials, the resistance against antimicrobials among bacteria of the normal intestinal flora of animals increases (van den Bogaard and Stobberingh, 1999). Resistance in the endogenous flora is considered a good indicator of the selection pressure caused by antimicrobial use in that population and of resistance problems in expected pathogens (Murray, 1992). These bacteria develop a reservoir of transferable resistance genes from which antimicrobial resistance can spread to other bacteria, including those responsible for infections in animals and humans (NORM/NORM-VET, 2002).

Escherichia coli, *Enterococcus faecalis* and *Enterococcus faecium* were chosen as indicator bacteria according to the ARBAO guidelines (ARBAO, 2004). Enterococci are known to acquire antimicrobial resistance with relative ease and to be able to spread their resistance genes to other species (Kühn et al., 2000).

Enterococci and *E. coli* were isolated from broiler caecal and cattle faecal samples collected at slaughter. About 30% of the cattle samples were taken from dairy cows.

Enterococcus spp. in broilers and cattle

Enterococci were isolated from 97% of broiler caecal samples and from 79% of bovine faecal samples. *Enterococcus faecium* was isolated from 61% of the broiler samples and from 19% of the bovine samples. *E. faecalis* was isolated from 10% of the broiler samples, but from only 4% of the bovine samples. Because of the small number of *E. faecalis* isolates from cattle, these were excluded from the results. The material in resistance testing was constituted of 303 enterococci isolates from broilers and 70 isolates from cattle.

Results and comments

The MIC distribution and the occurrence of resistance among enterococci from broiler chickens and cattle are presented in Tables 11 and 12. Because of inherent resistance, virginiamycin resistance in *E. faecalis* and flavomycin resistance in *E. faecium* were excluded from the results.

Antimicrobial resistance was rarer among bovine isolates than among isolates acquired from broilers. Differences in resistance against feed additives and coccidiostats in cattle and broiler isolates may be because their use pattern in these species is not the same. The most obvious example was narasin, which is used as a coccidiostat in broiler production; 72% of the broiler *E. faecium* isolates, but only 1% of the cattle isolates, were resistant to it.

BROILERS

In poultry, low infection prevalence and absence of many significant infections, coupled with favourable production conditions, have kept the incidence of secondary bacterial infections negligible. The need for antimicrobials is rare (MAF, 2003b), and in practice no therapeutic antimicrobials are used for broilers. There is some use of penicillin V, ampicillin, sulpha-trimethoprim and oxytetracycline for broiler parents.

The comparatively common resistance to erythromycin (27 and 33%) and oxytetracycline (36 and 24%) in *E. faecium* and *E. faecalis* isolates, respectively, cannot be explained by their use; the reason may be co-selection or their use over recent years. Multiple resistance-transfer agents can collect and recombine extant resistance gene cassettes in almost any combination. Consequently, treatment with any given antimicrobial agent can result in selection for bacteria resistant not only to that specific agent, but by genetic linkage of resistance genes also to other unrelated antimicrobial agents; periodic exposure to any antimicrobial will maintain a multiresistance array in a bacterial population. Furthermore, the host-commensal ecosystem can serve as a relatively stable reservoir of resistant microorganism long after the cessation of antimicrobial treatment (Summers, 2002).

Although the use of Zn-bacitracin ended in 1992, resistance to bacitracin was 30% in broiler *E. faecium* isolates and 39% in *E. faecalis* isolates. Cross-resistance between avoparcin and the related glycopeptide vancomycin has been demonstrated (Klare et al., 1995), and the high occurrence of *vanA* enterococci has been associated with the use of avoparcin in animal production (Kühn et al., 2000). Avoparcin was prohibited in the European Union in 1997, but Finland had already voluntarily terminated its use in 1996. Coccidiostats are widely used in broiler production (Table 7).

E. faecium

Most *E. faecium* isolates from broilers, 89%, were resistant to at least one antimicrobial: 30% were resistant to one antimicrobial, 37% to two, 9% to three, and 12% to four or more antimicrobials.

The prevalence of vancomycin resistance was small in broiler *E. faecium* isolates, 3%. The MIC of six isolates was ≥ 128 mg l^{-1}, and of one isolate 8 mg l^{-1}.

Of the isolates resistant to more than one antimicrobial, 94% were resistant to narasin, a finding in accordance with Swedish results: of the *E. faecium* isolated from broilers in Sweden, 98% resistant to more than one antimicrobial were resistant to narasin (SVARM, 2002). Of the isolates resistant to oxytetracycline, 82% were resistant to at least one other antimicrobial.

The use of virginiamycin ceased in 1990. Resistance to virginiamycin was 11%. A small proportion (2%) of the *E. faecium* isolates was resistant to ampicillin, avilamycin and chloramphenicol. No resistance was detected to gentamicin, neomycin or streptomycin. Resistance to virginiamycin can be explained by its previous use.

Of the isolates resistant to three or more antimicrobials, the following combinations were the most prevalent: oxytetracycline, bacitracin and narasin (2%), erythromycin, bacitracin and narasin (2%), oxytetracycline, erythromycin, virginiamycin and narasin (3%), oxytetracycline, virginiamycin, bacitracin and narasin (3%), oxytetracycline, erythromycin, bacitracin and narasin (1%), and oxytetracycline, erythromycin, virginiamycin, bacitracin and narasin (2%).

E. faecalis

Of the *E. faecalis* isolates from broilers, 63% were resistant to at least one antimicrobial, and 33% to more than one. Resistance to bacitracin was most common (39%), followed by resistance to erythromycin and oxytetracycline.

The use of flavomycin was stopped in 1996. Rare resistance to flavomycin (2%) was detected in broiler *E. faecalis* isolates. Resistance to narasin was 13%. Resistance to gentamicin (4%), streptomycin (4%) and vancomycin (2%) was rare. The microbiological cut-off value for vancomycin resistance is 8 mg l^{-1}, and the MIC of the isolate resistant to vancomycin was 8 mg l^{-1}. No resistance was detected to ampicillin, avilamycin, chloramphenicol or neomycin.

Of the isolates resistant to three or more antimicrobials, the following combinations were the most prevalent: bacitracin, erythromycin and oxytetracycline (2%), bacitracin, flavomycin and narasin (2%), bacitracin, gentamicin and vancomycin (2%), bacitracin, erythromycin, narasin and oxytetracycline (2%), and bacitracin, erythromycin, narasin, oxytetracycline, and streptomycin (4%).

CATTLE

As yet there are no data available on the consumption of antimicrobials divided between species in Finland. According to a survey carried out in 2001, penicillins were by far the largest group of antimicrobials used for the therapeutic treatment of cattle, representing 80% of the total consumption of antimicrobials (Rantala, 2003). The second largest group were aminoglycosides (6%) and trimethoprim-sulphonamide combinations (5%). The large proportion of aminoglycosides is due to the fact that nearly all intramammary products contain an aminoglycoside (MAF, 2003b). The use of fluoroquinolones is apparently very limited.

E. faecium

Of the *E. faecium* isolates from cattle, 26% were resistant to at least one antimicrobial. Resistance to erythromycin was most common (17%), followed by oxytetracycline (4%). Twenty percent of the isolates were resistant to one antimicrobial, 3% to two and 3% to three antimicrobials. All isolates resistant to two or more antimicrobials were resistant to erythromycin. Resistance to erythromycin and oxytetracycline can be explained by the use of macrolides and tetracyclines for cattle.

In spite of the widespread use of penicillins in cattle, no resistance to ampicillin was detected in bovine *E. faecium*. Of the therapeutic antimicrobials, no resistance was detected to chloramphenicol, gentamicin or neomycin. Chloramphenicol is no longer used, and gentamicin has never been used for cattle in Finland. Neomycin and dihydrostreptomycin/streptomycin are used in intramammary preparations, streptomycins in combination with a betalactam antimicrobial. Dihydrostreptomycin is used also in an oral antimicrobial product. Streptomycin resistance (3%) was rare.

Although antimicrobial feed additives have not been used for cattle in Finland, a moderate proportion of *E. faecium* isolates were resistant to bacitracin (9%). All isolates were sensitive to vancomycin, virginiamycin and avilamycin. Two isolates (3%) were resistant to at least three antimicrobials. One isolate was resistant to bacitracin, erythromycin and narasin, and one isolate to erythromycin, oxytetracycline and streptomycin.

Table 11.
Distribution of MICs for *Enterococcus faecalis* from broilers (n=46).

Substance	% resistant	Distribution (%) of MICs (mg l^{-1})														
	(95 % CI)	≤ 0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	0 (0.0-7.7)				87.0	10.9	2.2									
Avilamycin	0 (0.0-7.7)					19.6	71.7	8.7								
Bacitracin[1]	39 (25.1-54.6)						2.2	39.1	17.4	2.2	39.1					
Chloramphenicol	0 (0.0-7.7)						15.2	80.4	4.3							
Erythromycin	33 (19.5-48.0)			4.3	8.7	23.9	30.4	32.6								
Flavomycin	2 (0.1-11.5)					6.5	43.5	43.5	4.3				2.2			
Gentamicin	4 (0.5-14.8)							32.6	60.9	2.2				4.3		
Narasin	13 (4.9-26.3)		26.1	50.0	10.9		4.3	8.7								
Neomycin	0 (0.0-7.7)								6.5	34.8	45.7	13.0				
Oxytetracycline	24 (9.4-33.9)			8.7	56.5	8.7	2.2	4.3	6.5	4.3	8.7					
Streptomycin	4 (0.5-14.8)									2.2	43.5	50.0				4.3
Vancomycin	2 (0.1-11.5)				13.0	69.6	15.2	2.2								

Bold vertical lines indicate microbiological cut-off values for resistance. Hatched fields denote range of dilutions tested for each substance. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration.

[1] MIC in U ml^{-1}.

Table 12.
Distribution of MICs for *Enterococcus faecium* from broilers (n=257) and cattle (n=70).

Substance		% resistant	Distribution (%) of MICs (mg l^{-1})														
		(95 % CI)	≤ 0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	Broilers	2 (0.4-3.9)		8.9	15.2	22.2	20.2	25.3	6.6	0.8	0.4	0.4					
	Cattle	0 (0.0-5.1)			12.9	55.7	31.4										
Avilamycin	Broilers	2 (0.6-4.5)			0.4	0.8	10.1	66.5	12.5	7.8	1.6	0.4					
	Cattle	0 (0.0-5.1)				2.9	22.9	42.9	30.0	1.4							
Bacitracin[1]	Broilers	30 (24.4-36.0)				16.7	6.6	5.4	12.5	25.7	3.1	30.0					
	Cattle	9 (3.2-17.7)					1.4	4.3	8.6	41.4	35.7	8.6					
Chloramphenicol	Broilers	2 (0.6-4.5)						32.7	54.1	11.3	1.9						
	Cattle	0 (0.0-5.1)						34.3	64.3	1.4							
Erythromycin	Broilers	27 (21.2-32.3)			26.5	30.0	11.3	5.8	26.5								
	Cattle	17 (9.2-28.0)			8.6	15.7	31.4	27.1	17.2								
Gentamicin	Broilers	0 (0.0-1.4)					2.3	24.9	52.5	17.9	2.3						
	Cattle	0 (0.0-5.1)						51.4	42.9	4.3	1.4						
Narasin	Broilers	72 (66.0-78.0)		0.4	7.4	13.6	6.2	8.6	53.3	7.0	3.5						
	Cattle	1 (0.0-7.7)		1.4	25.7	68.6	2.9	1.4									
Neomycin	Broilers	0 (0.0-1.4)					2.3	19.8	46.3	24.5	5.8	1.2					
	Cattle	0 (0.0-5.1)						22.9	28.6	38.6	5.7	2.9	1.4				
Oxytetracycline	Broilers	36 (30.3-42.4)			24.9	35.0	3.5	0.8	2.3	3.1	7.8	10.5	12.1				
	Cattle	4 (0.9-12.0)			54.3	38.6	2.9			1.4	1.4		1.4				
Streptomycin	Broilers	0 (0.0-1.4)									67.7	30.4	1.9				
	Cattle	3 (0.4-9.9)									52.9	31.4	12.9			1.4	1.4
Vancomycin	Broilers	3 (0.9-5.0)				86.8	8.6	1.9	0.4				0.4	1.9			
	Cattle	0 (0.0-5.1)				71.4	7.1	21.4									
Virginiamycin	Broilers	11 (7.7-15.8)			10.5	32.3	31.5	10.1	4.3	8.2	1.2	1.9					
	Cattle	0 (0.0-5.1)			37.1	5.7	45.7	10.0	1.4								

Bold vertical lines indicate microbiological cut-off values for resistance. Hatched fields denote range of dilutions tested for each substance. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration.

[1] MIC in U ml^{-1}.

Escherichia coli in broilers and cattle

E. coli isolates were isolated from 99% of broiler caecal and 95% of bovine faecal samples. The material included 356 *E. coli* isolates from cattle and 300 isolates from broilers. The MIC distribution and the occurrence of resistance among *E. coli* from broilers and cattle are presented in Table 13. Overall, resistance in broiler and cattle isolates was rare. Of the broiler isolates 77%, and of the cattle isolates 93% were sensitive to all antimicrobials tested.

BROILERS

Of the broiler isolates, 14% were resistant to one antimicrobial, 5% to two, 2% to three, and 3% to four or more antimicrobials.

Resistance to ampicillin and oxytetracycline were the most prevalent resistance traits (11 and 10%, respectively) in *E. coli* from broilers. Eight percent were resistant to sulphamethoxazole, and 4% to trimethoprim. Ampicillin and sulphonamide-trimethoprim are used in broiler production, though infrequently, and the resistance can be explained by their use. The oxytetracycline resistance figures may reflect their previous use or co-selection of resistance.

No resistance was detected to ceftiofur or florfenicol. Occasional isolates were resistant to chloramphenicol (<1%), gentamicin (<1%), neomycin (2%) and streptomycin (3%). None of these substances is registered for use in broilers in Finland.

Fluoroquinolone resistance was rare: five broiler isolates had a slightly increased MIC, 1 mg l^{-1}; these isolates were resistant also to nalidixic acid.

CATTLE

Of the bovine *E. coli* isolates, 5% were resistant to one antimicrobial, 1% to two, 1 % to three and <1% to five antimicrobials. All isolates resistant to two or more antimicrobials were resistant to streptomycin. Resistance to streptomycin was most prevalent, though only 5%, followed by resistance to ampicillin and sulphamethoxazole (2%), reflecting the use of these antimicrobials (Rantala, 2003) assuming that consumption has remained roughly the same over the last few years.

No resistance was detected to ceftiofur, florfenicol, gentamicin or neomycin. Of these antimicrobials only neomycin is currently used for cattle. Resistance to chloramphenicol, oxytetracycline and trimethoprim was < 1%.

One bovine isolate had an increased MIC, 0.25 mg l^{-1}, just above the microbiological cut-off value for resistance to enrofloxacin; the isolate was also resistant to nalidixic acid.

Table 13.
Distribution of MICs for *Escherichia coli* from broilers (n=300) and cattle (n=356).

Substance		% resistant	Distribution (%) of MICs (mg l^{-1})															
		(95 % CI)	≤ 0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Ampicillin	Broilers	11 (8.0-15.5)						6.0	51.0	28.3	3.3			11.3				
	Cattle	2 (0.8-4.0)					0.3	6.2	47.2	43.0	1.4	0.6		1.4				
Ceftiofur	Broilers	0 (0.0-1.2)				29.3	62.0	8.3	0.3									
	Cattle	0 (0.0-1.0)				28.7	68.8	2.5										
Chloramphenicol	Broilers	<1 (0.1-2.4)							4.0	60.7	33.3	1.3	0.7					
	Cattle	<1 (0.0-1.6)							5.6	74.4	19.7		0.3					
Enrofloxacin	Broilers	2 (0.5-3.9)	32.3	61.3	4.7			1.7										
	Cattle	<1 (0.0-1.6)	34.0	58.7	7.0	0.3												
Florfenicol	Broilers	0 (0.0-1.2)								49.0	47.3	3.7						
	Cattle	0 (0.0-1.0)								65.2	33.7	1.1						
Gentamicin	Broilers	<1 (0.01-1.8)					6.7	63.7	25.7	3.7			0.3					
	Cattle	0 (0.0-1.0)					12.9	75.8	10.7	0.6								
Nalidixic acid	Broilers	2 (0.9-4.8)							17.0	71.3	8.7	0.7	0.3	0.3		1.7		
	Cattle	1 (0.3-2.9)						1.1	22.5	71.1	3.7	0.6	1.1					
Neomycin	Broilers	2 (0.5-3.9)							90.3	8.0	1.0		0.7					
	Cattle	0 (0.0-1.0)							96.3	3.7								
Oxytetracycline	Broilers	10 (7.1-14.4)					0.3	27.7	44.7	12.7	4.3	1.0	0.3	0.7	8.3			
	Cattle	<1 (0.2-2.4)					0.6	51.4	44.9	2.2					0.8			
Streptomycin	Broilers	3 (1.6-6.0)								13.3	71.0	12.3	0.7	1.3	0.7	0.7		
	Cattle	5 (3.2-8.2)							0.3	26.7	62.1	5.6	0.3	1.7	1.7	0.3	1.4	
Sulphamethoxazole	Broilers	8 (5.5-12.1)												90.0	1.0	0.7		8.3
	Cattle	2 (0.6-3.6)												98.3			0.3	1.4
Trimethoprim	Broilers	4 (1.8-6.5)				45.7	37.0	12.7	0.7	0.3			3.7					
	Cattle	<1 (0.0-1.6)				51.4	41.3	6.7		0.3			0.3					

Bold vertical lines indicate microbiological cut-off values for resistance. Hatched fields denote range of dilutions tested for each substance. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration.

Resistance in animal pathogens

Monitoring of resistance in animal pathogens is important for detecting emerging resistance that may pose a risk for human and animal health. Animal pathogens have the capacity to rapidly spread between animals and may, in consequence, be repeatedly exposed to antimicrobials. Emergence of new resistance mechanisms and loss of susceptibility in animal bacterial pathogen populations will be detected at an earlier stage in these bacterial populations (Franklin et al., 2001).

However, data on resistance in pathogenic bacteria are biased for several reasons: requisition varies among different veterinarians, some infections are more likely to generate isolates, and the isolates from some infections are more likely to be sent for susceptibility testing (Aarestrup, 2000). Furthermore, these samples are often derived from severe or recurrent clinical cases, including therapy failures (Franklin et al., 2001).

Escherichia coli in pigs

The material included 123 *E. coli* isolates from porcine enteritis. Some of the isolates probably originated from herds with diarrhoeal problems and a frequent use of antimicrobials.

Results and comments

The MIC distribution and occurrence of resistance are presented in Table 14. In total, 72% of the isolates were resistant to at least one antimicrobial: 17% were resistant to one antimicrobial, 12% to two, 12% to three, 15% to four, and 15% to five or more antimicrobials.

High prevalences of oxytetracycline (49%) and streptomycin (46%) resistance were detected. Resistance to sulphamethoxazole was 36%, and to trimethoprim 32%. Resistance to ampicillin was 17%.

Of the isolates resistant to three or more antimicrobials, the following combinations were the most prevalent: oxytetracycline, streptomycin, sulphamethoxazole and trimethoprim (7%) and enrofloxacin, nalidixic acid, oxytetracycline, trimethoprim, streptomycin and sulphamethoxazole (3%).

In 2001, the most common antimicrobials for therapeutic use in pigs were penicillins (33%), tetracyclines (30%) and trimethoprim-sulphonamide combinations (20%) (Rantala, 2003). Assuming that consumption has remained roughly stable during the last few years, the resistance to oxytetracycline, sulphamethoxazole, trimethoprim and ampicillin (17%) can be explained by their use in pig production in Finland. The resistance to streptomycin probably reflects its use in the past.

Of the fluoroquinolones, enrofloxacin and danofloxacin are registered for use in pigs. In spite of their apparently limited use, fluoroquinolone resistance was observed in 19% of the isolates. The isolates were also resistant to nalidixic acid.

A small portion of the isolates (4%) was resistant to chloramphenicol. Medicinal products containing chloramphenicol used for production animals were withdrawn from the market in 1993, and the resistance probably reflects its previous use. Resistance to florfenicol, registered for use in pigs, was found in 2% of the analysed isolates.

No resistance to ceftiofur or gentamicin was detected. No products containing these substances are approved for veterinary use in Finland.

Table 14.
Distribution of MICs for *Escherichia coli* from porcine enteritis 2002-2003 (n=123).

Substance	% resistant	Distribution (%) of MICs (mg l^{-1})															
	(95 % CI)	≤ 0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Ampicillin	17 (10.9-24.9)						12.2	50.4	15.4	4.9	0.8	1.6	14.6				
Ceftiofur	0 (0.0-3.0)				52.8	41.5	4.1	1.6									
Chloramphenicol	4 (1.3-9.2)							20.3	64.2	8.9	2.4	4.1					
Enrofloxacin	19 (12.2-26.7)	37.4	38.2	5.7	7.3	8.9	0.8		0.8	0.8							
Florfenicol	2 (0.2-5.8)								73.2	22.8	2.4	1.6					
Gentamicin	0 (0.0-3.0)					36.6	57.7	5.7									
Nalidixic acid[1]	21 (13.6-28.5)						1.6	31.1	40.2	5.7	0.8		4.1	8.2	8.2		
Neomycin	6 (2.3-11.4)							91.1	3.3			5.7					
Oxytetracycline	49 (39.7-58.0)					0.8	33.3	14.6	1.6	0.8			2.4	46.3			
Streptomycin	46 (37.3-55.6)							3.3	19.5	23.6	7.3	0.8	8.9	13.8	4.9	17.8	
Sulphamethoxazole	36 (27.3-44.9)												60.2	3.3	0.8		35.8
Trimethoprim	32 (23.6-40.7)				35.0	17.9	6.5	7.3	1.6		1.6	30.1					

Bold vertical lines indicate microbiological cut-off values for resistance. Hatched fields denote range of dilutions tested for each substance. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration.

[1] n=122.

Staphylococcus intermedius in dogs

Ninety-five isolates of *Staphylococcus intermedius* acquired from clinical samples of dogs were tested for their antimicrobial resistance.

Results and comments

The MIC distributions and occurrence of resistance are presented in Table 15. Penicillin resistance was more of a rule than an exception: in the cloverleaf test 87% of the isolates were β-lactamase positive, and the nitrocefin-test detected 52% of the strains as positive. Resistance to oxytetracycline was detected in 40%, to neomycin in 26% and to streptomycin in 27% of the samples tested. Resistance to macrolides and lincosamides was also common; 25% and 23% of strains were resistant to erythromycin and clindamycin, respectively. Less resistance was found to trimethoprim-sulphamethoxazole (7%) and chloramphenicol (6%). One isolate was resistant to cephalotin (1%). This result may be due to a methodological error or abundant production of β-lactamase, as the isolate was tested *mecA*-negative by PCR. No resistance was detected to avilamycin, gentamicin, oxacillin, vancomycin or virginiamycin.

Seventy-nine percent of the strains were resistant to at least one antimicrobial. Resistance to three or more antimicrobials was detected in 32% of the isolates. Isolates resistant to streptomycin (n=26) were also resistant to neomycin, except one. Out of 23 isolates resistant to erythromycin 20 were also resistant to clindamycin. A typical multiresistance pattern for six or seven antimicrobials (12 strains out of 15) included resistance to clindamycin, erythromycin, neomycin, oxytetracycline, penicillin and streptomycin.

Table 15
Distribution of MICs for *Staphylococcus intermedius* from canine infections 2002-2003 (n=95).

Substance	% resistant	Distribution (%) of MICs (mg l^{-1})													
	(95 % CI)	≤ 0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	>256
Avilamycin	0 (0.0-3.8)					1.1	25.3	65.3	6.3	2.1					
Cephalothin	1 (0.0-5.7)		84.2	11.6	3.2		1.1								
Chloramphenicol	6 (2.4-13.2)						1.1	76.8	14.7	1.1	6.3				
Clindamycin	23 (15.1-32.9)					76.8		2.1	3.2	17.9					
Erythromycin[1]	25 (16.2-34.4)				71.3	4.3			24.5						
Gentamicin	0 (0.0-3.8)				96.8	3.2									
Neomycin	26 (17.8-36.4)					70.5	3.2	16.8	6.3	3.2					
Oxacillin	0 (0.0-3.8)				34.7	46.3	18.9								
Oxytetracycline	40 (30.1-50.6)				54.7	4.2	1.1	1.1			16.8	16.8	5.3		
Penicillin	77 (67.1-84.9)	13.7	9.5	8.4	10.5	6.3	11.6	3.2	36.8						
Streptomycin	27 (18.7-37.5)						58.9	11.6	1.1	1.1			9.5	14.7	3.2
Trim.-sulpha[2]	7 (2.4-13.7)				60.9	28.3	4.3	2.2	4.3						
Vancomycin	0 (0.0-3.8)					91.6	8.4								
Virginiamycin	0 (0.0-3.8)				69.5	21.1	9.5								

Bold vertical lines indicate microbiological cut-off values for resistance. Hatched fields denote range of dilutions tested for each substance. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration.

[1] n=94.

[2] n=92, concentration of trimethoprim given, tested with sulphamethoxazole in concentration ration 1:20.

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Appendix 1: Materials and methods, resistance monitoring

Sampling strategy

Animal pathogens

Clinical isolates originated from diagnostic submissions or postmortem examinations: *Escherichia coli* from enteritis in pigs, and *Staphylococcus intermedius* from various canine, mostly skin, infections.

Indicator bacteria

Indicator bacteria, *E. coli, Enterococcus faecalis* and *E. faecium*, were collected from broiler chicken caeca and cattle faeces. The samples were isolated from healthy animals. The sampling period for broiler samples was from April 2002 to March 2003, and for bovine samples from February 2003 to December 2003.

The number of randomly taken samples from each production unit was proportioned to the annual slaughtering volume. Each isolate represents one herd or flock. The broiler and cattle slaughter production units accounted for 98 and 99 %, respectively, of the total production of these animals in Finland.

The broiler *E. coli* (n=300) isolates were randomly selected from 458 isolates collected, and 257 *E. faecium* isolates from 346 isolates.

Zoonotic bacteria

Salmonella isolates from warm-blooded animals were collected according to the Finnish *Salmonella* control programme. Isolates from domestic food were also included. At least one isolate from each notified incident was included, and more than one if isolates from one incident had different sensitivity profiles.

Campylobacter isolates were obtained in a survey of the prevalence of thermophilic *Campylobacter* in Finnish cattle in 2003. The animals sampled were chosen randomly and the number of samples per abattoir was based on the number of slaughtered animals in each plant in 2002. In total, 993 intestinal and 1460 carcass surface samples were examined according to the modified NMKL 119 (1990) method. Ninety randomly chosen intestinal isolates of *Campylobacter jejuni* were tested for antimicrobial susceptibility.

Isolation and identification of bacteria

Zoonotic bacteria

Salmonella

Salmonella serotypes were isolated and identified according to a modification of the NMKL standard Nr 71 (1999), or according to ISO standard 6579:1993 or 6579:2002, at local municipal or slaughterhouse laboratories. Serotyping of the isolates was performed at EELA, Kuopio Department.

Campylobacter spp.

Campylobacter spp. were isolated and identified according to a modification of the NMKL standard Nr 119 (1990) at EELA, Department of Bacteriology.

Indicator bacteria

Escherichia coli

One or five grams of intestinal content from chicken caeca or bovine faeces was diluted in 9 ml of peptone saline broth. After mixing, 10 µl of the suspension was spread on MacConkey agar (Difco, Le Pont de Claix, France) and incubated overnight at 44°C. A typical lactose-positive colony was subcultivated on TSA agar (Becton Dickinson, Le Pont de Claix, France) and incubated overnight at 37°C. Oxidase negative colonies were further cultivated in lactose tryptone lauryl sulfate broth (Oxoid, Hampshire, UK) and incubated at 37°C overnight, followed by the addition of Kovac's reagent to gas-positive tubes containing LTLSB to determine the indole reaction.

Enterococci

One or five grams of intestinal content from chicken caeca or bovine faeces was diluted in 9 ml of peptone saline broth. After mixing, 10 µl of the suspension was spread on Slanetz-Bartley agar (Merck, Darmstadt, Germany) and incubated for 48 h at 44.5°C. A typical colony was plated on bile-esculine agar (Difco) and incubated at 37°C overnight. Typical colonies (positive reaction) were cultivated on blood agar. *Enterococci* were identified to species level with the following tests: arginine dihydrolase, motility agar, mannitol, arabinose, raffinose, sorbitol and melibiose.

Animal pathogens

Animal pathogens were isolated and identified at EELA, Department of Bacteriology, Kuopio Department, or at Oulu or Seinäjoki Regional Unit according to standard procedures.

Staphylococcus intermedius isolates were isolated on blood agar plates as greyish white colonies with a beta-haemolytic zone. They were further identified according to Igimi et al. (1990), and with API Staph ID 32 (Biomerieux, Marcy L'Etoile, France).

Escherichia coli were isolated on blood agar plates, and identified as typical colonies on EMB agar (Becton Dickinson). The isolates were further tested for indole production.

Susceptibility testing

Susceptibility testing was performed with a microdilution broth method: VetMIC™

(National Veterinary Institute, Department of Antibiotics, Sweden). The testing was performed following the standards of the National Committee of Clinical Laboratory Standards (NCCLS, 2002), except for *Campylobacter*. Susceptibility testing was performed at EELA, Department of Bacteriology, or at the Kuopio Department of EELA.

Panels with different concentration ranges were used, and the MIC data for each animal species were united to include the concentrations in the panels used. Microbiological cut-off values for resistance were determined on the basis of microbiological criteria: an isolate was regarded as resistant to a specific antimicrobial when its MIC was distinctly higher than those of inherently susceptible isolates of the bacterial species in question. The microbiological cut-off values were suggested by repre-

Table 16
Microbiological cut off values (mg l^{-1}) for antimicrobial resistance used in this report. Isolates with MIC values higher than the given figures are considered resistant.

Antimicrobial agent	*Salmonella*	*Escherichia coli*	*Enterococcus* spp.	*Staphylococcus intermedius*	*Campylobacter jejuni*
Ampicillin	>8	>8	>8		>16
Avilamycin			>16	>16	
Bacitracin[1]			>32		
Ceftiofur	>2	>2			
Cephalotin				>1	
Chloramphenicol	>16	>16	>16	>16	
Clindamycin				>2	
Enrofloxacin	>0.125	>0.125			>0.5
Erythromycin			>4	>2	>8
Flavomycin			>16		
Florfenicol	>16	>16			
Gentamicin	>4	>4	>256	>2	>4
Nalidixic acid	>16	>16			>16
Narasin			>2		
Neomycin	>4	>4	>256	>2	
Oxacillin				>2	
Oxytetracycline	>8	>8	>4	>2	>2
Penicillin				>0,125	
Streptomycin	>32	>16	>256	>32	
Sulphamethoxazole	>256	>256			
Trimethoprim	>4	>4			
Trimethoprim/sulphamethoxazole[2]				>2	
Vancomycin			>4	>4	
Virginiamycin			>8	>4	

[1] MIC in U ml^{-1}.

[2] Concentration of trimethoprim given, tested with sulphamethoxazole in concentration ration 1:20.

sentatives of various Nordic monitoring programmes on antimicrobial resistance at a meeting in Oslo, 13th February 2004 (Table 16).

Bacitracin values are given in units ml^{-1} (SVARM, 2002).

Quality assurance system

All departments of EELA participate in external quality assurance programmes for veterinary pathogens. The Kuopio Department also participates in proficiency tests on isolation, identification and serotyping of *Salmonella*, and the Department of Bacteriology in proficiency tests for antimicrobial susceptibility testing (broth dilution method).

For susceptibility tests the following bacteria were included as quality controls on at least a weekly basis: *E. coli* ATCC 25922, *E. faecalis* ATCC 29212, *S. aureus* ATCC 29213 and *C. jejuni* ATCC 22560.

The method for isolation, identification and serotyping of *Salmonella* at Kuopio Department and the VetMIC™ test at Department of Bacteriology (since may 2004) are accredited according to standard SFS-EN ISO/IEC 17025 by the Finnish Centre for Metrology and Accreditation.

Confidence limits

Inverse beta function (MS Excel BETAINV) was used to calculate 95% confidence intervals for the prevalences of resistance (Rutledge and Warren, 1999).

2002

01/2002
Kalaterveyspäivä 13.3.2002
Luentokokoelma

02/2002
Kotimaisten kevytjuustojen laatututkimus
Loppuraportti 12.3.2002

03/2002: Mari Eskola
Study on Trichothecenes, Zearalenone and Ochratoxin A in Finnish Cereals: Occurence and Analytical Techniques
Väitöskirja

04/2002
Riskinarviointi Echinococcus granulosus –loisesta Suomessa
Riskinarviointiraportti

05/2002: Meri Kokkonen
Automatisoidun näytteenkäsittelymenetelmän kehittäminen ja käyttöönotto okratoksiini A:n ja zearalenonin määrityksessä
Pro Gradu –tutkielma

06/2002
Klassisen sikaruton maahantulo ja leviäminen Suomessa
Kvalitatiivinen riskinarviointi

07/2002
Eläinrokotteet

Aiemmin tässä sarjassa julkaistuja

2004

01/2004
Kalaterveyspäivä 2004 – Fiskhälsodagen 2004
Luentokokoelma – Förläsningsserie

02/2004
Paratuberkuloosiriski suomalaisessa emolehmätuotannossa ja eri toimenpiteiden vaikutus siihen
Kuvaileva riskinarviointi

03/2004
Salmonella in Pork Production in Finland
Kvantitatiivinen riskinarviointi

04/2004: Perttu Koski
The Occurrence and Prevention of the M74 Syndrome, a Thiamine Deficiency Disease in Baltic Salmon
Väitöskirja

05/2004: Anna-Liisa Myllyniemi
Development of microbiological methods for the detection and identification of antimicrobial residues in meat
Väitöskirja

2003

01/2003
Kalaterveyspäivä 13.3.2003
Luentokokoelma

02/2003
Economic Impacts of The Finnish Salmonella Control Programme for Broiler
Riskinarviointiraportti

03/2003: Elina Lahti
Cattle and Reindeer as Possible Sources of Escherichia Coli O157 Infection in Humans
Väitöskirja

04/2003
Salmonella in broiler production in Finland
Riskinarviointiraportti

05/2003
Yleiskuvaus kampylobakteerien aiheuttamasta riskistä
Riskinarviointiraportti

06/2003
Kotimaiset kevytjuustot ja kuluttajan valinnat
Loppuraportti



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