Eläinlääkintä- ja elintarviketutkimuslaitos

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FINRES-Vet 2004
Finnish Veterinary Antimicrobial Resistance Monitoring and Consumption of Antimicrobial Agents

EELA

LÄÄKELAITOS
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NATIONAL AGENCY
FOR MEDICINES

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TARKASTUSKESKUS

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Kuvailulehti

Tämä on toinen FINRES-Vet-ohjelman tuloksista kertova raportti. Raportissa esitetään vuoden 2004 resistenssituloksia sekä eläimille käytettyjen mikrobilääkkeiden ja rehun lisäaineiden kulutustietoja.

Ensimmäisen FINRES-Vet-raportin (2002-2003) mukaan eläimistä ja elintarvikkeista eristettyjen bakteerien resistenssitilanne Suomessa on hyvä. Tilanne on pysynyt samanlaisena myös vuonna 2004. Hyvä tilanne johtunee muun muassa tiukasta mikrobilääkepolitiikastamme, jonka mukaan vain eläinlääkärit voivat määrätä mikrobilääkkeitä eläimille. Tiettyjen eläimille tautia aiheuttavien bakteerien resistenssitilanne on kuitenkin huolestuttava, minkä takia mikrobilääkkeiden hallittu käyttö eläinten lääkinnässä on tärkeää myös tulevaisuudessa. Hallitun käytön edistämiseksi on eläinten tärkeimpiin tulehdus- ja tartuntatauteihin annettu mikrobilääkkeiden käyttösuositukset.

Mikrobilääkkeiden ja rehun lisäaineiden kulutus Suomessa
Eläinten lääkinnässä käytettiin vuonna 2004 mikrobilääkkeitä 13 300 kg (aktiivista lääkeainetta). Määrä on pysynyt samana vuodesta 2000 lähtien.

Vuonna 2004 kaikista eläimille käytetyistä mikrobilääkkeistä ß-laktaamien osuus oli 66 %, sulfonamidi-trimetopriimivalmisteiden 17 % ja tetrasykliinien 10 %. Penisilliinejä sisältävistä eläinlääkevalmisteista 86 % oli ß-laktamaasille herkkiä penisilliinejä.

Injektiovalmisteissa annettujen mikrobilääkkeiden osuus kasvoi vuonna 2004 pääasiassa penisilliini- ja tetrasykliiniryhmissä tapahtuneiden muutosten takia. Kasvu voi johtua nautojen terveydentilan muutoksista, esimerkiksi lisääntyneistä hengitystieinfektioista.

Suun kautta annettavien mikrobilääkkeiden määrä väheni hieman vuodesta 2003, johtuen pääasiassa tetrasykliinien, mutta jossain määrin myös sulfonamidien käytön vähenemisestä. Fluorokinolonien käyttö oli edelleen vähäistä.

Aminoglykosidien, esimerkiksi streptomysiinin, käyttömäärät ovat vakiintuneet viimeisten kahden vuoden aikana. G-penisilliinin käyttö on lisääntynyt nautojen umpeenpanohoidoissa.

Kaikkien mikrobilääkkeiden käyttö lypsykauden aikana käytettävinä utareen sisäisinä lääkkeinä (intramammaareina) väheni aminopenisilliinejä lukuun ottamatta.

Väheneminen todennäköisesti johtui pääasiassa lypsylehmien määrän pienenemisestä (13 % vuodesta 2000 vuoteen 2004).

Suomen rehuteollisuus luopui vapaaehtoisesti antimikrobisten kasvunedistäjien käytöstä 1990-luvulla. EU kielsi avoparsiinin käytön 1997 sekä basitrasiinin, spiramysiinin, tylosiinin ja virginiamysiinin käytön kasvun edistämiseen 1999. Suomessa virginiamysiinin käyttö loppui jo vuonna 1990, basitrasiinin käyttö 1992 ja flavomysiinin ja avoparsiinin käyttö 1996. Tällä hetkellä kasvunedistäjiä ei käytetä Suomessa lainkaan. Monensiini- ja narasiini -kokkidiostaatteja käytetään kokkidioosin ennaltaehkäisyyn broileri- ja kalkkunatuotannossa.

Zoonoosia aiheuttavien bakteerien resistenssi

Kansallisessa salmonellavalvontaohjelmassa seurataan salmonellan esiintyvyyttä naudoissa, sioissa, siipikarjassa sekä lihassa. Ohjelman tavoitteena on pitää salmonellan esiintyvyys tuotantoeläimissä ja lihassa alle yhden prosentin. Valvontaohjelman tulosten perusteella salmonellaa todetaan tuotantoeläimissä ja niistä saatavissa elintarvikkeissa vain vähän.

FINRES-Vet-ohjelmassa ovat mukana kotimaisista elintarvikkeista, naudoista, sioista ja siipikarjasta eristetyt salmonellat. Vuonna 2004 mukaan otettiin myös lemmikkieläimistä eristetyt salmonellat. Resistenssiä todettiin hyvin vähän. Tuotantoeläimistä eristetyissä salmonelloissa resistenssiä todettiin vain yhdessä sialta eristetyssä moniresistentissä *S.* Typhimurium DT 104- bakteerissa. Kotimaisista elintarvikkeista eristettiin kolme salmonellaa, jotka olivat herkkiä kaikille testatuille mikrobilääkkeille. Myös kolmesta koirasta, neljästä kissasta ja yhdestä hevosesta eristetyt *S.* Typhimurium –bakteerit olivat herkkiä kaikille testatuille mikrobilääkkeille. Resistenssiä todettiin vain vähän myös eksoottisilta lemmikeiltä (kilpikonnat, käärmeet, liskot ja siili) eristetyissä salmonelloissa.

Kampylobakteerien valvontaohjelman yhteydessä eristettiin broilereilta *C. jejuni* -bakteereita. Sioista eristettiin *C. coli* -bakteereita teurastuksen yhteydessä samoista näytteistä kuin indikaattoribakteereita. Resistenssiä todettiin *C. jejuni* -bakteereilla vain vähän. Tavallisimpia olivat oksitetrasykliini-, ampisilliini- ja nalidiksiinihappo-resistenssit. Resistenssi oli harvinaista myös *C. coli* -bakteereilla. Tavallisinta oli enrofloksasiini-, nalidiksiinihappo-, oksitetrasykliini- ja erytromysiiniresistenssi.

Indikaattoribakteerien resistenssi

FINRES-Vet-ohjelmassa tutkitaan *Escherichia coli*-, *Enterococcus faecalis*- and *Enterococcus faecium* -bakteerien mikrobilääkeresistenssiä. Vuonna 2004 indikaat-

toribakteereita eristettiin sioista. Sikojen massalääkitysten tarve on huomattavasti vähentynyt sen jälkeen kun terveydenhuolto-ohjelmat otettiin käyttöön tavallisissa sikaloissa. Pahimpia sikatauteja ei Suomessa esiinny, ja joitakin maailmanlaajuisesti tärkeitä, tautia aiheuttavia bakteereita, esimerkiksi salmonellaa, todetaan suomalaisissa sikaloissa vain harvoin.

Suurin osa (91 %) *E. faecalis* –bakteereista oli resistenttejä ainakin yhdelle testatulle mikrobilääkkeelle. Tavallisinta oli oksitetrasykliiniresistenssi (86 %), seuraavaksi yleisintä oli erytromysiini- (35 %) ja streptomysiiniresistenssi (21 %, korkea-asteinen resistenssi). Tetrasykliiniresistenssin yleisyys voi selittyä suun kautta annettujen tetrasykliinien käytöllä.

E. coli -bakteerit olivat tavallisimmin resistenttejä oksitetrasykliinille ja streptomysiinille (16 ja 15 %). Kaksitoista prosenttia oli resistenttejä sulfametoksatsolille ja kahdeksan trimetopriimille. Ampisilliiniresistenssiä todettiin kuudella prosentilla kannoista.

Indikaattori -*E. colit* ja sikojen suolitulehduksista eristetyt *E. colit* olivat resistenttejä samoille mikrobilääkkeille. Resistenssi oli kuitenkin selvästi yleisempää tautia aiheuttavilla *E. coleilla*.

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

Eläimille tautia aiheuttavien bakteerien resistenssi

Moniresistenssi oli tavallista sikojen suolitulehduksista eristetyillä *E. coli* -bakteereilla: peräti 54 % oli resistenttejä ainakin kolmelle mikrobilääkkeelle. Resistenssi on pysynyt suurin piirtein samalla tasolla vuodesta 2002 lähtien. Kuten vuosina 2002 ja 2003, myös vuonna 2004 resistenssi oli tavallista oksitetrasykliinille (51 %), streptomysiinille (54 %), sulfametoksatsolille (51 %) ja trimetopriimille (44 %). Näitä resistenssejä tavattiin säännöllisesti moniresistenteillä bakteereilla. Enrofloksasiiniresistenssiä todettiin 10 %:lla tutkituista kannoista.

Koirista eristetyistä *S. intermedius* -bakteereista 83 % tuotti β-laktamaasia. Oksitetrasykliiniresistenssi oli myös tavallista (47 %); melko yleistä oli resistenssi myös streptomysiinille, erytromysiinille, klindamysiinille ja fusidiinihapolle. Ensimmäisen kerran Suomessa todettiin eläimestä eristetty, metisilliiniresistentti koagulaasipositiivinen stafylokokki: koirasta eristetyn *S. intermedius* -bakteerin resistenssi varmistettiin osoittamalla *mecA*-geeni.

Beskrivning

Det här är den andra rapporten över resultaten av programmet FINRES-Vet. I rapporten presenteras resultaten av resistensundersökningarna år 2004 och information om förbrukade mängder antibiotika och tillsatser i foder för djur.

Enligt den första FINRES-Vet-rapporten (2002-2003) är resistensläget för bakterier som isolerats från djur och livsmedel bra i Finland. Läget har förblivit likadant även år 2004. Det torde bero på den strikta antibiotikapolicyn. Endast veterinärer kan ordinera antibiotika till djur. Resistensläget för vissa bakterier som förorsakar sjukdom hos djur är ändå oroväckande och därför är det viktigt att antibiotika även framöver används på ett behärskat sätt inom veterinärmedicinen. För att främja en behärskad användning har rekommendationer getts om användningen av antibiotika mot de viktigaste inflammationssjukdomarna och smittsamma sjukdomarna hos djur.

Förbrukning av antibiotika och fodertillsatser i Finland
Inom veterinärmedicinen förbrukades år 2004 13 300 kg (aktivt läkemedel) antibiotika. Mängden har hållit sig oförändrad allt sedan år 2000.

År 2004 var andelen ß-laktamer 66 %, sulfonamidtrimetoprimpreparat 17 % och tetracykliner 10 % av samtliga antibiotika som användes för behandling av djur. Av alla läkemedel inom veterinärmedicinen som innehöll penicilliner var 86 % penicilliner som är känsliga för ß-laktamas.

Andelen antibiotika som gavs som injektion ökade år 2004 huvudsakligen till följd av ändringar som skett i grupperna penicillin och tetracyklin. Ökningen kan bero på förändringar i nötdjurens hälsa, såsom en ökad mängd infektioner i luftvägarna.

Mängden peroral antibiotika minskade något från år 2003 huvudsakligen till följd av att användningen av tetracykliner, men i någon mån också sulfonamider minskat. Användningen av fluorokinoloner var fortsättningsvis blygsam.

Mängderna använda aminoglykosider, såsom streptomycin, har stabiliserats under de senaste två åren. Användningen av penicillin G har ökat i nötdjurs sinläggningsterapi.

Aminopenicillinerna undantagna minskade användningen av samtliga antibiotika i intramammarier. Minskningen berodde huvudsakligen på att antalet mjölkkor minskat (med 13% från år 2000 till år 2004).

Den finska foderindustrin avstod frivilligt från att använda växtfrämjande antibiotika på 1990-talet. EU förbjöd användning av avoparcin år 1997 och användning av bacitracin, spiramycin, tylosin och virginiamycin för växtbefrämjande ändamål år 1999. I Finland slutade man använda virginiamycin redan år 1990, bacitracin år 1992 och flavomycin och avoparcin år 1996.

För närvarande används tillväxtbefrämjande medel inte alls i Finland. Monensin och narasinkoccidiostater används för att förebygga koccidios vid kyckling och kalkonproduktion.

Resistensen hos zoonotiska bakterier

I det nationella salmonellakontrollprogrammet följer man upp förekomsten av salmonella hos nötdjur, svin, fjäderfä och kött. Målet med programmet är att hålla förekomsten av *Salmonella* i produktionsdjur och kött under en procent. Enligt resultaten av kontrollprogrammet konstateras endast sällan salmonella i produktionsdjur och i animaliska livsmedel.

Programmet FINRES-Vet omfattar salmonellor som isolerats från inhemska livsmedel, nötdjur, svin och fjäderfä. År 2004 togs också salmonellor som isolerats från sällskapsdjur med. Förekomsten av resistens var mycket låg. Bland salmonellor som isolerats från produktionsdjur konstaterades resistens endast i en multiresistent *S.* Typhimurium DT 104 som isolerats från ett svin. Från inhemska livsmedel isolerades tre salmonellabakterier som var känsliga mot samtliga testade antibiotika. Antibiotikakänsligheten testades också hos *S.* Typhimurium från tre hundar, fyra katter och en häst. Alla isolat var känsliga mot samtliga testade antibiotika. Förekomsten av resistens var låg också bland salmonellor som isolerats från exotiska sällskapsdjur (sköldpaddor, ormar, ödlor och en igelkott).

Från kyckling isolerades *C. jejuni* i samband med kontrollprogrammet för campylobacter; *C. coli* - isolerades åter i samband med slakt i samma prover som indikatorbakterierna. Förekomsten av resistens var låg bland *C. jejuni* -bakterier: resistens var vanligast mot oxitetracyklin (10 %), nästvanligast mot ampicillin och nalidixinsyra.

Resistens är sällsynt också hos *C. coli*. Vanligast var resistens mot enrofloxacin och nalidixinsyra, nästvanligast mot oxitetracyklin och erytromycin.

Resistens hos indikatorbakterier

I programmet FINRES-Vet undersöks resistensen mot antibiotika hos bakterierna

Escherichia coli, *Enterococcus faecalis* och *Enterococcus faecium*. År 2004 isolerades indikatorbakterier från svin. Behovet av massmedicinering av svin har minskat betydligt efter att hälsovårdsprogram togs i bruk i vanliga svingårdar. De viktigaste svinsjukdomarna förekommer inte i Finland och vissa globalt viktiga bakterier som förorsakar sjukdomar, såsom salmonella, konstateras endast sällan i finska svingårdar.

Huvuddelen (91 %) av *E. faecalis* –isolaten var resistenta mot åtminstone ett undersökt antibiotikum. Vanligast var oxitetracyklinresistens (86 %), nästvanligast var resistens mot erytromycin (35 %) och streptomycin (21 %, höggradig resistens). Att resistens mot tetracyklin är så vanligt kan bero på användningen av perorala tetracykliner.

E. coli var oftast resistenta mot oxitetracyclin och streptomycin (16 ja 15 %). Tolv procent var resistenta mot sulfametoxazol och åtta procent mot trimetoprim. Ampicillinresistens konstaterades hos sex procent av isolaten.

Indikator- *E. coli* och *E. coli* som isolerats från enteriter hos svin var resistenta mot samma antibiotika. Resistensen var som väntat ändå klart vanligare hos sjukdomsalstrande *E. coli*.

De konstaterade resistenserna beror delvis på nuvarande och tidigare användning av antibiotika och delvis på co-selektion av resistensfaktorer.

Resistens hos sjukdomsframkallande bakterier

Multiresistens var vanligt hos *E. coli* som isolerats från enteriter hos svin: hela 54 % var resistenta mot minst tre antibiotika. Resistensen har hållit sig på i stort sett samma nivå sedan år 2002. Liksom åren 2002 och 2003 var resistens även år 2004 vanligt mot oxitetracyklin (51 %), streptomycin (54 %), sulfametoxazol (51 %) och trimetoprim (44 %). Sådana resistenser påträffades regelbundet hos multiresistenta bakterier. Enrofloxasinresistens konstaterades hos 10 % av de undersökta isolaten.

Av *S. intermedius* -isolaten som isolerats från hundar producerade 83 % ß-laktamas. Oxitetracyklinresistens var också allmänt (47 %); rätt allmän var också resistens mot streptomycin, erytromycin, klindamycin och fusidinsyra. För första gången i Finland inrapporterades en från djur isolerad meticillinresistent koagulaspositiv stafylokock. Hos en *S. intermedius* -stam isolerad från hund konstaterades en *mecA*-gen.

Description

The current FINRES-Vet report is second of its kind. Resistance data are presented for the year 2004. The report also contains data on the consumption of antimicrobial agents and feed additives in animals.

The first FINRES-Vet report (2002-2003) showed an overall favourable resistance situation among bacteria isolated from animals and food in Finland, and the data from 2004 are fairly similar. This is probably the outcome of a strict policy regarding antimicrobial agents. Only veterinarians are allowed to prescribe antimicrobials used for treating animals. However, the resistance data of some animal pathogens are of concern, indicating that there is a need to further enforce the prudent use of antimicrobials. Recommendations for using antimicrobial agents in the treatment of the most significant infectious diseases in animals have been published.

Use of therapeutic antimicrobials and feed additives for animals in Finland
The total amount of antimicrobial products used in Finland for animals in 2004 was 13 300 kg of active substance. The volume has remained steady from 2000.

Beta-lactam antibiotics accounted for 66%, sulfonamide-trimethoprim for 17%, and tetracyclines for 10% of the total veterinary antimicrobial sales in 2004. Penicillins sensitive to beta-lactamase accounted for 86% of the veterinary beta-lactam preparations sold.

The volume of injectables increased in 2004 mainly due to changes in the penicillin and tetracycline groups. The increase may reflect changes in cattle health, for instance an increase of respiratory infections.

The consumption of antimicrobial products used orally for animals shows a slight decrease from 2003, which is due to diminishing sales of tetracyclines and, to lesser degree, sulfonamides. The use of fluoroquinoles remains small.

The use of aminoglycosides such as streptomycin has stabilised during the last two years and the use of penicillin G has increased in dry cow treatment of mastitis.

The amount of antimicrobials used for intramammary treatment during lactation has decreased for all antimicrobial groups except aminopenicillins. The reduction may be associated with the diminishing number (13% from 2000 to 2004) of dairy cows.

The Finnish feed industry voluntarily stopped the use of antimicrobial growth promoters in the 1990s. The European Union banned the use of avoparcin in 1997 and the use of bacitracin, spiramycin, tylosin and virginiamycin for growth promotion in 1999. In Finland, the use of virginiamycin was stopped already in 1990, the use of bacitracin in 1992 and the use of flavomycin and avoparcin in 1996.

At present, no growth promoters are used in Finland. The coccidiostats monensin and narasin are used as prophylactic anti-parasitic agents in broiler and turkey production.

Resistance in zoonotic bacteria

The prevalence of *Salmonella* in cattle, pigs and poultry, as well as in meat, 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 at 1% or less. The programme's results show that *Salmonellae* in production animals and foods of animal origin are rare in Finland.

Salmonella isolates from domestic food, cattle, pigs and poultry were included in the FINRES-Vet programme. In 2004, also resistance data on pet isolates were included.

Resistance was rare. In the production animal isolates included, resistance was detected only in one multiresistant *S.* Typhimurium DT 104 from a pig. Three isolates from domestic food were included, and these were sensitive to every antimicrobial drug tested.

Antimicrobial susceptibility was tested in three *Salmonella* isolates from dogs, four from cats, and one from a horse. All were *S.* Typhimurium, and were sensitive to all the antimicrobials tested. The prevalence of resistance among the isolates from exotic pets (turtles, snakes, lizards and a hedgehog) was also rare.

Isolates of *Campylobacter jejuni* were collected from broilers in association with the Finnish *Campylobacter* control programme, and porcine *Campylobacter coli* were collected at slaughter from the same samples as indicator bacteria.

Resistance to antimicrobial agents was rare among the *C. jejuni* isolates, the most common were resistance to oxytetracycline, ampicillin and nalidixic acid.

Antimicrobial resistance was rare also among *C. coli* isolates. The most common were resistance to enrofloxacin, nalidixic acid, oxytetracycline and erythromycin.

Resistance in indicator bacteria

Indicator bacteria analysed in the FINRES-Vet programme are *Escherichia coli*, *Enterococcus faecalis* and *Enterococcus faecium*. They were collected from pigs in 2004. The need for mass medication of pigs has greatly diminished after the establishment of health programs for conventional pig herds. Finland is free from major swine diseases and even some pathogens common worldwide, such as *Salmonella*, are only rarely isolated from Finnish piggeries.

Most isolates of *E. faecalis* (91%) were resistant to at least one antimicrobial drug in the test panel. Resistance to oxytetracycline was most common (86%), followed by resistance to erythromycin (35%) and streptomycin (21%, high-level). The high prevalence of tetracycline resistance may result from the use of orally administered tetracyclines.

The most common resistance traits in *E. coli* were resistance to oxytetracycline and streptomycin (16 and 15%, respectively). Twelve percent were resistant to sulfamethoxazole and 8% to trimethoprim. Resistance to ampicillin was detected in 6% of the isolates.

Indicator *E. coli* and those isolated from porcine enteritis were resistant to the same antimicrobials. As expected, resistance was much more common among pathogenic than indicator *E. coli*.

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

Resistance in animal pathogens

Multiresistance was common in *E. coli* isolated from pigs with enteritis; as many as 54% of the isolates were resistant to at least three antimicrobials. The occurrence of resistance has remained roughly at the same level since 2002. As in 2002 and 2003, in 2004 resistance to oxytetracycline (51%), streptomycin (54%), sulfamethoxazole (51%), and trimethoprim (44%) was common. These antimicrobials were also frequently included in the patterns of the multiresistant strains. Resistance to enrofloxacin was 10%.

Eighty-three percent of *S. intermedius* isolated from dogs produced beta-lactamase. Resistance to oxytetracycline was also common, 47%. Resistance to streptomycin, erythromycin, clindamycin and fusidic acid was also relatively common. The first methicillin-resistant coagulase-positive staphylococcus isolate from an animal in Finland was now reported: one *S. intermedius* isolate from a clinical sample of a dog was confirmed to be methicillin-resistant by *mecA*-PCR.

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Johdanto

FINRES-Vet ohjelma käynnistyi Suomessa vuonna 2002. Ohjelmassa seurataan ihmisten terveyden kannalta merkittävien, zoonoosia aiheuttavien bakteerien mikrobilääkeresistenssiä zoonoosidirektiivin 2003/99/EC edellyttämällä tavalla. Lisäksi seurataan indikaattoribakteerien ja tiettyjen eläimille tautia aiheuttavien bakteerien resistenssiä.

Viime vuosina tiettyjen zoonoosia aiheuttavien bakteerien mikrobilääkeresistenssi on lisääntynyt eri puolilla maailmaa. Ihmiset voivat saada tartunnan joko suoraan eläimistä tai niistä saatavista elintarvikkeista. Indikaattoribakteerit muodostavat eräänlaisen resistenssigeenien varaston, josta ne voivat siirtyä tautia aiheuttaviin bakteereihin. Lisäksi tietyn populaation indikaattoribakteerien resistenssi kuvaa ko. populaatioon kohdistunutta, mikrobilääkkeiden käytön aiheuttamaa valintapainetta.

Eläimille tautia aiheuttavien bakteerien resistenssin seuraaminen on tärkeää, koska sitä seuraamalla voidaan havaita ihmisten ja eläinten terveyden kannalta merkityksellisen resistenssin lisääntyminen. On kuitenkin huomioitava se, että tautitapauksista eristettyjen, eläimille tautia aiheuttavien bakteerien resistenssitiedot voivat olla väärin painottuneita, koska bakteerit on usein eristetty vakavista tai uusiutuvista infektioista.

FINRES-Vet-ohjelman tavoitteena on

- seurata tärkeimmistä tuotantoeläinlajeista ja lemmikkieläimistä eristettyjen bakteerien mikrobilääkeresistenssiä
- analysoida resistenssin levinneisyydessä tapahtuvia muutoksia sekä
- havaita uusien resistenttien kloonien ja fenotyyppien kehittyminen sekä seurata mikrobilääkkeiden kulutusta

Ensimmäisessä FINRES-Vet-raportissa (2002-2003) todettiin Suomen resistenssitilanteen olevan sekä eläimistä että elintarvikkeista eristetyillä bakteereilla pääosin hyvä. Tämä johtunee pääasiassa tiukasta mikrobilääkepolitiikastamme; vain eläinlääkärit voivat määrätä mikrobilääkkeitä eläimille. Joidenkin eläimille tautia aiheuttavien bakteerien resistenssitilanne on kuitenkin huolestuttava, minkä takia mikrobilääkkeiden hallittu käyttö on entistä tärkeämpää myös tulevaisuudessa. Eläinten tärkeimpiin tulehdus- ja tartuntatauteihin annettujen mikrobilääkkeiden käyttösuositusten tarkoituksena onkin edistää mikrobilääkkeiden hallittua käyttöä eläinlääkinnässä.

Tämä on toinen FINRES-Vet-ohjelman tuloksista kertova raportti. Vuonna 2002 indikaattoribakteereita kerättiin broilereilta, vuonna 2003 naudoilta ja vuonna 2004 sioilta. Zoonoosia aiheuttavista bakteereista mukana ovat *Salmonella* ja *Campylobacter*, eläimille tautia aiheuttavista bakteereista koirien *Staphylococcus intermedius* ja sikojen *Escherichia coli* ja indikaattoribakteereista *Escherichia coli*, *Enterococcus faecalis* and *E. faecium*.

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

Kiitokset
FINRES-Vet-ohjelman koordinoijat kiittävät Elintarvikeviraston ja teurastamoiden lihantarkastushenkilökuntaa näytteiden keräämisestä.

Introduktion

Programmet FINRES-Vet kördes i gång i Finland år 2002. I programmet följer man upp resistensen hos zoonotiska bakterier som är viktiga med tanke på människans hälsa på det sätt som zoonosdirektivet 2003/99/EC förutsätter. Man följer också upp resistensen hos indikatorbakterier och vissa bakterier som förorsakar sjukdom hos djur.

På senare år har resistensen hos vissa zoonotiska bakterier ökat på olika håll i världen. Människan kan få smitta antingen direkt från ett djur eller från animaliska livsmedel. Indikatorbakterierna bildar ett slags resistensgenförråd, från vilket de kan övergå till sjukdomsalstrande bakterier. Resistensen hos indikatorbakterierna i en viss population beskriver också selektionstrycket som riktats mot populationen i fråga till följd av att antibiotika använts. Deras resistens beskriver också selektionstrycket som riktats mot populationen till följd av att antibiotika använts.

Det är viktigt att resistensen hos bakterier som förorsakar sjukdom hos djur följs upp, eftersom man så kan upptäcka om resistens som är viktig med tanke på människans och djurens hälsa ökar. Det är ändå bra att hålla i minnet att informationen om resistensen hos bakterier som isolerats från sjukdomsfall och som förorsakar sjukdom hos djur kan vara felvinklad, eftersom bakterierna ofta isolerats från allvarliga eller upprepade infektioner.

Målet med programmet FINRES-Vet är att

- följa upp resistensen mot antibiotika hos bakterier som isolerats från de viktigaste slagen av produktionsdjur och sällskapsdjur
- analysera förändringar som sker i resistensens förekomst och
- notera uppkomsten av nya resistenta kloner och fenotyper och följa upp förbrukningen av antibiotika

I den första FINRES-Vet-rapporten (2002-2003) konstaterades resistensläget i Finland huvudsakligen vara bra hos såväl bakterier som isolerats från djur som bakterier som isolerats från livsmedel. Det torde bero på den strikta antibiotikapolicyn. Endast veterinärer kan ordinera antibiotika till djur. Resistensläget för vissa bakterier som förorsakar sjukdom hos djur är dock oroväckande och därför är det allt viktigare att antibiotika även framöver används på ett behärskat sätt. Syftet med rekommendationerna om användning av antibiotika mot de viktigaste inflammationssjukdomarna och smittsamma sjukdomarna hos djur är också att främja ett behärskat bruk av antibiotika inom veterinärmedicinen.

Det här är den andra rapporten över resultaten av programmet FINRES-Vet. År 2002 insamlades indikatorbakterier från kyckling, år 2003 från nötdjur och år 2004 från svin. Zoonotiska bakterier som togs med var *Salmonella* och *Campylobacter*, bakterier som förorsakar sjukdomar hos djur var *Staphylococcus intermedius* hos hund och *Escherichia coli* hos svin och indikatorbakterier var *Escherichia coli*, *Enterococcus faecalis* och *E. faecium*.

Forskningsanstalten för veterinärmedicin och livsmedel (EELA) koordinerar programmet FINRES-Vet. Läkemedelsverket följer upp förbrukningen av antibiotika för djur och Kontrollcentralen för växtproduktion (KTTK) förbrukningen av läkemedelsfoder och tillsatser i foder.

Tack
Koordinerarna av programmet FINRES-Vet tackar köttbesiktningspersonalen på Livsmedelsverket och i slakterierna för insamlandet av prover.

Introduction

The FINRES-Vet programme was launched in Finland in 2002. The programme monitors antimicrobial resistance in zoonotic agents that are a threat to public health, as required in the Zoonosis Directive 2003/99/EC. In addition, FINRES-Vet monitors antimicrobial resistance in indicator bacteria and certain animal pathogens.

In recent years there has been a significant increase in antimicrobial resistance in certain zoonotic bacteria worldwide. Humans may become infected with zoonotic organisms by direct contact with animals or food of animal origin. Indicator bacteria can create a pool of resistance genes, which may be transferred to pathogenic bacteria. Furthermore, the resistance of indicator bacteria in a certain population reflects the selection pressure caused by the use of antimicrobials.

Monitoring of antimicrobial resistance of animal pathogens is important since it may reveal emerging resistance, which is a risk for human and animal health. It must, however, be emphasised that the data on resistance in pathogenic bacteria isolated from diagnostic submissions may be biased, because the samples are mostly obtained from complicated or recurrent cases.

FINRES-Vet programme has the following objectives:

- to monitor resistance to antimicrobial agents in major food-producing animals and pets,
- to analyse trends in resistance prevalence, and
- to monitor the emergence of resistant clones, the development of new resistance phenotypes and the use of antimicrobial agents.

The first FINRES-Vet report (2002-2003) revealed an overall favourable resistance situation among bacteria isolated from animals and food in Finland. This is probably the outcome of the strict antimicrobial policy; antimicrobials used for treating animals are prescribed only by veterinarians. However, the resistance data from some animal pathogens were of concern indicating that there is a need to further enforce the prudent use of antimicrobials. Recommendations for using antimicrobial agents to treat the most significant infectious diseases in animals have been given to promote the prudent use of antimicrobials in animal therapeutics.

This is the second FINRES-Vet report. In 2002, indicator bacteria were collected from broilers, in 2003 from cattle, and in 2004 from pigs. Zoonotic bacteria obtained for analysis are *Salmonella* and *Campylobacter*, animal pathogens *Staphylococcus intermedius* from dogs and *Escherichia coli* from pigs, and indicator bacteria are *E. coli*, *Enterococcus faecalis* and *E. faecium*.

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 and the consumption of feed additives and medicated feeding stuffs by the Plant Production Inspection Centre.

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.

Use of therapeutic antimicrobials and feed additives for animals in Finland

Antimicrobials for treatment of animals

The National Agency for Medicines monitors the quantity of veterinary medicinal products used in Finland. The sales figures of antimicrobial products are collected from pharmaceutical wholesale companies.

The figures include products that have marketing authorisation as well as those sold under special licence. Products authorised for human use but prescribed for animals are not included. It is unlikely that their absence skews the figures markedly, as the proportion of human products used in canine practice accounts for about 10% and in feline practice for about 5% of all antimicrobials used for these species.

Volume of use

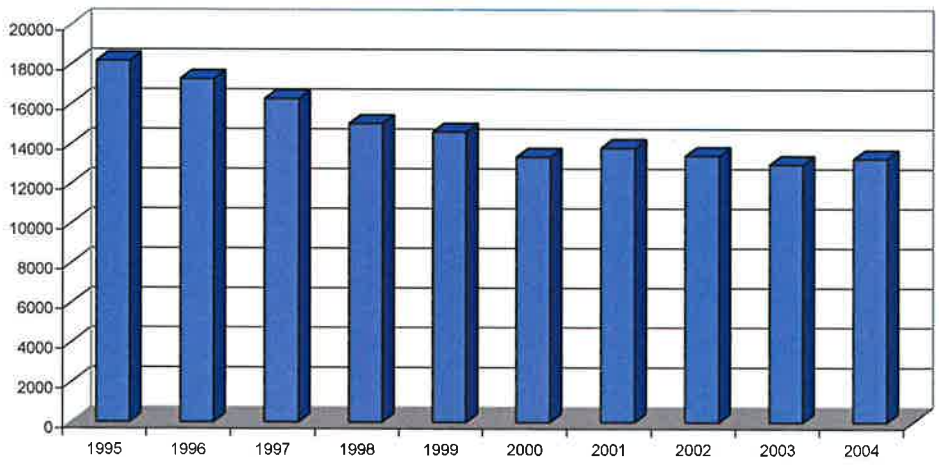

Figure 1. Total sales of veterinary antimicrobial medicines in Finland, kg of active substance

Table 1. Total amount of antimicrobial products authorised for veterinary use expressed as kg active substance

ATCvet code	Substance class	2000	2001	2002	2003	2004
QG01AA, QJ01AA, QD06AA,	Tetracyclines	2341	1937	1980	1757	1263
QJ01CE, QJ01R, QJ51R	Penicillin G	5503	6235	6054	6076	6754
QJ01CA, QJ01CR	Aminopenicillins	522	532	637	698	798
QJ01D, QJ51RD01, QJ51CF, QJ51CR	Other beta-lactam antimicrobials	0	0	0	0	0
QJ51RD, QJ01DA	Cephalosporins	1214	1153	1055	1133	1048
QJ51CR, QJ51CF	Cloxacillin	151	149	105	145	140
QA07AA, QJ01G, QJ01R, QJ51R	Aminoglycosides	610	632	385	291	280
QJ01E	Sulfonamides and trimethoprim	2818	2490	2342	2086	2286
QJ01F, QJ51FF90, QJ01FA94	Macrolides and lincosamides	523	492	422	538	526
QJ01MA, QJ01MB	Fluoroquinolones, quinoxalines	127	101	95	81	79
QJ01XX, QJ01B	Other substances	156	103	97	186	107
		13 965	13 824	13 172	12 991	13 280

The total amount of antimicrobial products, calculated as kg of the active substance, used for animals up to 2004 is given in Figure 1. The volume diminished consistently over several years and from about 2000 it has remained steady. Table 1 shows the breakdown of the overall consumption into main antimicrobial groups.

Injectable and orally administered antimicrobial products

Table 2. Antimicrobial substances used in injectables expressed in kgs in 1999-2004

ATCvet code	Substance class	2000	2001	2002	2003	2004
QG01AA, QJ01A	Tetracyclines, doxicyclin	188	196	143	265	291
QJ01CE, QJ01R, QJ51R	Penicillin G	5257	5981	5799	5840	6529
QJ01CA, QJ01CR	Aminopenicillins	59	76	115	133	145
QJ01E	Sulfonamides and trimethoprim	492	599	474	425	442
QJ01F	Macrolides and lincosamides	63	63	70	49	44
QJ01MA	Fluoroquinolones	69	70	70	69	66
QJ01BA, QJ01GA, QJ01DA	Other substances	1	2	0	2	1
		6129	6987	6671	6783	7518

The amount of antimicrobial medicines given in injectable form is shown in Table 2. The volume of injectables increased in 2004, mainly due to the changes in the penicillin and tetracycline groups. The increase may reflect changes in cattle health, for instance increase of respiratory infections.

Table 3. Total amount of per oral antimicrobial products authorised for veterinary use expressed as kg active substance

ATCvet code	Substance class	2000	2001	2002	2003	2004
QJ01A, QD06AA, QS03CA	Tetracyclines	2030	1672	1799	1380	967
QJ01CA, QJ01CR	Aminopenicillins	440	424	508	536	620
QJ01DA	Other beta-lactam antimicrobials (Cephalosporins)	949	939	887	998	938
QA07AA, QJ01R	Aminoglycosides	166	150	142	125	123
QJ01E	Sulfonamides and trimethoprim	2326	1892	1868	1661	1844
QJ01F	Macrolides and lincosamides	461	428	357	497	481
QJ01MA, QJ01MB	Fluoroquinolones, quinoxalines	59	31	44	12	12
QJ01XX, QJ01B	Other substances	156	101	87	100	104
		6587	5637	5692	5309	5090

The consumption of antimicrobial products used orally for animals shows a slight decrease (Table 3), which is due to diminishing sales of tetracyclines and, to lesser degree, sulfonamides. Fluoroquinole use remains small.

Intramammary antimicrobials

Table 4. Total sales of antimicrobials for intramammary use for dry cow period expressed in kgs

ATCvet code	Substance class	2000	2001	2002	2003	2004
QJ51CR, QJ51CF, QJ51RD	Aminopenicillins, cephalosporins, cloxacillins	125	125	112	100	92
QJ51RC	Penicillin G	29	29	32	34	43
QJ51RC	Aminoglycosides and other substances	75	70	53	43	45
Total		229	224	197	177	179

Table 4 presents the quantity of antimicrobials used for dry cow treatment of mastitis. The use of aminoglycosides such as streptomycin has stabilised during the last two years and the use of penicillin G has increased.

Table 5. Total sales of antimicrobials for intramammary use during lactation period expressed in kgs

ATCvet code	Substance class	2000	2001	2002	2003	2004
QJ51CR, QJ51CF, QJ51RD	Cephlosporin and cloxacillin	295	245	207	184	164
QJ51CR	Aminopenicillins	24	25	25	24	26
QJ51RC	Penicillin G	217	225	223	202	182
QJ51RC	Aminoglycosides and other substances	373	414	194	126	115
Total		909	909	649	536	488

Table 6. The use of antimicrobials for intramammary use calculated as the number of single-dose applicators per 1000 cows and day (DDDcow / 1000 cows at risk and day)

Indication	2000	2001	2002	2003	2004
For therapy during lactation*	3.77	3.73	3.64	3.38	3.45
For dry cow treatment**	0.57	0.59	0.58	0.57	0.56
Total	4.34	4.32	4.22	3.95	4.01

*calculated as total no. of tubes/2 (daily dose per cow)/days in a year/no. of cows/1000

**calculated as total no. of tubes/4 (daily dose per cow)/days in a year/no. of cows/1000

The amount of antimicrobials used for intramammary treatment during lactation has decreased for all antimicrobial groups except aminopenicillins (Table 5). The change may be due to the diminishing number (13% from 2000 to 2004) of dairy cows. Table 6 demonstrates that the use of intramammary antimicrobials in defined daily doses (DDDs) per 1000 cows at risk is fairly steady over the five-year period.

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 European Union banned the use of avoparcin in 1997 and the use of bacitracin, spiramycin, tylosin and virginiamycin for growth promotion in 1999. In Finland, the use of virginiamycin was stopped already in 1990, the use of bacitracin in 1992 and the use of flavomycin and avoparcin in 1996.

Table 7. The use of antimicrobial feed additives, coccidiostats and growth promoters in Finland in 1996-2004 (kg active substance/year).

	1996	1997	1998	1999	2000	2001	2002	2003	2004
Amprolium (and ethopabate)			427 (27)	148 (9)	74 (5)	79	22	0	0
Avoparcin	47	0	0	0	0	0	0	0	0
Dimetridazole	204	63	42	0	0	0	0	0	0
Flavomycin	7	0	0	0	0	32	3	0	0
Lasalocid sodium			3024	3019	2 796	3624	3349	176	0
Carbadox	1 841	1 123	3286	1082	0	0	0	0	0
Olaquindox	2 882	2 883	730	0	0	0	0	0	0
Madmuramycin ammonium	0	0	0	0	0	0	8	43	1,5
Monensin	3 653	4 375	632	353	0	1475	1969	4422	5808
Narasin	2 232	1 959	2866	2568	2 549	2101	5569	5769	5518
Salinomycin	1 705	3 657	2320	3246	2 829	3272	28	3	*10
Nifursol				188	0	0	0	0	0
Robenidine hydrochloride	0	0	0	0	67	0	0	0	0

* Used in exported feed mixtures

Table 7 presents the total sales of feed additives in Finland in 1993-2004. At present, no growth promoters are used in Finland. The coccidiostats monensin and narasin are used as prophylactic anti-parasitic agents in broiler and turkey production.

Resistance in zoonotic bacteria

In recent years there have been significant increases in the developed countries in the occurrence of resistance in non-typhoidal *Salmonella enterica* and *Campylobacter.* Drug resistance in food borne bacterial enteric pathogens is an almost inevitable consequence of the antimicrobial use in food-producing animals (Threlfall *et al.*, 2000). Zoonotic bacteria may become resistant in an animal, and thereafter be transferred into humans via the food chain or directly from animals.

The FINRES-Vet programme observes *Salmonella* isolated from production animals, domestic food and pets as well as *Campylobacter* from domestic animals. In 2004, *Campylobacter* were collected from broilers and pigs. Data on trends and sources of zoonotic agents in animals, feedstuffs, food and humans in Finland are available in another report (MAF, 2004).

Salmonella in production animals, domestic food and pets

The prevalence of *Salmonella* in cattle, pigs and poultry as well as in meat 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 at 1% or less (EELA, 2003a and b). The results from the programme show that *Salmonellae* in production animals and foods of animal origin are uncommon in Finland.

Isolates from the national control programme and domestic food were included in the previous report; this report contains also resistance data on pet isolates.

It should be noted that the breakpoint for resistance to enrofloxacin has been increased from > 0.12 mg l^{-1} to > 0.25 mg l^{-1} after the publication of the previous FINRES-Vet report. Details of sampling and isolation procedures are described in Appendix 1.

Table 8. Distribution of MICs for *Salmonella* in production animals (n=31).

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	1024	2048	>2048
Ampicillin	3 (0.1-16.7)					9.7	77.4	9.7					3.2						
Ceftiofur	0 (0.0-11.2)					6.5	87.1	6.5											
Chloramphenicol	3 (0.1-16.7)							9.7	61.3	25.8					3.2				
Enrofloxacin	0 (0.0-11.2)		22.6	45.2	32.3														
Florfenicol	3 (0.1-16.7)								64.5	32.3		3.2							
Gentamicin	0 (0.0-11.2)					22.6	74.2		3.2										
Nalidixic acid	0 (0.0-11.2)							3.2	67.7	25.8	3.2								
Neomycin	0 (0.0-11.2)							90.3	9.7										
Oxytetracycline	3 (0.1-16.7)						3.2	80.6	12.9					3.2					
Streptomycin	3 (0.1-16.7)									35.5	48.4	12.9		3.2					
Sulfamethoxazole	3 (0.1-16.7)										87.1	6.5	3.2						3.2
Trimethoprim	0 (0.0-11.2)				71.0	19.4	9.7												

Bold vertical lines indicate epidemiological 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.

Results and comments

Of the 31 isolates obtained from domestic production animals, 18 were identified as *S.* Typhimurium, 3 *S.* Infantis, 3 S. Tennessee, 2 *S.* Livingstone and 5 were other serovars. Fifteen isolates originated from cattle, 7 from pigs, 8 from poultry (*Gallus gallus*) and one from a turkey.

Resistance was rare (Table 8). In the isolates included, resistance was detected only in one multiresistant *S.* Typhimurium DT 104 from a pig. This isolate was resistant to oxytetracycline, streptomycin, chloramphenicol, florfenicol, ampicillin and sulfamethoxazole.

Three isolates from domestic food were included. Of these, two were *S.* Typhimurium and one was *S.* Infantis. The isolates were sensitive to every antimicrobial drug tested.

Antimicrobial susceptibility was tested in three *Salmonella* isolates from dogs, four from cats, and one from a horse. All were *S.* Typhimurium, and were sensitive to all the antimicrobials tested.

Table 9. Distribution of MICs for *Salmonella* in exotic pets (n=35).

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	1024	2048	>2048
Ampicillin	0 (0.0-10.0)					14.3	71.4	14.3											
Ceftiofur	0 (0.0-10.0)					31.4	60.0	8.6											
Chloramphenicol	0 (0.0-10.0)							2.9	68.6	28.6									
Enrofloxacin	3 (0.1-14.9)		42.9	28.6	25.7		2.9												
Florfenicol	0 (0.0-10.0)								65.7	34.3									
Gentamicin	0 (0.0-10.0)					40.0	60.0												
Nalidixic acid	3 (0.1-14.9)							2.9	77.1	17.1					2.9				
Neomycin	0 (0.0-10.0)							94.3	5.7										
Oxytetracycline	3 (0.1-14.9)						25.7	68.6	2.9		2.9								
Streptomycin	3 (0.1-14.9)								14.3	37.1	31.4	14.3	2.9						
Sulfamethoxazole	0 (0.0-10.0)										97.1	2.9							
Trimethoprim	0 (0.0-10.0)				65.7	11.4	2.9												

Bold vertical lines indicate epidemiological 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.

The prevalence of resistance among the 35 isolates obtained from 25 exotic pets (turtles, snakes, lizards and a hedgehog) is presented in Table 9. Of the isolates, 15 belonged to subspecies *enterica*, 9 to subsp. *salamae*, 6 to subsp. *diarizonae* and 5 to subsp. *arizonae*. Resistance was rare also among these isolates: one was resistant to oxytetracycline, one to streptomycin, and one to nalidixic acid and enrofloxacin.

Campylobacter jejuni in broilers

Isolates of *C. jejuni* were collected from broilers in association with the Finnish *Campylobacter* control programme between June and October. Details of isolation procedures are described in Appendix 1.

Table 10. Distribution of MICs for *Campylobacter jejuni* in broilers (n=69).

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	6 (1.6-14.2)					1.4	1.4	24.6	52.2	10.1	4.3	5.8			
Enrofloxacin	0 (0.0-5.2)		5.8	36.2	52.2	5.8									
Erythromycin	0 (0.0-5.2)				2.9	11.6	71.0	14.5							
Gentamicin	0 (0.0-5.2)					37.7	62.3								
Nalidixic acid	4 (0.9-12.2)								8.7	72.5	14.5	4.3			
Oxytetracycline	10 (4.2-19.8)				82.6	7.2				2.9	5.8		1.4		

Bold vertical lines indicate epidemiological 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.

Table11. Distribution of MICs for *Campylobacter coli* in pigs (n=100).

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	0 (0.0-3.6)					3.0	11.0	16.0	26.0	40.0	4.0				
Enrofloxacin	9 (4.2-16.4)		23.0	36.0	31.0	1.0	1.0		2.0	6.0					
Erythromycin	3 (0.6-8.5)				1.0	3.0	25.0	19.0	38.0	11.0	1.0	2.0			
Gentamicin	0 (0.0-3.6)					1.0	55.0	43.0	1.0						
Nalidixic acid	12 (6.4-20.0)								3.0	46.0	39.0	4.0		2.0	6.0
Oxytetracycline	4 (1.1-9.9)				42.0	34.0	11.0	9.0			2.0		2.0		

Bold vertical lines indicate epidemiological 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.

Results and comments

Resistance to antimicrobial agents was rare among the *C. jejuni* isolates (Table 10). Of the isolates, 20% were resistant to one antimicrobial; none of the strains was resistant to two or more antimicrobials. Oxytetracycline resistance was most common (10%), followed by resistance to ampicillin (6%) and nalidixic acid (4%).

In poultry, low infection prevalence and the absence of many significant infections, together with favourable production conditions, have kept the incidence of secondary bacterial infections negligible. Antimicrobial treatments are seldom necessary (MAF, 2003) and in practice no therapeutic antimicrobials are used for broilers. However, penicillin V, ampicillin, sulfa-trimethoprim and oxytetracycline are sometimes used to treat broiler breeding stock.

Campylobacter coli in pigs

Campylobacter coli and indicator bacteria were collected at slaughter and isolated from the same samples of porcine large intestine. Thermophilic *Campylobacter* were isolated from 62% (291/473) of the samples. Of these isolates, 91% were *C. coli* and 9% *C. lari*. One hundred *C. coli* isolates were randomly selected for susceptibility testing. Details of sampling and isolation procedures are described in Appendix 1.

Results and comments

Antimicrobial resistance was rare among *C. coli* isolates (Table 11). Of the isolates, 14% were resistant to at least one antimicrobial. The most common traits were resistance to enrofloxacin and nalidixic acid; 12 isolates were resistant to nalidixic acid. Of them, 9 were also resistant to enrofloxacin.

The observed resistance was likely caused by the use of antimicrobial agents for pigs. A single point mutation may lead to resistance to quinolones. The simplicity of this mechanism may contribute to the development of resistance to nalidixic acid and enrofloxacin. The occurrence of enrofloxacin resistance can be explained by the use of fluoroquinolones and the oxytetracycline resistance by the use of tetracyclines for pigs. Erythromycin resistance may be the consequence of the use of macrolides such as tylosin. No resistance was detected to gentamicin, which has not been used for pigs in Finland.

Resistance in indicator bacteria

Resistance among indicator bacteria among a certain population reflects the selection pressure caused by antimicrobial use. Indicator bacteria can also be considered as a pool of resistance genes, from which the resistance determinants can spread to pathogenic bacteria.

Indicator bacteria analysed in the FINRES-Vet programme are *Escherichia coli*, *Enterococcus faecalis* and *Enterococcus faecium*. Of these bacteria, Enterococci are known to acquire antimicrobial resistance relatively often and to be able to spread their resistance genes to other species (Kühn *et al.*, 2000).

The need for mass medication of pigs has greatly diminished after the establishment of health programs for conventional pig herds. The first health programme for piggeries was established in 1994 by a big cooperative slaughterhouse, and after that other major slaughterhouse companies started their own programs. Today the health classes are combined to a national system called (National) Health Class, and nearly 80% of the piggeries have joined the Health Class. In this class the farrowing units must prove that they are free from swine enzootic pneumonia and *Salmonella*. The Health Class also includes control for *Sarcoptes scabiei* infestation, swine dysentery and progressive atrophic rhinitis. Finland is free from major swine diseases and even some worldwide common pathogens, e.g. *Salmonella*, are only rarely found in Finnish piggeries.

No data are yet available on the consumption of antimicrobials divided between species in Finland. According to a survey carried out in 2002, penicillins, tetracyclines and trimethoprim-sulfonamides were the antimicrobials used most often for pigs (Rantala, 2003). Of the feed additives, avilamycin has never been used in Finland. The use of Zn-bacitracin was ended in 1992 and the use of all antimicrobial growth promoters in pig feed in 1999 (Table 7).

Indicator bacteria were isolated from broilers in 2002, from cattle in 2003 and from pigs in 2004. The samples were collected from large intestine of pigs originating from different farms. Details of sampling and isolation procedures are described in Appendix 1.

Enterococcus spp. in pigs

The number of enterococci isolates tested for antimicrobial susceptibility was 198. *Enterococcus faecalis* were isolated from 36% but *Enterococcus faecium* from only 6% of the samples.

Table 12. Distribution of MICs for *Enterococcus faecalis* from pigs (n=170).

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	2048	>2048
Ampicillin	0 (0.0-2.2)		1.2	2.4	87.1	9.4											
Avilamycin	2 (0.6-5.9)				2.4	58.8	30.6	5.3	0.6	1.8	0.6						
Bacitracin[1]	0 (0.0-2.2)					1.8	7.1	72.4	18.2	0.6							
Chloramphenicol	1 (0.1-4.2)					1.2	14.1	72.4	11.2	1.2							
Erythromycin	35 (28.1-43.0)			7.6	30.0	19.4	7.6		1.2	1.2	1.2	31.8					
Flavomycin	7 (3.7-12.0)					47.1	36.5	7.1	2.4	1.8	0.6	1.2	3.5				
Gentamicin	2 (0.6-5.9)												97.6	0.6			1.8
Narasin	0 (0.0-2.2)		18.2	63.5	15.3	2.9											
Neomycin	1 (0.1-4.2)								1.2	4.1	51.2	41.2	1.2		1.2		
Oxytetracycline	86 (79.7-90.7)			1.8	8.2	3.5	0.6	1.2	9.4	22.9	48.8	3.5					
Streptomycin	21 (14.8-27.5)												79.4			20.6	
Vancomycin	<1 (0.0-3.2)				11.2	68.8	19.4	0.6									

Bold vertical lines indicate epidemiological 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 13. Distribution of MICs for *Enterococcus faecium* from pigs (n=28).

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	2048	>2048
Ampicillin	0 (0.0-12.3)		14.3	3.6	60.7	14.3		7.1									
Avilamycin	0 (0.0-12.3)				7.1	39.3	42.9	10.7									
Bacitracin[1]	7 (0.9-23.5)					10.7		10.7	32.1	39.3		7.1					
Chloramphenicol	0 (0.0-12.3)					3.6	39.3	50.0	7.1								
Erythromycin	21 (8.3-41.0)			17.9	7.1	21.4	32.1	7.1	7.1			7.1					
Gentamicin	0 (0.0-12.3)												100				
Narasin	0 (0.0-12.3)		7.1	39.3	53.6												
Neomycin	0 (0.0-12.3)								75.0	17.9	7.1						
Oxytetracycline	32 (15.9-52.4)			10.7	57.1				7.1	7.1	14.3	3.6					
Streptomycin	14 (4.0-32.7)												85.7		3.6	10.7	
Vancomycin	0 (0.0-12.3)				78.6		21.4										
Virginiamycin	4 (0.1-18.4)			42.9	7.1	21.4	17.9	7.1		3.6							

Bold vertical lines indicate epidemiological 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}

Results and comments

The MIC distribution and the occurrence of resistance among enterococci from pigs are presented in Tables 12 and 13. Because of the inherent resistance, virginiamycin resistance in *E. faecalis* and flavomycin resistance in *E. faecium* were excluded from the results.

Most isolates of *E. faecalis* (91%) were resistant to at least one antimicrobial drug in the test panel: 38% were resistant to one, 44% to two, 7% to three and 2% to four or more antimicrobials. Resistance to oxytetracycline was most common (86%), followed by resistance to erythromycin (35%) and streptomycin (21%, high-level) (Table 12). One isolate (direct culture) was resistant to vancomycin. The samples were not enriched in vancomycin broth. All *E. faecalis* isolates were sensitive to ampicillin, bacitracin and narasin.

The most prevalent *E. faecalis* phenotype with resistance to three or more antibiotics was found in four isolates. This type was resistant to tetracycline, erythromycin and streptomycin. The high prevalence of tetracycline resistance in *E. faecalis* in pigs may result from the use of orally administered tetracyclines.

The MIC for erythromycin was higher than 32 mg l^{-1} in 33% of *E. faecalis* and in 7% of *E. faecium* isolates. Erythromycin resistance can at least partly be explained by the therapeutic use of antimicrobials belonging to the macrolide group. Resistance to streptomycin may reflect its use in the past, or may be a consequence of co-selection resulting from the use of other antimicrobials. Genetic linkage and co-expression imply that the use of any antibiotic that is a substrate for one resistance mechanism will co-select for resistance to the others and thus maintain the entire gene set (Sundsfjord *et al.*, 2004).

The number of *E. faecium* isolates was small, and the results should be considered with caution. Resistance to oxytetracycline, erythromycin and streptomycin (high-level) was comparatively common (14-32%) (Table 13). All isolates were sensitive to avilamycin and vancomycin, but moderate resistance to bacitracin was detected (7%). Four isolates (14%) were multiresistant.

Escherichia coli in pigs

Table 14. Distribution of MICs for *Escherichia coli* from pigs (n=391).

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	1024	2048	>2048
Ampicillin	6 (4.0-9.0)						4.6	47.6	38.9	2.8			6.1						
Ceftiofur	0 (0.0-0.9)			0.5	19.9	72.9	6.6												
Chloramphenicol	1 (0.4-3.0)							4.3	67.8	26.3	0.3	0.5			0.8				
Enrofloxacin	<1 (0.2-2.2)	8.7	78.0	12.3	0.3	0.5			0.3										
Florfenicol	0 (0.0-0.9)								44.5	53.5	2.0								
Gentamicin	0 (0.0-0.9)					10.7	71.9	16.4	1.0										
Nalidixic acid	<1 (0.2-2.2)							22.0	72.9	3.8	0.5			0.5	0.3				
Neomycin	1 (0.3-2.6)							90.0	9.0	0.3		0.8							
Oxytetracycline	16 (12.8-20.4)						21.0	57.5	5.1		0.3	0.5	0.3	15.3					
Streptomycin	15 (11.2-18.5)								12.3	63.9	9.2	2.3	2.6	5.9	3.1	0.8			
Sulfamethoxazole	12 (8.5-15.1)										88.2				0.3			0.3	11.3
Trimethoprim	8 (5.2-10.8)				70.3	19.7	1.5	0.5	0.3			0.3	7.4						

Bold vertical lines indicate epidemiological 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.

E. coli were isolated from 94% of the intestinal samples. The material included 391 *E. coli* isolates. The MIC distribution and the occurrence of resistance are presented in Table 14. Seventy-one percent of the *E. coli* isolates were sensitive to all antimicrobials in the test panel.

It should be noted that the breakpoint for resistance to enrofloxacin has been increased from > 0.12 mg l^{-1} to > 0.25 mg l^{-1} after the publication of the previous FINRES-Vet report. In order to make comparisons possible, the occurrence of resistance has been recalculated for the *E. coli* strains isolated in 2002 and 2003.

Of the isolates, 15% were resistant to one antimicrobial, 5% to two, 3% to three, and 5% to four or more antimicrobials in the test panel.

The most common resistance characteristics found were resistance to oxytetracycline and streptomycin (16 and 15%, respectively). Twelve percent were resistant to sulfamethoxazole and 8% to trimethoprim. Resistance to ampicillin was detected in 6% of the isolates.

Assuming that the antimicrobial usage has remained roughly at the same level as in 2002 (Rantala, 2003), resistance to oxytetracycline, sulfamethoxazole, trimethoprim and ampicillin can be explained by the use of these antimicrobials in pig production. The resistance to streptomycin may, as with enterococci, be explained by previous use or co-selection.

No resistance to ceftiofur, florfenicol or gentamicin was detected. Occasional isolates were resistant to chloramphenicol (1%) and neomycin (1%). Of these antimicrobials, only florfenicol is registered for use in pigs in Finland.

Enrofloxacin resistance was rare: two multiresistant isolates had a slightly increased MIC of 0.5 mg l^{-1}. These isolates were resistant also to nalidixic acid. One multiresistant isolate had a MIC of 4 mg l^{-1} and was also resistant to nalidixic acid.

Table 15. Occurrence of resistance in *Escherichia coli* from pigs, 2004. Data for broilers and cattle are given for comparison (FINRES-Vet 2002-2003).

		Resistance (%) (95% confidence intervals inside brackets)		
Substance	**Cut-off value (mg l^{-1})**	**Broilers 2002 (n=300)**	**Cattle 2003 (n=356)**	**Pigs 2004 (n=391)**
Ampicillin	>8	11 (8.0-15.5)	1 (0.8-4.0)	6 (4.0-9.0)
Ceftiofur	>2	0 (0.0-1.2)	0 (0.0-1.0)	0 (0.0-0.9)
Chloramphenicol	>16	<1 (0.1-2.4)	<1 (0.0-1.6)	1 (0.4-3.0)
Enrofloxacin	>0.25	2 (0.5-3.9)	0 (0.0-1.0)	<1 (0.2-2.2)
Florfenicol	>16	0 (0.0-1.2)	0 (0.0-1.0)	0 (0.0-0.9)
Gentamicin	>4	<1 (0.0-1.8)	0 (0.0-1.0)	0 (0.0-0.9)
Nalidixic acid	>16	2 (0.9-4.8)	1 (0.3-2.9)	<1 (0.2-2.2)
Neomycin	>4	2 (0.5-3.9)	0 (0.0-1.0)	1 (0.3-2.6)
Oxytetracycline	>8	10 (7.1-14.4)	<1 (0.2-2.4)	16 (12.8-20.4)
Streptomycin	>16	3 (1.6-6.0)	5 (3.2-8.2)	15 (11.2-18.5)
Sulfamethoxazole	>256	8 (5.5-12.1)	2 (0.6-3.6)	12 (8.5-15.1)
Trimethoprim	>4	4 (1.8-6.5)	<1 (0.0-1.6)	8 (5.2-10.8)

Table 15 presents the occurrence of resistance in *E. coli* from broilers, cattle and pigs from the years 2002-2003, 2003 and 2004, respectively.

Various resistance phenotypes of multiresistant isolates and their numbers are presented in Table 16.

Indicator *E. coli* and *E. coli*, obtained from porcine enteritis, were resistant to the same antimicrobials (Fig 2). As expected, resistance was much more common among pathogenic than indicator *E. coli*.

Table 16. Resistance phenotypes of multiresistant indicator *Escherichia coli*. The total number of isolates was 391. The shaded fields indicate resistance.

No. of isolates	STR	SMX	OTC	AMP	TMP	CHL	NEO	NAL	EF
2	■	■	■	■	■			■	■
2	■	■	■	■	■	■			
5	■	■	■	■	■				
1	■	■	■	■					
4	■	■	■		■				
2	■	■	■				■		
2		■	■		■	■			
2	■	■		■	■				
1	■			■				■	■
2	■		■	■					
3	■	■	■						
1	■		■		■				
4		■	■		■				
1	■	■		■					
1	■	■			■				

STR=streptomycin, SMX=sulfamethoxazole, OTC=oxytetracycline, AMP=ampicillin, TMP=trimethoprim, CHL=chloramphenicol, NEO=neomycin, NAL=nalidixic acid, EF=enrofloxacin

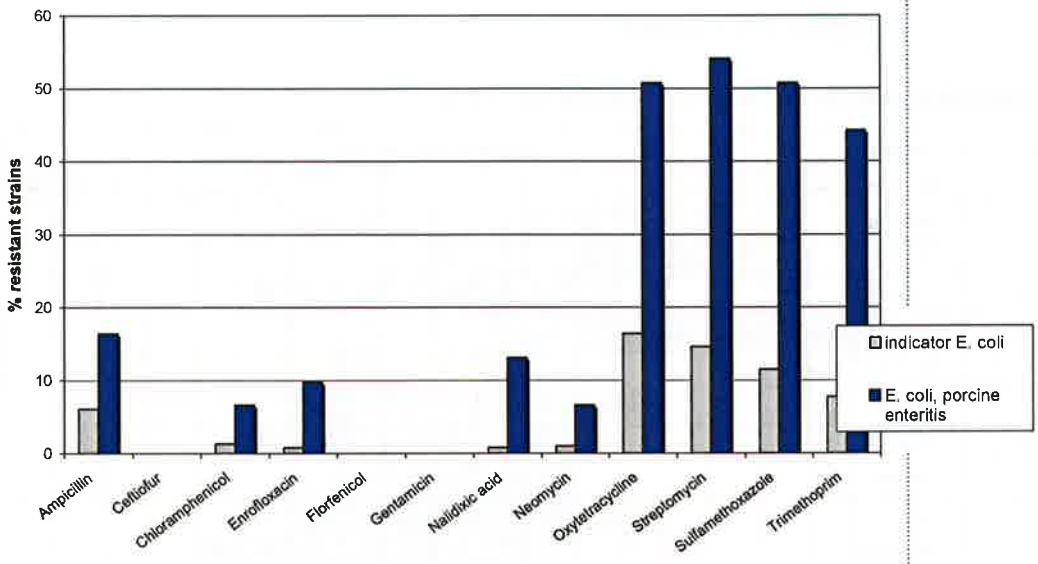

Figure 2. Antimicrobial resistance in *Escherichia coli* isolated from healthy and diarrhoeic pigs in 2004

Resistance in animal pathogens

Pathogenic bacteria were obtained from clinical or post-mortem samples submitted to EELA. Details of isolation procedures are described in Appendix 1.

Escherichia coli in pigs

The material in 2004 included 61 *E. coli* isolates from pigs with enteritis. The samples were taken from the gastrointestinal tract. At least part of the samples originated from herds with diarrhoeal problems and frequent use of antimicrobials.

It should be noted that the breakpoint for resistance to enrofloxacin has been increased from > 0.12 mg l^{-1} to > 0.25 mg l^{-1} after the publication of the previous report (FINRES-Vet 2002-2003). In order to make comparison possible, the occurrence of resistance has been recalculated for the *E. coli* strains isolated in 2002 and 2003.

Results and comments

Table 17. Distribution of MICs for *Escherichia coli* from porcine enteritis (n=61).

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	1024	2048	>2048
Ampicillin	16 (8.2-28.1)						1.6	59.0	19.7	3.3			16.4						
Ceftiofur	0 (0.0-5.9)				37.7	59.0	3.3												
Chloramphenicol	7 (1.8-16.0)							16.4	62.3	13.1	1.6	1.6		1.6	3.3				
Enrofloxacin	10 (3.7-20.2)	27.9	50.8	6.6	4.9	9.8													
Florfenicol	0 (0.0-5.9)								67.2	32.8									
Gentamicin	0 (0.0-5.9)					44.3	42.6	13.1											
Nalidixic acid	13 (5.8-24.2)							45.9	39.3	1.6			1.6	4.9	6.6				
Neomycin	7 (1.8-16.0)							90.2	3.3			6.6							
Oxytetracycline	51 (37.7-63.9)						23.0	26.2			1.6	1.6		47.5					
Streptomycin	54 (40.9-66.9)							1.6	21.3	21.3	1.6	1.6	14.8	6.6	6.6	24.6			
Sulfamethoxazole	51 (37.7-63.9)										49.2								50.8
Trimethoprim	44 (31.6-57.6)				41.0	11.5	3.3						44.3						

Bold vertical lines indicate epidemiological 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.

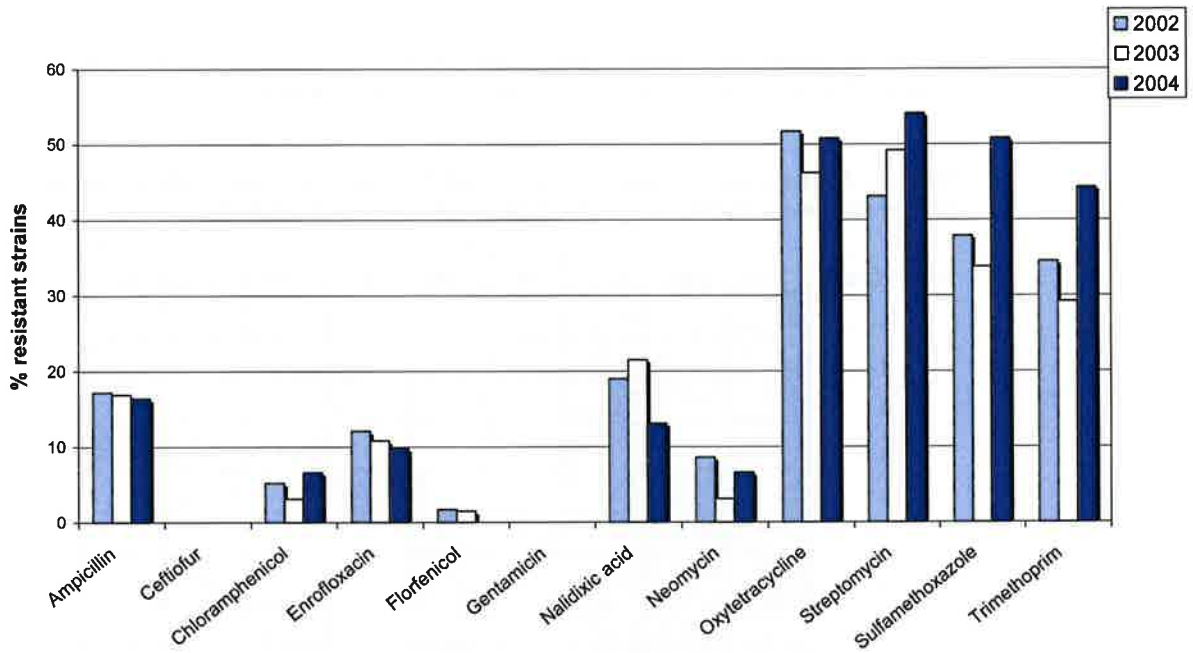

Figure 3. Antimicrobial resistance in *Escherichia coli* isolated from porcine enteritis in 2002 (n=58), 2003 (n=65) and 2004 (n=61)

The MIC distribution and occurrence of resistance are presented in Table 17, and the resistance percentages from 2002, 2003 and 2004 in Figure 3.

Multiresistance was common; as many as 54% of the strains were resistant to at least three antimicrobials. Thirteen percent of the isolates were resistant to three, 28% to four, and 13% to five or more antimicrobials in the test panel. The occurrence of resistance has remained at the same level since 2002 (Figure 3). As in 2002 and 2003, in 2004 resistance to oxytetracycline (51%), streptomycin (54%), sulfamethoxazole (51%), and trimethoprim (44%) was common. These antimicrobials were frequently included in the patterns of the multiresistant strains: 85% of the isolates resistant to streptomycin and oxytetracycline, 94% of the isolates resistant to sulfamethoxazole, and 88% of the isolates resistant to trimethoprim were resistant also to at least two other antimicrobials.

Enrofloxacin and danofloxacin are the fluoroquinolones authorised for use in pigs in Finland. In 2002 and 2003, when calculated with the new breakpoint of > 0.25 mg l^{-1}, 12% and 11% of the isolates, respectively, were resistant to enrofloxacin. In 2004 the percentage was 10%. Thirteen percent of the isolates were resistant to nalidixic acid.

Of the isolates studied, 16% were resistant to ampicillin and 7% to chloramphenicol - a surprisingly high percentage considering that chloramphenicol was withdrawn from the production-animal market in 1993. Since the isolates resistant to chloramphenicol were multiresistant, the resistance can be a consequence of co-selection of resistance genes. Also neomycin resistance (7%) was found only in the multiresistant isolates.

No resistance was detected to ceftiofur, gentamicin or florfenicol. Florfenicol is registered for use in pigs in Finland, but no products containing ceftiofur or gentamicin are approved for veterinary use.

Resistance to the same antimicrobials was detected in *E. coli* from healthy pigs (Fig. 2). Resistance was much more rare among indicator bacteria.

Table 18. Resistance phenotypes of multiresistant *Escherichia coli* from porcine enteritis. The total number of isolates was 61.The shaded fields indicate resistance.

No. of isolates	STR	SMX	OTC	AMP	TMP	CHL	NEO	NAL	EF
1	■	■	■	■	■	■	■		
1	■	■	■	■			■	■	■
1	■	■	■	■	■	■			
1	■		■	■			■	■	■
1	■	■	■		■	■		■	
1	■	■	■	■	■				
1	■	■	■		■			■	
1	■	■	■		■		■		
11	■	■	■		■				
1	■	■	■			■			
3	■	■		■	■				
1	■	■						■	■
1		■			■			■	■
1	■	■	■						
3		■	■		■				
1			■					■	■
2	■	■			■				
1	■							■	■

STR=streptomycin, SMX=sulfamethoxazole, OTC=oxytetracycline, AMP=ampicillin, TMP=trimethoprim, CHL=chloramphenicol, NEO=neomycin, NAL=nalidixic acid, EF=enrofloxacin

Among the isolates resistant to three or more antimicrobials, the following combinations were the most prevalent: resistance to oxytetracycline, streptomycin, sulfamethoxazole and trimethoprim, resistance to oxytetracycline, sulfamethoxazole and trimethoprim and resistance to streptomycin, sulfamethoxazole, trimethoprim and ampicillin. Resistance phenotypes of multiresistant isolates are presented in Table 18.

The resistance to oxytetracycline, sulfamethoxazole, trimethoprim and ampicillin can be explained by the use of these antimicrobials in pig production in Finland. The resistance to streptomycin may reflect the past use of this antibiotic or may be a consequence of co-selection resulting from the use of other antimicrobials. Earlier it was thought that once an antimicrobial was withdrawn from clinical use, the resistance genes would eventually disappear. However, it has been shown that after a long time period of exposure to some antimicrobials, certain bacterial species may adapt so that they are able to keep their resistance genes stable after the removal of the antimicrobials (Franklin, 1999).

Staphylococcus intermedius in dogs

Forty-six isolates of *Staphylococcus intermedius* were collected from clinical samples of dogs and tested for antimicrobial resistance.

Results and comments

Table 19. Distribution of MICs for *Staphylococcus intermedius* from dogs (n=46).

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	>256
Avilamycin	0 (0.0-7.7)						2.2	34.8	63.0							
Cephalothin[1]	2 (0.1-11.5)		6.5	78.3	13.0	2.2										
Chloramphenicol	7 (1.4-17.9)							2.2	80.4	10.9		4.3	2.2			
Clindamycin	17 (7.8-31.4)				71.7	10.9							17.4			
Enrofloxacin	4 (0.5-14.8)			8.7	73.9	13.0	4.3									
Erythromycin	17 (7.8-31.4)				30.4	50.0	2.2						17.4			
Fusidic acid[2]	14 (5.2-27.4)				70.5	15.9	4.5		2.3	6.8						
Gentamicin	2 (0.1-11.5)					95.7	2.2			2.2						
Neomycin	15 (6.3-28.9)						82.6	2.2	10.9	4.3						
Oxacillin[1]	2 (0.1-11.5)					34.8	50.0	15.2								
Oxytetracycline	46 (30.9-61.0)					54.3					6.5	21.7	17.4			
Penicillin	83[3]	13.0	4.3	8.7	10.9	13.0	8.7	15.2	10.9	15.2						
Streptomycin	20 (9.4-33.1)							54.3	26.1				2.2	10.9	6.5	
Trim.-sulfa[4]	7 (1.4-17.9)					67.4	26.1		4.3	2.2						
Vancomycin	0 (0.0-7.7)						82.6	15.2	2.2							
Virginiamycin	0 (0.0-7.7)					73.9	17.4	8.7								

Bold vertical lines indicate epidemiological cut-off values. 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] one isolate was considered resistant to cephalotin and oxacillin due to a positive result in *mecA* PCR

[2] n=44

[3] denotes beta-lactamase production

[4] concentration of trimethoprim given, tested with sulfamethoxazole in concentration ratio 1:20.

Table 20. Resistance phenotypes of multiresistant *S. intermedius* from clinical isolates of dogs (n=46). The shaded fields indicate resistance.

No. of isolates	PEN	OTC	FUS	SXT	STR	EF	NEO	CHL	CLI	ERY	GEN	OXA	CEP
1	■	■			■	■	■	■	■	■			
1	■	■			■		■	■	■	■			
1	■	■		■	■		■		■	■			
1	■				■		■		■	■		■	■
1	■	■			■		■		■	■			
1	■				■		■		■	■			
1			■		■				■	■			
1	■								■	■	■		
1	■				■		■	■					
1	■		■			■							
1	■	■			■								
2	■	■	■										

PEN=penicillin, OTC=oxytetracycline, FUS=fusidic acid, SXT=trimethoprim-sulfamethoxazole, STR=streptomycin, EF=enrofloxacin, NEO=neomycin, CHL=chloramphenicol, CLI=clindamycin, ERY=erythromycin, GEN=gentamicin, OXA=oxacillin, CEP=cephalothin

The MIC distributions and the occurrence of resistance are presented in Table 19. Eighty-three percent of the isolates produced beta-lactamase in the nitrocefin test. Resistance to oxytetracycline was also common (46% of the isolates). Resistance to streptomycin was detected in 20%, to neomycin in 15% and to erythromycin and clindamycin in 17% of the isolates. Resistance was found also to fusidic acid (14% of the isolates), trimethoprim-sulfamethoxazole (7%), chloramphenicol (7%) and enrofloxacin (4%). No resistance was detected to avilamycin, vancomycin or virginiamycin. All isolates were tested for *mecA* gene by PCR, and one *S. intermedius* isolate was found to have the gene and was thus confirmed to be methicillin-resistant. The MIC for oxacillin of the isolate was 2 mg l^{-1} and that for cephalothin 0.25 mg l^{-1}; however, the isolate was classified resistant to all betalactams based on the PCR result.

Of the isolates, 86% were resistant to at least one antimicrobial. Multiresistance was detected in 28% of the isolates. The eight isolates resistant to erythromycin were also resistant to clindamycin (Table 20). Four multiresistant isolates had a resistance pattern including clindamycin, erythromycin, neomycin, oxytetracycline, penicillin and streptomycin. One isolate was additionally resistant to chloramphenicol, one to sulfamethoxazole, and one to enrofloxacin and chloramphenicol.

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Appendix 1: Materials and methods, resistance monitoring

Sampling strategy

Zoonotic bacteria

Salmonella isolates from production animals were collected in accordance with the Finnish salmonella control programme. Isolates from domestic food and pets were included. Of the isolates collected in accordance with the control programme, one isolate from each notified incident was included.

Campylobacter coli and indicator bacteria were isolated from the same porcine samples. A hundred randomly chosen *C. coli* isolates from pigs were tested for antimicrobial susceptibility. *C. jejuni* were collected from broilers in connection with the Finnish *Campylobacter* control programme between June and October.

Indicator bacteria

Indicator bacteria, *E. coli*, *Enterococcus faecalis* and *E. faecium*, were collected from porcine colon or rectum. The samples were isolated from healthy animals. The sampling period was January to December.

The number of randomly taken samples from each slaughterhouse was proportional to the annual number of slaughtered animals. Each isolate represents one herd. The slaughterhouses accounted for 85% of the total slaughter volume in Finland in 2003.

Animal pathogens

Clinical isolates originated from diagnostic submissions or postmortem examinations: *Escherichia coli* was isolated from pigs with enteritis. The samples were taken from the gastrointestinal tract. *Staphylococcus intermedius* was isolated from various canine infections, mostly cases of dermatitis.

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 6579:2002, at local community or slaughterhouse laboratories. Serotyping of the isolates was performed at EELA, Kuopio Department.

Campylobacter

C. jejuni were isolated at slaughterhouse laboratories and confirmed at EELA, Department of Bacteriology according to a modification of the NMKL 119:1990. *C. coli* were isolated at the Department of Bacteriology according to the same method.

Indicator bacteria

Enterococci

Five grams of intestinal content 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 37°C. A typical colony was plated on bile-esculine agar (Difco) and incubated at 37°C overnight. Colonies with a positive esculine reaction were cultivated on blood agar. Non-motile, ribose positive enterococci were identified to species level with the following tests: arginine dihydrolase, mannitol, arabinose, raffinose, sorbitol and melibiose.

Escherichia coli

Five grams of intestinal content 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 blood agar and incubated overnight at 37°C. Oxidase-negative and indole positive colonies were further cultivated in lactose tryptone lauryl sulfate broth (Oxoid, Hampshire, UK) and incubated at 37°C overnight.

Animal pathogens

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

Isolates of *Staphylococcus intermedius* were grown 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 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 or Merck). The isolates were further tested for indole production.

Susceptibility testing

Susceptibility testing was performed with a microdilution broth method: VetMIC™ (Department of Antibiotics, National Veterinary Institute, Uppsala, Sweden). The testing was performed following the standards of the Clinical and Laboratory Standards Institute (former National Committee of Clinical Laboratory Standards) (NCCLS, 2002), except for *Campylobacter*, for which the standard has not yet been approved. Susceptibility testing was performed at EELA, Department of Bacteriology.

Table 21. Epidemiological cut-off values (mg l^{-1}) used in this report. Isolates with MIC values higher than the given figures are considered resistant.

Antimicrobial agent	*Salmonella enterica*	*Escherichia coli*	*Enterococcus* spp.	*Staphylococcus intermedius*	*Campylobacter* spp.
Ampicillin	>8	>8	>8		>16
Avilamycin			>16	>16	
Bacitracin[1]			>32		
Ceftiofur	>2	>2			
Cephalotin				>1	
Chloramphenicol	>16	>16	>16	>16	
Clindamycin				>2	
Enrofloxacin	>0.25	>0.25		>0.5	>0.5
Erythromycin			>4	>2	>8
Flavomycin			>16		
Florfenicol	>16	>16			
Fucidic acid				>0.5	
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
Streptomycin	>32	>16	>256	>32	
Sulfamethoxazole	>256	>256			
Trimethoprim	>4	>4			
Trim.-sulfa[2]				>2	
Vancomycin			>4	>4	
Virginiamycin			>8	>4	

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

[2] concentration of trimethoprim given, tested with sulfamethoxazole in concentration ratio 1:20

Panels with different concentration ranges were used and the MIC data for each animal species were combined to include the concentrations in the panels used. Cut-off values for resistance (Table 21) 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.

Bacitracin values are given in units ml^{-1} (SVARM, 2004).

Production of beta-lactamase was tested with nitrocefin disc test (AB Biodisk, Solna, Sweden). Polymerase chain reaction (PCR) for *mecA* gene detection was performed according to Murakami *et al.* (1991).

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.

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 33560.

Kuopio Department is accredited for isolation, identification and serotyping of *Salmonella*, and the Department of Bacteriology for performing the VetMIC™ test for *E. coli*, *Salmonella*, Enterococci and Staphylococci according to SS-EN ISO/IEC 17025, by the Finnish Centre for Metrology and Accreditation.

Appendix 2: Population statistics

Table 22. Number of farm animals and holdings in Finland (situation 1st December 2004) and animals slaughtered in 2004.

Animal category	Holdings	Livestock (live animals)	Slaughtered animals
Cattle			
calves (under one year)	21 681	328 400	
dairy cows and heifers	18 107	463 700	
meat production animals	1 869	115 600	
in total			315 395
Chickens			
broilers	143	5 573 229	52 422 471
laying hens	1 653	3 069 195	1 023 596
parent birds for meat production line			463 828
Pigs			
sows and gilts	2 425	191 200	62 020
breeding animals	2 717	44 949	
fattening pigs	1 828	1 243 800	2 306 475

Table 22 presents the number of farm animals and holdings in Finland (situation December 1, 2004) and animals slaughtered in 2004. Data on holdings and live animals originate from the Information Centre of the Ministry of Agriculture and Forestry, Farm survey 2004, and data on slaughtered animals from meat inspection statistics of the National Food Agency.

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