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CONTRIBUTORS AND PARTICIPANTS

Editors:

Dag Seeger Halvorsen	NORM, Department of Microbiology, University Hospital of North Norway
Hilde Kruse	NORM-VET, Norwegian Zoonosis Centre

Authors:

Hege Salvesen Blix	Norwegian Institute of Public Health
Kari Grave	VETLIS / Norwegian School of Veterinary Science
Dag Seeger Halvorsen	NORM, Department of Microbiology, University Hospital of North Norway
Einar Heldal	Norwegian Institute of Public Health
Merete Hofshagen	NORM-VET, Norwegian Zoonosis Centre
Bjørn Iversen	Norwegian Institute of Public Health
Hilde Kruse	NORM-VET, Norwegian Zoonosis Centre
Jørgen Lassen	Norwegian Institute of Public Health
Pia Littauer	Department of Microbiology, University Hospital of North Norway
Madelaine Norström	NORM-VET, Norwegian Zoonosis Centre
Per Sandven	Norwegian Institute of Public Health
Gunnar Skov Simonsen	NORM, Dept. of Microbiology, University Hospital of North Norway and Norw. Inst. of Public Health
Martin Steinbakk	NORM, Department of Microbiology, University Hospital of North Norway
Yngvar Tveten	Telelab A/S

Institutions participating in NORM-VET:

Municipal Food Control Authorities	
Norwegian Food Control Authority	
Norwegian Animal Health Authority	
National Agricultural Inspection Service	
Norwegian Institute of Public Health	Jørgen Lassen / Trine-Lise Stavnes
National Veterinary Institute	Hanne Tharaldsen / Bjarne Bergsjø
Norwegian Zoonosis Centre	Madelaine Norström / Hilde Kruse / Merete Hofshagen

Institutions participating in NORM:

Aker University Hospital, Department of Bacteriology	Signe H. Ringertz / Bitten Rasmussen
Akershus University Hospital, Department of Microbiology	Martin Steinbakk / Siri Haug
Bærum Hospital, Central Laboratory, Section of Microbiology	Fredrik Müller / Miriam Sundberg
Central Hospital of Buskerud, Department of Microbiology	Hjørdis Iveland / Ann Elise Johansen
Central Hospital of Nordland, Department of Microbiology	Liisa Mortensen / Karstein Korsvik
Central Hospital of Nord-Trøndelag, Levanger, Department of Microbiology	Arne Mehl / Eldbjørg Berg
Central Hospital of Nord-Trøndelag, Namsos, Department of Microbiology	Gerd Skjervold / Lise Haaland
Central Hospital of Oppland, Lillehammer, Department of Microbiology	Ingunn Haavemoen / Kari Ødegaard
Central Hospital of Hedmark, Elverum, Laboratory of Microbiology	Linda Schildman / Lene Bjøntegård
Central Hospital of Østfold, Department of Microbiology	Eivind Ragnhildstveit / Eva Madsen
Central Hospital of Rogaland, Department of Microbiology	Elisebet Haarr / Tone Roa
Central Hospital of Sogn og Fjordane, Department of Microbiology	Reidar Hjetland / Berit Ose
Central Hospital of Vest-Agder, Department of Microbiology	Sølvi Noraas / Torill S. Larsen
Central Hospital of Vestfold, Department of Microbiology	Rolf Schøyen / Astrid Lia
Central Hospital of Hordaland, Haugesund, Department of Microbiology	Liv J. Sønsteby / Pirrko-L. Kellokumpu
County Hospital of Møre og Romsdal, Molde, Department of Microbiology	Einar Vik / Margreet B. Sandhaug
County Hospital of Møre og Romsdal, Ålesund, Department of Microbiology	Reidar Hide / Fillip Angeles
Haukeland Hospital, Department of Immunology and Microbiology	Asbjørn Digranes / Hilde Bekkeheien
National Hospital, University of Oslo, Institute of Medical Microbiology	Mette Walberg / Magli Bøvre
National Cancer Hospital, Laboratory of Microbiology	Sunniva R. Fagerås
Norwegian Institute of Public Health, Laboratory of Enteric Pathogens	Jørgen Lassen / Trine-Lise Stavnes
Telelab A/S, Skien	Yngvar Tveten / Inger Johanne Lunde
Ullevål University Hospital, Department of Microbiology	Gaute Syversen / Thea Bergheim
University Hospital of North Norway, Department of Microbiology	Gunnar S. Simonsen / Siv-H. Barkhald
University Hospital of Trondheim, Department of Microbiology	Trond Jacobsen / Mariann Hulsund
Laboratory of Clinical Medicine, Oslo	Wibeke Aasnæs / Anne K. Andersen

NORM-VET steering group:

Norwegian Animal Health Authority	Gunnar Hagen
Norwegian Food Control Authority	Nina Krefting Aas
National Agricultural Inspection Service	Ellen Mari Grande
National Veterinary Institute	Kåre Fossum
Norwegian Zoonosis Centre	Hilde Kruse

NORM reference group:

E. Arne Høiby	Norwegian Institute of Public Health
Reidar Hjetland	Central Hospital of Sogn og Fjordane, Department of Microbiology
Eirik Holten	Akershus University Hospital, Department of Microbiology
Asbjørn Digranes	Haukeland University Hospital, Department of Immunology and Microbiology
Inger Sofie Samdal Vik	County Hospital of Møre og Romsdal, Department of Microbiology

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I. INTRODUCTION

Antimicrobial resistance is an increasing problem worldwide. It affects the treatment of infectious diseases in both humans and animals, thereby resulting in increased morbidity and mortality, as well as higher costs. It is well established that there is an association between the use of antimicrobial agents and the occurrence of resistance. The selective pressure excerted by the use of antimicrobials is a key issue in the epidemiology of resistance. Moreover, resistance can be disseminated through the spread of resistant pathogenic bacteria themselves or by horizontal transfer of resistance genes from one type of bacteria to another. Such transfer is not limited to closely related bacteria; it can also take place between bacteria of different evolutionary origins and/or ecological sources. Thus, antimicrobial usage and resistance in one compartment can have consequences for the occurrence of resistance in another compartment. When addressing antimicrobial resistance – the occurrences, causes, consequences and preventive measures – a holistic approach is needed, encompassing both usage and resistance in human and veterinary medicine, as well as in food production.

Several countries have implemented monitoring programmes for antimicrobial resistance and antimicrobial usage in recent years. Some programmes focus primarily on human consumption and resistance in human pathogens, whereas others also include data concerning veterinary medicine and food production. The EU supported this broad approach in 1998 through the Copenhagen recommendations and again in 2001 at a follow-up conference in Visby, Sweden. The World Health Organization has published similar guidelines. In response to the growing concern about antimicrobial resistance, the Norwegian Ministry of Health and Social Affairs issued a national action plan against antimicrobial resistance (2000–2004) in March 2000. Again, the importance of monitoring both the human and veterinary sectors, including food production, was emphasized.
The NORM surveillance programme for antimicrobial resistance in human pathogens was established in Norway in 1999 and is coordinated by the Department of Microbiology at the University Hospital of North Norway in Tromsø. The NORM-VET monitoring programme for antimicrobial resistance in the veterinary and food production sectors was established in 2000 and is coordinated by the Norwegian Zoonosis Centre in Oslo. The consumption of antimicrobial agents in humans is monitored by the Norwegian Institute of Public Health on the basis of reports from wholesalers. This reporting was made mandatory from 1 January 2002. Data on veterinary therapeutic use are similarly reported to the WHO Collaborating Centre, whereas consumption data on feed additives, including antibacterial growth promoters and coccidiostats, are collated at the Norwegian Agricultural Inspection Service.

This report, which is the third annual joint report from NORM and NORM-VET, presents data for 2002. In addition to resistance data, the NORM/NORM-VET reports present data on the consumption of antimicrobial agents in humans and animals in Norway. The present report together with the earlier reports and reports from the years to come form a basis for the detection, interpretation and evaluation of trends regarding antimicrobial usage and occurrence of resistance in Norway. The NORM and NORM-VET programmes are valuable tools for setting policies, assessing risks and evaluating interventions.

The editors would like to thank the Reference Center for Detection of Antimicrobial Resistance in Tromsø for fruitful cooperation and all those who contributed to data collection and the writing of this report for excellent work.

Tromsø / Oslo, September 2003

II. SAMMENDRAG

Norsk overvåkingssystem for antibiotikaresistens hos mikrober (NORM) overvåker forekomsten av antibiotikaresistens blant sykdomsfremkallende bakterier fra mennesker. Programmet koordineres av Mikrobiologisk Avdeling, Universitetssykehuset i Nord-Norge. NORM-VET har tilsvarende oppgaver innen veterinærmedisin og matproduksjon og koordineres av Norsk zoonosesenter i Oslo. NORM ble etablert i 1999 og NORM-VET i 2000. De to programmene samarbeider nært og utgir blant annet en felles årsrapport. Den foreliggende rapport presenterer data for året 2002 og er den tredje årsrapporten fra NORM/NORM-VET. Årsrapportene gir i tillegg til resistensdata en oversikt over forbruket av antibakterielle midler til mennesker og dyr. Rapportene brukes også til å formidle data fra relevante prosjekter selv om disse ikke er en del av den opprinnelige planen for overvåkingsprogrammene.

Forbruk av antibiotika til dyr

Det norske totalsalget av antibakterielle midler godkjent for terapeutisk bruk til dyr utenom fisk var 5 890 kg i 2002. Dette er en økning på 3% sammenlignet med 2001. Siden 1995 er det likevel en reduksjon på 38%. Forbruket er lavt sammenlignet med en rekke andre land, og forbruksmønsteret er gunstig. Andelen av rene penicillin-preparater økte fra 25% av totalsalget i 1995 til 38% i 2002. β-laktamase-følsomme penicilliner utgjorde 87% av totalsalget av rene penicillinpreparater i 2002. Kombinasjonspreparater av sulfonamider og trimetoprim eller baquiloprim økte sin andel av totalsalget fra 11% i 1995 til 24% i 2002, mens andelen av penicilliner kombinert med aminoglykosider (dihydrostreptomycin) sank fra 35% til 24% i samme periode. Tetracyklinenes andel av totalsalget sank fra 5% i 1995 til 3% i 2002. Sulfonamidene utgjorde 14% av salget i 1995, mens det i 2002 ikke ble solgt veterinære farmasøytiske spesialpreparater som kun inneholdt sulfonamider. Den gunstige situasjonen når det gjelder forbruk av antibiotika til landdyr kan tilskrives en generelt restriktiv legemiddelpolitikk når det gjelder antibiotika, samt en holdningskampanje for en kritisk bruk av antibiotika innenfor husdyrproduksjonen.

Totalsalget av veterinære antibakterielle midler godkjent for terapeutisk bruk til oppdrettsfisk i Norge var 1 219 kg i 2002. Kinoloner utgjorde 82% av dette salget. I løpet av de siste 15 årene har forbruket av antibakterielle midler i oppdrettsnæringen blitt redusert med 98% samtidig som produksjonen av oppdrettsfisk er mangedoblet. Denne betydelige reduksjonen kan tilskrives innføringen av effektive vaksiner og bedrede miljøforhold i oppdrettsnæringen.

Avoparcin ble brukt som antibakterielt vekstfremmende fôrtilskudd i norsk broiler- og kalkunproduksjon fra 1986 inntil det ble forbudt i 1995. Samme år innførte husdyrnæringene et selvpålagt forbud mot bruk av alle antibakterielle vekstfremmere. Forbruket av slike stoffer har vært minimalt etter 1995, og lik null etter 1998.

Det årlig forbruket av koksidiostatika har vært stabilt de siste seks årene, selv om forbruksmønsteret har endret seg. Narasin har dominert siden 1996, mens bruken av andre ionofore koksidiostatika har sunket tilsvarende.

Forbruk av antibiotika hos mennesker

Totalforbruket av antibakterielle midler til systemisk bruk (ATC gruppe J01) hos mennesker var 17.1 DDD/1000 innbyggere/døgn i 2002. Dette er en liten økning på 2% fra 2001. Forbruket til humant bruk i Norge kan sammenliknes med forbruket i Sverige og Danmark og er lavt i forhold til mange land i Europa. Forskrivningsmønsteret er fortsatt preget av smalspektrete antibiotika. En økning ble observert for mange grupper av antibiotika i 2002, et viktig unntak var smalspektrete penicilliner (J01CE), som ble redusert. Penicilliner (J01C) er fortsatt den viktigste antibiotika gruppen og representerer 42% av totalforbruket. Andelen har vært stabil over år, men det ses nå en dreining fra β-laktamase følsomme penicilliner til penicilliner med utvidet spektrum og β-laktamase resistente penicilliner. Tetracyklinene (J01A) utgjorde 18% av totalforbruket. 2002 var det første året uten nedgang i tetracyklin-forbruket siden 1993 da det høyeste forbruket noensinne ble registrert. Makrolidene (J01FA) representerer 12 % av totalforbruket. Salget har vært ganske stabilt, men fra 2000 har vi sett en økning i forbruket. Forskrivnings-mønsteret av makrolider er stabilt, og erythromycin er hyppigst brukt. Salget av cefalosporinene øker, og salg av sulfonamider og trimetoprim er redusert. I tillegg er det observert en liten, men stabil økning av kinolonforbruket. Kinolonene representerer kun en liten del av totalforbruket, men økningen utgjør 57% siden 1996. Økningen i ATC gruppe J01X er hovedsakelig forårsaket av metenamin, et profylaktisk urinveisantiseptikum.

Sykehusene sto for 7.7% av det totale antibiotika-forbruket til systemisk bruk hos mennesker i 2002. Forbruksmønsteret er forskjellig på sykehus og i almenpraksis. Penicilliner (J01C) utgjør 45% av forbruket på sykehus, etterfulgt av cefalosporinene. Sykehusforbruket innbefatter omtrent halvparten av alt salg av cefalosporiner. Forskrivningsmønsteret ser ut til å være endret til et høyere forbruk av 3. generasjons cefalosporiner og et lavere forbruk av 1. generasjons cefalosporiner.

Resistens hos kliniske isolater fra dyr

Staphylococcus intermedius fra hudinfeksjon hos hund

Resistens var utbredt blant de undersøkte isolatene. Bare 8% av isolatene var følsomme for alle undersøkte antibiotika, og 44% var resistente mot minst tre antibiotika. Prevalensen av resistens mot henholdsvis penicillin (86%), fusidinsyre (59%) og tetracyklin (53%) var særlig høy. En moderat andel av isolatene var resistente mot henholdsvis klindamycin (15%), erytromycin (18%), streptomycin (22%) og trimetoprim (13%). Resistens mot henholdvis gentamicin, cefalotin og ciprofloxacin ble ikke påvist. Dataene for 2002 indikerer en økning sammenlignet med NORM-VET 2000 i prevalensen av resistens mot alle undersøkte antibiotika med unntak av cefalosporiner og fluorokinoloner hvor resistens fortsatt er på et meget lavt nivå.

***Escherichia coli* fra enteritt hos gris**
En moderat forekomst av resistens ble observert. Tilsammen 56% av isolatene var resistente mot minst ett og 21% mot minst tre av de undersøkte antibiotika. En høy andel av isolatene var resistente mot oxytetracyklin (41%) og streptomycin (54%). Forekomsten av resistens mot henholdsvis ampicillin, trimetoprim og sulfa var moderat (8-25%). Kinolonresistens ble ikke påvist. Resultatene fra 2002 samsvarer med tilsvarende fra NORM-VET 1999.

***Escherichia coli* fra septikemi hos fjærfe**
En moderat forekomst av resistens ble observert. Tilsammen 37% av isolatene var resistente mot minst ett og 12% mot minst tre av de undersøkte antibiotika. Resistens mot sulfa var hyppigst (25%), fulgt av resistens mot ampicillin (12%), streptomycin (10%), oxytetracyklin (8%) og trimetoprim (8%). Prevalensen av resistens mot kinoloner var lav; tre isolater (6%) var resistente mot nalidiksinsyre, hvorav ett (2%) også var resistent mot enrofloxacin.

Resistens hos indikatorbakterier

Resultatene fra 2002 indikerer en relativ lav forekomst av resistens blant *E. coli* og *Enterococcus* spp. fra prøver av feces og kjøtt fra en representativ gruppe av friske norske griser og broilere. Virginiamycinresistens hos *Enterococcus faecalis* og flavomycinresistens hos *E. faecium* er ekskludert fra resultatene for enterokokker på grunn av naturlig resistens.

***Escherichia coli* fra gris**
Tilsammen 26% av *E. coli*-isolatene fra grisefeces og 23% av *E. coli*-isolatene fra svinekjøtt var resistente mot minst ett av de undersøkte antibiotika. Resistensmønstrene var i hovedsak de samme som for *E. coli* fra enteritt hos gris, men resistensfrekvensene var betydelig lavere for indikatorisolatene. Resistensfrekvensene og forekomsten av multiresistens var noe høyere for *E. coli* fra feces enn for svinekjøttisolatene. Hyppigst ble det påvist resistens mot streptomycin (21%), fulgt av sulfa (11%), tetracyklin (6%), ampicillin (4%) og trimetoprim (3%). Fluorokinolonresistens ble ikke påvist. Ett isolat (0.5%) var imidlertid resistent mot nalidiksinsyre.

***Escherichia coli* fra broiler**
Tilsammen 33% av *E. coli*-isolatene fra broilerfeces og 23% av *E. coli*-isolatene fra broilerkjøtt var resistente mot minst ett av de undersøkte antibiotika.
Resistensmønstrene samt resistensfrekvenser var i hovedsak de samme som for *E. coli* fra septikemi hos fjærfe. Imidlertid var forekomsten av resistens for mange av antibiotikumene noe lavere blant broilerkjøttisolatene sammenlignet med de andre gruppene. Totalt sett ble resistens mot sulfa hyppigst påvist (16%), fulgt av ampicillin (10%), oxytetracyklin (8%), streptomycin (4%) og trimetoprim (1%). Prevalensen av resistens mot kinoloner var lav; to isolater (0.7%) var resistente mot både nalidiksinsyre og enrofloxacin, og to (0.7%) var resistente mot kun nalidiksinsyre.

***Enterococcus* spp. fra gris**
Tilsammen 56% av enterokokkene fra grisefeces og 20% av enterokokkene fra svinekjøtt var resistente mot minst ett av de undersøkte antibiotika. Multiresistens (resistens mot minst tre antibiotika) ble sjelden påvist (1.6%). Resistens mot oxytetracyklin (27%) var hyppigst, fulgt av resistens mot streptomycin (7%). Resistensfrekvensene for oxytetracyklin og streptomycin var betydelig høyere for de fekale isolatene enn for svinekjøttisolatene, og høyere for *E. faecalis* enn for *E. faecium*. En lav andel (<3.2%) av isolatene var resistente mot henholdsvis bacitracin, erytromycin, narasin, neomycin, avilamycin og kloramfenikol. Resistens mot henholdsvis vankomycin, ampicillin og gentamicin ble ikke påvist. Resistensfrekvensene for svinekjøttisolatene samsvarer med tilsvarende data fra NORM-VET 2000.

***Enterococcus* spp. fra broiler**
Tilsammen 77% av enterokokkene fra broilerfaeces og 54% av enterokokkene fra broilerkjøtt var resistente mot minst ett av de undersøkte antibiotika. Multiresistens ble sjelden påvist (4.9%). Narasinresistens ble hyppigst observert (40%), fulgt av resistens mot oxytetracyklin (22%), bacitracin (20%), erytromycin (10%) og vankomycin (1.9%). Andelen isolater resistente mot henholdsvis tetracyklin og erytromycin var betydelig høyere for isolatene fra feces enn for broilerkjøttisolatene. Koksidiostatika, i all hovedsak narasin, brukes rutinemessig i norsk broilerproduksjon. Avoparcin, som gir kryssresistens mot vankomycin, ble rutinemessig benyttet som vekstfremmer i norsk broiler- og kalkunproduksjon fra 1986 inntil det ble forbudt i 1995. Liksom i andre studier var det en species-forskjell når det gjaldt vankomycinresistens blant tilfeldig utvalgte enterokokkisolater; 3.8% av *E. faecium* og ingen av *E. faecalis* var resistente. Forekomsten av vancomycinresistens blant indikator-enterokokker hos norske broilere synes å ha holdt seg på samme nivå fra 2000 til 2002. Ved bruk av en selektiv metode som påviser tilstedeværelse av vankomycinresistente enterokokker (VRE), ble VRE imidlertid isolert fra 91% av faecesprøver der hver prøve representerte én broilerflokk. Denne andelen samsvarer med tilsvarende tidligere undersøkelser. Følgelig synes utbredelsen av VRE i norske broilerflokker å ha vedvart på samme nivå syv år etter at forbudet mot avoparcin ble iverksatt.

Resistens hos zoonosebakterier og andre enteropatogene bakterier

***Salmonella* spp.**
Salmonella, med unntak av *S. enterica* subsp. *diarizonae* hos sau, påvises sjelden hos matproduserende dyr i Norge. I 2002 ble fem tilfeller påvist i *Salmonella*-overvåkingsprogrammet, og alle var følsomme for alle de undersøkte antibiotika. Alle 21 isolater av *S. enterica* subsp. *diarizonae* fra friske sauer var også følsomme, hvilket indikerer at resistens ikke er utbredt hos denne bakterietypen som forekommer endemisk i den norske sauepopulasjonen. Multiresistent *S.* Typhimurium DT104 (ACSSuT) ble isolert fra en hest på en gård i nærheten av en storfebesetning der samme bakterietype ble påvist i 2001, den første kjente påvisningen av denne bakterietypen noensinne hos norske dyr.
Av de humane salmonellosetilfellene som ble rapportert i 2002, var 75% oppgitt å ha blitt smittet i utlandet. Andelen *S.* Typhimurium isolater (unntatt DT104) som var følsomme for alle de undersøkte antibiotika, var høyere for kategorien "smittet i Norge" (72%) enn for kategorien "smittet i utlandet" (53%). Multiresistens ble hyppigere påvist i sistnevnte katergori (22%) enn førstnevnte (8%).

For kinolonresistens var det en signifikant forskjell mellom de to kategoriene; 10.9% av isolatene fra gruppen "smittet i utlandet" var resistente mot nalidiksinsyre og 1.1% mot ciprofloxacin, sammenlignet med ingen i gruppen "smittet i Norge".
Resistensprofilene for isolatene av multiresistent DT104 var tilnærmet like for gruppene "smittet i Norge" og "smittet i utlandet." Alle isolatene var resistente mot ampicillin, tetracyklin, streptomycin, sulfa og kloramfenikol. Tilsammen 23% var også resistente mot nalidiksinsyre.
Hovedandelen av *S.* Enteritidis-isolatene var ervervet utenlands. Andelen isolater som var resistente mot henholdsvis tetracyklin, kloramfenikol og ampicillin, var betydelig lavere enn for *S.* Typhimurium (inkludert de som ble smittet i Norge). Nalidiksinsyreresistens var derimot mer utbredt blant *S.* Enteritidis enn blant *S.* Typhimurium.

***Campylobacter* spp.**
Resultatene fra 2002 viser at forekomsten av resistens hos *Campylobacter jejuni* fra norske broilere er lav. Totalt 94.4% av isolatene var følsomme for alle de undersøkte antibiotika. Kun ett isolat (0.6%) var resistent mot fluorokinoloner, mens 1.9% var resistente mot nalidiksinsyre. Nivået av resistens og resistensmønstrene for *C. jejuni* fra norske broilere samsvarer med *C. jejuni* fra mennesker smittet i Norge med unntak av en høyere forekomst av kinolonresistens, særlig nalidiksinsyre, blant humanisolatene. Dette forholdet ble også påvist i NORM/NORM-VET 2001.
Resistens var betydelig mer utbredt blant *C. jejuni* fra pasienter smittet i utlandet (79% resistente mot minst ett antibiotikum) enn pasienter smittet i Norge (11%). Dette skyldes en utbredt forekomst av resistens mot ciprofloxacin/nalidiksinsyre og tetracyklin blant isolatene ervervet i utlandet.
Bare to av 29 undersøkte *C. coli* var ervervet i Norge. Tilsammen 76% av *C. coli* isolatene var resistente mot minst ett antibiotikum. Kinolonresistens var utbredt; 66% av isolatene var resistente mot både nalidikinsyre og ciprofloxacin.

***Shigella* spp.**
Hovedandelen av *Shigella*-isolatene var ervervet i utlandet. I likhet med hva som rapporteres fra andre land, var resistens utbredt. Resistensfrekvensene var særlig høye (>55%) for tetracyklin og trimetoprim/sulfa, fulgt av ampicillin og kloramfenikol. Fluorokinolonresistens var lite utbredt og ble kun observert blant *S. flexneri* (4.3%). Imidlertid var en betydelig andel av isolatene av *S. flexneri* (17.4%) og *S. sonnei* (11.8%) nalidiksinsyreresistente, hvorav mange også viste redusert følsomhet for ciprofloxacin, noe som igjen indikerer en utvikling av fluorokinolonresistens.

Resistens hos kliniske isolater fra mennesker

Forekomsten av antibiotikaresistens i humane kliniske isolater var fortsatt meget lav i Norge i 2002. Det ble bare påvist mindre endringer fra 2001 til 2002 for bakterietyper som ble undersøkt begge år. Det ble funnet tre isolater av *E. coli* og ett isolat av *Klebsiella oxytoca* med utvidet β-lactamaseproduksjon (ESBL), to isolater av methicillinresistente *Staphylococcus aureus* (blant 726 isolater), fem isolater av *Streptococcus pneumoniae* med nedsatt følsomhet for penicillin (blant 538 isolater), og syv isolater av multiresistent *Mycobacterium tuberculosis* (seks MDR isolater blant 180 ikke tidligere behandlede og ett MDR isolat blant 12 tidligere behandlede). De to tilfellene av MRSA-infeksjon og de syv tilfellene av multiresistent tuberkulose var sannsynligvis alle importerte fra utlandet. Det ble kun påvist ett enterokokkisolat med overførbar vankomycinresistens.
Forekomst av fucidinresistens blant *S. aureus* i blodkulturisolater var 8.0 % i 2002. Dette er høyere enn hva som ble beskrevet i blodkultur fra 2000 (1.9 %) og i 2001 (5.1%). Vi er kjent med et nasjonalt klonalt utbrudd av fucidinresistente *S. aureus* som forårsaker hudlidelsen bulløs impetigo. Hvorvidt det er den samme bakterieklon som er representert i blodkulturmaterialet til NORM 2002, er uavklart. Flere forskningsgrupper ønsker nå å undersøke dette forholdet nærmere.
Enterococcus spp. fra blodkultur ble i 2002 inndelt i *E. faecalis* og *E. faecium* for å få frem den vesentlig lavere følsomheten for β-laktamantibiotika blant *E. faecium* sammenlignet med *E. faecalis* (38.3% versus 98.9% følsomhet for ampicillin). Høygradig gentamicin-resistens ble påvist hos 9.6% av *E. faecalis*-isolatene, og dette er økning sammenlignet med 2001 (4.5%). Samlet er dog mer enn 92% av alle enterokokkisolatene fortsatt følsomme for gentamicin.
Makrolidresistens hos luftveispatogener er et økende problem internasjonalt. Kun 5.2% av pneumokokkene fra blodkultur var resistente mot erytromycin i NORM 2002. Dog rapporteres en økning sammenlignet med 2001 (2.2 %). For *Streptococcus pyogenes* (gruppe A streptokokker) var 3.7 % av isolatene resistente mot erytromycin. Overraskende var hele 15.6 % av alle *S. pyogenes* isolatene resistente mot doxycyklin. Gruppe A streptokokker funnet i sårprøver var mer resistente (23.0 %) enn gruppe A streptokokker funnet i bakteriologiske prøver fra luftveiene (10.4 %).

Konklusjon

Antibiotikaresistens er fortsatt et begrenset problem i Norge både når det gjelder mennesker og dyr. Det lave forbruket av antibiotika og det fordelaktige forbruksmønsteret må opprettholdes for å bevare den gunstige situasjonen. Resultatene som presenteres i denne rapporten, viser at norske strategier når det gjelder antibiotikabruk og antibiotikaresistens hittil har vært vellykkede både i husdyrholdet og i helsevesenet. Faren for økende resistensproblemer er imidlertid til stede i form av økt antibiotikaforbruk i Norge og import av resistens fra andre land. Det er derfor nødvendig med fortsatt aktiv innsats for å sikre at vi også i fremtiden kan gi tilfredsstillende antibiotikabehandling til dem som trenger det. NORM/NORM-VET-rapporten er et viktig bidrag til arbeidet med å forebygge utvikling og spredning av antibiotikaresistens.

III. SUMMARY

The NORM surveillance programme for antimicrobial resistance in human pathogens was established in 1999. It is coordinated by the Department of Microbiology at the University Hospital of North Norway in Tromsø. The NORM-VET monitoring programme for antimicrobial resistance in the veterinary and food production sectors was established in 2000. The Norwegian Zoonosis Centre in Oslo is the coordinator of NORM-VET. Successful collaboration has been established between NORM and NORM-VET and a joint report is issued annually. The current report, which is the third joint report, presents data for the year 2002. In addition to data on antimicrobial resistance, the NORM/NORM-VET reports include data on consumption of antimicrobial agents in humans and animals. The joint report also presents data from specific surveys or projects that are not part of the continuous monitoring through NORM or NORM-VET.

Use of antimicrobial agents in animals

In 2002, the total sale of antibacterial drugs approved for therapeutic use in animals (excluding fish) in Norway was 5,890 kg. This is a 3% increase compared to 2001. Still, this amount is considered low compared to many other countries and represents a 38% decrease since 1995. Furthermore, the patterns of use are favourable. The proportion of the total sale accounted for by pure penicillin preparations increased from 25% in 1995 to 38% in 2002. β-lactamase sensitive penicillins accounted for 87% of the veterinary penicillin preparations sold in 2002. The proportion accounted for by sulfonamides in combination with trimethoprim or baquiloprim increased from 11% in 1995 to 24% in 2002, and the proportion of combined preparations of penicillins and aminoglycosides (dihydrostreptomycin) decreased from 35% to 24% in the same period. The proportion of the total sales accounted for by sulfonamides decreased gradually from 14% in 1995 to 0% in 2002, and the proportion of tetracyclines declined from 5% to 3%. This favourable situation regarding use of antimicrobials in terrestrial animals is mainly attributed to restrictive antimicrobial drug legislation in Norway as well as a campaign focusing on prudent use of antimicrobials in food producing animals.

In 2002, the total sales of antibacterial drugs for therapeutic use in farmed fish was 1 219 kg of active substance. Quinolones accounted for 82% of this. During the past 15 years, the total use of antibacterials in farmed fish has decreased by 98%. In the same period, the total production of fish has increased massively. This significant decrease in antibacterial use is mainly attributed to the introduction of effective vaccines and improved health management in Norwegian aquaculture.

The antibacterial growth promoter avoparcin was used in Norwegian broiler and turkey production from 1986 until it was prohibited in 1995. The same year, Norwegian food animal production industries voluntarily abandoned the use of all antibacterial growth promoters. Since 1995, the consumption of such agents in Norwegian animal husbandry has been very low, and since 1998 zero. The total use of coccidiostats has remained at the same level for the past six years, but the pattern of use has changed. Since 1996, narasin has been the most commonly used coccidiostat while the use of other ionophores has decreased correspondingly.

Use of antimicrobials in humans

The overall consumption of antibacterials for systemic use (ATC group J01) in humans in 2002 was 17.1 DDD/1000 inhabitants/day, which is a 2% increase compared to 2001. The consumption in Norway is comparable to Sweden and Denmark, but low compared to the majority of other European countries. Further, the prescription pattern is characterised by the use of narrow spectrum drug groups. An increase was observed for several antibacterial subgroups in 2002, except for the β-lactamase sensitive penicillins (J01CE). Still penicillins (J01C) were commonly used and accounted for 42% of the total antimicrobial use in Norway. The sales of penicillins have been stable over years. In 2002, however, there was a shift from β-lactamase-sensitive penicillins to penicillins with extended spectrum and β-lactamase-resistant penicillins. The tetracyclines (J01A) accounted for 18% of the total use. 2002 was the first year with no decrease since 1993, when the highest sale ever was recorded. The macrolides (J01FA) represent 12% of the total use in 2002. The sale has been fairly stable in the 1990s, however, since 2000 an increase was observed. The macrolide prescription pattern remained unchanged, with erythromycin as the most commonly prescribed substance. The sales of cephalosporins are increasing whereas the sales of sulfonamides and trimethoprim are decreasing. Further, there has been a small but stable increase in quinolone use. Quinolones represent only a minor fraction (2.6%) of total antibacterial sales, but sales have increased with 57% since 1996. The increase of ATC group J01X is mainly due to the urinary prophylactic agent methenamine. Sales to hospitals accounted for 7.7% of total sale in 2002. Penicillins (J01C) accounted for 45% of the use in hospitals followed by the cephalosporins (J01D). Around half of the total amount of cephalosporins sold in Norway was used in hospitals. The prescription pattern has changed towards more 3rd generation cephalosporins and less 1st generation cephalosporins.

Resistance in animal clinical isolates

***Staphylococcus intermedius* from skin infections in dogs**

Resistance was widespread. Only 8% of the isolates were susceptible to all antimicrobials included, and 44% were resistant to at least three drugs. The prevalence of resistance to penicillin (86%), fucidic acid (59%) and tetracycline (53%), respectively, was particularly high. A moderate proportion of the isolates were resistant to clindamycin (15%), erythromycin (18%), streptomycin (22%) and trimethoprim (13%), respectively. No resistance to gentamicin, cephalothin or ciprofloxacin was observed. The data for 2002 indicate an increase as compared to NORM-VET 2000 in the prevalence of resistance to all antimicrobials included except cephalosporins and fluoroquinolones to which resistance has remained at a very low level.

***Escherichia coli* from enteritis in pigs**
A moderate occurrence of resistance was observed. In total, 56% of the isolates were resistant to at least one of the antimicrobials included and 21% to at least three antimicrobials. A high prevalence of resistance to oxytetracycline (41%) and streptomycin (54%) was observed. The occurrence of resistance to ampicillin, trimethoprim and sulfamethoxazole was moderate (8-25%). No quinolone resistance was observed. The results obtained in 2002 are similar to those from 1999.

***Escherichia coli* from septicaemia in poultry**
A moderate occurrence of resistance was observed. In total, 37% were resistant to at least one of the antimicrobials included and 12% to at least three antimicrobials. Resistance to sulfamethoxazole was most common (25%), followed by resistance to ampicillin (12%), streptomycin (10%), oxytetracycline (8%) and trimethoprim (8%). The prevalence of resistance to quinolones was low; three isolates (6%) were resistant to nalidixic acid, one (2%) of these also to enrofloxacin.

Resistance in indicator bacteria

The data obtained in 2002 indicate a relatively low occurrence of antimicrobial resistance in generic *E. coli* and *Enterococcus* spp. from faecal and meat samples from a representative group of healthy Norwegian pigs and broilers. It should be noted that due to the presence of intrinsic resistance, virginiamycin for *Enterococcus faecalis* and flavomycin for *E. faecium* were excluded from the results.

***Escherichia coli* from pigs**
In total, 26% of the faecal isolates and 23% of the meat isolates were resistant to at least one of the antimicrobials included. The resistance patterns were in general similar to those that were observed for the clinical *E. coli* from pigs, but the resistance frequencies were considerably lower as compared to the latter category. The resistance frequencies and the occurrence of multiresistance were somewhat higher for the faecal *E. coli* than for the meat isolates. The most frequent resistance traits observed were resistance to streptomycin (21%), sulfamethoxazole (11%), tetracycline (6%), ampicillin (4%), and trimethoprim (3%). No resistance to fluoroquinolones was observed. However, one faecal isolate (0.5%) was resistant to nalidixic acid.

***Escherichia coli* from broilers**
In total, 33% of the faecal isolates and 23% of the broiler meat isolates were resistant to at least one of the antimicrobials included. The resistance patterns and resistance frequencies were in general similar to those that were observed for *E. coli* from septicaemia in broilers. However, for several antimicrobials the occurrence of resistance was somewhat lower among the broiler meat isolates as compared to the other two categories. Altogether, resistance to sulfamethoxazole was most common (16%) followed by resistance to ampicillin (10%), oxytetracycline (8%), streptomycin (4%) and trimethoprim (1%). The prevalence of quinolone resistance was low; two isolates (0.7%) resistant to both nalidixic acid and enrofloxacin, and two isolates (0.7%) resistant to nalidixic acid only.

***Enterococcus* spp. from pigs**
In total, 56% of the isolates from the faecal samples and 20% of the isolates from the meat samples were resistant to at least one of the antimicrobials included. Multiresistance (resistance to at least three of the drugs included) was rarely (1.6%) observed. Altogether, resistance to oxytetracycline (27%) was most commonly observed, followed by resistance to streptomycin (7%). The resistance frequencies for oxytetracycline and streptomycin were considerably higher for the faecal isolates as compared to the meat isolates, and higher for *E. faecalis* as compared to *E. faecium*. Resistance to bacitracin, erythromycin, narasin, neomycin, avilamycin and chloramphenicol, respectively, was low (<3.2%). No resistance to vancomycin, ampicillin or gentamicin was observed. The resistance frequencies for the meat isolates were more or less at the same level as observed for pork isolates in NORM-VET 2000.

***Enterococcus* spp. from broilers**
In total, 77% of the enterococcal isolates from the faecal samples and 54% from the meat samples were resistant to at least one of the antimicrobials included. Multiresistance was rarely observed (4.9%). Altogether, resistance to narasin was most commonly observed (40%), followed by resistance to oxytetracycline (22%), bacitracin (20%), erythromycin (10%) and vancomycin (1.9%). For tetracycline and erythromycin, the resistance prevalences were considerably higher for the faecal isolates as compared to the meat isolates. Coccidiostats, mainly narasin, are routinely used in Norwegian broiler production. Avoparcin, which confers cross-resistance to vancomycin, was routinely used as a growth promoter in Norwegian broiler and turkey production from 1986 until it was banned in 1995. As observed in other studies, there was a species difference with regard to vancomycin resistance in randomly selected enterococcal isolates; 3.8% of the *E. faecium* and none of the *E. faecalis* isolates were resistant. The occurrence of vancomycin resistance among indicator enterococci in broilers in Norway seems to have remained at the same level from 2000 to 2002. Using a selective method that detects the presence of VRE, vancomycin resistant enterococci (VRE) were isolated from 91% of faecal samples from broilers, each representing a different flock. This figure corresponds to the figures obtained in earlier studies. Thus, the prevalence of VRE in Norwegian broiler flocks seems to have remained at the same level for at least seven years following the ban on avoparcin.

Resistance in zoonotic and other enteropathogenic bacteria

***Salmonella* spp.**
Salmonella, apart from *S. enterica* subsp. *diarizonae* in sheep, is rarely isolated from food producing animals in Norway. In 2002, five isolates were detected in the *Salmonella* surveillance programme, all of which were susceptible to the antimicrobials included. Also, all 21 isolates of *S. enterica* subsp. *diarizonae* from healthy sheep were susceptible, indicating that resistance is not widespread among this type of bacteria that occur endemically in the Norwegian sheep population. A multiresistant *S.* Typhimurium DT104 (ACSSuT) was isolated from a horse on a farm with contact with a cattle

farm on which the same strain was detected in 2001, the first detection of this variant ever in Norwegian animals.
I 2002, 75% of the human cases of salmonellosis were reported as being infected abroad. The proportion of *S.* Typhimurium isolates (excluding DT104) susceptible to all antimicrobials was higher for the category "infected in Norway" (72%) than for the "infected abroad" category (53%). Multiresistance was more common in the latter category (22%) as compared to the former (8%). A significant discrepancy between the two categories was observed for quinolone resistance; in the category "infected abroad" 10.9% and 1.1% of the isolates were resistant to nalidixic acid and ciprofloxacin, respectively, as opposed to none in the category "infected in Norway". The resistance profiles for the multiresistant DT104 isolates were almost identical for the two categories. All isolates were resistant to ampicillin, tetracycline, streptomycin, sulfonamides and chloramphenicol. Altogether 23% were also resistant to nalidixic acid. The vast majority of the *S.* Enteritidis isolates had been acquired abroad. The proportion resistant to tetracycline, chloramphenicol and ampicillin, respectively, was considerably lower than for *S.* Typhimurium (including those acquired in Norway). Resistance to nalidixic acid on the other hand was more widespread among *S.* Enteritidis as compared to *S.* Typhimurium.

***Campylobacter* spp.**
The results obtained in 2002 show that the prevalence of resistance in *Campylobacter jejuni* from Norwegian broilers is low. A total of 94.4% of the isolates were susceptible to all the antimicrobials included. Only one isolate (0.6%) was fluoroquinolone resistant, while 1.9% were resistant to nalidixic acid. The level of resistance and the resistance patterns for *C. jejuni* from Norwegian broilers corresponds to *C. jejuni* from humans infected within Norway except for a higher prevalence of resistance to quinolones, particularly nalidixic acid, among the human isolates. This relationship was also observed in NORM/NORM-VET 2001.
Resistance was significantly more widespread in the *C. jejuni* isolates derived from patients infected abroad (79% resistant to at least one antimicrobials) than patients infected in Norway (11%). These discrepancies are explained by the widespread occurrence in isolates derived from patients infected abroad of resistance to nalidixic acid/ciprofloxacin and to tetracycline.
Only two of the 29 isolates of *C. coli* tested were acquired in Norway. In total, 76% of the isolates were resistant to at least one of the antimicrobials included. Resistance to quinolones was widespread; 66% of the isolates were resistant to both nalidixic acid and ciprofloxacin.

***Shigella* spp.**
The vast majority of the *Shigella* isolates tested had been acquired abroad. As is the case in reports from other countries, resistance was widespread. The resistance frequencies were particularly high (>56%) for tetracycline and trimethoprim/sulfonamides, followed by ampicillin and chloramphenicol. Resistance to fluoroquinolones was less prevalent and only observed in *S. flexneri* (4.3%). However, a considerable proportion of *S. flexneri* (17.4%) and *S. sonnei* (11.8%) were resistant to nalidixic acid, many of which also expressed reduced susceptibility to ciprofloxacin, indicating that fluoroquinolone resistance could be developing.

Resistance in clinical isolates from humans

The overall prevalence of antimicrobial resistance in human clinical isolates was still very low in Norway in 2002. Only minor changes were observed from 2001 to 2002. Three blood culture isolates were detected of *E. coli* and one isolate of *Klebsiella* spp. producing extended spectrum β-lactamases (ESBL). Two methicillin resistant *Staphylococcus aureus* (MRSA) (out of 726 isolates), five *Streptococcus pneumoniae* not susceptible to penicillin (out of 538 isolates), and seven multiresistant *Mycobacterium tuberculosis* (six MDR isolates among 180 cases not previously treated and one MDR among 12 cases previously treated). All MRSA and MDR patients had probably acquired their infections abroad. One enterococcal isolate harbouring transferable vancomycin resistance was detected.
The prevalence of resistance to fucidic acid among *S. aureus* blood culture specimens was higher in 2002 compared to previous years (1.9% in 2000 and 5.1% in 2001). At present a specific clone of *S. aureus* with resistance to fucidic acid causes the skin infection impetigo bullosa in Norway. Whether this clone of fucidic acid resistant *S. aureus* is part of the NORM 2002 blood culture sample remains to be investigated. Several research groups want to investigate this issue.
Blood culture isolates of *Enterococcus* spp. were speciated as *E. faecalis* and *E. faecium* in 2002 thus demonstrating the much higher prevalence of β-lactam resistance in *E. faecium* (38.8% ampicillin susceptibility) than in *E. faecalis* (98.9% ampicillin susceptibility). The prevalence of high-level resistance to gentamicin was higher among *E. faecalis* isolates in 2002 (9.6%) than in 2001 (4.5%). Such an increase may indicate future problems with aminoglycoside resistant enterococci even though the prevalence of gentamicin resistance still is low compared to other countries.
Resistance to macrolides among respiratory tract pathogens is a worldwide problem. Only 5.2% of *Streptococcus pneumoniae* blood culture isolates were resistant to erythromycin, an increase compared to 2001 (2.2%). Among the *S. pyogenes* (group A streptococci) isolates 3.8% were resistant to erythromycin. Surprisingly, 15.6% of the *S. pyogenes* isolates were resistant to doxycyklin. Group A streptococcal isolates from wound specimens were more resistant (23.0%) than respiratory tract specimens (10.4%).

Conclusion

Antimicrobial resistance is still a limited problem in Norway. The relatively low consumption of antimicrobial agents as well as the advantageous patterns of use must be maintained to preserve this favourable situation. The data presented in this report show that Norwegian antimicrobial policies in food production and healthcare have succeeded. However, the situation may rapidly change if the use of antimicrobial agents in Norway increases or if resistant clones are imported from abroad. A continued effort is needed to prevent the development and spread of antimicrobial resistance and thus ensure the effectiveness of antimicrobials when such treatment is needed. The NORM/NORM-VET report is a vital component of the work aimed at preventing the development and spread of antimicrobial resistance.

IV. POPULATION STATISTICS

Population statistics for human and animal populations are presented in order to facilitate comparison of Norwegian data with corresponding figures from other countries. The data are collected by Norwegian authorities as shown in the various tables below.

TABLE 1. Human population in Norway as of January 1st, 2002.
(Data provided by Statistics Norway)

Age group	All	Males	Females
0 to 4 years	296 361	151 908	144 453
5 to 14 years	609 939	313 148	296 791
15 to 24 years	541 206	276 399	264 807
25 to 44 years	1 326 038	675 532	650 506
45 to 64 years	1 074 701	543 417	531 284
65 years and older	675 821	281 530	394 291
All age groups	4 524 066	2 241 934	2 282 132

TABLE 2. Livestock population in Norway as of July 31st, 2002.
(Data provided by Register of Production Subsidies (herds) and Register of Slaughtered Animals (animals))

Animal category	Herds	Animals*
Cattle	24 937	952 100
Dairy cows**	16 988	254 600
Suckling cows**	4 221	39 600
Combined production (cows)**	1 475	34 400
Goats	1 387	73 200
Dairy goats**	615	46 000
Sheep	-	2 410 100
Breeding sheep > 1 year**	20 008	941 700
Pigs	4 148	741 400
Breeding animals > 6 months**	2 435	56 700
Fattening pigs for slaughter until July31st **	3 743	407 400
Egg laying hens (>20 weeks of age)	3 112	3 108 800
Broilers for slaughter until July 31st	394	7 203 400
Turkeys, ducks and geese for slaughter	218	246 000
Ostriches	42	537

*Animal numbers are rounded to the nearest hundred, with the exception of ostriches
**Included in above total

TABLE 3. Number of animals slaughtered approved for human consumption in 2002.
(Data provided by Statistics Norway (terrestrial animals) and Directorate of Fisheries (fish))

Animal category	Slaughtered animals
Horse	2 410
Cattle	346 143
Goats	21 120
Sheep	1 236 620
Pigs	1 328 230
Broilers	40 932 389
Farmed salmon*	466 620
Farmed trout*	86 556

*Amount in metric tons, ungutted fish

TABLE 4. Live animals (excluding fish) imported to Norway in 2002.
(Data provided by the Norwegian Animal Health Authority)

	Live animals	
Animal species	Individuals	Consignments
Cattle	0	0
Sheep/goat	33	1
Pig	2	1
Reindeer*	2 439	26
Fur animals	2 663	11
Gallus gallus - day old chicks	31 030	8
Gallus gallus - eggs	240	2
Turkey	5 689	2
Ducks and geese	38	2

*For slaughter

V. CONSUMPTION OF ANTIMICROBIAL AGENTS

A. ANIMAL CONSUMPTION

Antibacterial growth promoters and coccidiostats

Data on the usage of various substances and categories of feed additives were obtained through annual reports from the Norwegian Agricultural Inspection Service. Table 5 summarizes the total sales of antibacterial growth promoters and coccidiostats in Norway in 1995–2002.

The glycopeptide avoparcin was licensed for the Norwegian market as a growth promoter in broilers and turkeys in 1986. It was prohibited in 1995 due to a reported association between its use and the occurrence of vancomycin resistant enterococci in animal husbandry. The same year, the Norwegian food animal production industry voluntarily abandoned the use of all antibacterial growth promoters. The measures resulted in an immediate reduction in the use of these substances (Table 5). In 1998, the streptogramin virginiamycin was officially prohibited due to reports from other countries of an association between its use and the occurrence of enterococci that were resistant to quinupristin-dalfopristin, a streptogramin combination preparation used in human medicine. Antibacterial growth promoters have not been used in Norwegian animals since 1998.

Coccidiostats are still used in Norwegian poultry production. The total sales of coccidiostats, in kilograms of active substance, are at the same level as before the ban on antibacterial growth promoters was implemented. However, the pattern of use has changed. The use of coccidiostats has been dominated by narasin since 1996, while the use of other ionophores has decreased correspondingly.

TABLE 5. Total sales, in kilograms of active substance, of antibacterial growth promoters and coccidiostats in Norway in 1995-2002. Data were obtained through annual reports from the Norwegian Agricultural Inspection Service.

Group of substances / Active substances	Total sales in kg active substance							
	1995	1996	1997	1998	1999	2000	2001	2002
Avoparcin	419*	Prohibited	Prohibited	Prohibited	Prohibited	Prohibited	Prohibited	Prohibited
Zincbacitracin	129	64	27	0	0	0	0	0
Virginiamycin	0	0	0	0*	Prohibited	Prohibited	Prohibited	Prohibited
Total antibacterial growth promoters	**548**	**64**	**27**	**0**	**0**	**0**	**0**	**0**
Lasalocid	996	480	471	193	208	80	96	514
Monensin	3 422	891	561	485	557	776	629	521
Salinomycin	214	27	0	0	27	233	12	0
Narasin	24	3 508	3 343	3 530	4 062	4 486	4 195	4 470
Total ionophore coccidiostats	**4 656**	**4 906**	**4 375**	**4 208**	**4 854**	**5 575**	**4 932**	**5 505**
Amprolium/etopabat	156	116	582	174	201	135	159	74
Total other coccidiostats	**156**	**116**	**582**	**174**	**201**	**135**	**159**	**74**

*Prohibited part of the year

Therapeutic usage of veterinary antibacterial drugs

Sales data for antibacterial drugs were collected from all Norwegian drug wholesalers. The majority of substances included are approved as pharmaceutical formulations for food animals, horses and/or dogs and cats. Thus the figures represent overall sales data for veterinary antibacterial drugs. Antimicrobials authorized for human use, but prescribed for animals, are not included. Such drugs are primarily used in small animal practices.

Table 6 summarizes the sales (in kg of active substance) in 2002 of veterinary antibacterial drugs approved for therapeutic use in domestic animals in Norway. The data are organized according to the main groups of substances (ATCvet) and show the total use for the various routes of administration. The total sale of veterinary antibacterial drugs is given in Figure 1. Figure 2 illustrates the proportion of the total sale of the various main groups of antibacterial substances. Both figures present annual sales data for the period 1995–2002. In 2002, the sales of veterinary antibacterials approved for therapeutic use in animals in Norway amounted to 5,890 kg of active substance (Table 6). The consumption of veterinary antibacterial drugs decreased by 40% from 1995 to 2001, while an increase of 3% was observed in 2002 compared to the preceding year. This increase was mainly caused by a change in the prescribing patterns for intramammary drugs and antibacterial drugs indicated for use in horses. The approved/recommended dosages for these "new" drugs were several times higher than the drugs formerly used, creating higher sales figures. This clearly illustrates the weaknesses of using kg active substance as a unit of measurement in drug statistics.

The proportion accounted for by pure penicillin preparations rose from 25% in 1995 to 38% in 2002. Altogether 94% of the veterinary penicillin preparations sold in 2002 were β-lactamase-sensitive penicillins. From 1995 to 2002, the sale of sulfonamides in combination with trimethoprim or baquiloprim increased from 11% to 24%, whereas combination preparations of penicillins and aminoglycosides decreased from 35% to 24% during the same period. The proportion of sulfonamides decreased gradually from 14% in 1995 to 0% in 2002, and the proportion of tetracyclines declined from 5% to 3% during the same period.

TABLE 6. Sales in 2002 (in kilograms of active substance) of veterinary antibacterial drugs approved in Norway for therapeutic use in animals, excluding fish. The data were obtained from Norwegian drug wholesalers.

Groups of substances	ATCvet code	Active substance or combinations of substances	Gastro-intestinal (QA07)	Uterine (QG01)	Systemic individual (QJ01)	Systemic herds (QJ01)	Intra-mammary (QJ51)
Tetracyclines	QG01AA07	Oxytetracycline		2			
	QJ01AA02	Doxycycline			< 0.1		
	QJ01AA06	Oxytetracycline			92	93	
Beta-lactam	QJ01CA01	Ampicillin			23		
antibacterials	QJ01CA04	Amoxicillin			66	70	
	QJ01CE09	Benzylpenicillinprocain*			1 929		
	QJ01CE90/QJ51CE90	Penethamate hydroiodide*			9		
	QJ01CR02/QJ51RV01	Amoxicillin+clavulanic acid			132		6
	QJ51CA51	Ampicillin+cloxacillin					2
Sulfonamides and	QJ01EQ10	Sulfadiazine+trimethoprim			1 280		
trimethoprim**	QJ01EQ13	Sulfadoxine+trimethoprim			111		
Lincosamides	QJ01FF01	Clindamycin			8		
	QJ01FF02	Lincomycin			7		
Aminoglycosides	QA07AA01	Neomycin	31				
	QA07AA90	Dihydrostreptomycin (DHS)	150				
Quinolones	QJ01MA90	Enrofloxacin			23		
Other antibacterials	QJ01XX92	Tiamulin			8	179	
Combinations of	QG01AE99	Sulfadimidine+procaine		235			
antibacterials	QJ01RA01	Benzylpenicillinprocain *+DHS			606		790
	QJ01RA01	Spiramycin+metronidazole			6		
	QJ51RC25	Penethamate hydroiodide*+ DHS					32
		Total per route of administration	**181**	**237**	**4 300**	**342**	**830**
						Total:	**5 890**

*Calculated as benzylpenicillin
**Includes baquiloprim

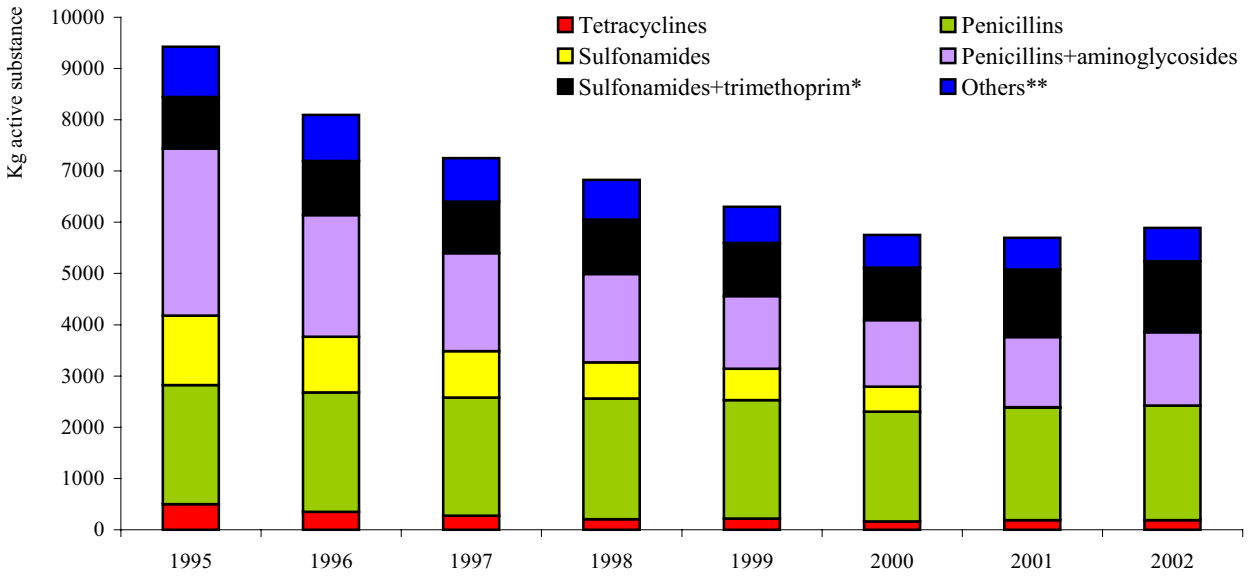
In Norway, medicated feeds and premixes for farmed fish are approved by the drug authorities and classified as pharmaceutical specialities. Sales figures, in kg of active substance, of such products and premixes containing antibacterial drugs are presented in Table 7. Quinolones is the antibacterial class most commonly used in farmed fish. In 2002, quinolones accounted for 82% (in kg) of the total antibacterial use in fish.

Altogether, 1,219 kg of veterinary antibacterial drugs for therapeutic use in farmed fish were sold in 2002. This is twice the amount that was sold in 2001 and reflects that the calculated percentage of farmed fish receiving one antibacterial drug treatment increased from on average 2% in 2001 to 4% in 2002 (Kari Grave, unpublished data). The increase is explained by natural annual variations.

Overall, the annual use of antibacterial drugs for fish declined by 98% during the period 1987-2002. In the same period, the total production of farmed fish increased massively. This significant decrease in the use of antibacterial drugs in aquaculture is mainly attributed to the introduction of effective vaccines and to improved health management.

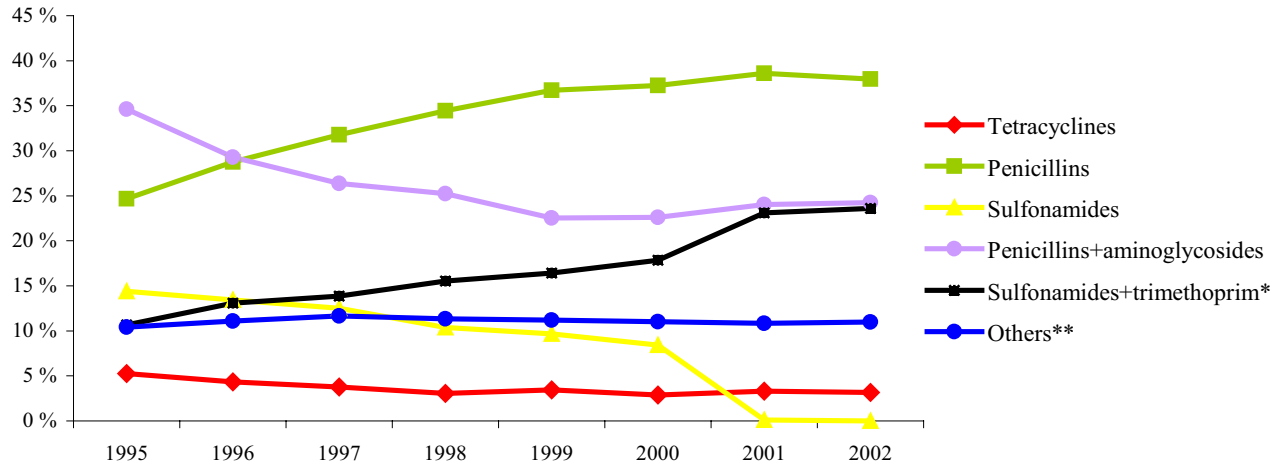
TABLE 7. Total sales (in kilograms of active substance) of veterinary antibacterial drugs for therapeutic use in farmed fish in Norway in 1995-2002. Data were obtained from Norwegian drug wholesalers and feed mills.

Groups of substances	ATCvet code	Active substance	1995	1996	1997	1998	1999	2000	2001	2002
Tetracyclines	QJ01AA06	Oxytetracycline	70	27	42	55	25	15	12	11
Amphenicols	QJ01BA90	Florfenicol	64	64	123	135	65	148	109	205
Antibacterial quinolones	QJ01MB07	Flumequine	182	105	74	53	7	52	7	5
	QJ01MB91	Oxolinic acid	2 800	841	507	436	494	470	517	998
Total			**3 116**	**1 037**	**746**	**679**	**591**	**685**	**645**	**1 219**



*Includes small amounts of baquiloprim.
**Includes ATCvet codes: QAA7AA01; QA07AA51; QA07AA90; QG01AE99; QJ01FA01; QJ01FF01; QJ01FF02; QJO1MA90; QJ01RA9; QJ01XX92

FIGURE 1. Sales (in kilograms of active substance) of veterinary antibacterial drugs (QA07AA, QG01AA, QG01AE, QJ01, QJ51) for therapeutic use in Norway in 1995–2002, fish not included.



*Includes small amounts of baquiloprim.
**Includes ATCvet codes: QAA7AA01; QA07AA51; QA07AA90; QG01AE99; QJ01FA01; QJ01FF0; QJ01FF02; QJO1MA90; QJ01RA91; QJ01XX92

FIGURE 2. Sales (as percentage of total sales) of veterinary antibacterial drugs (QA07AA, QG01AA, QG01AE, QJ01, QJ51) in Norway in 1995–2002, fish not included.

B. HUMAN CONSUMPTION

The overall consumption of antibacterials for systemic use (ATC group J01) in humans in 2002 was 17.1 DDD/1,000 inhabitants/day. Total sales of antibacterials have remained stable for many years. In 2002 however, a 2% increase was reported compared to 2001. An increase was observed for several antibacterial subgroups. The main exception was a 4% decrease among the β-lactamase sensitive penicillins (J01CE). The sales of benzylpenicillin, mainly used in hospitals, was stable, hence the decrease was due to phenoxymethylpenicillin. This peroral penicillin formulation is mainly used in ambulatory care.

TABLE 8. Human consumption of antibacterial agents in Norway 1996-2002 by ATC groups. The consumption is presented as Defined Daily Doses(DDD)/1,000 inhabitants/day and % change 1996-2002. Collection of data on human consumption of antimicrobial agents is presented in Appendix 2.

ATC	Groups of substances	1996	1997	1998	1999	2000	2001	2002	Change (%) 1996-2002
J01A	Tetracyclines	3.66	3.55	3.37	3.19	3.17	3.11	3.13	- 14
J01B	Amphenicols	0.005	0.005	0.004	0.005	0.004	0.003	0.002	
J01CA	Penicillins with extended spectrum	1.73	1.87	1.90	1.96	2.01	2.1	2.23	+ 29
J01CE	β-lactamase sensitive penicillins	5.08	5.32	5.12	5.01	4.66	4.68	4.48	- 12
J01CF	β-lactamase resistant penicillins	0.21	0.24	0.27	0.32	0.35	0.41	0.50	+138
J01CR	Combination of penicillins	0.01	0.02	0.01	0.01	0.01	0.01	0.01	
J01D	Cephalosporins, monobactams, carbapenems	0.44	0.42	0.44	0.47	0.52	0.55	0.58	+ 32
J01E	Sulfonamides and trimethoprim	1.57	1.45	1.34	1.26	1.17	1.16	1.15	- 27
J01F	Macrolides, lincosamides and streptogramins	1.5	1.58	1.61	1.59	1.59	1.8	1.98	+ 32
J01G	Aminoglycosides	0.05	0.05	0.05	0.05	0.04	0.06	0.06	
J01M	Quinolones	0.28	0.28	0.30	0.33	0.35	0.40	0.44	+ 57
J01X	Other antibacterials	1.90	2.06	2.2	2.34	2.39	2.55	2.57	+ 35
	Total	**16.4**	**16.8**	**16.6**	**16.6**	**16.3**	**16.8**	**17.1**	

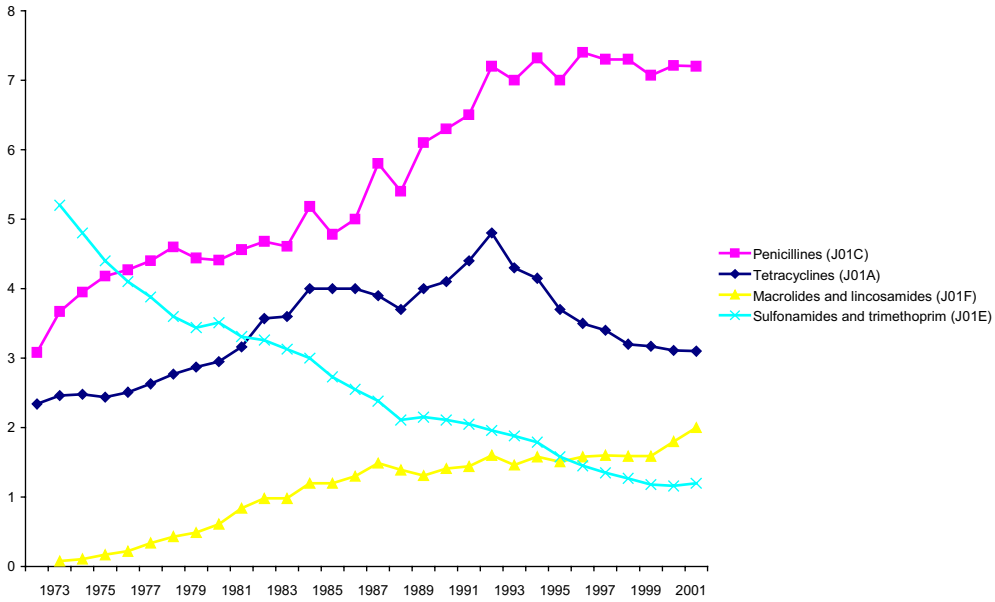


FIGURE 3. Sales of penicillins (J01C), tetracyclines (J01A), macrolides and lincosamides (J01F), and sulfonamides and trimethoprim (J01E) in DDD/1000 inhabitants/day in Norway in 1973-2002.

The penicillins (ATC group J01C) accounted for 42% of the total antimicrobial use in Norway in 2002 (Figure 4). The sale of penicillins has been stable over years. There has, however, been a shift in the use of β-lactamase-sensitive penicillins (31% of J01 in 1996 to 26% in 2002) towards penicillins with extended spectrum (11% and 13%) and to β-lactamase-resistant penicillins (1.3% and 2.4%), respectively (Table 8). Tetracyclines (J01A) accounted for 18% of the total use. The sale has been steadily decreasing over years and 2002 was the first year with no such decrease since 1993. The macrolides (J01FA) accounted for 12% of the total use in 2002. The sale has been fairly stable for some years. In 2002 an increase of 10% compared to 2001 was reported and the prescription pattern of macrolides remained unchanged (Figure 5). The increase in the ATC group J01X was mainly caused by the urinary prophylactic agent methenamine (represents 12.5% of total use) and its sale has increased by 48% since 1996. The sale of cephalosporins has increased over the years and accounted for 3% of the total sale of antibacterials. Only half of the amount was used in hospitals. The prescription pattern of cephalosporines has changed (Figure 6) and more 2nd and 3rd generation cephalosporins, as well as carbapenems are now being prescribed.

The sales of sulfonamides and trimethoprim have decreased by 27% since 1996. There has been a small, but stable increase in quinolone use over the years. This group accounts for only a minor fraction (2.6%) of total sale of antibacterials, but the increase has been 57% since 1996. The pattern of antibacterial use in hospitals differs from the sales related to general practice (Figure 7). Sales to hospitals accounted for 7.7% of total sales in the country. Penicillins (J01C) accounted for 45% of the use in hospitals and in ambulatory care. Next to penicillins, the most important groups used in general practice were the tetracyclins (19%), the macrolides (13%) and methenamine (13%). Cephalosporins (J01D) were the second most commonly used group in hospitals after penicillins. Although the use of antibacterials outside hospitals accounts for 92% of the total human sale of antimicrobials, there is uncertainty whether this use has a larger impact on the development of bacterial resistance compared to the use of more broad-spectrum antibacterials in hospitals.

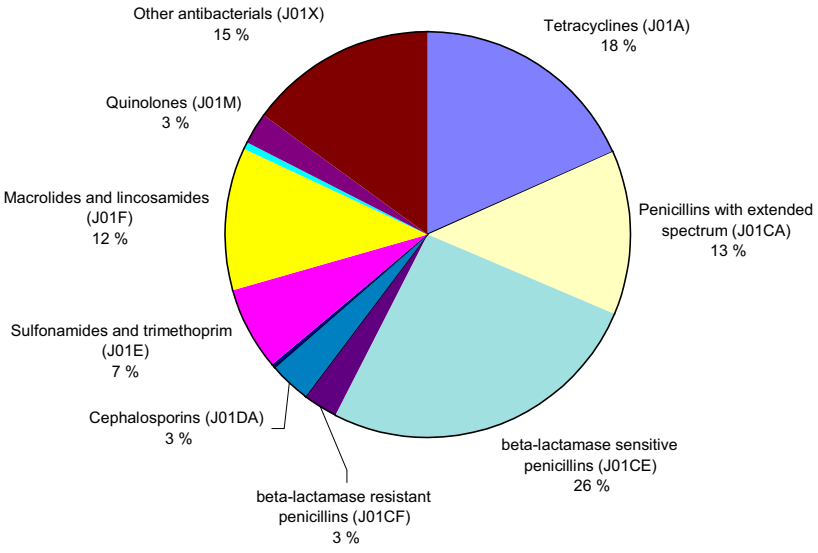


FIGURE 4. Relative amounts of antibacterial agents for systemic use in 2002 in Defined Daily Doses (DDD) (total sale in the country). Groups of antibacterials are represented by ATC numbers as follows: Tetracyclines (J01A), penicillins with extended spectrum (J01CA), β-lactamase sensitive penicillins (J01CE), β-lactamase resistant penicillins (J01CF), cephalosporins, carbapenems and monobactams (J01D), sulfonamides and trimethoprim (J01E), macrolides and lincosamides (J01F), quinolones (J01M) and other antibacterials (J01X).

TABLE 9. Human consumption of single antibacterial agents for systemic use in Norway (ATC group J01). Sales given in DDD/1000 inhabitants/day. Collection of data on human consumption of antibacterial agents is presented in Appendix 2.

ATC	Substance	1996	1997	1998	1999	2000	2001	2002
A07AA09	Vancomycin	0.001	0.001	0.001	0.001	0.001	0.001	0.001
J01A A02	Doxycycline	2.49	2.47	2.34	2.20	2.10	2.1	2.03
J01A A04	Lymecycline	0.11	0.10	0.09	0.09	0.14	0.19	0.26
J01A A06	Oxytetracycline	0.36	0.30	0.27	0.25	0.24	0.22	0.21
J01A A07	Tetracycline	0.70	0.68	0.67	0.65	0.69	0.64	0.62
J01B A01	Chloramphenicol	0.005	0.005	0.004	0.005	0.004	0.003	0.002
J01C A01	Ampicillin	0.09	0.09	0,09	0.09	0.09	0.08	0.09
J01C A02	Pivampicillin	0.20	0.17	0.15	0.14	0.13	0.11	0.11
J01C A04	Amoxicillin	0.75	0.85	0.85	0.87	0.83	0.89	0.94
J01C A08	Pivmecillinam	0.69	0.75	0.81	0.86	0.96	1	1.09
J01C A09	Azlocillin	0.0001	0.0001					
J01C A11	Mecillinam	0.003	0.003	0.003	0.004	0.004	0.005	0.005
J01C E01	Benzylpenicillin	0.19	0.19	0.21	0.23	0.21	0.23	0.24
J01C E02	Phenoxymethylpenicillin	4.89	5.13	4.91	4.78	4.45	4.45	4.24
J01C F01	Dicloxacillin	0.13	0.16	0.19	0.22	0.25	0.31	0.39
J01C F02	Cloxacillin	0.08	0.08	0.08	0.10	0.10	0.09	0.11
J01C F05*	Flucloxacillin							0.0001
J01C R02	Amoxicillin and enzyme inhibitor	0.01	0.02	0.01	0.01	0.01	0.01	0.01
J01C R05	Piperacillin and enzyme inhibitor					0.0001	0.0006	0.0014
J01D A01	Cefalexin	0.25	0.22	0.22	0.22	0.26	0.27	0.29
J01D A03	Cefalotin	0.04	0.04	0.04	0.05	0.05	0.05	0.05
J01D A05	Cefoxitin	0.0004	0.0004	0.0004	0.0004	0.0004	0.0003	0.0002
J01D A06	Cefuroxim	0.11	0.11	0.12	0.13	0.13	0.14	0.15
J01D A10	Cefotaxim	0.01	0.02	0.03	0.04	0.04	0.05	0.05
J01D A11	Ceftazidim	0.02	0.01	0.01	0.01	0.01	0.01	0.01
J01D A13	Ceftriaxone	0.001	0.004	0.007	0.008	0.011	0.01	0.01
J01D A63	Ceftriaxone, combinations	0.00003	0.0001	0.0001	0.0001			
J01D F01	Aztreonam	0.0008	0.0007	0.0005	0.0008	0.001	0.001	0.001
J01D H02	Meropenem		0.002	0.004	0.008	0.012	0.014	0.017
J01D H51	Imipenem and enzyme inhibitor	0.006	0.007	0.007	0.006	0.006	0.005	0.005
J01E A01	Trimethoprim	0.93	0.90	0.87	0.84	0.79	0.8	0.8
J01E B02	Sulfamethizole	0.001		0.0002	0.001	0.002	0.002	0.0001
J01E C20	Sulfonamides, combinations	0.003	0.003	0.003	0.0004			
J01E E01	Sulfamethoxazol and trimethoprim	0.64	0.55	0.47	0.42	0.38	0.36	0.36
J01F A01	Erythromycin	1.03	1.04	1.06	1.01	1.00	1.13	1.2
J01F A02	Spiramycin	0.06	0.05	0.04	0.03	0.02	0.02	0.02
J01F A09	Clarithromycin	0.17	0.22	0.24	0.26	0.26	0.3	0.36
J01F A10	Azithromycin	0.14	0.17	0.17	0.18	0.19	0.21	0.24
J01FA15	Telithromycin							0.0001
J01F F01	Clindamycin	0.10	0.10	0.11	0.11	0.12	0.14	0.16
J01F F02	Lincomycin	0.001						
J01GA01*	Streptomycin							0.0015
J01G B01	Tobramycin	0.02	0.03	0.03	0.03	0.02	0.03	0.04
J01G B03	Gentamicin	0.007	0.006	0.006	0.006	0.006	0.008	
J01G B06*	Amikacin							0.0009
J01G B07	Netilmicin	0.02	0.02	0.02	0.02	0.02	0.02	0.007

ATC	Substance	1996	1997	1998	1999	2000	2001	2002
J01M A01	Ofloxacin	0.07	0.07	0.06	0.06	0.05	0.05	0.05
J01M A02	Ciprofloxacin	0.19	0.20	0.23	0.26	0.29	0.34	0.38
J01MA12*	Levofloxacin							0.001
J01M B02	Nalidixic acid	0.02	0.01	0.01	0.01	0.01	0.01	
J01X A01	Vancomycin	0.005	0.005	0.005	0.004	0.005	0.005	0.006
J01X A02	Teicoplanin	0.0009	0.0009	0.001	0.0007	0.0012	0.0013	0.0013
J01X B01	Colistin	0.002	0.004	0.003	0.003	0.003	0.003	0.003
J01X C01	Fusidic acid	0.003	0.003	0.003	0.003	0.003	0.01	0.01
J01X D01	Metronidazole	0.052	0.056	0.056	0.060	0.063	0.065	0.069
J01X D02	Tinidazole	0.001						
J01X E01	Nitrofurantoin	0.39	0.38	0.38	0.37	0.37	0.36	0.35
J01X X05	Methenamin	1.44	1.61	1.75	1.91	1.95	2.08	2.13
J01XX08	Linezolid							0.002
P01AB01	Metronidazole	0.20	0.18	0.18	0.18	0.18	0.18	0.19

* Drugs not licenced for the Norwegian market

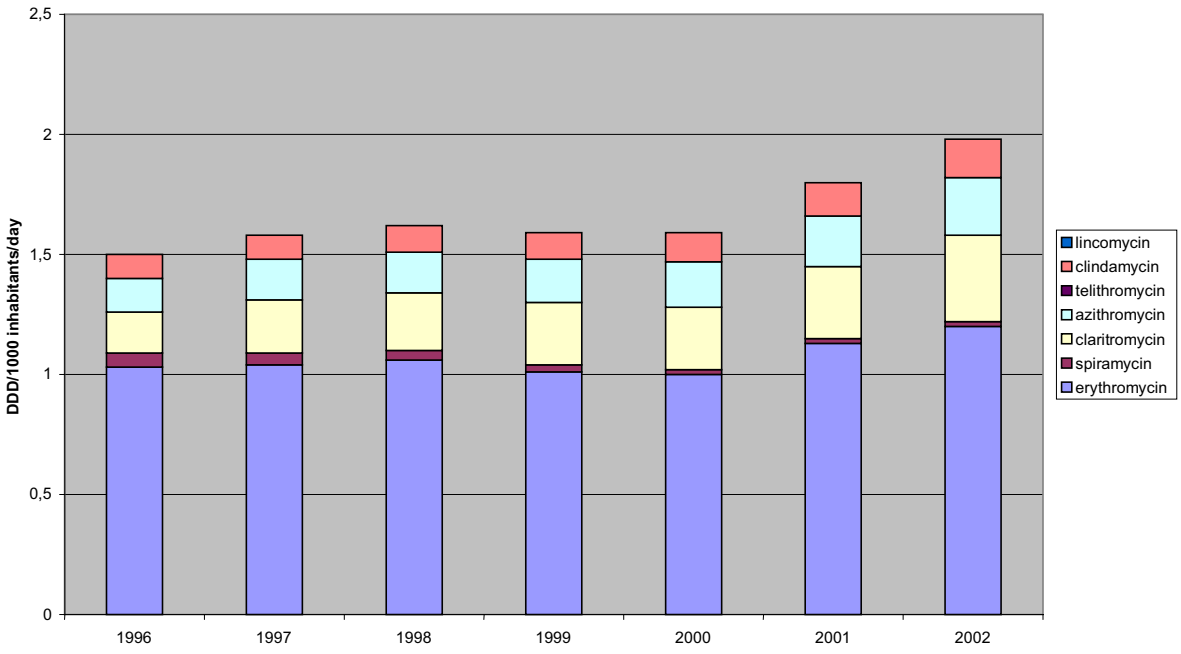


FIGURE 5. Sales of macrolides and lincosamides (J01F) in Norway 1996-2002

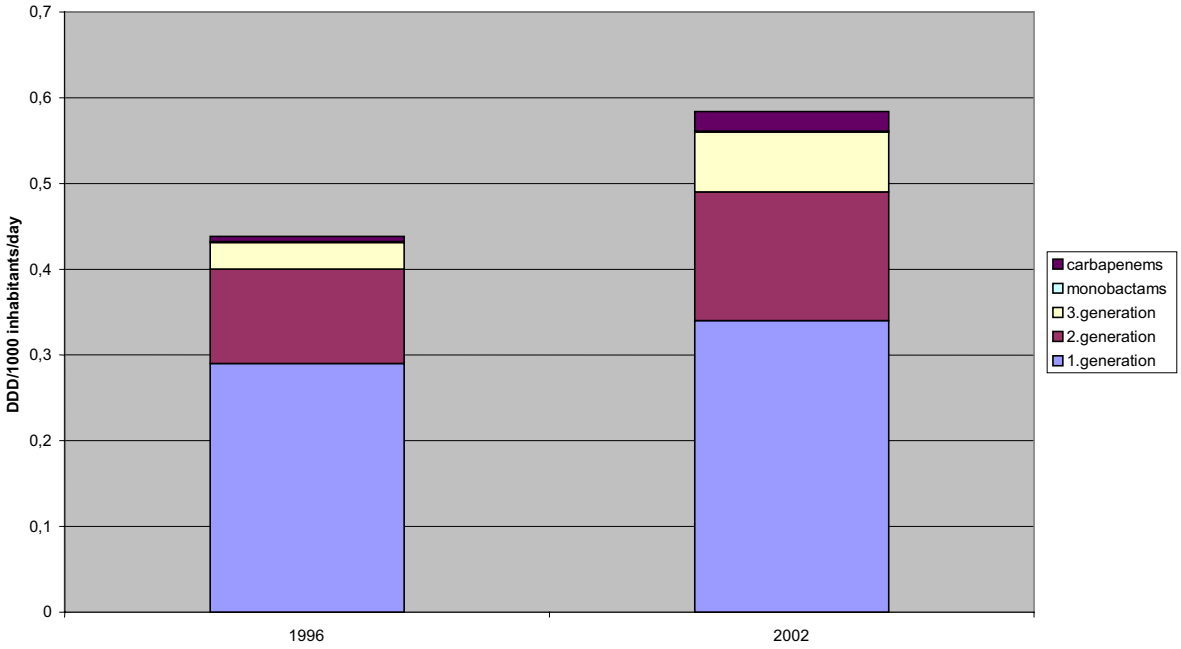


FIGURE 6. Sales of cephalosporins and carbapenems (J01D) in Norway in 1996 and 2002.

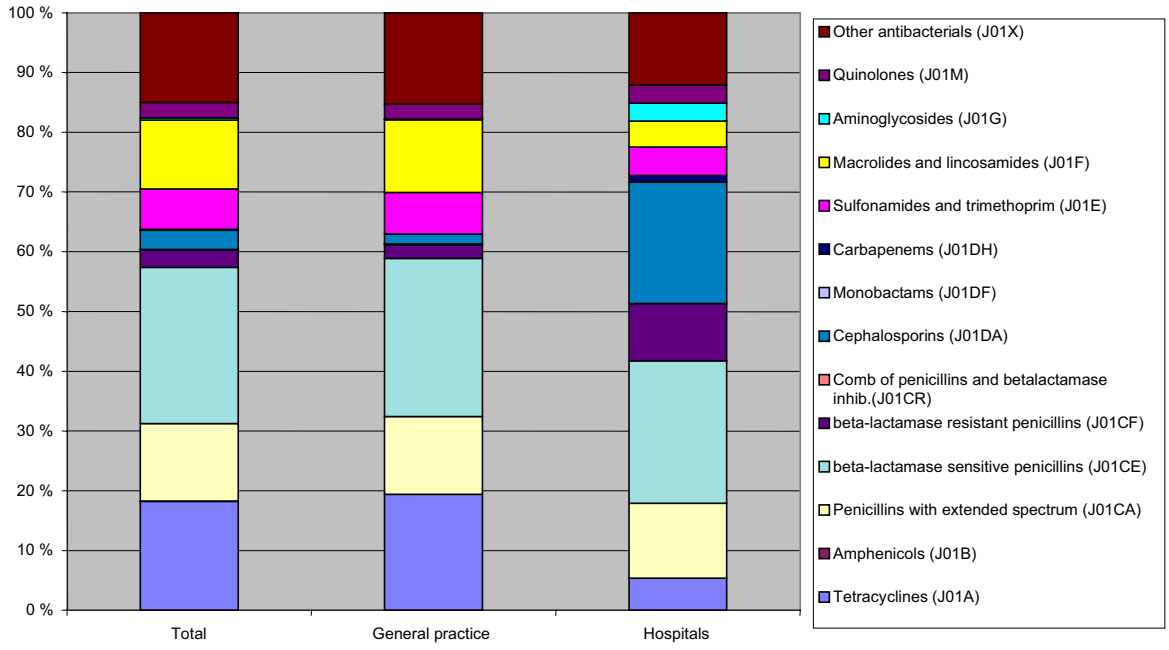


FIGURE 7. Proportions of antibacterial agents for systemic use in hospitals and general practice in Norway 2002.

VI. OCCURRENCE OF ANTIMICROBIAL RESISTANCE

A. ANIMAL CLINICAL ISOLATES

As proposed in the NORM-VET plan, the clinical isolates included in 2002 were from diagnostic samples from skin infections (including otitis externa) in dogs (*Staphylococcus intermedius*) and from septicaemia in poultry and enteritis in pigs (pathogenic *E. coli*). Sampling, laboratory methods and data processing are described in Appendix 3.

Staphylococcus intermedius from dogs

A total of 99 clinical isolates of *Staphylococcus intermedius* from dogs were susceptibility tested. Of these, 47 were isolated from otitis externa and the remaining 52 from other skin infections. The results are presented in tables 10 and 11 and figure 8.

TABLE 10. Antimicrobial resistance in *Staphylococcus intermedius* from skin infections (incl. otitis externa) in dogs (n=99).

Substance	% Resistant	Distribution (%) of MIC values (mg/L)														
	[95% CI*]	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥512
Oxytetracycline	53 [42.2-62.7]					47.5					4.0	41.4	7.1			
Chloramphenicol	2 [0.3-7.1]							5.1	84.8	8.1		2.0				
Penicillin	86** [77.7-92.1]		14.1		12.1	6.1	3.0	2.0	10.1	4.0	48.5					
Oxacillin	0 [0.0-3.7]					71.7	28.3									
Cephalothin	0 [0.0-3.7]			96.0	3.0	1.0										
Trimethoprim	12 [6.4-20.2]			1.0			2.0	41.4	40.4	3.0	5.1	7.1				
TMS***	2 [0.3-7.1]				29.3	38.4	30.3		2.0							
Erythromycin	18 [11.2-27.2]				8.1	68.7	4.0	1.0					18.2			
Clindamycin	15 [8.7-23.8]						83.8	1.0	2.0	1.0	12.1					
Streptomycin	22 [14.5-31.7]							46.5	27.3	3.0	1.0	1.0	1.0	3.0	9.1	8.1
Gentamicin	0 [0.0-3.7]				41.4	54.6	4.0									
Neomycin	0 [0.0-3.7]						74.8	6.1	12.1	7.1						
Ciprofloxacin	0 [0.0-3.7]	2.0	52.5	42.4	3.0											
Vancomycin	0 [0.0-3.7]						96.0	4.0								
Fucidic acid	59 [48.7-68.7]		15.2	22.2	4.0			4.0	3.0	12.1	18.2	7.1	7.1		7.1	
Avilamycin	1 [0.0-5.5]						46.5	48.5	3.0	1.0		1.0				
Virginiamycin	0 [0.0-3.7]					93.9	6.1									

Bold vertical lines denote breakpoints for resistance. White fields denote range of dilutions tested for each antimicrobial. MIC-values higher than the highest concentration tested for are given as the lowest MIC-value above the range. MIC-values equal to or lower than the lowest concentration tested are given as the lowest tested concentration.

*CI = Confidence Interval.

**All, except one resistant isolate, were β-lactamase positive. All susceptible isolates were β-lactamase negative.

***TMS = Trimethoprim/sulfamethoxazole. Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulfamethoxazole).

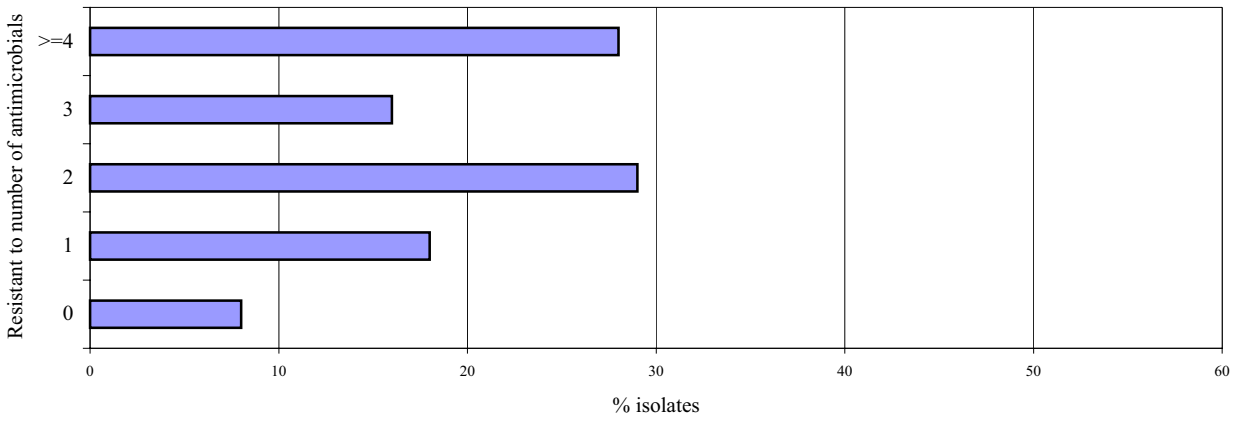


FIGURE 8. Antimicrobial resistance profiles for *Staphylococcus intermedius* from skin infections (incl. otitis externa) in dogs (n=99). Proportion of isolates susceptible to all antimicrobials included and proportion of isolates resistant to one, two, three, or four or more antimicrobials.

TABLE 11. Number and percentages of *Staphylococcus intermedius* from skin infections in dogs (n=99) expressing different resistance patterns.

Resistant to number of antimicrobials	Resistance pattern (resistance is indicated with hatched areas where the number of isolates resistant to the respective antimicrobials is presented)																	Number (%) of isolates from each sample type expressing the respective resistance patterns	
	Oxytetracycline	Chloramphenicol	Penicillin	Oxacillin	Cephalothin	Trimethoprim	TMS*	Erythromycin	Clindamycin	Streptomycin	Gentamicin	Neomycin	Ciprofloxacin	Vancomycin	Fucidic acid	Avilamycin	Virginiamycin	Skin, other than ears, n =52	Ear, n =47
0																		6 (12%)	2 (4%)
1			15															9 (17%)	6 (13%)
															2			1 (2%)	1 (2%)
	1																		1 (2%)
2			14												14			6 (12%)	8 (17%)
	11		11															6 (12%)	5 (11%)
	2														2			2 (4%)	
						1									1				1 (2%)
			1													1			1 (2%)
3	11		11												11			3 (6%)	8 (17%)
			3							3					3				3 (6%)
	1		1							1									1 (2%)
			1					1							1			1 (2%)	
4	7		7			7									7			5 (10%)	2 (4%)
	2		2							2					2			1 (2%)	1 (2%)
	1		1			1	1											1 (2%)	
5			2					2	2	2					2			1 (2%)	1 (2%)
	2		2					2		2					2			1 (2%)	1 (2%)
	1		1					1	1	1								1 (2%)	
	1		1					1	1						1			1 (2%)	
	1		1						1	1					1			1 (2%)	
6	6		6					6	6	6					6			3 (6%)	3 (6%)
	2	2	2					2	2	2								2 (4%)	
	1		1			1		1	1						1				1 (2%)
7	1		1			1	1	1		1					1				1 (2%)
	1		1			1		1	1	1					1			1 (2%)	
Total	52	2	85	0	0	12	2	18	15	22	0	0	0	0	58	1	0	52	47

* Trimethoprim/sulfamethoxazole.

COMMENTS

The data indicate a moderate to high occurrence of resistance among *Staphylococcus intermedius* from skin infections in dogs. Only 8% of the isolates were susceptible to all antimicrobials included, and 44% were resistant to at least three drugs (Figure 8). Thus, multiresistance seems to be widespread among *S. intermedius* from skin infections in Norwegian dogs. It should be noted that likely there has been a selection bias towards isolates from dogs with recurrent disease or with treatment failures. This may have caused a higher occurrence of resistance as compared to *S. intermedius* from the general canine population. Stratification of the isolates by anatomical origin (otitis externa versus other skin infections) did not reveal any significant (p=0.05) differences regarding prevalence of resistance to the antimicrobials included in the test panel.

The prevalence of resistance to penicillin (β-lactamase production) was high (86%) (Table 10). This is an increase as compared to NORM-VET 2000 (77%). In a retrospective Norwegian study of resistance in *S. intermedius* from canine dermatitis (otitis externa excluded), the prevalence of penicillin resistance was 46% for the period 1986-1987 and 59% for the period 1993-1994 (Kruse et al, 1996). Thus, the occurrence of penicillin resistance among *S. intermedius* from skin infections in dogs seems to have increased over time. Penicillin is widely used for different indications in dogs. However, the above data indicate that penicillinase sensitive penicillins are not likely to be effective for the treatment of recurrent pyoderma in dogs.

A high proportion of the isolates were resistant to fucidic acid (59%) and tetracycline (53%), respectively (Table 10), which is an increase as compared to NORM-VET 2000 (46% and 36%). Moreover, the prevalence of resistance to these two drugs seems to have increased considerable as compared to the data for 1986-1987 (1% and 20%) and 1993-1994 (45% and 28%) (Kruse et al., Vet. Res. Comm., 1996). It should be noted that the latter study is based on different sampling strategy and methodology as compared to what is used in NORM-VET. Fucidic acid is frequently used as a topical antimicrobial against skin infections, including otitis externa, in dogs in Norway. Tetracycline is also being used, both systemically as well as topically.

A large variety of resistance patterns were observed (Table 11). However, a total of 33% of the isolates were resistant to at least penicillin G, fucidic acid and oxytetracycline.

A moderate proportion of the isolates were resistant to the lincosamid clindamycin (15%) and the macrolide erythromycin (18%), respectively (Table 10), which is an increase as compared to NORM-VET 2000 (7% and 11%). Altogether 14 of the 15 clindamycin resistant isolates were also resistant to erythromycin, which most probably is a result of cross-resistance. Lincosamides and macrolides are commonly used for treatment of pyoderma in dogs.

A moderate proportion of the isolates were resistant to the aminoglycoside streptomycin (22%) and to trimethoprim (13%) (Table 10), which is an increase compared to NORM-VET 2000 (9% and 4%). Streptomycin is rarely used in dogs today, whereas a trimethoprim/ sulfamethoxazole combination frequently is prescribed for use in dogs.

No resistance to gentamicin, cephalotin, or ciprofloxacin was observed, which is similar to what was presented in NORM-VET 2000. No veterinary preparations containing gentamicin are licensed in Norway. The fluoroquinolone enrofloxacin is licensed for use in dogs. However, its use in pets is very limited. Although no veterinary preparations containing cephalosporins are licensed in Norway, it is known that there is some use in dogs with pyoderma of human preparations containing cephalosporins.

The data from 2002 indicate an increase in the prevalence of resistance to all antimicrobials included except cephalosporins and fluoroquinolones to which resistance have remained negligible. At present, there are no indications of an increased use in dogs of the antimicrobials for which an increased prevalence of resistance was observed. However, several of the preparations used for skin infections in dogs are licensed for humans, and no data regarding the amount used in companion animals are available.

Assumingly, currently the most commonly used antimicrobial for skin infections in dogs is a trimethoprim/sulfamethoxazole combination followed by erythromycin, lincomycin or clindamycin. The present data indicates that these drugs still will be effective for treatment of most cases of *S. intermedius* skin infections. In case of recurrent or chronic pyoderma/otitis in dogs, however, it is recommendable to perform susceptibility testing.

Escherichia coli from pigs and poultry

A total of 39 clinical isolates of *Escherichia coli* from enteritis in pigs and 52 clinical isolates of *E. coli* from septicaemia in poultry were susceptibility tested. The results are presented in table 12 and and 13 and figure 9.

TABLE 12. Antimicrobial resistance in *Escherichia coli* from enteritis in pigs (n=39) and from septicaemia in poultry (n=52).

Substance	Animal species	% Resistant	[95% CI*]	Distribution (%) of MIC values (mg/L)														
				0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline	Pigs	41	[25.6-57.9]						53.8	5.1			2.6			38.5		
	Poultry	8	[2.1-18.5]						48.1	44.2						7.7		
Chloramphenicol	Pigs	0	[0.0-9.0]							20.5	71.8	7.7						
	Poultry	0	[0.0-6.9]							5.8	76.9	17.3						
Florfenicol	Pigs	0	[0.0-9.0]							7.7	66.7	23.1	2.6					
	Poultry	0	[0.0-6.9]								61.5	38.5						
Ampicillin	Pigs	13	[4.3-27.4]						20.5	46.2	17.9	2.6			12.8			
	Poultry	12	[4.4-23.4]						9.6	65.4	13.5				11.5			
Ceftiofur	Pigs	0	[0.0-9.0]				61.5	38.5										
	Poultry	0	[0.0-6.9]				53.8	44.2	1.9									
Trimethoprim	Pigs	15	[5.9-30.5]			12.8	35.9	28.2	5.1	2.6				15.4				
	Poultry	8	[2.1-18.5]				13.5	38.5	38.5	1.9				7.7				
Sulfamethoxazole	Pigs	23	[11.1-39.3]												76.9			23.1
	Poultry	25	[14.0-39.0]												73.1	1.9		25.0
Streptomycin	Pigs	54	[37.2-69.9]							5.1	30.8	7.7		2.6	20.5	7.7	17.9	7.7
	Poultry	10	[3.2-21.0]								17.3	57.7	13.5	1.9	3.8		5.8	
Gentamicin	Pigs	3	[0.1-13.5]					56.4	38.5	2.6				2.6				
	Poultry	2	[0.1-10.3]					13.5	67.3	15.4	1.9				1.9			
Neomycin	Pigs	0	[0.0-9.0]						87.2	10.3	2.6							
	Poultry	2	[0.1-10.3]						25.0	65.4	7.7				1.9			
Apramycin	Pigs	3	[0.1-13.5]							5.1	74.4	15.4	2.6		2.6			
	Poultry	0	[0.0-6.9]								19.2	63.5	17.3					
Enrofloxacin	Pigs	0	[0.0-9.0]	92.3	7.7													
	Poultry	2	[0.1-10.3]	63.5	28.8	1.9	3.8		1.9									
Nalidixic acid	Pigs	0	[0.0-9.0]						17.9	59.0	23.1							
	Poultry	6	[1.2-16.0]							59.6	34.6					3.8	1.9	

Bold vertical lines denote breakpoints for resistance. White fields denote range of dilutions tested for each antimicrobial. MIC-values higher than the highest concentration tested for are given as the lowest MIC-value above the range. MIC-values equal to or lower than the lowest concentration tested are given as the lowest tested concentration.

*CI = Confidence Interval

TABLE 13. Number (%) of *Escherichia coli* resistant to antimicrobials presented by animal/sample category and resistance phenotype.

Resistant to number of antimicrobials	Resistance pattern (resistance is indicated with hatched areas where the number of isolates resistant to the respective antimicrobials is presented)													Number of isolates		Number (%) of isolates from each sample type expressing the respective resistance patterns					
																Pigs			Broilers		
	Oxytetracycline	Chloramphenicol	Florfenicol	Ampicillin	Ceftiofur	Trimethoprim	Sulfa methoxazole	Streptomycin	Gentamicin	Neomycin	Apramycin	Enrofloxacin	Nalidixic acid	Pigs	Broilers	Enteritis n = 39	Indicator, faeces n = 187	Indicator, meat n = 137	Septicaemia n = 52	Indicator, faeces n = 141	Indicator, meat n = 155
0														260	247	17 (43.6)	138 (73.8)	105 (76.6)	33 (63.5)	94 (66.6)	120 (77.4)
1								34						33	1	1 (2.6)	18 (9.6)	14 (10.2)		1 (0.7)	
							32							2	30			2 (1.5)	6 (11.5)	9 (6.4)	15 (9.7)
				25										4	21		3 (1.6)	1 (0.7)	2 (3.8)	12 (8.5)	7 (4.5)
	15													3	12		2 (1.1)	1 (0.7)	1 (1.9)	8 (5.7)	3 (1.9)
													2	1	1		1 (0.5)		1 (1.9)		
									1						1				1 (1.9)		
						1								1			1 (0.5)				
2							21	21						17	4	1 (2.6)	7 (3.7)	9 (6.6)	1 (1.9)	2 (1.4)	1 (0.6)
	15							15						14	1	11 (28.2)	2 (1.1)	1 (0.7)		1 (0.7)	
	8						8								8					6 (4.3)	2 (1.3)
				5			5								5					3 (2.1)	2 (1.3)
	3			3										2	1		2 (1.1)			1 (0.7)	
						2	2							1	1		1 (0.5)				1 (0.6)
				1				1						1		1 (2.6)					
												1	1		1						1 (0.6)
								1					1		1				1 (1.9)		
3	6						6	6						6		2 (5.1)	2 (1.1)	2 (1.5)			
						3	3	3						2	1		1 (0.5)	1 (0.7)			1 (0.6)
				2			2	2						1	1		1 (0.5)		1 (1.9)		
	2					2	2							1	1	1 (2.6)			1 (1.9)		
							1	1	1						1					1 (0.7)	
				1			1						1		1					1 (0.7)	
4				6		6	6	6						4	2	3 (7.7)	1 (0.5)		1 (1.9)	1 (0.7)	
	2			2			2	2						1	1		1 (0.5)				1 (0.6)
	2					2	2	2						2			1 (0.5)	1 (0.7)			
	1						1	1		1				1			1 (0.5)				
		1				1	1	1						1			1 (0.5)				
	1			1		1	1								1				1 (1.9)		
						1	1					1	1		1				1 (1.9)		
5	4			4		4	4	4						4		1 (2.6)	3 (1.6)				
	1			1			1	1		1					1				1 (1.9)		
6	1			1		1	1					1	1		1						1 (0.6)
	1			1			1	1		1			1		1					1 (0.7)	
	1					1	1	1	1		1			1		1 (2.6)					
Total	63	1	0	53	0	25	105	103	3	3	1	3	8	363	348	39	187	137	52	141	155

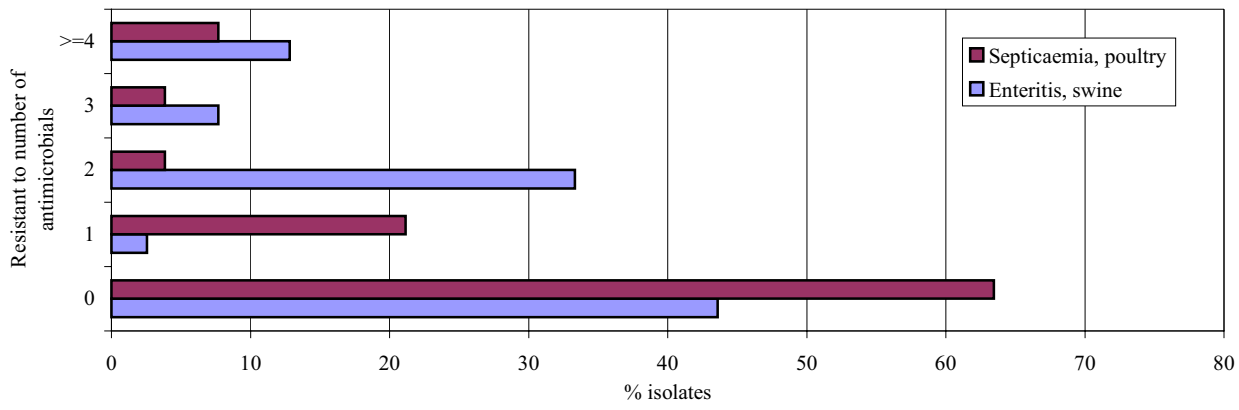


FIGURE 9. Antimicrobial resistance profiles for *Escherichia coli* from diagnostic samples from enteritis in pigs (n=39) and septicaemia in poultry (n=52). Proportion of isolates susceptible to all antimicrobials included and resistant to one, two, three, or four or more of the antimicrobials.

COMMENTS

PIGS

The data presented indicate a moderate occurrence of antimicrobial resistance in *E. coli* from enteritis in pigs. In total, 56% of the isolates were resistant to at least one of the antimicrobials included in the test panel; 3% to one antimicrobial only, 33% to two, 8% to three and 13% to four or more antimicrobials.

A high prevalence of resistance to oxytetracycline (41%) and streptomycin (54%), respectively, was observed. Moreover, a high correlation between resistance to oxytetracycline and streptomycin was found; 15 out of the 16 isolates resistant to oxytetracycline were also resistant to streptomycin. Concurrent resistance to oxytetracycline and streptomycin was also the most frequent resistance pattern observed (Table 13). Both drugs are common therapeutics in pig production, the latter drug in combination with penicillin.

The occurrence of resistance to ampicillin, trimethoprim and sulfamethoxazole was moderate (8-25%). Ampicillin and trimethoprim/sulfonamides are also commonly used therapeutics in pig production in Norway.

No quinolone resistance was observed. The use of fluoroquinolones in animals, including pigs, in Norway is very limited. No resistance to ceftiofur was observed, whereas a small proportion (3%) of the isolates were resistant to gentamicin. No preparations containing cephalosporins or the aminoglycoside gentamicin are approved for veterinary use in Norway.

The results obtained in 2002 are comparable with what was documented in an earlier survey regarding *E. coli* from enteritis in pigs (NORM-VET 1999) except that no resistance to chloramphenicol was observed in 2002 in contrast to 1999 (5%). All veterinary preparations containing chloramphenicol were withdrawn from the Norwegian market in 1992. Nevertheless, various surveys have shown that *E. coli* with reduced susceptibility to chloramphenicol still can be found in areas where chloramphenicol was used in earlier years. Of the generic faecal *E. coli* included in NORM-VET 2002, one isolate (0.5%) was resistant to chloramphenicol (Table 14).

The resistance patterns for the enteritis isolates were in general similar to those that were observed for generic faecal *E. coli* from healthy pigs and pork (Table 13). However, the resistance frequencies were considerably higher for the enteritis isolates. Moreover, the proportion of isolates being resistant to a least one antimicrobial was more than twice as high for the enteritis isolates (56% versus 26% for pork isolates and 23% for isolates from healthy pigs) (Figures 9 and 10).

POULTRY

The data presented indicate a moderate occurrence of antimicrobial resistance in *E. coli* from septicaemia in poultry. In total, 37% of the isolates were resistant to at least one of the antimicrobials included in the test panel; 21% to one antimicrobial only, 4% to two, 4% to three, and 8% to four or more antimicrobials.

Resistance to sulfamethoxazole was most common (25%), followed by resistance to ampicillin (12%), streptomycin (10%), oxytetracycline (8%) and trimethoprim (8%). There is some use of tetracycline and amoxicillin (cross-resistance with ampicillin) for clinical purposes in poultry, whereas streptomycin and trimethoprim are not used in Norwegian poultry production. Sulfonamides are rarely used in Norwegian poultry production today, but were commonly used in earlier years. All trimethoprim resistant isolates were at the same time resistant to sulfamethoxazole indicating that exposure to sulfonamides might have co-selected for trimethoprim resistance.

The prevalence of resistance to quinolones was low; three isolates (6%) were resistant to nalidixic acid, and one (2%) of these was also resistant to enrofloxacin. No quinolone preparations are licensed for use in poultry in Norway. However, veterinarians in Norway may apply for authorisation to use drugs for which no marketing authorisation has been granted. Sulfaclozin (1996-2002) and minor amounts of enrofloxacin (1992-2002) in preparations for flock treatment of poultry has been sold in Norway with such exemption. In addition, flumequine (cross-resistance with nalidixic acid) was used for clinical purposes to a very limited extent in the 1980s and early 1990s.

One isolate (2%) was resistant to the aminoglycoside gentamicin. Also one faecal indicator *E. coli* (1%) expressed this resistance trait (Table 14). No preparations containing gentamicin are licensed for use in animals in Norway. There are no indications that gentamicin has been used in poultry in Norway.

The resistance patterns for the septicaemia isolates were in general similar to those that were observed for indicator *E. coli* from healthy broilers and broiler meat (Table 13). Moreover, the resistance frequencies were in general at the same level. However, for several antimicrobials the occurrence of resistance was somewhat lower among the broiler meat isolates as compared to the other two categories. With regard to quinolone resistance, this trait was more frequent among the septicaemia isolates as compared to the indicator *E. coli*.

B. INDICATOR BACTERIA FROM ANIMALS, FOOD AND FEED

The prevalence of acquired antimicrobial resistance among certain bacteria of the normal enteric microflora can serve as an indicator of the selective antimicrobial pressure in the various populations. These bacteria form a reservoir of transferable resistance genes from which antimicrobial resistance can be spread to other bacteria, including those responsible for infections in animals or humans. Thus, monitoring of resistance among so-called indicator bacteria of the normal enteric microflora from healthy animals as well as indicator bacteria from feed and food is important in order to get a better understanding of the resistance situation, to detect trends, and to evaluate the effects of interventions.

In NORM-VET, *Escherichia coli* and *Enterococcus* spp. serve as indicator bacteria.

In 2002, indicator bacteria from pigs and broilers were included in the monitoring programme. In addition, data from wild cervids are presented, representative of a population that has not been directly exposed to antimicrobials. Data from a survey regarding dog feed of both imported or Norwegian origin are also presented. Such dog feed may come in contact not only with pets, but also small children.

Sampling, laboratory methods and data processing are described in Appendix 3.

Escherichia coli from pigs and broilers

A total of 205 faecal and 205 meat samples from pigs and a total of 166 faecal and 212 meat samples from broilers were collected. *E. coli* was isolated and susceptibility tested from 187 (91%) of the faecal and from 137 (67%) of the meat samples from pigs, and from 141 (85%) of the faecal and from 155 (73%) of the meat samples from broilers. The results are presented in tables 13 and 14 and figure 10.

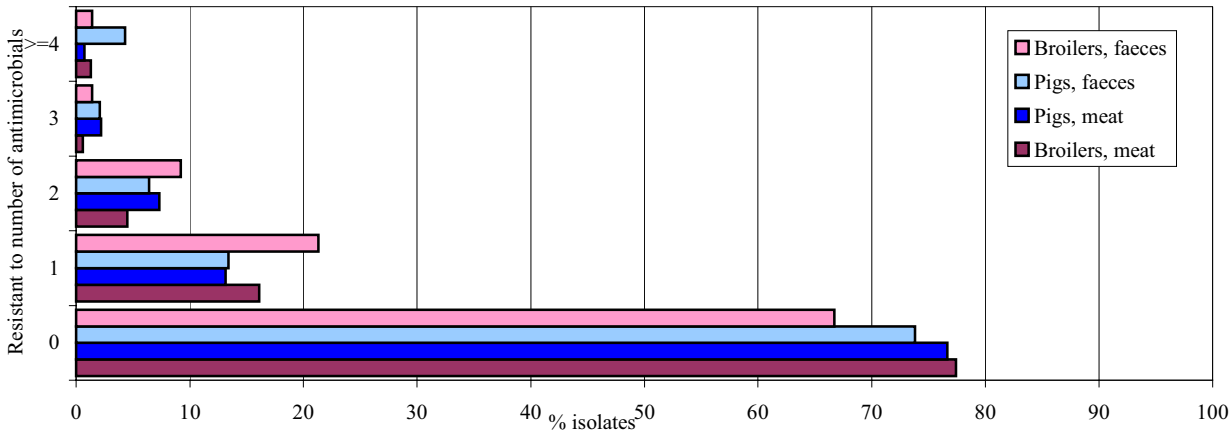


FIGURE 10. Antimicrobial resistance profiles for *Escherichia coli* isolates from porcine faecal (n=187) and meat (n=137) samples, and broiler faecal (n=141) and meat (n=155) samples. Proportion of isolates susceptible to all antimicrobials included and resistant to one, two, three, or four or more antimicrobials.

TABLE 14. Antimicrobial resistance in *Escherichia coli* from faecal (n=187) and meat samples (n=137) from pigs and faecal (n=141) and meat samples (n=155) from broilers.

Substance	Animal species	Sample type	% Resistant	[95% CI*]	Distribution (%) of MIC values (mg/L)														
					0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥512
Oxytetracycline	Pigs	Faeces	7	[4.2-12.2]					1.6	64.2	25.7	1.1			0.5	0.5	6.4		
		Meat	4	[1.8-8.3]					2.2	71.5	21.2	0.7	0.7			0.7	2.9		
	Broilers	Faeces	12	[7.2-18.6]						49.6	35.5	1.4	1.4		1.4	0.7	9.9		
		Meat	5	[1.8-9.1]					1.3	52.3	40.6	1.3		0.6			3.9		
Chloramphenicol	Pigs	Faeces	<1	[0.0-2.9]							9.1	51.9	38.0	0.5	0.5				
		Meat	0	[0.0-2.7]							12.4	55.5	29.9	2.2					
	Broilers	Faeces	0	[0.0-2.6]							3.5	52.5	42.6	1.4					
		Meat	0	[0.0-2.4]							4.5	55.5	40.0						
Florfenicol	Pigs	Faeces	0	[0.0-1.5]							5.3	38.5	52.9	3.2					
		Meat	0	[0.0-2.7]							5.1	40.9	51.1	2.9					
	Broilers	Faeces	0	[0.0-2.6]							2.8	28.4	62.4	6.4					
		Meat	0	[0.0-2.4]							1.9	34.8	59.4	3.9					
Ampicillin	Pigs	Faeces	6	[3.0-10.3]					0.5	15.0	60.4	17.6	0.5		0.5	5.4			
		Meat	<1	[0.0-4.0]				0.7		16.8	57.7	23.4	0.7		0.7				
	Broilers	Faeces	14	[8.3-20.2]						9.2	57.4	18.4	1.4			13.5			
		Meat	7	[3.6-12.3]					0.6	14.2	55.5	21.3	1.3			7.1			
Ceftiofur	Pigs	Faeces	0	[0.0-1.5]				50.3	46.5	3.2									
		Meat	0	[0.0-2.7]				48.2	49.6	2.2									
	Broilers	Faeces	0	[0.0-2.6]				37.6	58.2	4.3									
		Meat	0	[0.0-2.4]				36.8	61.3	1.9									
Trimethoprim	Pigs	Faeces	5	[2.2-8.9]			3.7	31.6	50.3	8.0	1.1	0.5			4.8				
		Meat	2	[0.2-5.2]			3.6	27.7	55.5	10.2	1.5				1.5				
	Broilers	Faeces	<1	[0.0-3.9]			1.4	36.2	49.6	11.3		0.7			0.7				
		Meat	2	[0.4-5.6]			2.6	18.7	58.7	17.4	0.6				1.9				
Sulfamethoxazole	Pigs	Faeces	11	[6.7-16.0]												89.3			10.7
		Meat	11	[6.3-17.4]												89.1			10.9
	Broilers	Faeces	17	[11.2-24.3]												82.3	0.7		17.0
		Meat	16	[10.2-22.2]												84.5			15.5
Streptomycin	Pigs	Faeces	21	[15.3-27.4]							1.1	39.6	34.8	2.1	1.6	6.4	7.5	4.8	2.1
		Meat	20	[14.0-28.2]								32.8	43.8	2.2	0.7	6.6	8.0	5.1	0.7
	Broilers	Faeces	5	[2.0-10.0]								25.5	61.0	7.8	0.7	2.8	0.7	1.4	
		Meat	2	[0.4-5.6]								31.0	61.3	4.5	1.3	1.3		0.6	
Gentamicin	Pigs	Faeces	0	[0.0-1.5]				0.5	31.0	61.0	7.0	0.5							
		Meat	0	[0.0-2.7]					23.4	66.4	10.2								
	Broilers	Faeces	<1	[0.0-3.9]					9.2	70.9	17.0	2.1				0.7			
		Meat	0	[0.0-2.4]					14.8	72.3	10.3	1.9	0.6						
Neomycin	Pigs	Faeces	<1	[0.0-2.9]						61.5	33.7	3.7	0.5			0.5			
		Meat	0	[0.0-2.7]						48.2	48.9	2.2	0.7						
	Broilers	Faeces	<1	[0.0-3.9]						42.6	50.4	6.4			0.7				
		Meat	0	[0.0-2.7]						48.2	48.9	2.2	0.6						
Apramycin	Pigs	Faeces	0	[0.0-1.5]							3.7	46.0	43.9	5.9	0.5				
		Meat	0	[0.0-2.7]								37.2	52.6	9.5	0.7				
	Broilers	Faeces	0	[0.0-2.6]						0.7	0.7	28.4	54.6	14.9	0.7				
		Meat	0	[0.0-2.4]								29.7	60.6	8.4	1.3				
Enrofloxacin	Pigs	Faeces	0	[0.0-1.5]	59.9	38.0	1.6	0.5											
		Meat	0	[0.0-2.7]	54.7	44.5	0.7												
	Broilers	Faeces	0	[0.0-2.6]	44.7	51.8	2.1	1.4											
		Meat	1	[0.0-3.5]	47.7	50.3	0.7		0.6	0.6									
Nalidixic acid	Pigs	Faeces	<1	[0.0-2.9]						2.7	35.3	59.9	1.6			0.5			
		Meat	0	[0.0-2.7]						2.9	40.9	51.1	5.1						
	Broilers	Faeces	1	[0.2-5.0]						0.7	36.2	58.9	2.1	0.7	0.7	0.7			
		Meat	1	[0.0-4.6]						3.9	35.5	57.4	1.9				0.6	0.6	

Bold vertical lines denote breakpoints for resistance. White fields denote range of dilutions tested for each antimicrobial. MIC-values higher than the highest concentration tested for are given as the lowest MIC-value above the range. MIC-values equal to or lower than the lowest concentration tested are given as the lowest tested concentration.

*CI = Confidence Interval

COMMENTS

PIGS

The data presented indicate a relatively low occurrence of antimicrobial resistance among generic *E. coli* from faecal and meat samples from a representative group of healthy Norwegian pigs.

In total, 26% of the faecal isolates and 23% of the meat isolates were resistant to at least one of the antimicrobials included in the test panel (Figure 10). This is considerable less as compared to the clinical isolates from pigs (56%) (Table 12), but at a similar level as what was observed for faecal generic *E. coli* isolates from healthy cattle in NORM-VET 2001.

The resistance patterns were in general similar to those that were observed for the clinical *E. coli* isolates from pigs. However, the resistance frequencies were considerably lower for the indicator *E. coli* than for the clinical isolates. The resistance frequencies and the occurrence of multiresistance were somewhat higher for the faecal *E. coli* than for the meat isolates.

Altogether, the most frequent resistance traits observed were resistance to streptomycin (21%), sulfamethoxazole (11%), tetracycline (6%), ampicillin (4%) and trimethoprim (3%), respectively (Table 14). All these drugs are common therapeutics in pig production, - sulfonamides and trimethoprim as a combination preparation and streptomycin in combination with penicillin.

The resistance frequencies for the meat isolates were more or less at the same level as what was observed for pork isolates in NORM-VET 2000 and in a Norwegian survey from 1998 (Kruse, H. SNT-report no. 1, 1999).

No resistance to fluoroquinolones was observed. However, one faecal isolate (0.5%) was resistant to nalidixic acid. This isolate also had an MIC value for enrofloxacin just below the breakpoint for resistance indicating that fluoroquinolone resistance might be developing. The use of fluoroquinolones in animals, including pigs, in Norway is very limited.

No resistance to ceftiofur or gentamicin was observed. No preparations containing cephalosporins or the aminoglycoside gentamicin are approved for veterinary use in Norway.

One isolate (0.5%) of faecal *E. coli* was resistant to chloramphenicol. All veterinary preparations containing chloramphenicol were withdrawn from the Norwegian market in 1992. Nevertheless, various surveys have shown that *E. coli* with reduced susceptibility to chloramphenicol still can be found in areas where this antimicrobial was used in earlier years.

BROILERS

The data presented indicate a relatively low occurrence of antimicrobial resistance among generic *E. coli* from faecal and meat samples from a representative group of healthy Norwegian broilers.

In total, 33% of the faecal isolates and 23% of the broiler meat isolates were resistant to at least one of the antimicrobials included in the test panel (Figure 10). The corresponding figure for broiler meat in NORM-VET 2000 is 36%.

The resistance patterns as well as the resistance frequencies were in general similar to those that were observed for the septicaemia *E. coli* isolates (Table 12). However, for several antimicrobials the occurrence of resistance was somewhat lower among the broiler meat isolates as compared to the other two categories.

Altogether, resistance to sulfamethoxazole was most commonly observed (16%) followed by resistance to ampicillin (10%), oxytetracycline (8%), streptomycin (4%) and trimethoprim (1%) (Table 14). There is some use of tetracycline and amoxicillin (cross-resistance with ampicillin) for clinical purposes in broilers, whereas streptomycin and trimethoprim are not used in Norwegian broiler production. Sulfonamides are rarely used in Norwegian broiler production today, but were commonly used in earlier years. All trimethoprim resistant isolates were at the same time resistant to sulfamethoxazole indicating that exposure to sulfonamides might have co-selected for trimethoprim resistance.

Compared to the data from NORM-VET 2000, the data indicate a decrease in the resistance prevalences for streptomycin, sulfonamides and trimethoprim.

Quinolone resistance was rarely observed; two broiler meat isolates (1%) were resistant to both nalidixic acid and enrofloxacin, whereas two faecal isolates (1%) were resistant to nalidixic acid but still susceptible to enrofloxacin. No quinolone preparations are licensed for use in broilers in Norway. However, veterinarians in Norway may apply for authorisation to use drugs for which no marketing authorisation has been granted. Sulfaclozin (1996-2002) and minor amounts of enrofloxacin (1992-2002) in preparations for flock treatment of broilers has been sold in Norway with such exemption. In addition, flumequine (cross-resistance with nalidixic acid) was used for clinical purposes to a very limited extent in the 1980s and early 1990s.

One faecal isolate (1%) was resistant to the aminoglycoside gentamicin. Also one *E. coli* (2%) isolated from septicaemia in broilers expressed this resistance trait. No preparations containing gentamicin are licensed for use in animals in Norway. There are no indications that gentamicin has been used in broilers in Norway.

Enterococcus spp. from pigs and broilers

A total of 205 faecal and 205 meat samples from pigs and 166 faecal and 212 meat samples from broilers were collected. *E. faecium* or *E. faecalis* was isolated from 95 (46%) of the faecal and 95 (46%) of the meat samples from pigs, and from 149 (90%) of the faecal and 175 (83%) of the meat samples from broilers. *E. faecium* was isolated from 36 faecal and 31 meat samples from pigs and from 116 faecal and 42 meat samples from broilers. *E. faecalis* was isolated from 59 faecal and 64 meat samples from pigs and from 33 faecal and 133 meat samples from broilers. All these isolates were susceptibility tested. The results are presented in tables 15 and 16 and figure 11.

The faecal samples from broilers were also examined for the presence of vancomycin resistant *Enterococcus* spp. (VRE) using a selective method.

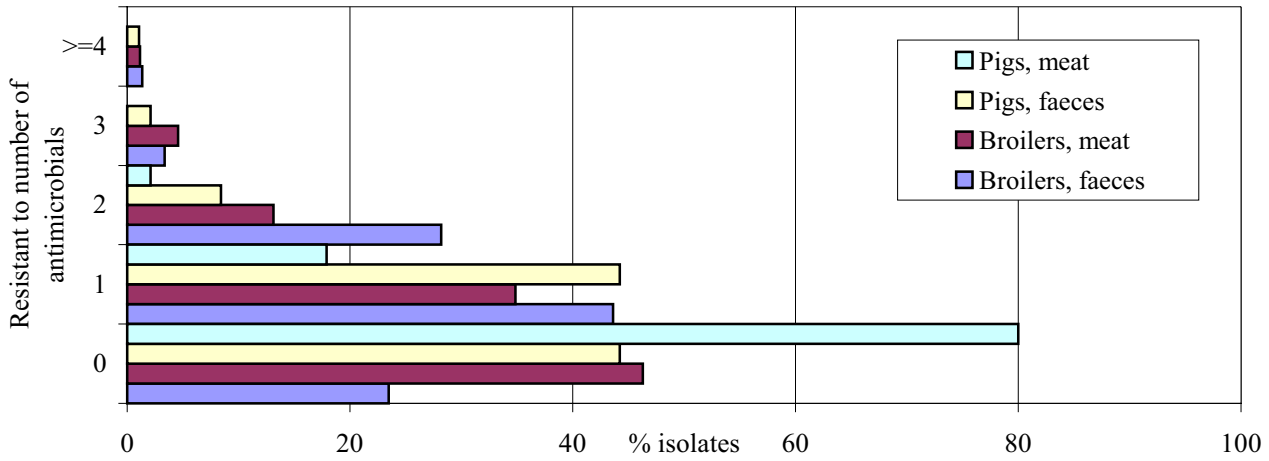


FIGURE 11. Antimicrobial resistance profiles for *E. faecalis* and *E. faecium* from porcine faecal (n=95) and meat (n=95) samples, and broiler faecal (n=149) and meat (n=175) samples. Proportion of isolates susceptible to all antimicrobials included and resistant to one, two, three, or four or more antimicrobials. Resistance to virginiamycin and flavomycin are excluded for *E. faecalis* and *E. faecium*, respectively, due to inherent resistance.

TABLE 15. Antimicrobial resistance in *Enterococcus faecium* from faecal (n=36) and meat samples (n=31) from pigs, and faecal (n=116) and meat samples (n=42) from broilers.

Substance	Animal species	Sample type	%Resistant	[95% CI*]	Distribution (%) of MIC values (mg/L)														
					0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	≥ 2048
Oxytetracycline	Pigs	Faeces	22	[10.1-39.2]			16.7	55.6	5.6				8.3	13.9					
		Meat	3	[0.1-16.7]			9.7	54.8	29.0	3.2			3.2						
	Broilers	Faeces	19	[12.3-27.3]			37.9	37.1	4.3	1.7		1.7	8.6	6.0	2.6				
		Meat	5	[0.6-16.2]			28.6		61.9	2.4	2.4				4.8				
Chloramphenicol	Pigs	Faeces	0	[0.0-9.7]					8.3	16.7	69.4	5.6							
		Meat	0	[0.0-16.7]						32.3	54.8	12.9							
	Broilers	Faeces	0	[0.0-3.1]					22.4	36.2	41.4								
		Meat	0	[0.0-8.4]					7.1	28.6	61.9	2.4							
Ampicillin	Pigs	Faeces	0	[0.0-9.7]		16.7	11.1	44.4	13.9	13.9									
		Meat	0	[0.0-16.7]		16.1		25.8	54.8	3.2									
	Broilers	Faeces	0	[0.0-3.1]		13.8	14.7	29.3	15.5	21.6	5.2								
		Meat	0	[0.0-8.4]		9.5	11.9	26.2	38.1	14.3									
Erythromycin	Pigs	Faeces	3	[0.1-14.5]			16.7	5.6	22.2	52.8	2.8								
		Meat	13	[3.6-29.8]			54.8		9.7	22.6	6.5	6.5							
	Broilers	Faeces	9	[4.2-15.3]			12.1	9.5	53.4	16.4	2.6	2.6	1.7	1.7					
		Meat	0	[0.0-8.4]			4.8	16.7	47.6	31.0									
Streptomycin	Pigs	Faeces	6	[0.7-18.7]								13.9	38.9	33.3	5.6			2.8	5.6
		Meat	0	[0.0-16.7]						3.2		16.1	64.5	12.9	3.2				
	Broilers	Faeces	0	[0.0-3.1]							3.4	12.9	45.7	36.2	1.7				
		Meat	0	[0.0-8.4]							2.4	9.5	47.6	40.5					
Gentamicin	Pigs	Faeces	0	[0.0-9.7]					5.6	19.4	50.0	16.7	8.3						
		Meat	0	[0.0-16.7]					3.2	32.3	45.2	19.4							
	Broilers	Faeces	0	[0.0-3.1]					2.6	19.8	50.0	26.7	0.9						
		Meat	0	[0.0-8.4]						28.6	42.9	26.2	2.4						
Neomycin	Pigs	Faeces	0	[0.0-9.7]						8.3	44.4	33.3	11.1		2.8				
		Meat	0	[0.0-16.7]					3.2	29.0	29.0	25.8	12.9						
	Broilers	Faeces	0	[0.0-3.1]					0.9	14.7	46.6	29.3	6.0	2.6					
		Meat	0	[0.0-8.4]						14.3	50.0	33.3	2.4						
Vancomycin	Pigs	Faeces	0	[0.0-9.7]				83.3	13.9	2.8									
		Meat	0	[0.0-16.7]				96.8	3.2										
	Broilers	Faeces	3	[1.0-8.6]				61.9	28.6	4.8						3.4			
		Meat	5	[0.6-16.2]				62.0	29.0	5.0						5.0			
Bacitracin	Pigs	Faeces	11	[3.1-26.1]			2.8		2.8	5.6	5.6	41.7	30.6	11.1					
		Meat	0	[0.0-16.7]				9.7	3.2	6.5	19.4	45.2	16.1						
	Broilers	Faeces	19	[12.3-27.3]			3.4	16.4	13.8	5.2	6.9	21.6	13.8	19					
		Meat	36	[21.6-52.0]			4.8	2.4	21.4	4.8		7.1	23.8	35.7					
Avilamycin	Pigs	Faeces	6	[0.7-18.7]				2.8	16.7	44.4	19.4	11.1	5.6						
		Meat	0	[0.0-16.7]			3.2	3.2	9.7	51.6	32.3								
	Broilers	Faeces	0	[0.0-3.1]			7.8	22.4	25.0	37.9	6.0	0.9							
		Meat	2	[0.1-12.6]			2.4	9.5	26.2	50.0	4.8	4.8	2.4						
Virginiamycin	Pigs	Faeces	0	[0.0-9.7]			25.0	36.1	22.2	16.7									
		Meat	0	[0.0-16.7]			12.9	19.4	25.8	41.9									
	Broilers	Faeces	3	[0.5-7.4]			21.6	28.4	27.6	18.1	1.7	1.7	0.9						
		Meat	2	[0.1-12.6]			16.7	40.5	23.8	14.3	2.4	2.4							
Flavomycin**	Pigs	Faeces								2.8					2.8	94.4			
		Meat														100			
	Broilers	Faeces							0.9	3.4	1.7	5.2	2.6	3.4	1.7	81.0			
		Meat									2.4		2.4	2.4		92.9			
Narasin	Pigs	Faeces	11	[3.1-26.1]	5.6	2.8	27.8	50.0	2.8	5.6	5.6								
		Meat	0	[0.0-16.7]	6.5	29.0	58.1	6.5											
	Broilers	Faeces	67	[57.9-75.7]	2.6	3.4	9.5	14.7	2.6	11.2	54.3	1.7							
		Meat	76	[60.6-88.0]		2.4	9.5	2.4	9.5	16.7	52.4	7.1							

Bold vertical lines denote breakpoints for resistance. White fields denote range of dilutions tested for each antimicrobial. MIC-values higher than the highest concentration tested for are given as the lowest MIC-value above the range. MIC-values equal to or lower than the lowest concentration tested are given as the lowest tested concentration.

* CI = Confidence Interval

** *E. faecium* inherently resistant to flavomycin

TABLE 16. Antimicrobial resistance in *Enterococcus faecalis* from faecal (n=59) and meat samples (n=64) from pigs and faecal (n=33) and meat samples (n=133) from broilers.

Substance	Animal species	Sample type	%Resistant	[95% CI*]	Distribution (%) of MIC values (mg/L)													
					0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	≥ 2048
Oxytetracycline	Pigs	Faeces	56	[42.4-68.9]			15.3	22.0	6.8			11.9	23.7	18.6	1.7				
		Meat	16	[7.8-28.9]			15.6	51.6	14.1		3.1	7.8	4.7	3.1					
	Broilers	Faeces	45	[28.1-63.7]			6.1	45.5	3.0			6.1	21.2	12.1	6.1				
		Meat	23	[16.4-31.4]			18.0	51.9	6.8			9.8	9.8	3.0	0.8				
Chloramphenicol	Pigs	Faeces	2	[0.04-9.1]						22.0	76.3		1.7						
		Meat	0	[0.0-5.6]					1.6	32.8	65.6								
	Broilers	Faeces	0	[0.1-10.6]					3.0	42.4	54.5								
		Meat	0	[0.0-2.7]					3.0	36.1	60.9								
Ampicillin	Pigs	Faeces	0	[0.0-6.1]			10.2	81.4	8.5										
		Meat	0	[0.0-5.6]		3.1	17.2	62.5	17.2										
	Broilers	Faeces	0	[0.1-10.6		3.0	18.2	66.7	6.1	6.1									
		Meat	0	[0.0-2.7]		1.5	21.8	72.2	3.8	0.8									
Erythromycin	Pigs	Faeces	2	[0.04-9.1]			10.2	11.9	45.8	30.5				1.7					
		Meat	0	[0.0-5.6]			7.8	6.2	35.9	50.0									
	Broilers	Faeces	24	[11.1-42.3]			12.1	18.2	12.1	33.3	3.0	3.0	6.1	12.1					
		Meat	11	[5.9-17.0]			7.5	7.5	24.1	50.4	1.5	1.5	6.8	0.8					
Streptomycin	Pigs	Faeces	17	[8.4-29.0]						3.4			6.8	16.9	47.5			8.5	16.9
		Meat	3	[3.8-10.8]									7.8	40.6	45.3			3.1	3.1
	Broilers	Faeces	3	[0.1-15.8]									6.1	48.5	33.3			9.1	3.0
		Meat	3	[0.8-7.5]						0.8		0.8	9.0	44.4	37.6			4.5	3.0
Gentamicin	Pigs	Faeces	0	[0.0-6.1]						3.4	23.7	33.9	39.0						
		Meat	0	[0.0-5.6]						10.9	31.2	46.9	9.4				1.6		
	Broilers	Faeces	0	[0.0-11.0]				3.0			45.5	39.4	12.1						
		Meat	0	[0.0-2.7]					0.8	6.0	33.8	47.4	12.0						
Neomycin	Pigs	Faeces	2	[0.04-9.1]								13.6	13.6	28.8	37.3			5.1	1.7
		Meat	2	[0.0-8.4]							1.6	25.0	34.4	31.2	4.7			1.6	1.6
	Broilers	Faeces	3	[0.1-15.8]						3.0		9.1	30.3	27.3	27.3				3.0
		Meat	0	[0.0-2.7]							1.5	16.5	34.6	33.8	12.8			0.8	
Vancomycin	Pigs	Faeces	0	[0.0-6.1]				15.3	74.6	10.2									
		Meat	0	[0.0-5.6]				20.3	70.3	9.4									
	Broilers	Faeces	0	[0.0-11.0]				39.4	54.5	3.0	3.0								
		Meat	0	[0.0-2.7]				23.3	66.2	10.5									
Bacitracin	Pigs	Faeces	0	[0.0-6.1]						6.8	42.4	50.8							
		Meat	3	[3.8-10.8]					3.1	17.2	21.9	40.6	14.1	3.1					
	Broilers	Faeces	15	[5.1-31.9]					6.1	9.1	18.2	39.4	12.1	15.2					
		Meat	17	[11.3-24.8]					0.8	4.5	32.3	36.1	9.0	17.3					
Avilamycin	Pigs	Faeces	0	[0.0-6.1]				13.6	25.4	52.5	1.7	6.8							
		Meat	0	[0.0-5.6]			1.6	18.8	40.6	35.9	1.6	1.6							
	Broilers	Faeces	0	[0.0-11.0]				15.2	21.2	63.6									
		Meat	0	[0.0-2.7]			0.8	30.8	29.3	36.8	1.5	0.8							
Virginiamycin**	Pigs	Faeces								3.4	16.9	74.6	5.1						
		Meat						3.1	4.7	3.1	3.1	82.8	3.1						
	Broilers	Faeces							6.1	9.1	21.2	60.6	3.0						
		Meat								3.0	14.3	69.2	12.8		0.8				
Flavomycin	Pigs	Faeces	2	[0.04-9.1]					25.4	66.1	6.8					1.7			
		Meat	2	[0.0-8.4]					42.2	42.2	9.4	3.1	1.6	1.6					
	Broilers	Faeces	3	[0.1-15.8]					48.5	45.5	3.0					3.0			
		Meat	0	[0.0-2.7]					48.9	33.8	10.5	3.0	3.8						
Narasin	Pigs	Faeces	2	[0.04-9.1]	5.1	37.3	45.8	6.8	3.4	1.7									
		Meat	0	[0.0-5.6]	10.9	53.1	32.8	3.1											
	Broilers	Faeces	9	[1.9-24.3]	9.1	39.4	33.3	3.0	6.1	6.1	3.0								
		Meat	11	[6.5-17.9]	16.5	45.9	21.8	2.3	2.3	10.5	0.8								

Bold vertical lines denote breakpoints for resistance. White fields denote range of dilutions tested for each antimicrobial. MIC-values higher than the highest concentration tested for are given as the lowest MIC-value above the range. MIC-values equal to or lower than the lowest concentration tested are given as the lowest tested concentration.

*CI = Confidence Interval

** *E. faecalis* inherently resistant to virginiamycin

COMMENTS

The material included 190 enterococcal isolates from pigs and 324 enterococcal isolates from broilers.

A higher proportion of the samples from poultry yielded *E. faecalis or E. faecium* as compared to the pig samples; 90% of the faecal and 83% of the meat samples from broilers versus 46% of the faecal and 46% of the meat samples from pigs.

Isolation frequencies of *E. faecium* and *E. faecalis*, respectively, differed for pigs and broilers. For broilers, *E. faecium* dominated among the selected faecal isolates, whereas *E. faecalis* dominated among the selected meat isolates. For pigs, *E. faecalis* was more frequently selected than *E. faecium* regardless of sample type.

E. faecalis is reported to be inherently resistant to the streptogramin virginiamycin, while *E. faecium* is reported to be susceptible to this antimicrobial. The situation is reversed for flavomycin. The data obtained are in accordance with these phenomenons. The use of virginiamycin in animal production in Norway has always been negligible, and the substance has been banned since 1998. Flavomycin has never been approved in Norway.

PIGS

It should be noted that resistance to virginiamycin for *E. faecalis* and to flavomycin for *E. faecium* are excluded from the following results.

In total, 56% of the enterococcal isolates from the faecal samples and 20% of the isolates from the meat samples were resistant to at least one of the antimicrobials included in the test panel (Figure 11). Multiresistance (resistant to three or more of the drugs included) was rarely (1.6%) observed.

Altogether, resistance to oxytetracycline (27%) was the most commonly observed resistance trait, followed by resistance to streptomycin (7%) (Tables 15 and 16). Tetracycline and streptomycin are common therapeutics in Norwegian pig production, the latter one in combination with penicillin. The resistance prevalences for oxytetracycline and streptomycin were considerably higher for the faecal isolates as compared to the meat isolates, and higher for *E. faecalis* as compared to *E. faecium*.

A low proportion of the isolates were resistant to bacitracin (3.2%), erythromycin (3.2%), narasin (2.6%), neomycin (1.1%) and avilamycin (1.1%). Less than 1% of the isolates were resistant to chloramphenicol, and no resistance to vancomycin, ampicillin or gentamicin was observed. No resistance to virginiamycin was observed in *E. faecium*, whereas 2% of *E. faecalis* were resistant to flavomycin. No antibacterial growth promoters are used in Norwegian pig production. There is some use of neomycin as an oral therapeutic against enteritis. No macrolides or lincosamides are licensed for use in pigs in Norway. However, a veterinary spiramycin formulation was available in the 1990s. Moreover, veterinarians in Norway may apply for authorisation to use drugs for which no marketing authorisation has been granted, and it is known that since 1998 at least 8.1 kg (1.5 kg in 2002) of the macrolide tylosin has been sold with such exemption in Norway for therapeutic use in pigs. All veterinary preparations containing chloramphenicol were withdrawn from the Norwegian market in 1992.

The resistance frequencies for the meat isolates were more or less at the same level as observed for pork isolates in NORM-VET 2000 and in a Norwegian survey from 1998 (Kruse, H. SNT-report no. 1, 1999).

E. faecium

Of the *E. faecium* isolates from porcine faecal and meat samples, respectively, 42% (faecal) and 16% (meat) were resistant to at least one of the antimicrobials included in the test panel (flavomycin excluded).

Resistance to oxytetracycline was most commonly observed (13%), followed by resistance to erythromycin (7%), narasin (6%), bacitracin (6%), streptomycin (3%), and avilamycin (3%) (Table 15). For oxytetracycline, bacitracin and streptomycin, the resistance frequencies were higher for the faecal isolate as compared to the meat isolates. For erythomycin, the prevalence of resistance was higher for the meat isolates as compared to the faecal isolates.

E. faecalis

Of the *E. faecalis* isolates from porcine faecal and meat samples, respectively, 64% (faecal) and 22% (meat) were resistant to at least one of the antimicrobials included in the test panel (virginiamycin excluded). Resistance to oxytetracycline was the most commonly observed resistance trait (35%), followed by resistance to streptomycin (10%) (Table 16). However, the resistance frequencies to both these drugs were considerably higher for the faecal isolate as compared to the meat isolates. The prevalence of resistance to neomycin, chloramphenicol, erythromycin, bacitracin, flavomycin, and narasin, respectively, was low (1-2%). No resistance to vancomycin, ampicillin or gentamicin was observed.

BROILERS

It should be noted that resistance to virginiamycin for *E. faecalis* and to flavomycin for *E. faecium* are excluded from the following results.

In total, 77% of the enterococcal isolates from the faecal samples and 54% of the isolates from the meat samples were resistant to at least one of the antimicrobials included in the test panel (Figure 12). Multiresistance was rarely (4.9%) observed. Altogether, resistance to narasin was most commonly observed (40%), followed by resistance to oxytetracycline (22%), bacitracin (20%), erythromycin (10%), and vancomycin (2%) (Tables 15 and 16). For tetracycline and erythromycin, the resistance prevalences were considerably higher for the faecal isolates as compared to the meat isolates. Resistance to streptomycin (1.5%), neomycin (0.3%) and avilamycin (0.3%), respectively, was rarely observed. No resistance to ampicillin, chloramphenicol or gentamicin was observed. In total, 3% of *E. faecium* were resistant to virginiamycin and 0.6% of *E. faecalis* were resistant to flavomycin. The resistance frequencies observed for the broiler meat isolates are comparable to the frequencies observed for broiler meat isolates in NORM-VET 2000 and in an earlier Norwegian survey from 1998 (Kruse, H. SNT-report no. 1, 1999), except that resistance to tetracycline seems to have decreased somewhat (27% and 40% of *E. faecium* and 32% and 41% of *E. faecalis* classified as resistant in 2000 and 1998, respectively).

Coccidiostats are routinely used in Norwegian broiler production and since 1996 the use of coccidiostats has been dominated by the ionophore narasin. The high level of narasin resistance among enterococci from broilers, *E. faecium* in particular, is likely a result of the selection pressure exerted by the common use of narasin in broiler production.

There is some use of tetracycline for clinical purposes in Norwegian broiler production. In the 1990s, a spiramycin preparation was licensed for therapeutic use in poultry. Cross-resistance between erythromycin and spiramycin is common. Bacitracin was used as a growth promoter in earlier years. However, during the 1990s the usage of bacitracin as a growth promoter has been negligible, and since 1997 no such use has been recorded in animal production in Norway. The growth promoter virginiamycin was banned in 1998. However, the use has always been negligible.

Avoparcin, which confers cross-resistance to vancomycin, was routinely used as a growth promoter in Norwegian broiler and turkey production from 1986 until it was banned in 1995. Studies have shown that this use has selected for an extensive occurrence of vancomycin resistant enterococci (VRE) in Norwegian broiler production, and that VRE have persisted and remained at a high prevalence level for at least six years after the ban was implemented.

Of the randomly selected enterococcal isolates included in NORM-VET 2002, 1.9% were vancomycin resistant (2.7% for the faecal isolates and 1.1% for the broiler meat isolates). For *E. faecium*, this figure was 3.8% (3.4% for the faecal isolates and 4.8% for the broiler meat isolates) and for *E. faecalis,* 0% (Tables 15 and 16). In NORM-VET 2000, 3.4% of the broiler meat isolates were vancomycin resistant; 4.8% for *E. faecium* and 0% for *E. faecalis*. Thus, the prevalence of vancomycin resistance among indicator enterococci in broilers in Norway seems to have remained at the same level from 2000 to 2002. In a small survey conducted in 1998 (Kruse, H. SNT-report no. 1, 1999), three (12%) out of 25 randomly selected *E. faecium* from broiler meat (each isolate representing a different sample) were vancomycin resistant and none out of 41 *E. faecalis*. Although the number of isolates included in 1998 was limited, the data indicate a decrease in the concentration of vancomycin resistant *E. faecium* in broiler meat products from 1998 to 2000-2002.

Using a selective method that detects the presence of VRE, VRE could be isolated from 141 (91%) out of 155 faecal samples from broilers included in NORM-VET 2002, each sample representing a different flock. This figure corresponds to the figures obtained in studies conducted in 1995, 1998, and 2001, respectively. Thus, the prevalence of VRE in Norwegian broiler flocks seems to have remained at the same level for at least seven years following the ban on avoparcin.

E. faecium

Of the *E. faecium* isolates from faeces and broiler meat samples, respectively, 79% (faecal) and 83% (meat) were resistant to at least one of the antimicrobials included in the test panel (flavomycin excluded). Resistance to narasin (70%) was most commonly observed, followed by resistance to bacitracin (23%), oxytetracycline (15%), erytromycin (7%), vancomycin (3.8%), and virginiamycin (3%) (Table 15). For tetracycline and erythromycin, the resistance prevalences were considerably higher for the faecal isolates as compared to the meat isolates. Resistance to avilamycin (0.6%) was rarely observed. No resistance to ampicillin, chloramphenicol or gentamicin was observed.

E. faecalis

Of the *E. faecalis* isolates from faeces and broiler meat samples, respectively, 67% (faecal) and 44 % (meat) were resistant to at least one of the antimicrobials included in the test panel (virginiamycin excluded). Resistance to oxytetracycline (28%) was most commonly observed, followed by resistance to bacitracin (17%), erytromycin (14%), narasin (11%), and streptomycin (3%) (Table 16). For tetracycline and erythromycin, the resistance prevalences were considerably higher for the faecal isolates as compared to the meat isolates.

Resistance to neomycin (0.6%) and flavomycin (0.6%) was rarely observed. No resistance to vancomycin, ampicillin, chloramphenicol, avilamycin or gentamicin was observed.

Escherichia coli and *Enterococcus* spp. from wild cervids

A total of 137 isolates of *Escherichia coli* from wild cervids were susceptibility tested; 48 from moose, 45 from red deer and 44 from roe deer. Also, a total of 19 enterococcal isolates were susceptibility tested; 13 *Enterococcus faecalis* – three from moose, five from red deer and five from roe deer, and six *E. faecium* – three from red deer and three from roe deer. The results are presented in tables 17 and 18.

TABLE 17. Antimicrobial resistance in *Escherichia coli* from wild cervids (n=137); moose (n=48), red deer (n=45) and roe deer (n=44).

Substance	% Resistant [95% CI*]		Distribution (%) of MIC values (mg/L)														
			0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline	1	[0.2-5.2]					1.5	20.4	40.1	35.8	0.7				1.5		
Chloramphenicol	0	[0.0-2.7]							10.2	49.6	40.1						
Florfenicol	0	[0.0-2.7]							6.6	34.3	57.7	1.5					
Ampicillin	0	[0.0-2.7]						8.0	72.3	17.5	1.5	0.7					
Ceftiofur	0	[0.0-2.7]				21.9	74.5	3.6									
Trimethoprim	<1	[0.0-4.0]			5.8	20.4	64.2	7.3		1.5			0.7				
Sulfamethoxazole	1	[0.2-5.2]												98.5			1.5
Streptomycin	<1	[0.0-4.0]							0.7	38	56.2	4.4		0.7			
Gentamicin	0	[0.0-2.7]				0.7	29.9	63.5	5.1	0.7							
Neomycin	0	[0.0-2.7]						47.4	48.2	4.4							
Apramycin	0	[0.0-2.7]							1.5	35	59.9	3.6					
Enrofloxacin	0	[0.0-2.7]	34.3		64.2	1.5											
Nalidixic acid	0	[0.0-2.7]						3.6	53.3	43.1							

Bold vertical lines denote breakpoints for resistance. White fields denote range of dilutions tested for each antimicrobial. MIC-values higher than the highest concentration tested for are given as the lowest MIC-value above the range. MIC-values equal to or lower than the lowest concentration tested are given as the lowest tested concentration.
*CI = Confidence Interval

TABLE 18. Antimicrobial resistance in *Enterococcus spp.* isolates from wild cervids (n=19): *E. faecalis* (n=13); moose (n=3), red deer (n=5) and roe deer (n=5), and *E. faecium* (n=6); red deer (n=3) and roe deer (n=3). Distribution of MICs (mg/L) is given as number of isolates.

Substance	Isolate	Number resistant	Distribution (N) of MIC values (mg/L)														
			0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	≥ 2048
Oxytetracycline	*E. faecalis*	1				8	4						1				
	E. faecium	1				2	3						1				
Chloramphenicol	*E. faecalis*	0						3	9	1							
	E. faecium	0								6							
Ampicillin	*E. faecalis*	0			2	11											
	E. faecium	0		1		1	4										
Erythromycin	*E. faecalis*	1			2	1	2	7				1					
	E. faecium	4			1	1			4								
Streptomycin	*E. faecalis*	1									1	1	8			2	1
	E. faecium	1										2	1	2			1
Gentamicin	*E. faecalis*	0							1	8	4						
	E. faecium	1							3			2				1	
Neomycin	*E. faecalis*	0								1	1	8	2			1	
	E. faecium	0						1	2			2	1				
Vancomycin	*E. faecalis*	0				1	9	2	1								
	E. faecium	0			2	4											
Bacitracin	*E. faecalis*	1				1				5	6	1					
	E. faecium	0								1	5						
Avilamycin	*E. faecalis*	0				4	6	3									
	E. faecium	0				2		4									
Virginiamycin	*E. faecalis**						1					8	4				
	E. faecium	3			2	1						3					
Flavomycin	*E. faecalis*	1					3	6	2	1				1			
	*E. faecium**								1	1	1			3			
Narasin	*E. faecalis*	0	1	3	9												
	E. faecium	0		1	2	3											

Bold vertical lines denote breakpoints for resistance. White fields denote range of dilutions tested for each antimicrobial. MIC-values higher than the highest concentration tested for are given as the lowest MIC-value above the range. MIC-values equal to or lower than the lowest concentration tested are given as the lowest tested concentration.
**E. faecalis* inherentyly resistant to virginiamycin and *E. faecium* inherently resistant to flavomycin.

COMMENTS

The occurrence of resistance in generic *E. coli* from wild cervids was very low. The resistance frequencies were considerably lower as compared to the levels observed in generic faecal *E. coli* from cattle, pigs and poultry in Norway. However, the data for cervids are similar to what was observed for *E. coli* from ovine meat samples in NORM-VET 2001 (originated mostly from lambs). In Norway, lamb production is very extensive, and the lambs spend a large part of their lives roaming freely on rough, upland grazing. Thus, similar to wild cervids, lambs in Norway experience a minimal exposure to antimicrobials.

The antimicrobials to which resistance was observed were oxytetracycline, trimethoprim, sulfamethoxazole and streptomycin. All these drugs are commonly used for therapy in Norwegian husbandry. It is biologically plausible that resistant bacteria from animal husbandry contaminate the environment from which resistant isolates and/or mobile genetic elements harbouring resistance genes are spread to wild cervids. Contamination may also originate from sludge and different kinds of waste, including sewage from humans and food leftovers. Furthermore, wild cervids may be exposed to antimicrobial residues in the environment that may select for resistant strains. Such residues may originate from antimicrobial use in agriculture, pets or human medicine.

The *E. coli* isolates from moose were susceptible to all antimicrobials included. One of the *E. coli* isolates from red deer was resistant to two antimicrobials (sulfamethoxazole and streptomycin). Of the *E. coli* isolates from roe deer, one isolate was resistant to oxytetracycline, whereas another was resistant to oxytetracycline, sulfamethoxazole and trimethoprim.

The number of enterococcal isolates included was too low to obtain a good indication of the resistance situation. Nevertheless, the data indicate a relatively low occurrence of resistance in enterococci from wild cervids in Norway, and furthermore that the same resistance traits as can be observed in isolates from animal husbandry, pets or humans may be encountered in enterococci from wild cervids.

Escherichia coli from feed

A total of 90 isolates of *Escherichia coli* from dog feed were susceptibility tested; 71 from feed of Norwegian origin and 19 from feed of foreign or unknown origin. The results are presented in table 19.

TABLE 19. Antimicrobial resistance in *Escherichia coli* from dog feed (n=90).

Substance	% Resistant		Distribution (%) of MIC values (mg/L)														
	[95% CI*]		0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Tetracycline	6	[1.8-12.5]					1.1	32.2	60.0	1.1				1.1	4.4		
Chloramphenicol	1	[0.0-6.0]							11.1	86.7	1.1						1.1
Kanamycin	1	[0.0-4.0]							37.8	55.6	3.3	2.2					1.1
Ampicillin	4	[1.2-11.0]						1.1	28.9	63.4	2.2			1.1		1.1	2.2
Cefuroxime	0	[0.0-4.0]						3.3	41.1	52.2	2.2	1.1					
Trimethoprim	6	[1.8-12.5]			1.1	4.4	23.3	60.0	5.6				1.1	4.4			
Sulfamethoxazole	7	[2.5-14.0]									2.2	10.0	31.1	37.8	12.2		6.7
Streptomycin	7	[2.5-14.0]						1.1	55.6	27.8	2.2	4.4	2.2	2.2	3.3	1.1	
Gentamicin	0	[0.0-4.0]				22.2	77.7										
Enrofloxacin	0	[0.0-4.0]	2.2	41.2	53.3	3.3											
Nalidixic acid	0	[0.0-4.0]							16.6	70.0	12.2	1.1					

Bold vertical lines denote breakpoints for resistance. White fields denote range of dilutions tested for each antimicrobial. MIC-values higher than the highest concentration tested for are given as the lowest MIC-value above the range. MIC-values equal to or lower than the lowest concentration tested are given as the lowest tested concentration.

*CI = Confidence Interval

COMMENTS

A moderate occurrence of resistance was observed in *E. coli* from dog feed. In total, 22% of the isolates were resistant to at least one of the antimicrobials included in the test panel; 1% to one, 2% to two and 6% to three or more antimicrobials. Of the five multiresistant isolates, three were of Norwegian and two of unknown origin.

Resistance to sulfamethoxazole, streptomycin, trimethoprim, oxytetracycline, and ampicillin, respectively, was most common. One of the isolates of Norwegian origin was resistant to chloramphenicol, whereas another Norwegian isolate was resistant to kanamycin. No preparations containing kanamycin are approved for veterinary use in Norway. All veterinary preparations containing chloramphenicol were withdrawn from the Norwegian market in 1992.

The results obtained are comparable to what was observed for dog feed in NORM-VET 2000 and NORM-VET 2001.

C. ZOONOTIC AND OTHER ENTEROPATHOGENIC BACTERIA

Zoonotic and other enteropathogenic bacteria represent a considerable public health problem. Furthermore, the increasing occurrence of antimicrobial resistance in such bacteria is a major public health concern. Therefore, it is of utmost importance to monitor the occurrence of antimicrobial resistance in zoonotic and other enteropathogenic bacteria at various stages in the farm-to-fork continuum.

In Norway, all *Salmonella* isolates from feed, animals and food are monitored for antimicrobial resistance as well as *Campylobacter* isolates from broiler and broiler meat. Regarding human isolates, all *Salmonella, Shigella* and *Yersinia enterocolitica* isolates are monitored, as well as a representative number of *Campylobacter* isolates.
Sampling, laboratory methods and data processing are described in Appendix 4.

SALMONELLA

Salmonella spp. from animals, feed and food

The situation regarding *Salmonella* spp. in food production animals in Norway is very good. Such animals are virtually free from *Salmonella* spp. except for an endemic occurrence of *S. enterica* subsp. *diarizonae* in sheep. To document this favourable situation, Norway runs an extensive surveillance programme that covers both live animals (cattle, pigs, and poultry) and meat (cattle, pigs, sheep and poultry). The *Salmonella* isolates examined in NORM-VET include those that might be detected in this programme in addition to isolates from other relevant projects and clinical submissions to the National Veterinary Institute.
In 2002, only five isolates of *Salmonella* were detected in the surveillance programme; four isolates of *S.* Typhimurium from pigs and one *S.* Javiana from cattle. All were susceptible to all antimicrobials included.
Multiresistant *S.* Typhimurium DT 104 (ACSSuT) was isolated from a horse on a farm in contact with a cattle farm on which the same strain was detected in 2001. A clinical strain of *S.* Typhimurium, not phagetypable, was cultured from a dog. This was resistant to oxytetracycline, ampicillin, sulfamethoxazole and streptomycin. A clinical *S.* Typhimurium strain that was isolated from a parrot was susceptible to all antimicrobials included.
A total of 21 isolates of *S. enterica* subsp. *diarizonae* from healthy sheep were susceptibility tested. In addition, a total of 27 *Salmonella* isolates from a project aiming to determine the hygienic conditions in feed mills, were isolated from the environment of the mills or from produced feed (n=25) as well as from seagulls (n=2) found nearby one of the mills. The results are presented in table 20.

COMMENTS
The isolation of multiresistant *S.* Typhimurium DT104 from the abovementioned horse illustrates the importance of following up all possible contacts when this variant has been isolated on a farm. Apart from this incident, only few isolates of *S.* Typhimurium were detected in food producing animals in 2002, and these were all susceptible to the antimicrobials included. There is reason to believe that the contamination in the latter cases originated from the surrounding environment. In NORM-VET 2001, *S.* Typhimurium from wild birds and a hedgehog were included, and these were all susceptible except one isolate being resistant to sulfamethoxazole. This indicates that the occurrence of antimicrobial resistance among strains of *S.* Typhimurium that occur endemically in the Norwegian wildlife and that may sometimes infect food-producing animals is low.
The data, although based on few isolates, indicate that resistance is not widespread among *S. enterica* subsp. *diarizonae* that occur endemically in the Norwegian sheep population. This is in accordance with the results presented in NORM-VET 2001.
All isolates from the feed mills were susceptible to all antimicrobials included in the test panel except one streptomycin resistant isolate.

TABLE 20. Antimicrobial resistance in *Salmonella enterica* subsp. *diarizonae* from sheep (n=21) and *S. enterica* subsp. *enterica* (*S.* Agona (n=8), *S.* Montevideo (n=6), *S.* Kentucky (n=2) and *S.* Senftenberg (n=9)) from feed mills (n=25) and from seagulls (*S.* Montevideo (n=2)).

Substance	Sample type	Number resistant	Distribution (n) of MIC values (mg/L)													
			0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline	Sheep	0					15	6								
	Feeding mills*	0					9	18								
Chloramphenicol	Sheep	0					1	10	10							
	Feeding mills*	0							13	14						
Florfenicol	Sheep	0						11	10							
	Feeding mills*	0							3	21	3					
Ampicillin	Sheep	0				8	12		1							
	Feeding mills*	0					19	8								
Ceftiofur	Sheep	0				20	1									
	Feeding mills*	0				2	22	3								
Trimethoprim	Sheep	0			9	12										
	Feeding mills*	0			10	14	3									
Sulfamethoxazole	Sheep	0											21			
	Feeding mills*	0											27			
Streptomycin	Sheep	0								1	16	4				
	Feeding mills*	1							1	11	13	1	1			
Gentamicin	Sheep	0			2	19										
	Feeding mills*	0				5	20	2								
Neomycin	Sheep	0					21									
	Feeding mills*	0					8	17	2							
Apramycin	Sheep	0					16	5								
	Feeding mills*	0						1	13	13						
Enrofloxacin	Sheep	0	20	1												
	Feeding mills*	0	21	6												
Nalidixic acid	Sheep	0							18	3						
	Feeding mills*	0							18	9						

Bold vertical lines denote breakpoints for resistance. White fields denote range of dilutions tested for each antimicrobial. MIC-values higher than the highest concentration tested for are given as the lowest MIC-value above the range. MIC-values equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Distribution of MICs (mg/L) is given as number of isolates.
*Including two isolates of *S.* Montevideo from seagulls

Salmonella from human clinical specimens

In 2002, 1,495 human cases of salmonellosis, excluding typhoid and paratyphoid fever, were reported in Norway (incidence rate 33.0 per 100 000). In 75% of the cases, the infection was reported as having been acquired abroad, whereas for 16% the infection was classified as domestically acquired. For the remaining cases, the place of acquisition was unknown. For *S.* Enteritidis, the proportion of cases reported as imported was particularly high - 84%. *S.* Enteritidis has never been detected in Norwegian poultry. About 50% of the *S.* Typhimurium infections were acquired in Norway, which is partly explained by the endemic occurrence of specific clones of this serovar in Norwegian wildlife. Data from surveillance programmes show that domestically produced food is not an important source of human salmonellosis acquired in Norway. The most likely sources in these cases are direct or indirect contamination from wildlife, imported food products, or secondary infections from other patients.

Thus, the isolates categorized as "infected in Norway" also partly reflect the resistance situation outside Norway.
One domestic outbreak of *S.* Typhimurium infection occurred in Norway in 2002; 48 confirmed cases in the Bergen area were associated with contact with hedgehogs.
For the *S.* Typhimurium infections acquired domestically, 8% of the isolates were caused by multiresistant DT104, as opposed to 16% for those *S.* Typhimurium infections acquired abroad. Of the multiresistant DT104 isolates with a known place of acquisition, 36% were acquired in Norway.
The proportion of DT104 among the domestically acquired *S.* Typhimurium isolates was reduced as compared to 2001, which is explained by the occurrence of a domestic outbreak of DT104-infections (28 confirmed cases) caused by imported helva in Norway in 2001.
In 2002, a total of 974 *Salmonella* isolates from humans, 205 isolates of *S.* Typhimurium and 769 isolates of *S.* Enteritidis, were susceptibility tested. The results are presented in tables 21 and 22 and figure 12.

TABLE 21. Antimicrobial resistance in *Salmonella* Typhimurium excluding DT104 from patients infected in Norway (n=83) and abroad (n=92), *S.* Typhimurium DT104 (n=30, including 10 from patients infected in Norway, 15 from patients infected abroad and 5 from patients with unknown place of infection), and *S.* Enteritidis from all patients (n=833, including 737 from patients infected abroad, 38 from patients infected in Norway, and 58 from patients with unknown place of infection).

Substance	Species**	Place of acquisition	Breakpoints (mm) S	Breakpoints (mm) R	Proportion of isolates (%)* S	Proportion of isolates (%)* I	Proportion of isolates (%)* R	Range (mm)		
Tetracycline	ST	Norway	≥ 21	≤ 17	83.1	1.2	15.7	6	-	30
	ST	Abroad			62.0	1.1	37.0	6	-	32
	DT104	All			0.0	0.0	100	8	-	12
	SE	All			94.1	0.8	5.0	6	-	≥ 36
Chloramphenicol	ST	Norway	≥ 24	≤ 23	81.9	-	18.1	6	-	≥ 36
	ST	Abroad			73.9	-	26.1	6	-	35
	DT104	All			0.0	-	100	6	-	6
	SE	All			98.0	-	2.0	6	-	≥ 36
Ampicillin	ST	Norway	≥ 25	≤ 11	75.9	9.6	14.5	6	-	34
	ST	Abroad			57.6	16.3	26.1	6	-	32
	DT104	All			0.0	0.0	100	6	-	6
	SE	All			80.0	15.4	4.7	6	-	≥ 36
TMS***	ST	Norway	≥ 26	≤ 19	94.0	2.4	3.6	6	-	≥ 36
	ST	Abroad			87.0	1.1	12.0	6	-	≥ 36
	DT104	All			100	0.0	0.0	27	-	34
	SE	All			96.4	0.2	3.4	6	-	≥ 36
Ciprofloxacin	ST	Norway	≥ 29	≤ 19	98.8	1.2	0.0	25	-	≥ 36
	ST	Abroad			90.2	8.7	1.1	17	-	≥ 36
	DT104	All			93.3	6.7	0.0	28	-	≥ 36
	SE	All			88.5	11.5	0.0	20	-	≥ 36
Nalidixic acid	ST	Norway	≥ 17	≤ 16	100	-	0.0	21	-	30
	ST	Abroad			89.1	-	10.9	6	-	30
	DT104	All			76.7	-	23.3	6	-	30
	SE	All			77.5	-	22.5	6	-	≥ 36

*S=Susceptible, I=Intermediately susceptible, R=Resistant. The breakpoints are according to the AFA recommendations for 2003.
** ST=*S.* Typhimurium excluding DT104, DT104=*S.* Typhimurium phagetype DT104, SE= *S.* Enteritidis
***TMS=Trimethoprim/sulfamethoxazole

COMMENTS

The breakpoints applied for *Salmonella* spp., *Yersinia enterocolitica and Shigella* spp. in this report are the ones currently recommended by AFA. These are different from the ones applied in NORM/NORM-VET 2001. For chloramphenicol and tetracycline in particular, the current breakpoints seems to be more in accordance with MIC-distributions and thus give a more correct picture of the situation. Consequently, the proportion of isolates classified as intermediately susceptible to these two drugs has decreased significantly from 2001 to 2002. However, based on the MIC-distributions it seems that the resistance breakpoint for chloramphenicol (Table 22) is still not optimal and perhaps should be lowered to somewhere in the range of 17-20 mm. Furthermore, based on the MIC-distributions it also seems that the susceptibility breakpoint for ampicillin ought to be lowered to about 20 mm.

The proportion of *S.* Typhimurium isolates (excluding DT104) susceptible to all antimicrobials was higher for the category "infected in Norway" (72%) than for the "infected abroad" category (53%) (Figure 12). For the category "infected in Norway", 14% of the isolates were resistant to one antimicrobial (predominantly chloramphenicol), 5% to two (tetracycline and ampicillin), 6% to three (tetracycline, ampicillin and chloramphenicol) and 2% to four antimicrobials. For the category "infected abroad", 16% of the isolates were resistant to one antimicrobial (mostly tetracycline or chloramphenicol), 9% to two (mostly tetracycline and ampicillin), 12% to three (mostly tetracycline, ampicillin and chloramphenicol) and 10% to four or more antimicrobials. Thus, multiresistance was more common in the category "infected abroad" (22%) as compared to the category "infected in Norway" (8%). A significant discrepancy for the two categories was observed for quinolones; in the category "infected abroad" 10.9% and 1.1% of the isolates were resistant to nalidixic acid and ciprofloxacin, respectively, as opposed to none among those from patients "infected in Norway". One of the 10 isolates classified as resistant to nalidixic acid was also resistant to ciprofloxacin, and six of them expressed reduced susceptibility to ciprofloxacin indicating that fluoroquinolone resistance might be developing. It is emphasized that the use of fluoroquinolones in Norway is limited in both human and veterinary medicine.

The resistance profiles for the multiresistant DT104 isolates were almost identical for isolates acquired in Norway and those acquired abroad. All isolates were resistant to ampicillin, tetracycline, streptomycin, sulfonamides and chloramphenicol. In addition, 23% of the isolates were resistant to nalidixic acid (27% of those acquired abroad, 30% of those acquired in Norway, and none of those with an unknown place of acquisition). This is an increase as compared to NORM/NORM-VET 2001 when only 8.7% of the isolates were resistant to nalidixic acid.

The vast majority of the *S.* Enteritidis isolates had been acquired abroad. The proportion of *S.* Enteritidis isolates resistant to tetracycline, chloramphenicol and ampicillin, respectively, was considerably lower than for *S.* Typhimurium including those acquired in Norway. Resistance to nalidixic acid on the other hand was more widespread among *S.* Enteritidis as compared to *S.* Typhimurium (Table 21). Of the nalidixic acid resistant *S.* Enteritidis isolates, 50% showed reduced susceptibility to ciprofloxacin indicating that fluoroquinolone resistance could be developing. In total, 97% of the isolates intermediately susceptible to ciprofloxacin were also

resistant to nalidixic acid. The resistance frequencies observed for *S.* Enteritidis in NORM/NORM-VET 2002 are in accordance with those in NORM/NORM-VET 2001 taking into account the change of breakpoints applied. Fourteen isolates of *S.* Typhi were susceptibility tested. One isolate was resistant to chloramphenicol. Four other isolates were resistant to nalidixic acid, whereas all isolates were susceptible to ciprofloxacin. Eleven isolates of *S.* Paratyphi A were also susceptibility tested. Two isolates were resistant to four antimicrobials (ampicillin, chloramphenicol, tetracycline and trimethoprim/ sulfamethoxazole). Three others were resistant to nalidixic acid, whereas all isolates were susceptible to ciprofloxacin. All infections with the "typhoid/paratyphoid"-group had been acquired outside Norway.

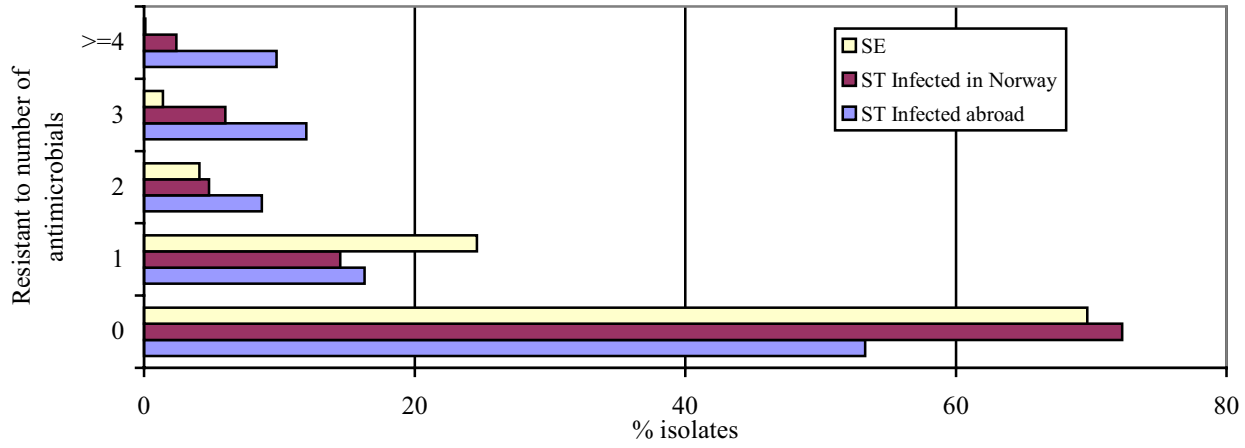


FIGURE 12. Antimicrobial resistance profiles for all *Salmonella* Enteritidis from humans (n=833) and for *Salmonella* Typhimurium (excluding DT104) from humans infected in Norway (n=83) and infected abroad (n=92). Proportion of isolates susceptible to all antimicrobials included and resistant to one, two, three, or four or more antimicrobials.

TABLE 22. Antimicrobial resistance in *Salmonella* Typhimurium excluding DT104 from patients infected in Norway (n=83) and abroad (n=92), *S.* Typhimurium DT104 (n=30) (including 10 from patients infected in Norway, 15 from patients infected abroad and 5 from patients with unknown place of infection), and *S.* Enteritidis (n=833, including 737 from patients infected abroad, 38 from patients infected in Norway, and 58 from patients with unknown place of infection). Distribution (%) of zone diameters (mm).

Substance	Species*	Place of acquisition	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	≥ 36
Tetracycline	ST	Norway	9.6		1.2	2.4	1.2	1.2									1.2		2.4	4.8	13.3	15.7	20.5	10.8	9.6	2.4	3.6						
	ST	Abroad	19.6	7.6		2.2	4.3	1.1				1.1		1.1			1.1	2.2	3.3	1.1	12.0	5.4	14.1	9.8	7.6	2.2	2.2		2.2				
	DT104	All			6.7	26.7	43.3	16.7	6.7																								
	SE	All	3.6	1.3	0.1										0.1	0.1	0.6	0.5	3.0	2.3	7.0	9.7	22.0	15.9	21.2	3.2	7.3	0.1	1.3	0.1	0.2		0.1
Chloramph.**	ST	Norway	7.2															1.2	1.2	8.4	15.7	24.1	15.7	3.6	15.7	3.6	2.4						1.2
	ST	Abroad	14.1	1.1		1.1									1.1			1.1		7.6	15.2	16.3	17.4	13.0	3.3	1.1	4.3		1.1	1.1		1.1	
	DT104	All	100																														
	SE	All	0.2													0.1	0.4	0.3	0.1	1.0	8.9	22.5	21.7	18.5	19.3	2.0	3.6	0.1	0.1	0.1	0.4	0.3	0.5
Ampicillin	ST	Norway	14.5														1.2	1.2	1.2	3.6	2.4	3.6	8.4	12.0	25.3	8.4	15.7		1.2		1.2		
	ST	Abroad	26.1														2.2	2.2	2.2	4.3	5.4	5.4	7.6	8.7	20.7	5.4	6.5	1.1	2.2				
	DT104	All	100																														
	SE	All	4.7								0.1		0.1	0.4	0.5	0.1	1.8	1.0	2.4	1.7	7.2	7.0	13.5	15.1	23.8	6.1	11.5	0.6	1.9		0.3		0.1
TMS***	ST	Norway	3.6																1.2			1.2		1.2	7.2		12.0	7.2	22.9	9.6	20.5	1.2	12.0
	ST	Abroad	10.9													1.1					1.1		2.2	5.4	3.3	2.2	8.7	5.4	15.2	14.1	13	3.3	14.1
	DT104	All																						10.0	13.3	20.0	30.0	6.7	6.7	10.0	3.3		
	SE	All	3.4																0.1		0.1		0.3	1.5	5.1	4.4	15.7	8.9	19.4	10.0	17.0	4.0	10.0
Ciprofloxacin	ST	Norway																				1.2				1.2		1.2	2.4	2.4	10.8	12.0	68.7
	ST	Abroad												1.1								1.1	1.1	2.2	4.3	3.3		1.1	2.2	4.3	7.6	8.7	63
	DT104	All																							6.7	6.7	6.7	3.3				3.3	73.3
	SE	All															0.1					0.3	1.2	2.8	7.2	3.5	5.3	1.4	3.4	3.2	10.4	7.6	53.7
Nalidixic acid	ST	Norway																2.4	3.6	6.0	26.5	28.9	18.1	8.4	3.6	1.2	1.2						
	ST	Abroad	10.9											2.2					4.3	8.7	19.6	18.5	18.5	9.8	2.2	1.1	4.3						
	DT104	All	23.3																		3.3	10.0	23.3	16.7	13.3	6.7	3.3						
	SE	All	22.3								0.1					0.1	0.6	1.0	3.2	8.0	17.7	19.1	18.0	4.9	3.3	0.3	0.8					0.1	0.4

Shaded areas in each row indicate resistance (dark blue), intermediate susceptibility (medium blue) and susceptibility (light blue). The breakpoints are according to the AFA recommendations for 2003.

* ST=*S.* Typhimurium excluding DT104, DT104=*S.* Typhimurium phagetype DT104, SE= *S.* Enteritidis

** Chloramph.= Chloramphenicol

*** TMS= Trimethoprim/sulfamethoxazole.

CAMPYLOBACTER

Campylobacter jejuni from broilers

The isolates of *Campylobacter jejuni* in broilers originate from the Norwegian action plan against *Campylobacter* spp. in broilers (www.zoonose.no). All broiler flocks slaughtered before 50 days of age are tested for the presence of *Campylobacter* spp. In addition, 100 samples of broiler meat products from retail level are tested monthly. In 2002, one isolate per positive farm as well as one isolate from each batch of positive broiler meat products were submitted for susceptibility testing.

A total of 161 isolates, 122 from cloacal samples and 39 from broiler meat, were susceptibility tested. The results are presented in table 23 and figure 13.

TABLE 23. Antimicrobial resistance in *Campylobacter jejuni* (n=161) from broiler cloacal samples (n=122) and from broiler meat products (n=39).

Substance	% Resistant [95% CI*]		Distribution (%) of MIC values (mg/L)													
			0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline	0	[0.0-2.3]				93.8	4.3	1.9									
Ampicillin	3	[1.0-7.1]					7.5	3.1	26.1	48.4	10.6	1.2	0.6	2.5			
Erythromycin	1	[0.2-4.4]			2.5	5.0	36.2	46.2	8.8				1.2				
Gentamicin	0	[0.0-2.3]				10.6	37.3	41.6	10.6								
Enrofloxacin	<1	[0.0-3.4]	4.3	28.0	59.0	5.6	1.2	1.2		0.6							
Nalidixic acid	2	[3.9-5.4]						1.2	16.1	61.5	17.4	1.9			1.9		

Bold vertical lines denote breakpoints for resistance. White fields denote range of dilutions tested for each antimicrobial. MIC-values higher than the highest concentration tested for are given as the lowest MIC-value above the range. MIC-values equal to or lower than the lowest concentration tested are given as the lowest tested concentration.
*CI = Confidence Interval

COMMENTS

The results show that the prevalence of resistance among *C. jejuni* isolates from Norwegian broilers is low (Table 23). There was no significant difference between the isolates from broiler meat products and cloacal samples (Figure 14).

A total of 94.4% of the isolates were susceptible to all antimicrobials included in the test panel. Altogether 4.3% were resistant to one antimicrobial (ampicillin, erythromycin or nalidixic acid) and 1.2% to two antimicrobials (nalidixic acid and erythromycin or enrofloxacin). This corresponds to the usage of antimicrobials in broilers production. Antimicrobials (except coccidiostats) are rarely used, and only for therapeutic purposes. If used, amoxicillin (cross-resistance with ampicillin) and tetracycline are the drugs of choice.

No quinolone preparations are licensed for use in broilers in Norway. However, several are approved for use in broilers in the EU, and may therefore also be used in broiler production in Norway if specifically applied for. The results are similar to what was observed in 2001, although the proportion of isolates resistant to the quinolones was slightly lower in 2002 as compared to 2001.

The level of resistance and the resistance patterns for *C. jejuni* isolated from Norwegian broilers corresponds to what was observed for *C. jejuni* isolated from humans infected within Norway except for a higher prevalence of resistance to quinolones, particularly nalidixic acid, among the human isolates (Figure 13). This relationship was also observed in NORM/NORM-VET 2001.

Campylobacter spp. from human clinical specimens

Of the 2,192 cases of human campylobacteriosis recorded in Norway in 2002 (incidence rate 48.5 per 100 000), 52% were reported as acquired abroad. The vast majority of cases were sporadic. Norwegian case-control studies have revealed that consumption of broiler meat purchased fresh and drinking untreated water are risk factors for domestically acquired campylobacteriosis.

A total of 147 isolates of *C. jejuni*, 37 from patients infected in Norway and 110 from patients infected abroad, as well as 29 isolates of *C. coli* were susceptibility tested. The results are presented in tables 24 and 25 and figure 13.

TABLE 24. Antimicrobial resistance in *Campylobacter jejuni* from patients infected in Norway (n=37) and abroad (n=110) and all *Campylobacter coli* (n=29).

Substance	Species	Place of acquisition	Breakpoints (mg/L) S	Breakpoints (mg/L) R	Proportion of isolates (%)* S	Proportion of isolates (%)* I	Proportion of isolates (%)* R	Range (mg/L)			MIC_{50}	MIC_{90}
Doxycycline	*C. jejuni*	Norway	≤1	≥4	94.6	2.7	2.7	0.047	-	12	0.19	0.5
	C. jejuni	Abroad			41.8	3.6	54.5	0.094	-	256	6	64
	C. coli	All			72.4	0.0	27.6	0.016	-	64	0.25	32
Erythromycin	*C. jejuni*	Norway	≤1	≥4	91.9	5.4	2.7	0.094	-	≥4	0.75	1
	C. jejuni	Abroad			78.2	15.5	6.4	0.25	-	256	0.75	2
	C. coli	All			69.0	20.7	10.3	0.094	-	256	0.75	256
Gentamicin	*C. jejuni*	Norway	≤2	≥8	97.3	2.7	0.0	0.125	-	4	0.5	1
	C. jejuni	Abroad			94.5	3.6	1.8	0.094	-	32	0.75	2
	C. coli	All			100.0	0.0	0.0	0.094	-	2	1	1.5
Ciprofloxacin	*C. jejuni*	Norway	≤0.125	≥4	56.8	40.5	2.7	0.064	-	≥12	0.125	0.38
	C. jejuni	Abroad			16.4	11.8	71.8	0.064	-	32	32	32
	C. coli	All			20.7	13.8	65.5	0.047	-	32	16	32
Nalidixic acid	*C. jejuni*	Norway	≤16	≥32	91.9	0.0	8.1	1	-	≥256	3	16
	C. jejuni	Abroad			28.2	0.0	71.8	1.5	-	256	256	256
	C. coli	All			34.5	0.0	65.5	1.5	-	256	256	256

*S=Susceptible, I=Intermediately susceptible, R=Resistant

TABLE 25. Antimicrobial resistance in *Campylobacter jejuni* from patients infected in Norway (n=37) and abroad (n=110) and all *Campylobacter coli* (n=29). Distribution (%) of MICs (mg/L).*

Substance	Species	Place of acuisition	% Resistant	Distribution (%) of MICs (mg/L).* ≤0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Doxycycline	*C. jejuni*	Norway	2.7	5.4	18.9	56.7	10.8	2.7	2.7			2.7				
	C. jejuni	Abroad	54.5		10.9	18.2	10.0	2.7	3.6	2.7	6.3	7.2	18.2	14.6	1.8	3.6
	C. coli	All	27.6	6.8	24.1	31.0	10.3			3.4	3.4	3.4	10.3	6.9		
Erythromycin	*C. jejuni*	Norway	2.7		2.7		37.8	51.3	5.4	2.7						
	C. jejuni	Abroad	6.4			8.2	25.5	44.6	15.5	4.5						1.8
	C. coli	All	10.3		3.4	10.3	34.5	20.7	20.7							10.3
Gentamicin	*C. jejuni*	Norway	0.0		5.4	8.1	40.5	37.8	5.4	2.7						
	C. jejuni	Abroad	1.8		3.6	11.8	26.4	34.5	18.2	3.6	0.9		0.9			
	C. coli	All	0.0		3.4	10.3	17.2	44.8	24.1							
Ciprofloxacin	*C. jejuni*	Norway	2.7	10.8	45.9	32.4	8.1					2.7				
	C. jejuni	Abroad	71.8	0.9	15.4	9.1	1.8		0.9	0.9			70.9			
	C. coli	All	65.5	10.3	10.3	13.8					6.9	10.3	48.3			
Nalidixic acid	*C. jejuni*	Norway	8.1					2.7	37.8	43.2	5.4	2.7				8.1
	C. jejuni	Abroad	71.8						9.1	15.4	2.7	0.9				71.8
	C. coli	All	65.5						10.3	24.1						65.5

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue). Non-shaded areas represent MIC values that are not covered by the standard test method.

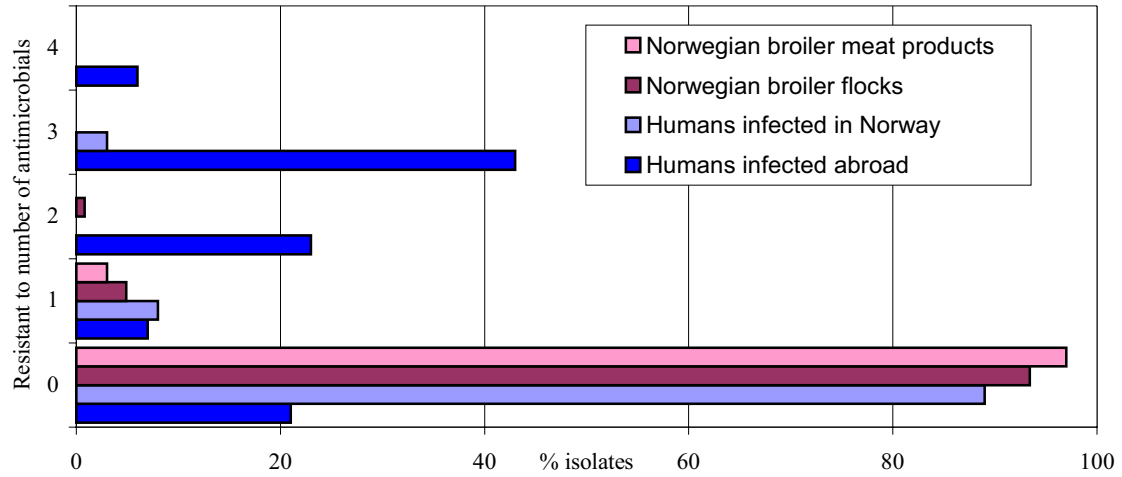


FIGURE 13. Antimicrobial resistance profiles for *Campylobacter jejuni* from Norwegian broiler flocks (n=122), Norwegian broiler meat products (n=39), humans infected in Norway (n=37) and humans infected abroad (n=110). Proportion of isolates susceptible to all antimicrobials included or resistant to one, two, three, or four or more of the antimicrobials. The human isolates were tested for susceptibility to doxycycline, erythromycin, gentamicin, ciprofloxacin and nalidixic acid, whereas the broiler/meat isolates in addition were tested for susceptibility to ampicillin and oxytetracycline rather than doxycycline.

COMMENTS

The data show that resistance was significantly more widespread among the *C. jejuni* isolates derived from patients infected abroad (21% susceptible to all antimicrobials included in the test panel) than patients infected in Norway (89% susceptible to all antimicrobials included) (Table 24). These discrepancies are explained by the widespread occurrence among isolates acquired abroad of resistance to ciprofloxacin/nalidixic acid (71.8% versus 2.7/8.1%) and to tetracycline (54.5% versus 2.7%) (Table 24).

The resistance frequencies for domestically acquired human isolates are in accordance with data for Norwegian broilers, although resistance to quinolones, particularly nalidixic acid, was more prevalent among the human isolates (Figure 14).

Only two of the 29 isolates of *C. coli* were acquired in Norway. In total, 76% of the *C. coli* isolates were resistant to at least one of the antimicrobials included, and 66% were resistant to two antimicrobials or more. Resistance to quinolones was widespread; 66% of the isolates were resistant to both nalidixic acid and ciprofloxacin (Table 24). *C. coli* is typically associated with pigs and pork

Yersinia enterocolitica from human clinical specimens

Most cases of *Yersinia enterocolitica* infection in Norway are domestically acquired. In 2002, only 24 % of the 117 reported cases were classified as imported.

A total of 53 isolates of *Y. enterocolitica* were susceptibility tested. The results are presented in tables 26 and 27.

TABLE 26. Antimicrobial resistance in *Yersinia enterocolitica* serogroup 0:3 from human clinical cases (n=53).

Substance	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 21	≤ 17	92.5	1.9	5.7	6 - 36
Chloramphenicol	≥ 24	≤ 23	83.0	-	17.0	6 - 36
Ampicillin	≥ 25	≤ 11	0.0	3.8	96.2	6 - 19
TMS**	≥ 26	≤ 19	77.4	11.3	11.3	6 - 36
Ciprofloxacin	≥ 29	≤ 19	90.6	7.5	1.9	18 - 36
Nalidixic acid	≥ 17	≤ 16	94.3	-	5.7	6 - 36

*S=Susceptible, I=Intermediately susceptible, R=Resistant. The breakpoints are according to the AFA recommendations for 2003.
**TMS=Trimethoprim/sulfamethoxazole.

COMMENTS

Compared to data from 2001 and taking into account the change of breakpoints applied, the resistance frequencies are quite similar, except for an increase in tetracycline resistance from 1.1% in 2001 to 5.7% in 2002.

All isolates expressed reduced susceptibility to ampicillin, an intrinsic resistance trait in strains of serogroup O:3.

TABLE 27. Antimicrobial resistance in *Yersinia enterocolitica* serogroup O:3 (n=53), *Shigella sonnei* (n= 51), *S. flexneri* (n=46) and *S. boydii* (n=18) from human clinical cases. Distribution (%) of zone diameters (mm).

Substance	Species*	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	≥ 36
Tetracycline	*Y. ent.*	3.8									1.9					1.9	1.9	1.9			5.7	1.9	9.4	13.2	7.5	20.8	1.9	15.1	5.7	1.9		5.7
	S. sonnei	72.5					2.0														3.9	11.8	2.0	7.8								
	S. flexneri	76.1	8.7																							13.0	2.2					
	S. boydii	55.6																		5.6			5.6	16.7		16.7						
Chloramph.**	*Y. ent.*	15.1														1.9				1.9	3.8	5.7	9.4	18.9	5.7	17.0	5.7	5.7		5.7		3.8
	S. sonnei	2.0																	2.0	13.7	9.8	17.6	15.7	29.4		7.8		2.0				
	S. flexneri	58.7	8.7	2.2		4.3	2.2															2.2						2.2	2.2	4.3		13.0
	S. boydii	5.6																				5.6	5.6			11.1		22.2	5.6	16.7	16.7	11.1
Ampicillin	*Y. ent.*	60.4	11.3	13.2	5.7	5.7						1.9			1.9																	
	S. sonnei	9.8					2.0					2.0	2.0	3.9	2.0	3.9	11.8	21.6	23.5	13.7	3.9											
	S. flexneri	80.4																2.2				4.3	4.3	6.5			2.2					
	S. boydii	11.1													5.6	5.6				16.7	27.8	22.2	5.6	5.6								
TMS***	*Y. ent.*	1.9								1.9	1.9	1.9		1.9	1.9			3.8	1.9		5.7	1.9	5.7	3.8	5.7	11.3	3.8	15.1	5.7	7.5		17.0
	S. sonnei	78.4						2.0			3.9												2.0					3.9	2.0	5.9		2.0
	S. flexneri	67.4																		4.3	2.2				2.2	2.2	2.2	6.5	2.2			10.9
	S. boydii	55.6														5.6							5.6	5.6		5.6	5.6			5.6		11.1
Ciprofloxacin	*Y. ent.*													1.9				1.9				3.8		1.9		7.5	1.9	5.7	11.3	7.5	3.8	52.8
	S. sonnei																					2.0		3.9		3.9	2.0		2.0	2.0	3.9	80.4
	S. flexneri	4.3																		4.3						2.2		2.2	8.7		4.3	73.9
	S. boydii																													5.6		94.4
Nalidixic acid	*Y. ent.*	5.7												1.9		1.9				1.9	1.9	9.4	9.4	15.1	13.2	20.8	1.9	9.4	3.8	1.9		1.9
	S. sonnei	7.8	2.0	2.0																	2.0	3.9	5.9	15.7	11.8	33.3	7.8	5.9	2.0			
	S. flexneri	15.2		2.2															2.2		4.3		10.9	4.3	10.9	19.6	13.0	8.7	6.5		2.2	
	S. boydii																						5.6	5.6	22.2	16.7	16.7	22.2	5.6			5.6

Shaded areas in each row indicate resistance (dark blue), intermediate susceptibility (medium blue) and susceptibility (light blue). The breakpoints are according to the AFA recommendations for 2003.

* *Y. ent. = Yersinia enterocolitica*

** Chloramph.= Chloramphenicol

*** TMS= Trimethoprim/sulfamethoxazole

Shigella spp. from human clinical specimens

It is emphasized that almost all the reported *Shigella* infections in Norway were acquired abroad, mostly in Egypt, India, Pakistan and Turkey. In 2002, only 8.9% of the reported shigellosis cases were classified as domestically acquired. Moreover, most of these are believed to be secondary cases to patients infected abroad. Thus, the resistance frequencies reported here predominantly relate to isolates originating in other countries.

The distribution of the *Shigella* species included in 2002 was as follows: *S. sonnei* 51 (43%), *S. flexneri* 46 (39%), *S. boydii* 18 (15%), and *S. dysenteriae* 4 (3%).

A total of 115 isolates of *Shigella* spp., 51 *S. sonnei*, 46 *S. flexneri* and 18 *S. boydii*, were susceptibility tested. The results are presented in table 28.

TABLE 28. Antimicrobial resistance in *S. sonnei* (n=51), *S. flexneri* (n=46) and *S. boydii* (n=18) from human clinical cases.

Substance	Species	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)		
		S	R	S	I	R			
Tetracycline	*S. sonnei*	≥ 21	≤ 17	25.5	0.0	74.5	6	-	28
	S. flexneri			15.2	0.0	84.8	6	-	31
	S. boydii			44.4	0.0	55.6	6	-	30
Chloramphenicol	*S. sonnei*	≥ 24	≤ 23	96.1	-	3.9	6	-	32
	S. flexneri			23.9	-	76.1	6	-	≥36
	S. boydii			94.4	-	5.6	6	-	≥36
Ampicillin	*S. sonnei*	≥ 25	≤ 11	3.9	84.3	11.8	6	-	25
	S. flexneri			17.4	2.2	80.4	6	-	31
	S. boydii			61.1	27.8	11.1	6	-	28
TMS**	*S. sonnei*	≥ 26	≤ 19	15.7	0.0	84.3	6	-	≥36
	S. flexneri			26.1	6.5	67.4	6	-	≥36
	S. boydii			38.9	5.6	55.6	6	-	≥36
Ciprofloxacin	*S. sonnei*	≥ 29	≤ 19	94.1	5.9	0.0	26	-	≥36
	S. flexneri			91.3	4.3	4.3	6	-	≥36
	S. boydii			100.0	0.0	0.0	34	-	≥36
Nalidixic acid	*S. sonnei*	≥ 17	≤ 16	88.2	-	11.8	6	-	33
	S. flexneri			82.6	-	17.4	6	-	35
	S. boydii			100.0	-	0.0	27	-	≥36

*S=Susceptible, I=Intermediately susceptible, R=Resistant. The breakpoints are according to the AFA recommendations for 2003.
**TMS=Trimethoprim/sulfamethoxazole

COMMENTS

As is the case in reports from other countries, resistance is widespread among *Shigella* isolates, regardless of the species. The resistance frequencies were particularly high for tetracycline and trimethoprim/ sulfamethoxazole, followed by ampicillin and chloramphenicol. These drugs are commonly used for various clinical purposes within human medicine in many parts of the world. For ampicillin and chloramphenicol there were species differences as resistance was highly prevalent among *S. flexneri* and less prevalent among *S. boydii* and *S. sonnei*.

Resistance to fluoroquinolones was not widespread, and only observed among *S. flexneri*. However, a considerable proportion of the *S. flexneri* and *S. sonnei* isolates were resistant to nalidixic acid, many of which also showed reduced susceptibility to ciprofloxacin, indicating that fluoroquinolone resistance might be developing. This picture is strengthened as compared to the data in NORM/NORM-VET 2001.

D. BACTERIA FROM HUMAN CLINICAL SPECIMENS

Escherichia coli in blood cultures

TABLE 29. *Escherichia coli* blood culture isolates (n=973). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Ampicillin	≤ 1	≥ 32	4.7	68.8	26.5	0.125 - ≥ 256	4	≥ 256
Amoxi/Clav**	≤ 0.5	≥ 32	0.6	97.2	2.2	0.125 - ≥ 256	4	8
Cefpirome	≤ 1	≥ 32	99.7	0.2	0.1	0.016 - ≥ 256	0.032	0.125
Ceftazidime	≤ 1	≥ 32	98.9	0.9	0.2	0.016 - 32	0.125	0.25
Cefuroxime	≤ 1	≥ 32	6.6	92.0	1.4	0.016 - ≥ 256	4	4
Ciprofloxacin	≤ 0.125	≥ 4	95.5	2.3	2.2	0.002 - ≥ 32	0.016	0.032
Gentamicin	≤ 2	≥ 8	98.4	0.4	1.2	0.016 - ≥ 256	0.5	1
Meropenem	≤ 0.5	≥ 4	100.0	0.0	0.0	0.004 - 0.25	0.016	0.032
Pip/Tazo***	≤ 8	≥ 32	99.0	0.4	0.6	0.016 - ≥ 256	2	4
TMS****	≤ 2	≥ 16	81.2	0.6	18.2	0.004 - ≥ 256	0.064	≥ 32

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**Amoxi/Clav=Amoxicillin/clavulanic acid.
***Pip/Tazo=Piperacillin/tazobactam
****TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 30. *Escherichia coli* blood culture isolates (n=973). Distribution (n) of MICs (mg/L).*

	≤0.008	0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Ampicillin					1		6	39	250	370	42	6	5	1	4	248
Amoxi/Clav**					2		3	42	237	495	136	36	6	1		14
Cefpirome		57	453	363	67	18	10	2	1							2
Ceftazidime		3	16	87	539	283	28	4	4	1	3		3			
Cefuroxime	1	1		1	1	2	8	50	387	435	59	12	5	5	2	2
Ciprofloxacin	443	417	38	9	20	18	2	1	2		3		18			
Gentamicin		1	3	7	57	324	447	102	15	4	2	5			1	4
Meropenem	114	722	118	2	5	11										
Pip/Tazo***		1	1	2	2	4	37	309	513	78	15	4		1	1	4
TMS****	2	42	181	361	117	50	20	11	4	1	5	1	175			

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue). Non-shaded areas represent MIC values that are not covered by the standard test method.
**Amoxi/Clav=Amoxicillin/clavulanic acid.
***Pip/Tazo=Piperacillin/tazobactam
****TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS

The isolates were generally susceptible to all classes of broad-spectrum antimicrobials, including aminoglycosides, quinolones, cephalosporins and carbapenems. The prevalence of ciprofloxacin- and gentamicin resistant *E. coli* isolates was low and similar to the NORM results previously reported (Figure 14 and 15). Ampicillin resistance, commonly caused by production of a plasmid-mediated β-lactamase (TEM-type) was slightly higher among blood culture isolates (26.5%) compared to urinary tract isolates (24.8%). Eleven isolates were reported to have MIC ≥ 2 mg/L for ceftazidime and/or cefpirome. All isolates were specifically examined for the presence of extended-spectrum β-lactamase (ESBL) production by a disc approximation test and combination Etests. Three of the suspected isolates produced ESBL and originated from different hospitals. Two of the isolates had MIC ≥ 256 mg/L for cefpirome, MIC ≥ 24 mg/L for ceftazidime and were highly resistant to ciprofloxacin (MIC ≥ 32 mg/L) and gentamicin (MIC mg/L ≥ 128). Six isolates were reported to have MICs ≥ 32 mg/L for piperacillin/ tazobactam. Norwegian breakpoints are similar to NCCLS and isolates are considered susceptible when MIC is ≤ 8 mg/L and resistant when MIC is ≥ 32 mg/L. These isolates were further examined by the laboratory of K-Res. Typically, β-lactamase production in these high-level piperacillin resistant strains was not reversed by tazobactam, indicating a possible hyperproduction of β-lactamases. Tazobactam seemed to be a less potent inhibitor than clavulanic acid in these isolates. The design of the Etest might also influence the *in vitro* results as the concentration of tazobactam is constant along the full length of the Etest strip,

independent of the piperacillin concentration. In contrast, the ratio of amoxicillin/clavulanic acid is constant at 2:1 along the full length of the Etest strip. As the inhibitor binds irreversibly to the β-lactamases, the relatively reduced amount of tazobactam versus clavulanic acid might not be sufficient to inhibit the β-lactamases. As the majority of the strains were susceptible to 3rd and 4th generation cephalosporins, the results are consistent with a TEM-1 β-lactamase.

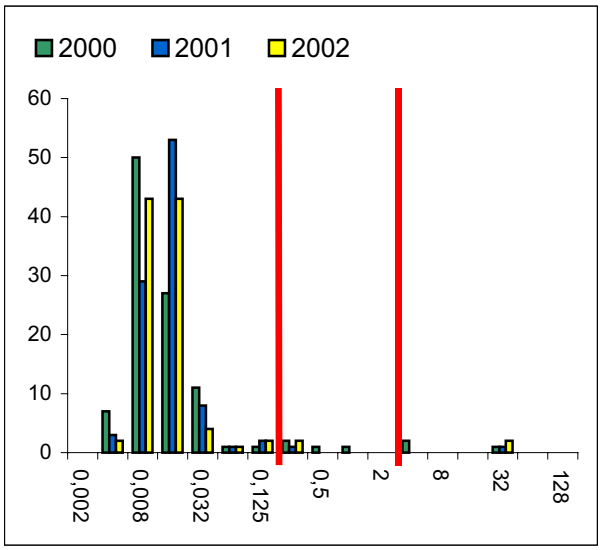


FIGURE 14. Distribution (%) of minimum inhibitory concentrations (MICs) of ciprofloxacin for *E. coli* blood culture isolates surveyed in NORM 2000-2002. AFA breakpoints are shown in red.

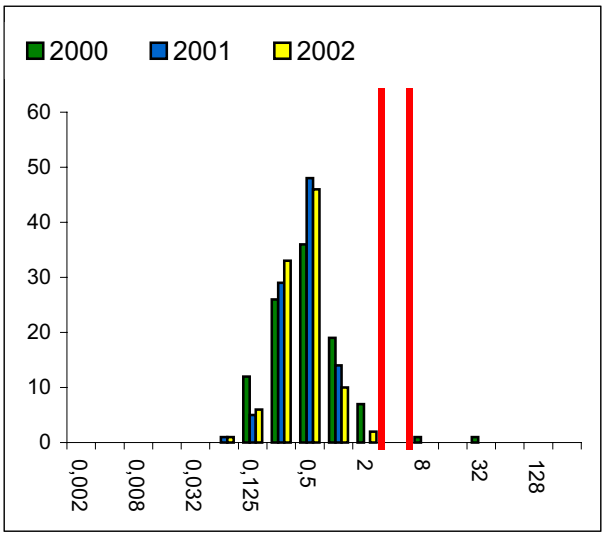


FIGURE 15. Distribution (%) of minimum inhibitory concentrations (MICs) of gentamicin for *E. coli* blood culture isolates surveyed in NORM 2000-2002. AFA breakpoints are shown in red.

Klebsiella spp. in blood cultures

TABLE 31. *Klebsiella* spp. blood culture isolates (n=327). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Ampicillin	≤ 1	≥ 32	1.2	46.0	52.8	1 - ≥ 256	32	≥ 256
Amoxi/Clav**	≤ 0.5	≥ 32	1.3	97.2	1.5	0.25 - ≥ 256	2	4
Cefpirome	≤ 1	≥ 32	99.4	0.3	0.3	0.016 - 128	0.032	0.125
Ceftazidime	≤ 1	≥ 32	98.2	1.5	0.3	0.016 - 32	0.125	0.5
Cefuroxime	≤ 1	≥ 32	33.7	64.7	1.6	0.032 - ≥ 256	2	4
Ciprofloxacin	≤ 0.125	≥ 4	94.5	4.9	0.6	0.004 - ≥ 32	0.032	0.064
Gentamicin	≤ 2	≥ 8	98.8	0.3	0.9	0.032 - 128	0.5	0.5
Meropenem	≤ 0.5	≥ 4	100.0	0.0	0.0	0.008 - 0.064	0.032	0.032
Pip/Tazo***	≤ 8	≥ 32	95.7	1.5	2.8	0.032 - ≥ 256	2	4
TMS****	≤ 2	≥ 16	95.4	0.6	4.0	0.016 - 64	0.125	0.5

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**Amoxi/Clav=Amoxicillin/clavulanic acid.
***Pip/Tazo=Piperacillin/tazobactam
****TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 32. *Klebsiella* spp. blood culture isolates (n=327). Distribution (n) of MICs (mg/L).*

	≤ 0.004	0.008	0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Ampicillin									4	7	15	45	83	84	33	9	46
Amoxi/Clav**							1	3	96	169	40	11	2	4		1	
Cefpirome			15	160	106	28	10	4	2		1					1	
Ceftazidime			3	19	85	132	48	20	13	3	1	1		1			
Cefuroxime				1		3	4	20	82	145	41	12	13	1	2		2
Ciprofloxacin	3	35	99	125	34	13	10	6			1			1			
Gentamicin				4	2	19	122	150	24	1	1		1		1	1	
Meropenem		5	130	180	12												
Pip/Tazo***				1		1	3	14	59	153	67	15	5	2			7
TMS****			1	41	99	109	43	10	7	2	2		1	12			

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue). Non-shaded areas represent MIC values that are not covered by the standard test method.
**Amoxi/Clav=Amoxicillin/clavulanic acid.
***Pip/Tazo=Piperacillin/tazobactam
****TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS

The 327 *Klebsiella* spp blood culture isolates included 214 *K. pneumoniae* subsp. *pneumoniae* and 50 *K. oxytoca*. The remaining 63 isolates were reported as Klebsiella species. Forty-six percent of the isolates were categorized as intermediately susceptible to ampicillin by the general Enterobacteriaceae breakpoints. As *Klebsiella* spp. harbour a chromosomal class A β-lactamase, such isolates should always be reported as resistant even though *in vitro* testing might reveal a low level of resistance. Class A β-lactamases are inhibited by clavulanic acid.

Norwegian breakpoints for piperacillin/tazobactam are similar to the NCCLS breakpoints. Isolates are considered susceptible when the MIC is ≤ 8 mg/L and resistant when MIC is ≥ 32 mg/L. The distribution of MICs to amoxicillin/clavulanic acid and piperacillin/tazobactam is quite similar (Figure 16), both with MIC_{50} = 2 mg/L and MIC_{90} = 4 mg/L. Due to different breakpoints, the proportion of susceptible isolates was much higher for piperacillin/tazobactam (95.7%) than to amoxicillin/clavulanic acid (1.3%). The majority of isolates were susceptible to all broad-spectrum antimicrobials, including gentamicin, ciprofloxacin, cephalosporins and carbapenems. In the NORM data, *K. oxytoca* is less susceptible than *K. pneumoniae* subsp. *pneumoniae* (Table 33), but there were too few isolates to draw any firm conclusion.

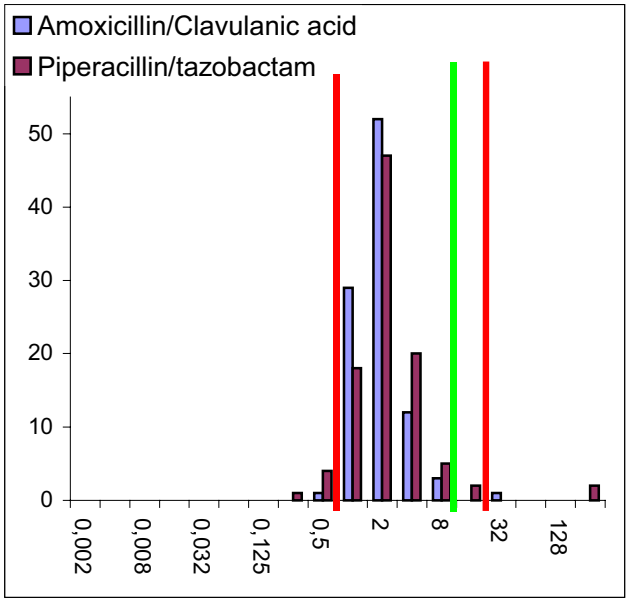


FIGURE 16. Distribution of minimum inhibitory concentrations (MICs) of amoxicillin/clavulanic acid and piperacillin/tazobactam for *Klebsiella* spp. blood culture isolates. AFA breakpoints for ampoxicillin/clavulanic acid are shown in red. The lower breakpoint for piperacillin/tazobactam is shown in green, whereas the upper breakpoint is common with the upper breakpoint for amoxicillin/clavulanic acid.

TABLE 33. Proportions (%) of resistant *K. pneumoniae* subsp. *pneumoniae* and *K. oxytoca* surveyed during NORM 2002.

	***K. pneumoniae* subsp. *pneumoniae* (n=214)**	***K. oxytoca* (n=50)**	**All (n=327)**
Ceftazidime	0.0 %	2.0 %	0.3 %
Ciprofloxacin	0.5 %	2.0 %	0.6 %
Gentamicin	0.5 %	2.0 %	0.9 %
TMS *	4.2 %	4.0 %	3.9 %

* Trimetoprim-sulfamethoxazol

Eight isolates were reported to have MIC ≥ 2 mg/L for ceftazidime and/or cefpirome. All isolates were specifically examined for the presence of extended-spectrum β-lactamase (ESBL) production by a disc approximation test and combination Etests. One of the suspected isolates, a *K. oxytoca* produced ESBL. This strain had MIC ≥ 128 mg/L for cefpirome, MIC ≥ 32 mg/L for ceftazidime and was also resistant to ciprofloxacin (MIC ≥ 32 mg/L) and gentamicin (MIC ≥ 16 mg/L).

Enterococcus spp. in blood cultures

TABLE 34. *Enterococcus* spp. blood culture isolates (n=252). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints mg/L		Proportion of isolates (%)*			MIC range	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Ampicillin	≤ 2	≥ 16	86.9	2.4	10.7	0.032 - 128	0.5	16
Gentamicin	≤ 512	≥ 1024	92.0	-	8.0	0.064 - ≥ 1024	8	256
Penicillin G	≤ 4	≥ 16	83.7	2.4	13.9	0.032 - ≥ 256	2	64
Streptomycin	≤ 512	≥ 1024	76.9	0.0	23.1	0.5 - ≥ 1024	64	≥ 1024
Vancomycin Screen			97.6	-	2.4			
β-lactamase	Neg	Pos	100.0	-	0.0			

*S=Susceptible, I=Intermediately susceptible, R=Resistant.

TABLE 35. *Enterococcus* spp. blood culture isolates (n=252). Distribution (n) of MICs (mg/L).*

	≤ 0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	≥ 1024
Ampicillin		1	5	7	40	85	78	3	1	2	8	15	6	1			
Gentamicin			1	1	2	2	4	24	69	93	22	4		2	7		20
Penicillin G		1		4	4	12	68	103	19	5	1	7	4	2	22		
Streptomycin				1		1	1		2	7	24	43	82	27	2	3	58

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue). Non-shaded areas represent MIC values that are not covered by the standard test method.

TABLE 36. *Enterococcus faecalis* blood culture isolates (n=188). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints mg/L		Proportion of isolates (%)*			MIC range	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Ampicillin	≤ 2	≥ 16	98.9	0.0	1.1	0.064 - 64	0.5	1
Gentamicin	≤ 512	≥ 1024	90.4	-	9.6	1 - ≥ 1024	8	256
Penicillin G	≤ 4	≥ 16	95.8	2.1	2.1	0.032 - ≥ 256	2	4
Streptomycin	≤ 512	≥ 1024	79.8	1.1	19.1	8 - ≥ 1024	64	≥ 1024
Vancomycin Screen			99.5	-	0.5			
β-lactamase	Neg	Pos	100.0	-	0.0			

*S=Susceptible, I=Intermediately susceptible, R=Resistant.

TABLE 37. *Enterococcus faecalis* blood culture isolates (n=188). Distribution (n) of MICs (mg/L).*

	≤ 0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	≥ 1024
Ampicillin			3	4	45	78	56	2					2				
Gentamicin							3	14	43	78	20	4		1	7		18
Penicillin G		1		1	2	6	65	94	11	4			2		2		
Streptomycin										2	16	31	75	25	1	2	36

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue). Non-shaded areas represent MIC values that are not covered by the standard test method.

TABLE 38. *Enterococcus faecium* blood culture isolates (n=47). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints mg/L		Proportion of isolates (%)*			MIC range	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Ampicillin	≤ 2	≥ 16	38.3	4.3	57.4	0.032 - 128	16	64
Gentamicin	≤ 512	≥ 1024	95.7	-	4.3	0.25 - ≥ 1024	4	8
Penicillin G	≤ 4	≥ 16	34.1	2.1	63.8	0.125 - ≥ 256	32	≥ 256
Streptomycin	≤ 512	≥ 1024	54.3	0.0	45.7	1 - ≥ 1024	64	≥ 1024
Vancomycin Screen			100.0	-	0.0			
β-lactamase	Neg	Pos	100.0	-	0.0			

*S=Susceptible, I=Intermediately susceptible, R=Resistant.

TABLE 39. *Enterococcus faecium* blood culture isolates (n=47). Distribution (n) of MICs (mg/L).*

	≤ 0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	≥ 1024
Ampicillin		1	2	1	2	2	7	3		2	8	14	4	1			
Gentamicin					1	2	1	9	18	11	1			1			2
Penicillin G				2		2	1	4	7	1		7	2	2	19		
Streptomycin							1		1	1	7	9	4	1	1		21

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue). Non-shaded areas represent MIC values that are not covered by the standard test method.

COMMENTS

The data for *Enterococcus* spp. (all species) blood culture isolates (n=252) are presented in tables 34 – 39. The dominating species were *E. faecalis* (n=188) and *E. faecium* (n=47), whereas *E. casseliflavus* (n=4), *E. gallinarum* (n=4) and others (n=9) represented less than 6% of the total. The vast majority of isolates were susceptible to the traditional combination therapy of ampicillin and aminoglycoside. Resistance data should be described separately for *E. faecalis* and *E. faecium* due to species-specific differences in resistance rates. As demonstrated in figure 17, *E. faecium* was less susceptible to β-lactams than *E. faecalis*. More than 57% of the 47 *E. faecium* isolates were resistant to ampicillin, whereas 98.9% of the *E. faecalis* isolates were susceptible. Due to modification of the breakpoints, the proportion of intermediately susceptible isolates was reduced compared to the results reported in NORM 2001. The occurrence of high-level resistance to gentamicin was higher in *E. faecalis* (9.6%) than in *E. faecium* (4.3%). In contrast, the occurrence of high-level resistance to streptomycin was higher in *E. faecium* (45.7%) compared to *E. faecalis* (19.1%). High-level resistance to gentamicin and streptomycin for both *E. faecalis* and *E. faecium* isolates have increased slightly from 2001 to 2002 (Table 40), but it is still low compared to many other countries.

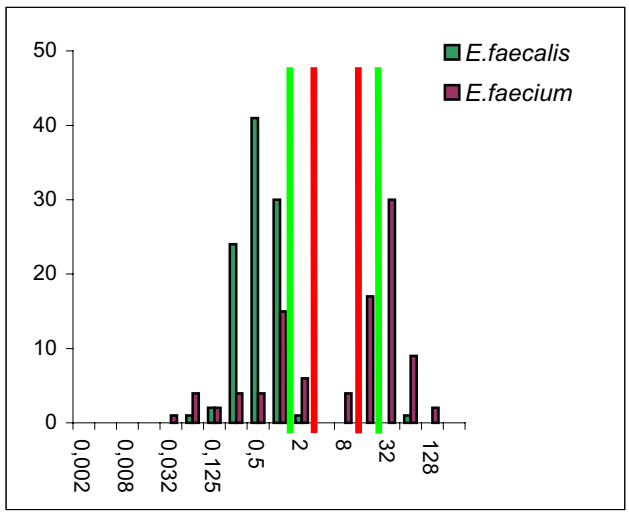


FIGURE 17. Distribution (%) of minimum inhibitory concentrations (MICS) of ampicillin for *E. faecalis* and *E. faecium* blood culture isolates. AFA old breakpoints are shown in green, whereas new breakpoints (valid from 2003) are shown in red.

TABLE 40. Proportions (%) of *E. faecalis* and *E. faecium* blood culture isolates with high-level resistance to gentamicin and streptomycin (MIC ≥ 1024 mg/L) surveyed in NORM 2001 and 2002.

	E. faecalis		*E. faecium*	
	2001	**2002**	**2001**	**2002**
Gentamicin	4.5 %	9.6 %	3.3 %	4.3 %
Streptomycin	12.3 %	19.1 %	60.0 %	45.7 %

All enterococcal isolates were screened on a Brain Heart Infusion agar containing 6 mg/L vancomycin. Suspected VREs were further analysed by a PCRs for the *van* gene complex. Six enterococcal isolates grew on the agar screen and PCR confirmed one *E. faecalis vanB* type and 5 *E. casseliflavus* harbouring *vanC* genes. Only the *E. faecalis vanB* isolate encodes transferable glycopeptide resistance.

Streptococcus pneumoniae in blood cultures

TABLE 41. *Streptococcus pneumoniae* blood culture isolates (n=538). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Cefotaxime	≤ 0.5	≥ 4	100.0	0.0	0.0	0.002 - 0.5	0.016	0.016
Cefuroxime	≤ 0.5	≥ 4	99.4	0.6	0.0	0.016 - 1	0.016	0.016
Chloramph.	≤ 4	≥ 8	99.4	0.0	0.6	0.064 - 32	2	2
Ciprofloxacin	≤ 0.125	≥ 4	1.6	96.8	1.6	0.064 - 32	1	2
Clindamycin	≤ 0.25	≥ 4	99.3	0.0	0.7	0.016 - ≥ 256	0.125	0.125
Doxycycline	≤ 1	≥ 4	98.0	0.0	2.0	0.032 - 32	0.125	0.25
Erythromycin	≤ 0.5	≥ 1	94.8	0.0	5.2	0.004 - ≥ 256	0.064	0.125
Oxacillin screen	≥ 20 mm	≤ 19 mm	98.2	-	1.8			
Pen G**	≤ 0.064	≥ 2	99.4	0.6	0.0	0.002 - 0.5	0.016	0.016
TMS***	≤ 0.5	≥ 4	97.6	1.4	1.0	0.032 - ≥ 32	0.125	0.25
Vancomycin	≤ 2	≥ 8	99.6	0.4	0.0	0.125 - 5	0.5	1

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**Pen G=Benzylpenicillin.
***TMS= Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 42. *Streptococcus pneumoniae* blood culture isolates (n=538). Distribution (n) of MICs (mg/L).*

	≤0.004	0.008	0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	≥128
Cefotaxime	7	127	363	34	3	1	1	2								
Cefuroxime			490	35	8	1	1		3							
Chloramph.					1			15	154	360	5		2	1		
Ciprofloxacin					4	4	10	181	256	74	6	2		1		
Clindamycin			11	27	162	314	20									4
Doxycycline				4	10	260	215	32	6		3	5	2	1		
Erythromycin	1		16	44	295	153		1	1	1	8	9	4	2	1	2
Pen G**	18	152	342	22	1	3										
TMS***				3	22	293	199	8	5	3	4			1		
Vancomycin						1	43	306	134	51	2					

	≤ 19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	≥ 34
Oxacillin disc	9	7	3	11	12	37	69	81	45	61	48	39	25	21	9	30

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue). Non-shaded areas represent MIC values that are not covered by the standard test method.
**Pen G=Benzylpenicillin.
***TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS

The pneumococcal isolates were generally susceptible to all relevant classes of antimicrobials. Nine *S. pneumoniae* blood culture isolates were non-susceptible to penicillin G according to the oxacillin screening test. Five of these isolates were intermediately susceptible to penicillin G confirmed with Etest and all were susceptible to 3rd generation cephalosporins.

Erythromycin resistance (MIC ≥ 1mg/L) was detected in 5.2% of the isolates, which is an increase compared to previous years (2.4% and 2.2% in 2000 and 2001, respectively) (Table 43). It should be noted that the breakpoint for erythromycin resistance has been altered from R ≥ 4 mg/L in 2001 to R ≥ 1 mg/L in 2002. Twenty-eight resistant isolates were detected in 2002. The majority showed low-level resistance, whereas only two isolates demonstrated high-level resistance (MIC ≥ 256 mg/L). These two isolates were concomitantly highly resistant to clindamycin (MIC ≥ 256 mg/L) indicating the presence of constitutively expressed Erm methylases. Strains that constitutively express the *erm* genes are resistant to both eythromycin and clindamycin. However, strains with an inducible *erm* gene are resistant to erythromycin and show *in vitro* susceptibility to clindamycin unless induced by erythromycin. Erythromycin low-level resistance in isolates that are clindamycin susceptible are usually caused by a *mef*-encoded efflux mechanism.

TABLE 43. Proportions (%) of *S. pneumoniae* blood culture isolates showing resistance to erythromycin (MIC ≥ 4 mg/L) and clindamycin (MIC ≥ 4 mg/L) surveyed during NORM 2000-2002

	2000 (n=167)	2001 (n=460)	2002 (n=538)
Erythromycin	2.4%	2.2%	4.8 %
Clindamycin	0.0%	0.9%	0.7 %

Doxycycline resistance was a limited (2.0%) problem among *S. pneumoniae* blood culture isolates. In contrast, group A streptococci from respiratory tract (10.4%) and wound specimens (23.0%) revealed a much higher prevalence of doxycycline resistance

Staphylococcus aureus in blood cultures

TABLE 44. *Staphylococcus aureus* blood culture isolates (n=726). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Cefuroxime	≤ 2	≥ 8	99.6	0.1	0.3	0.125 - ≥ 256	1	1
Clindamycin	≤ 1	≥ 4	99.3	0.0	0.7	0.016 - ≥ 256	0.064	0.125
Doxycycline	≤ 1	≥ 4	96.0	0.6	3.4	0.016 - 16	0.125	0.5
Erythromycin	≤ 1	≥ 4	96.7	0.1	3.2	0.016 - ≥ 256	0.125	0.25
Fucidic acid	≤ 0.5	≥ 1	92.0	-	8.0	0.016 - ≥ 256	0.064	0.25
Gentamicin	≤ 2	≥ 8	99.2	0.7	0.1	0.032 - 16	0.25	1
Oxacillin	≤ 2	≥ 4	99.7	0.0	0.3	0.064 - ≥ 256	0.25	0.5
Oxacillin screen			99.7	-	0.3			
Penicillin G**	≤ 0.064	≥ 0.25	25.5	4.3	70.2	0.008 - ≥ 256	0.5	4
β-lactamase	Neg	Pos	25.0	-	75.0			
Vancomycin screen			100.0	0.0	0.0			

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**Penicillin G=Benzylpenicillin.

TABLE 45. *Staphylococcus aureus* blood culture isolates (n=726). Distribution (n) of MICs (mg/L).*

	≤0.008	0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Cefuroxime					9	24	201	463	26	1						2
Clindamycin		2	41	424	250	2	2									5
Doxycycline		1	9	147	330	141	46	23	3	11	9	5				
Erythromycin		2	3	51	393	240	7	5	1	2		1				20
Fucidic acid		4	120	343	145	42	13	9	10	17	12	6	1			3
Gentamicin			2	7	78	281	279	63	10	4	1	1				
Oxacillin				5	99	316	277	25	2							2
Penicillin G**	3	62	99	21	31	36	134	169	92	38	15	10	15			

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue). Non-shaded areas represent MIC values that are not covered by the standard test method.
**Penicillin G=Benzylpenicillin.

COMMENTS

A total of 75.0% of *S. aureus* blood culture isolates were β-lactamase producers, compared to 74.5% in 2000 and 74.1% in 2001. The percentage of resistance to penicillin G, using an epidemiological breakpoint of S ≤ 0.064 mg/L was slightly lower (70.2%), but the specific assay for β-lactamases is more reliable for detection of true resistance to penicillin G.

Methicillin resistant *S. aureus* (MRSA) are diagnosed by their reduced susceptibility to oxacillin. Methicillin resistance is associated with presence of the *mecA* gene that encodes an altered penicillin binding protein (PBP2a or PBP2') with reduced affinity to β-lactams. Resistance to oxacillin indicates resistance to all β-lactam antimicrobials, including penicillins, cephalosporins, monobactams and carbapenems. AFA presently recommends a Mueller-Hinton agar containing 4 mg/L oxacillin and 2% NaCl as a screening agar for methicillin resistance. Only 0.3 % (n=2) of *S. aureus* blood culture isolates grew on the screening agar. These two isolates were confirmed as true MRSA by *mecA* PCR. Both isolates were identified in the same hospital, but were non-related according to PFGE analysis. Resistance to doxycycline and clindamycin remained unchanged compared to previous years. However, a marginal increase in macrolide resistant *S. aureus* was described in 2002 (3.2%) compared to 2001 (2.2%). The prevalence of resistance to fucidic acid was 8.0%, which is higher than the 1.9% and 5.1% reported for blood culture isolates in 2000 and 2001, respectively. NORM 2001 reported a much higher rate of resistance (20.8%) to fucidic acid among isolates from wound specimens. *S. aureus* from wound specimens were not surveyed in NORM 2002. It has been documented that isolates from localized infections frequently are more resistant than systemic isolates. For fusidic acid resistance in *S. aureus* in Norway, the discovery of a clonal outbreak of fucidic acid resistant *S. aureus* causing impetigo bullosa in the Nordic countries is more important (page 54 for more details by Y. Tveten). Whether the fucidic acid resistant isolates found in blood cultures in NORM 2002 were part of the same clonal outbreak remains to be investigated.

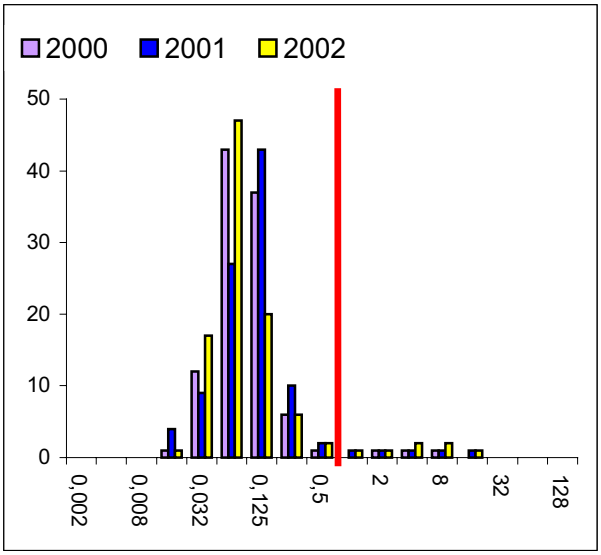


FIGURE 18. Distribution (%) of minimum inhibitory concentrations (MICs) of fucidic acid for *S. aureus* isolates from blood cultures surveyed during 2000 to 2002. The AFA breakpoint is shown in red.

Fusidic acid resistant *Staphylococcus aureus*

Since the introduction of fusidic acid in the 1960s there have been scattered reports of increased resistance, but the majority of studies have reported low prevalence of fusidic acid resistance among *S. aureus* [1]. In the Scandinavian countries, fusidic acid has been used extensively for topical treatment of superficial skin infections for many years, irrespective of the aetiology. Until recently, more than 90% of *S. aureus* isolates from Norway were susceptible to fusidic acid [2]. In the summer and early autumn of 1999 a marked increase in isolation frequencies of fusidic acid resistant *S. aureus* associated with impetigo among children was noted. From a low prevalence of 3% in 1992, the prevalence of fusidic acid resistant *S. aureus* has increased in the Telemark region and reached 40% in 2002. In the last three years, much of this increase seems to have been due to summer peaks of resistance (55% in September 2002), coinciding with outbreaks of impetigo among children.

Genetic typing with PFGE showed that about 80% of impetigo-associated fusidic resistant *S. aureus* belongs to a single DNA class, and corresponding isolates from Sweden and other regions of Norway are of the same DNA class [3, 4, 5]. In contrast, fusidic acid sensitive isolates are genetically heterogeneous. The impetigo associated fusidic acid resistant *S. aureus* showed MICs ranging from 2-4 mg/L, while MICs of fusidic acid resistant *S. aureus* showing other PFGE patterns varied from 1 to ≥ 32 mg/L. The majority of impetigo associated fusidic acid resistant *S. aureus* isolates are closely related members of a single clone. These results strongly suggest that a fusidic acid resistant *S. aureus* clone has spread epidemically in Scandinavia in recent years. Excessive and indiscriminate use of fusidic acid is likely to exacerbate this situation. New recommendations for treatment of impetigo is published from the Norwegian Medicines Agency.[6]

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MRSA infections in Norway

Infections with methicillin resistant *Staphylococcus aureus* (MRSA) have been notifiable in Norway since 1995, but colonisation without infection is not notifiable. Consistent discrimination between the two can be difficult. In 2002 there was once again a substantial increase in the number of reported cases with 142 cases compared to 88 and 121 the two previous years (Figure 19). Eighty-one of the cases were men (57%). Median age in 2002 was 35 years (range 0–95 years) and 42 years for all eight years reported. Less than half (31%) of the patients falling ill in 2002 were hospitalised at the time of diagnosis.

FIGURE 19. Reported cases of MRSA infection 1995–2002 and whether the infection was contracted abroad or not.

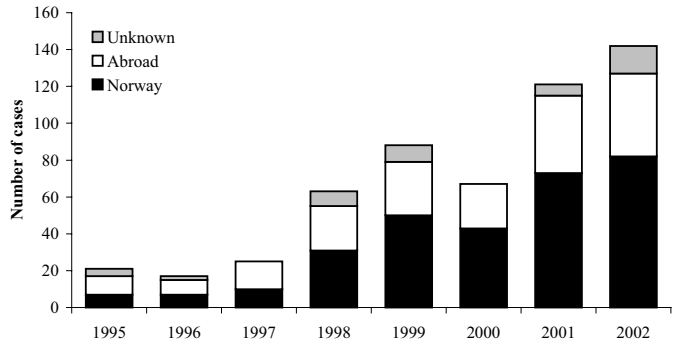

TABLE 46. Clinical picture of reported cases of MRSA infection in Norway 1995–2002.

Clinical picture	1995	1996	1997	1998	1999	2000	2001	2002	Total
Septicaemia	1		3	3	4	2	6	4	23
Septicaemia and meningitis				1					1
Meningitis				1					1
Osteomyelitis	2	1		2			2		7
RTI*, incl. otitis media	1	1	1	14	8	5	8	12	50
Urinary tract infection		1		4	3	3	2	9	22
Wound infection, abscess	17	14	19	36	71	54	97	116	424
Other, unknown			2	2	2	3	6	1	16
Total	21	17	25	63	88	67	121	142	544

* RTI = Respiratory tract infection

The number of cases of MRSA infections has increased by 17% from the previous year. MRSA was found in blood cultures in only five patients in 2002 and only 24 for all eight years reported. The overwhelming majority consists of wound infections or abscesses (Table 46). The number of serious infections is still very low with four clinical septicaemias and five positive blood cultures. The numbers are too small to ascertain whether there has been a true increase in serious infections. How large the true increase in the total number of infections is, has to be interpreted with caution. The proportion of patients who contracted the disease in Norway has been constant the past four years even as the total numbers have increased. The increase in the total numbers for the same period has mainly been in non-hospitalised patients, decreasing the proportion of hospitalised patients. This may indicate increased testing of patients outside hospitals. The national surveillance of MRSA in Norway is not satisfactory. Only MRSA infections are notifiable and not colonisations. Consequently only a part of the picture is seen and the ability to discover outbreaks is made difficult. Furthermore we are in a process to establish a national reference laboratory where all isolates are to be sent, analysed and compared genetically.

Streptococcus pyogenes in specimens from wounds and the respiratory tract

TABLE 47. *Streptococcus pyogenes* wound specimens and respiratory tract isolates (n=963). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Clindamycin	≤ 0.25	≥ 4	99.3	0.3	0.4	0.016 - ≥ 256	0.125	0.125
Doxycycline	≤ 1	≥ 4	84.3	0.1	15.6	0.016 - ≥ 256	0.125	16
Erythromycin	≤ 0.5	≥ 1	96.2	0.0	3.8	0.016 - ≥ 256	0.064	0.125
Penicillin G**	≤ 0.064	≥ 2	99.8	0.2	0.0	0.002 - 0.5	0.008	0.016
TMS***	≤ 0.5	≥ 4	99.6	0.1	0.3	0.004 - ≥ 32	0.064	0.125

*S=Susceptible, I=Intermediately susceptible, R=Resistant. **Penicillin G=Benzylpenicillin.
***TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 48. *Streptococcus pyogenes* wound specimens and respiratory tract isolates (n=963). Distribution (n) of MIC values (mg/L).

	≤ 0.004	0.008	0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	≥ 128	≥ 256
Clindamycin			4	57	267	602	26		3		1						3
Doxycycline			1	9	21	324	380	72	5	1		9	72	54	12	1	2
Erythromycin			64	120	396	340	3	3	2	4	10	8	2	2			9
Penicillin G**	5	481	468	6	1	1											
TMS***	1	4	36	132	386	324	68	7		1	1			3			

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue). Non-shaded areas represent MIC values that are not covered by the standard test method. **Penicillin G=Benzylpenicillin. ***TMS=Trimethoprim/sulfamethoxazole.

TABLE 49. *Streptococcus pyogenes* respiratory tract isolates (n=568). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Clindamycin	≤ 0.25	≥ 4	99.0	0.5	0.5	0.016 - ≥ 256	0.125	0.125
Doxycycline	≤ 1	≥ 4	89.4	0.2	10.4	0.016 - 64	0.25	8
Erythromycin	≤ 0.5	≥ 1	97.2	0.0	2.8	0.016 - ≥ 256	0.064	0.125
Penicillin G**	≤ 0.064	≥ 2	99.8	0.2	0.0	0.002 - 0.25	0.008	0.016
TMS***	≤ 0.5	≥ 4	99.5	0.2	0.3	0.008 - ≥ 32	0.064	0.125

*S=Susceptible, I=Intermediately susceptible, R=Resistant. **Penicillin G=Benzylpenicillin.
***TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 50. *Streptococcus pyogenes* respiratory tract isolates (n=568). Distribution (n) of MIC values (mg/L).

	≤ 0.004	0.008	0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	≥ 128	≥ 256
Clindamycin			2	41	177	329	13		3		1						2
Doxycycline			1	6	11	198	251	39	2	1		3	30	21	5		
Erythromycin			29	91	218	211	2	1	2	2	4	2		1			5
Penicillin G**	3	285	276	3			1										
TMS***		4	23	93	212	183	45	5		1				2			

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue). Non-shaded areas represent MIC values that are not covered by the standard test method. **Penicillin G=Benzylpenicillin. ***TMS=Trimethoprim/sulfamethoxazole.

TABLE 51. *Streptococcus pyogenes* wound specimens (n=395). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Clindamycin	≤ 0.25	≥ 4	99.7	0.0	0.3	0.016 - ≥ 256	0.125	0.125
Doxycycline	≤ 1	≥ 4	77.0	0.0	23.0	0.032 - ≥ 256	0.25	32
Erythromycin	≤ 0.5	≥ 1	94.7	0.0	5.3	0.016 - ≥ 256	0.064	0.125
Penicillin G**	≤ 0.064	≥ 2	99.7	0.3	0.0	0.004 - 0.125	0.008	0.016
TMS***	≤ 0.5	≥ 4	99.7	0.0	0.3	0.004 - ≥ 32	0.064	0.125

*S=Susceptible, I=Intermediately susceptible, R=Resistant. **Penicillin G=Benzylpenicillin.
***TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 52. *Streptococcus pyogenes* wound specimens (n=395). Distribution (n) of MIC values (mg/L).

	≤ 0.004	0.008	0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	≥ 128	≥ 256
Clindamycin			2	16	90	273	13										1
Doxycycline				3	10	126	129	33	3			6	42	33	7	1	2
Erythromycin			35	29	178	129	1	2		2	6	6	2	1			4
Penicillin G**	2	196	192	3	1	1											
TMS***	1		13	39	174	141	23	2						1			

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue). Non-shaded areas represent MIC values that are not covered by the standard test method. **Penicillin G=Benzylpenicillin. ***TMS=Trimethoprim/sulfamethoxazole.

COMMENTS

Group A streptococci (*S. pyogenes*) were introduced in the Norwegian surveillance system for the first time in 2002. Both respiratory tract isolates (n= 568) and wound specimens (n=395) were surveyed. All isolates were susceptible to penicillin G (Figure 20), which is the drug of choice for treating streptococcal infections in Norway. Resistance development to penicillin and other β-lactams has never been observed in clinical isolates. Surprisingly, 15.6% of all group A streptococcal isolates were resistant to tetracycline. Similar data have been reported from Sweden, possibly indicating clonal outbreaks. The isolates from wound specimens were more resistant (23.0%) than the respiratory tract isolates (10.4%) (Figure 21). Macrolide resistant group A streptococci is still a limited problem in Norway. Isolates from wound specimens were more often resistant (5.3%) than the respiratory tract isolates (2.8%). Only three isolates demonstrated high-level resistance to both erythromycin and clindamycin. Presence of the macrolide-lincosamide-streptogramin B (MLS_B) resistance gene *erm* (TR) was confirmed by PCR. The erythromycin ribosome methylation (*erm*) gene encodes a methylase that modifies the binding site on the ribosomes. Strains that express the *erm* gene constitutively are resistant to both erythromycin and clindamycin, whereas strains with an inducible *erm* gene are resistant to erythromycin and show *in vitro* susceptibility to clindamycin unless they are induced by erythromycin. Low-level resistance to erythromycin and suscebtibility to clindamycin is usually caused by an unrelated efflux mechanism.

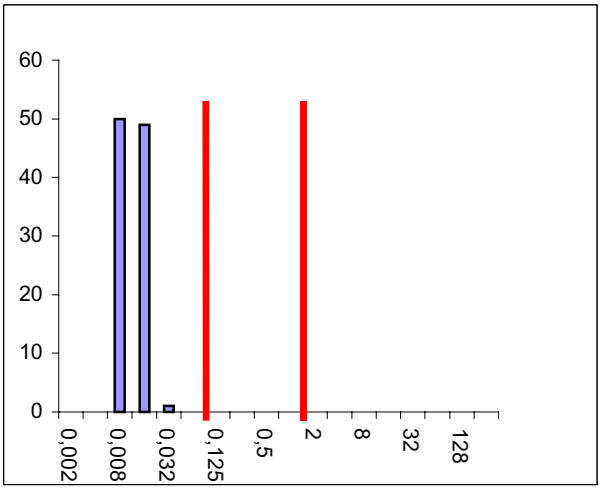

FIGURE 20. Distribution (%) of minimum inhibitory concentrations (MICs) of penicillin G for group A streptococci isolated from specimens from the respiratory tract or wounds. AFA breakpoints are shown in red.

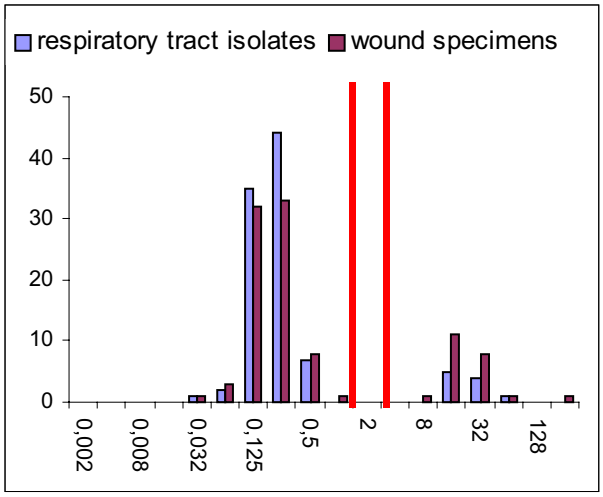

FIGURE 21. Distribution (%) of minimum inhibitory concentrations (MICs) of tetracycline for group A streptococci isolated from respiratory tract specimens and wound specimens.

Macrolide resistance in *Streptococcus pneumoniae* and *Streptococcus pyogenes*.

Macrolides are clinically important antibiotics in treating upper respiratory diseases caused by *S. pneumoniae* and *S. pyogenes* as an alternative to penicillin and other β-lactams. Unfortunately macrolide resistance in these two bacteria are increasing worldwide and therefore worrisome. The prevalence of macrolide resistance in Norway is still low, but it is increasing. The macrolide blocks the protein synthesis by binding to the ribosomes and inhibiting the elongation of the peptide chain. Two macrolide resistance mechanisms have been demonstrated in *S. pneumoniae* and *S. pyogenes;* target site modification and efflux[1,2]. Target site modifications are caused by a methylase, encoded by erythromycin ribosome methylase (*erm*) genes, which modifies a specific adenine residue of 23S rRNA, causing conformational changes in the prokaryotic ribosome. The modification affects the binding of macrolide, lincosamide, and streptogramin B (MLS_B) antibiotics due to overlapping binding sites in the ribosomal subunit and confers so-called MLS_B resistance, which might be inducible ($iMLS_B$) or constitutive ($cMLS_B$). An altered target site modification may occassionally be caused by specific point mutations in the peptidyl transferase region giving rise to different ML and MS_B phenotypes[3]. A macrolide efflux mechanism, encoded by macrolide efflux (*mef*) genes, causes a M type resistance. M type resistance is causing low-level resistance. It is specific for macrolides, affecting neither lincosamides nor streptogramin B. Macrolide resistance can be classified phenotypically by using a double disc diffussion test[4]. Erythromycin (30µg) and clindamycin (30µg) discs are placed 12-15 mm apart on PDMII agar supplemented with 5% defibrinated horse blood (non-hemolysed), which has been inoculated with a swab dipped into a bacterial suspension with a turbidity equivalent to a 0.5 McFarland standard. After 18-20 hours of incubation in 37˚C in CO_2, the abscence of zones around both discs indicates constitutive resistance (cMLS); blunting of the clindamycin zone proximal to the erythromycin disk ("D" shape) indicates inducible resistance (iMLS); resistance to erythomycin and susceptibility to clindamycin with no blunting of the zone around the clindamycin disc, indicates M type resistance. Isolates with reduced susceptibility can be examined for resistance genes by specific PCR's[5-7].

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Escherichia coli in urine

TABLE 53. *Escherichia coli* urinary tract isolates (n=1044). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Ampicillin	≥ 24	≤ 12	9.6	65.6	24.8	6 - 36
Ciprofloxacin	≥ 28	≤ 20	97.3	1.5	1.1	6 - ≥ 41
Mecillinam	≥ 20	≤ 16	92.6	4.8	2.6	6 - ≥ 41
Nalidixic acid	≥ 17	≤ 16	97.0	-	3.0	6 - 39
Nitrofurantoin	≥ 19	≤ 18	96.8	-	3.2	6 - ≥ 41
Sulfonamide	≥ 19	≤ 14	76.2	0.6	23.2	6 - ≥ 41
Trimethoprim	≥ 21	≤ 19	83.2	0.1	16.7	6 - 40

*S=Susceptible, I=Intermediately susceptible, R=Resistant.

TABLE 54. *Escherichia coli* urinary tract isolates (n=1044). Distribution (n) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Ampicillin	227	18	4	1	1		8	5	5	15	23	43	81	64	127
Ciprofloxacin	6			2		1	2				1				1
Mecillinam	9				4	2	3	1	3	5	11	9	11	6	13
Nalidixic acid	26	3			1	1						1		1	3
Nitrofurantoin	3	1	1	1		2	4	1	2	3	1	2	12	9	30
Sulfonamide	219	14			1	1						1	4	1	5
Trimethoprim	151	10				1		1	1		1	2	3	1	

	21	22	23	24	25	26	27	28	29	30	31	32	33	34	≥ 35
Ampicillin	95	81	68	48	42	23	13	9	5	2	1		1		1
Ciprofloxacin		1	1	2	4	2	2	3	4	9	34	83	127	142	617
Mecillinam	12	20	15	39	28	33	20	33	31	97	88	149	123	108	171
Nalidixic acid	11	16	23	64	93	113	170	149	131	123	39	36	17	10	9
Nitrofurantoin	26	58	65	118	180	173	131	103	42	36	14	11	1	6	8
Sulfonamide	10	7	21	40	59	63	79	82	54	96	50	69	34	39	62
Trimethoprim		1		3	3	18	23	72	50	132	100	125	83	101	133

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue). Non-shaded areas represent MIC values that are not covered by the standard test method.

COMMENTS

E. coli urinary tract isolates were analysed by disc diffusion methodology. A small zone diameter indicates resistance, whereas a large zone diameter indicates susceptibility. All samples were tested for urinary tract antimicrobials commonly prescribed in Norway. A high prevalence of susceptibility was seen for ciprofloxacin (97.3%), mecillinam (92.6%), nalidixic acid (97.0%), nitrofurantoin (96.8%) and trimetoprim (83.2%). The majority of isolates was intermediately susceptible to ampicillin (65.6%). The distribution of zone diameters was similar to the results reported in NORM 2001 for ampicillin. In NORM 2001, an increase in *Klebsiella* spp. urinary tract isolates non-susceptible to ciprofloxacin was recorded. Such a drift has not been documented for *E. coli* urinary tract isolates surveyed in NORM. Ciprofloxacin treatment should still be limited to complicated cases in order to prevent a future increase in quinolone resistance. As the AFA breakpoints have been modified for several of the urinary tract antimicrobials, the proportions of susceptible, intermediately susceptible and resistant isolates have been altered. Figure 22 shows how the new breakpoints better discriminate the resistant and the susceptible phenotypes regarding sulfonamide. In contrast, defining microbiological breakpoints for mecillinam is difficult as the population cannot be separated into distinct resistance phenotypes (Figure 23).

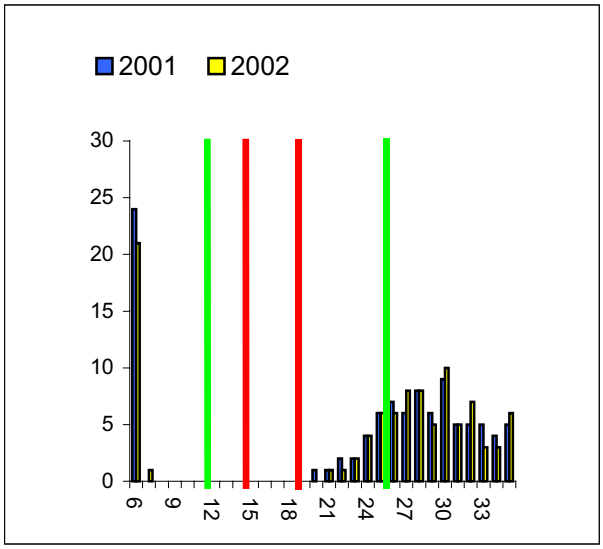

FIGURE 22. Distribution (%) of disc diffusion diameters (mm) of sulfonamide for *E. coli* urinary tract isolates from 2001 (blue) and 2002 (yellow) using a 250 µg disc. AFA old breakpoints are shown in green, whereas new breakpoints (valid from 2003) are shown in red. New breakpoints discriminate better the susceptible from the resistant phenotypes.

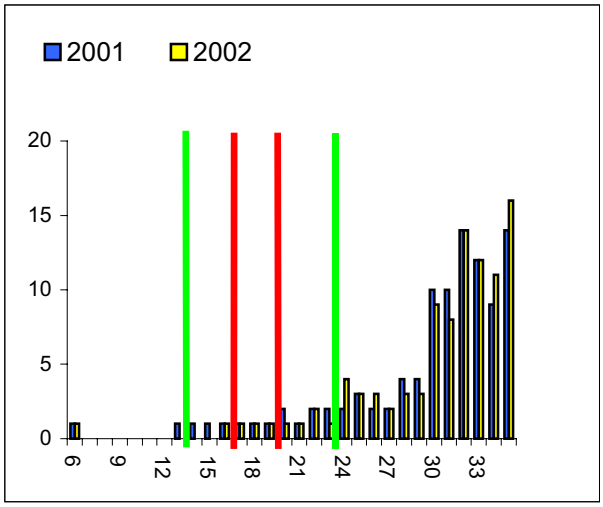

FIGURE 23. Distribution (%) of disc diffusion diameters (mm) of mecillinam for *E. coli* urinary tract isolates from 2001 (blue) and 2002 (yellow) using 10 µg discs. A small zone diameter indicates resistance, whereas a large zone diameter indicates susceptibility. AFA old breakpoints are shown in green, whereas new breakpoints (valid from 2003) are shown in red.

Mycobacterium tuberculosis

A total of 256 cases of tuberculosis were reported to the Norwegian Surveillance System for Communicable Diseases (MSIS) in 2002 (MSIS report 2003; 31:23). Of these patients 238 had not previously been treated with antituberculosis drugs. *Mycobacterium tuberculosis* was isolated in 178 cases, *M. bovis* in one and *M. africanum* in one case. Susceptibility tests were performed in all these 180 patients (Table 55).

TABLE 55. Antimicrobial susceptibility of *Mycobacterium tuberculosis* complex isolates from 180 patients not previously treated for tuberculosis.

Geographical origin of patients	No. of isolates	Resistance to antimicobial agents (isolates)				
		Isoniazid	Rifampicin	Ethambutol	Streptomycin*	MDR**
Norway	35	1			1	
Europe outside Norway	21	2	1	1	1	1
Asia	48	7	1	3	7	1
Africa	74	9	4	3	12	4
America	1					
2nd generation immigrants	1					
Total	180	19	6	7	21	6
Proportion of isolates resistant (%)		11	3	4	12	3

*Isolates from 46 patients were not tested for susceptibility to streptomycin.
**MDR= Multidrug resistance (combined resistance to rifampicin and isoniazid).

Susceptibility tests were also performed on *Mycobacterium tuberculosis* isolates from 12 patients who had previously received antituberculosis drug treatment. Three of them had strains resistant to isoniazid, one to ethambutol, two to streptomycin and one of these patients (born in Asia) had a multidrug resitant (MDR) isolate. Seven patients were therefore diagnosed with MDR tuberculosis is Norway in 2002.

Appendix 1
Collection of data on animal consumption of antimicrobial agents

Data sources

Feed additives

The Norwegian Agricultural Inspection Service is responsible for approving and monitoring sales of feed additives including antibacterial growth promoters and coccidiostats. Reliable data on the use of different substances and categories of feed additives can be obtained from this agency.

Antibacterial drugs for therapeutic use

In Norway, veterinary antimicrobials for therapeutic use in domestic animals or farmed fish are prescription drugs only. Moreover, veterinary antibacterial drugs have to be dispensed through pharmacies, which are only supplied by drug wholesalers. An exemption from the pharmacy/wholesaler monopoly has been granted for medicated feeds (i.e. feeds into which drugs for therapeutic use are mixed prior to sale). Medicated feeds have to be prescribed by veterinarians and produced by feed mills authorized by the Norwegian Medicines Agency. In Norway, medicated feeds produced and supplied by feed mills are only used for farmed fish. Medicated feeds for livestock are not produced in feed mills due to the small size of livestock herds compared to most other European countries. However, herd/flock treatment of livestock with antibacterial drugs is possible, again subject to veterinary prescription, through the drinking water or as a top dressing on the feed.

The sales figures for veterinary antibacterial drugs from wholesalers and feed mills are thought to roughly equal the use of these drugs. Sales figures for veterinary antibacterial drugs are therefore used as synonyms of veterinary antibacterial use.

Drug wholesalers and feed mills report their sales figures to the WHO Collaborating Centre for Drug Statistics and Methodology at the Norwegian Institute of Public Health. This reporting was made mandatory from January 1st 2002 to ensure that all the data are included. Data on annual sales of veterinary antibacterial drugs were obtained from the Norwegian Institute of Public Health.

Drug classification system

The Anatomical Therapeutic Chemical (ATC) classification system was used to categorize veterinary medicinal products (ATCvet).

Unit of measurement

The amount of active substance denoted in kilograms was chosen as the unit of measurement. Veterinary antibacterial use was calculated from sales figures for delivery of antibacterials from wholesalers to pharmacies, and from feed mills. The data for benzyl penicillin salts and esters (procaine penicillin and penethamate hydriodide) were converted to the corresponding values for benzyl penicillin.

Inclusion criteria

All veterinary antibacterial specialities included in this report belong to the following ATCvet groups: gastrointestinal infections (QA07AA), uterine infections (QG01AA+AE), and antibacterial drugs for systemic use (QJ), including intramammary dose applicators (QJ51). The QJ-group also includes medicated feeds and premixes for farmed fish that are approved by the drug authorities and classified as pharmaceutical specialities (QJ01).

Dermatological preparations (QD) and preparations intended for sensory organs (QS) are not included in the material. Human antibacterial preparations can be used in small animal practice. However, data on the use of these drugs in animals are not included in this report, as such use cannot be separated from use in humans.

Appendix 2
Collection of data on human consumption of antimicrobial agents

Data sources
In Norway, antibacterials are prescription drugs only (POM), and only allowed sold by pharmacies. Antibacterials are normally not reimbursed, exceptions are venereal diseases and chronic infections. Drug statistics on consumption of antibacterials for human use are based on sale of medicaments from drug wholesalers to pharmacies and hospitals in Norway. These data cover total sale of antibacterials for humans in Norway. Sale to hospitals represents around 8% of the total use of antibacterials for human use.
The figures presented should be regarded as maximum figures with the assumption that all medicaments sold from the wholesalers are actually consumed. The actual drug consumption will probably be somewhat lower. The data are collected by the Norwegian Institute of Public Health. Data on drug use have been collected since the beginning of the seventies.

Drug classification
The data are categorized according to the ATC classification system, and Defined Daily Doses (DDDs) are employed as units of measurement.

Unit of measurement
The ATC/DDD system is recommended by the WHO to serve as a tool for drug utilisation research in order to improve quality of drug use. One component of this is the presentation and comparison of drug consumption statistics at international and other levels.
The use of defined daily dose, DDD, as a unit of measurement, simplifies and improves the evaluation of drug consumption over time, nationally and internationally. The DDD is a theoretical unit of measurement, and does not necessarily reflect the recommended or Prescribed Daily Dose.

The basic **definition** of the unit is:
The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults.

The DDDs for the antiinfectives are as a main rule based on the use in infections of moderate severity. Some antiinfectives are only used in severe infections and their DDDs are assigned accordingly. The DDDs assigned are based on daily treatment.

Inclusion criteria
The antibacterials for human use included in this report belong to ATC J01 antibacterials for systemic use. Oral vancomycin (A07AA09) and oral and rectal metronidazole (P01AB01) are also included. The ATC/ DDD index version 2003 is used. Antibacterials used in dermatological preparations (ATC group D) and preparations intended for sensory organs (ATC group S) are not included in the material.

Appendix 3
Sampling, microbiological methods and data processing in NORM-VET

Sampling strategy

Clinical isolates from animals in 2002 were collected from diagnostic submissions: *Staphylococcus intermedius* from dogs with skin infections and *Escherichia coli* from enteritis in pigs and septicaemia in poultry.

The isolates of indicator bacteria (*Escherichia coli* and *Enterococcus* spp.) included in the NORM-VET monitoring programme 2002 were collected from healthy pigs (faecal and meat samples at slaughterhouses) and broilers (meat samples at slaughterhouses and faecal samples from live stock). The sampling period was from March to December. The Municipal Food Control Authorities collected the samples at slaughterhouses. To obtain a representative random sample from pigs, samples collected at each slaughterhouse were determined by the proportion of animals slaughtered there relative to the total number of animals slaughtered in Norway in 2001. Abattoirs that slaughtered >1% of the total delivered slaughter in 2001 were included. The meat samples from broilers were collected from all five broilers slaughterhouses in Norway. The faecal samples from broiler livestock were systematically sampled at four of the Regional Laboratories at the National Veterinary Institute from samples collected according to the Norwegian *Salmonella* control programme for live animals. The first sample on a specific weekday during the whole sampling period was collected at each laboratory.

In addition, indicator bacteria from faecal samples collected in the National Health Surveillance Programme for Cervids were included. From the species red deer, roe deer and moose, 50 samples each were collected for isolation of indicator bacteria.

A survey samples from dog food (chewing bones, frozen offal products and dried products like pigs' ears, ox penises, etc.) were collected by District Veterinary Officers as part of a survey conducted by the Norwegian Animal Health Authority.

Isolation and identification of bacteria

Escherichia coli

Bacteria were isolated and identified at the National Veterinary Institute. Five grams of material from each specimen were incubated in 45 ml of MacConkey broth (Oxoid). After incubation at 44°C for 24 h, a small amount of broth was plated onto the surface of lactose agar (Difco). Intestinal content was gathered on swabs and plated directly without broth enrichment. After incubation at 37°C for 24 h, a typical colony was plated onto blood agar (Heart infusion agar (Difco) containing 5% bovine blood). Colonies were identified as *E. coli* by typical appearance, lactose fermentation and a positive indole reaction.

***Enterococcus* spp.**

Bacteria were isolated and identified at the National Veterinary Institute. Five grams of material from each specimen were incubated in 45 ml of Azide dextrose broth (Oxoid). After incubation at 44°C for 24 h, a small amount of broth was plated onto the surface of Slanetz & Bartley agar (Oxoid). Intestinal content was gathered on swabs and plated directly without broth enrichment. After incubation at 44°C for 48h, a typical colony was plated onto blood agar (Heart infusion agar (Difco) with 5% bovine blood). Typical colonies were tested by negative catalase reaction and further identified by *ddl*-PCR.

For the selective isolation of vancomycin resistant enterococci (VRE), serial dilutions of the samples were plated out on Slanetz and Bartley's agar plates with and without 32 mg/L vancomycin. One colony of VRE from each positive sample was selected, and the isolates confirmed as *Enterococcus* spp. by phenotypic characterisation. The isolates were further identified to species level and tested for the presence of the *vanA* gene using PCR.

Staphylococcus intermedius

The isolates were either obtained from samples submitted to the National Veterinary Institute and cultivated on one blood agar plate (heart infusion agar (Difco) with 5% bovine blood), or blood agar plates with isolates were submitted directly from the Norwegian School of Veterinary Science. The plates were incubated in 5% CO_2 atmosphere at 37°C for 16-24 hrs. Greyish white colonies with a beta-haemolytic zone on blood agar were isolated and tested for cell morphology and Gram stain, production of catalase, β-galactosidase and fermentation of D-mannitol.

Susceptibility testing

Only one isolate per herd or product were tested for antimicrobial susceptibility. Bacterial isolates were tested for antimicrobial susceptibility at the National Veterinary Institute. MIC (minimum inhibitory concentration) values for isolates from dog food were obtained using Mueller-Hinton agar (MH) and Etest (AB Biodisk). For staphylococci, MH and Etest were used to determine MIC values for ciprofloxacin, fucidic acid and trimethoprim and all isolates were tested for production of β-lactamase using the cloverleaf method. The VetMIC™ microdilution method (Dept. of Antibiotics, National Veterinary Institute, Sweden) was used for the other bacteria and substances. In some cases, if out of range for the VetMIC™ plates, MIC values were obtained using MH and Etest. Breakpoints for antimicrobial resistance were determined on the basis of microbiological criteria, however, NCCLS breakpoints were used when appropriate (Appendix 6).

Quality assurance systems

The following bacteria were included as quality controls on a weekly basis, *E. coli* ATCC 25922, *E. faecalis* ATCC 29212 and *Staphylococcus intermedius* ATCC 29213. The following resistant bacteria were tested on a regular basis: and CCUG 35603, *E. faecium* CCUG 33829 and CCUG 36804 and *E. faecalis* CCUG 37389. The results were approved according to reference values given by NCCLS when available.

The participating laboratories at the National Veterinary Institute are accredited according to the requirements of NS-EN ISO/IEC 17025 and participate in an external quality assurance programme for veterinary pathogens. The programme is organized by the VLQAS.

Data processing

Susceptibility test results were recorded and processed in WHONET5, a program developed by the World Health Organization (WHO) for analysis of antimicrobial resistance data (ftp.who.int/data/cds/csreph). The susceptibility data were stored as continuous values (MIC). In addition data was imported into SAS, Enterprise guide V.2. to obtain exact 95% confidence intervals for the prevalence's of resistance. For this purpose the susceptibility data were categorised as susceptible or resistant, respectively, as defined by the relevant breakpoint. The function Proc freq, using exact binomial was used for the calculation of prevalences of resistance including 95% confidence intervals.

Appendix 4
Sampling, microbiological methods and data processing of zoonotic and other enteropathogenic bacteria

Sampling strategy - animals
Salmonella
Samples from animals were collected according to The Norwegian Salmonella Control Programme for Live Animals. Additional samples were obtained from animals during clinical examinations or necropsies at the National Veterinary Institute. One isolate of each serovar per incident was included for susceptibility testing.

Campylobacter jejuni
As part of the Norwegian action plan against *Campylobacter* in broilers (www.zoonose.no), cloacal samples from chickens were collected at farm level or at slaughter plants, and samples from fresh broiler products were collected at retail level. One isolate per positive farm or batch of products was included for susceptibility testing.

Sampling strategy - humans
Salmonella, Yersinia enterocolitica* and *Shigella
All the human isolates were obtained from clinical specimens. One isolate per patient was included for susceptibility testing.

Campylobacter
A total of 250 human isolates were obtained from clinical specimens. Five regional laboratories submitted the first five isolates each month to the National Reference Laboratory for Enteropathogenic Bacteria at the Norwegian Institute of Public Health. One isolate per patient was included for susceptibility testing.

Isolation and identification of bacteria
Isolation and identification of *Salmonella* from animals were carried out by the National Veterinary Institute according to the Nordic Committee on Food Analyses (NMKL) method number 71. Isolation and identification of *Campylobacter jejuni* from broilers were carried out by the Municipal Food Control Authorities according to the Nordic Committee on Food Analyses (NMKL) method number 119, with minor modifications.

Isolation and identification of bacteria from humans were performed according to conventional methods described in standard reference literature (e.g. the ASM Manual of Clinical Microbiology, Edwards and Ewings Identification of Enterobacteriaceae). The identification of all isolates from animals and humans were verified at the National Reference Laboratory for Enteropathogenic Bacteria at the Norwegian Institute of Public Health.

Susceptibility testing
The isolates from animals were tested for antimicrobial susceptibility at the National Veterinary Institute. MIC values were obtained using the VetMIC^{TM} microdilution method (Dept. of Antibiotics, National Veterinary Institute, Sweden).

The *Salmonella*, *Yersinia* and *Shigella* isolates from humans were tested for antimicrobial susceptibility at the Norwegian Institute of Public Health by an agar disc diffusion test using PDM II agar plates and PDM discs (AB Biodisk, Solna, Sweden). The *Campylobacter* isolates from humans were tested for antimicrobial susceptibility at the Norwegian Institute of Public Health by using Etest (AB Biodisk).

For animal isolates, microbiological breakpoints were mostly used. However, NCCLS breakpoints were applied when available and appropriate. For human isolates, breakpoints defined by AFA (Norwegian Reference Group on Antibiotic Susceptibility Testing) were applied.

Quality assurance systems
The National Veterinary Institute and the Reference Laboratory for Enteropathogenic Bacteria at the Norwegian Institute of Public Health have a quality assurance system according to the requirements of NS-EN ISO/IEC 17025.
Campylobacter jejuni subsp. *jejuni* CCUG 33057and CCUG 33560 were used as quality control at the National Veterinary Institute on a weekly basis. The National Veterinary Institute participates in an external quality assurance programme for veterinary pathogens. The programme is organized by the VLQAS (Veterinary Laboratories Agency Quality Assurance Unit, Loughborough, England).
The Norwegian Institute of Public Health participates in the external quality assessment programme for *Salmonella* organized by Enter-Net.

Data processing
Susceptibility data were recorded and processed in WHONET5, a program developed by the World Health Organization (WHO) for analysis of antimicrobial resistance data (ftp.who.int/data/cds/csreph).

Appendix 5
Sampling, microbiological methods and data handling in NORM

General considerations
NORM is based upon periodic sampling of bacteria from patients with respiratory tract infections, wound infections, urinary tract infections, or septicemiae. For enteric infections see Appendix 4. 2002 was the third year of surveillance, and all twenty-five laboratories in Norway participated in the surveillance system in addition to the National Institute of Public Health. The surveillance strategy is based on sampling and local testing of bacterial isolates from defined clinical conditions. All laboratories follow the same sampling strategy and use identical criteria for the inclusion of bacterial strains. Only one isolate per patient and infectious episode is included. All bacteria were identified using conventional methods as described in the ASM Manual of Clinical Microbiology (7^{th} ed). The surveillance period started in the beginning of January, and consecutive bacterial isolates were included up to a defined maximum of isolates for each surveillance category. The surveillance categories in 2002 were: *E. coli*, *Klebsiella* spp., *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Enterococcus* spp. from blood cultures; *Streptococcus pyogenes* from respiratory tract infections and from wound infections and *E. coli* from urinary tract infections. Blood culture isolates, respiratory tract isolates and isolates from wound specimens were tested using Etest (AB Biodisk, Solna, Sweden), while isolates from urinary tract infections were examined by a disc diffusion method in accordance with the Norwegian Reference Group on Antibiotic Susceptibility Testing (AFA). All resistance values were recorded either as MICs or mm inhibition zone sizes in order to monitor trends in the occurrence of resistance. Suspected MRSA (*S. aureus* with oxacillin MIC $\geq$ 4 mg/L) were to be confirmed by *mecA* PCR, and suspected VRE (enterococci growing on BHI with 6 mg/L vancomycin) were to be confirmed by PCRs for the *van* gene complex. A computer program (the NORM program) was used for the registration of patient data, sample data and resistance data. Data were analyzed by WHONET5 with the aid of a special program (NORMlink developed by John Stelling) converting the data base structure of NORM to a single file format. Baclink was subsequently used to convert data to the WHONET format

Blood culture isolates
Consecutive isolates of up to 50 each of *E. coli*, *S. aureus*, and pneumococci, up to 25 isolates of *Klebsiella* spp., and up to 20 isolates of enterococci from January until testing time in September to October were included in the surveillance. All isolates were identified to the species level using conventional bacteriological methods. All isolates were tested using Etest (AB Biodisk, Solna, Sweden). A total of 973 isolates of *E. coli*, 327 isolates of *Klebsiella* spp, 726 isolates of *S. aureus* and 252 isolates of enterococci were tested on PDM agar at 35ºC in ambient air, while the 538 isolates of pneumococci were tested on PDM (AB Biodisk, Solna, Sweden) agar supplemented with 5% lysed horse blood at 35ºC in 5% CO_2. All *S. aureus* isolates were tested for production of β-lactamase using either the nitrocefin disk, the acidometric agar plate (3.6 mg/L penicillin G and phenol red) or the clover leaf method. All *S. aureus* isolates were screened for methicillin-resistance using MH agar (Difco) with 4% NaCl and oxacillin 4 mg/L and a spot inoculum of 10^6 cfu/spot. All enterococci were screened for vancomycin resistance using BHI agar (Difco) and vancomycin 6 mg/L. The following strains were used for quality control: *E. coli* ATCC 25922, *E. faecalis* ATCC 29212, *S. pneumoniae* ATCC 49619, *S. aureus* ATCC 29213, *S. aureus* ATCC 43300 (heterogeneous methicillin resistance), and *S. aureus* CCUG 35600 (homogeneous methicillin resistance)

Respiratory tract isolates
Up to 50 consecutive isolates each of *S. pyogenes* from patients with respiratory tract infections were collected in each laboratory from January to March. All isolates were kept in a freezer and tested in batch using Etest (AB Biodisk, Solna Sweden). A total number of 568 *S. pyogenes* were included in the study. *S. pyogenes* were tested on PDM agar supplemented with 5% lysed horse blood at 35ºC in 5% CO_2. The following strain was used for quality control: *S. pneumoniae* ATCC 49619.

Wound specimens
Up to 50 consecutive isolates of *S. pyogenes* from patients with wound infections were collected in each laboratory from January to March. All isolates were kept in a freezer and tested in batch using Etest (AB Biodisk, Solna Sweden). A total of 395 *S. pyogenes* were included in the study. *S. pyogenes* were tested on PDM agar supplemented with 5% lysed horse blood at 35ºC in 5% CO_2. The following strain was used for quality control: *S. pneumoniae* ATCC 49619.

Urinary tract isolates
Up to 50 consecutive isolates of *E. coli* from patients with urinary tract infections were collected in each lab during January and February. All isolates were either kept on bench or in a freezer until tested in batch using a disk diffusion method with PDM agar and paper disk (AB Biodisk, Solna Sweden) at 35ºC in ambient air. The study included 1044 *E. coli* isolates. The following strain was used for quality control: *E. coli* ATCC 25922.

Mycobacterium tuberculosis
In the year 2002, antimicrobial susceptibility testing of *M. tuberculosis* was performed at the following institutions: National Institute of Public Health, Oslo, Ullevål University Hospital, Oslo, National Hospital, Oslo, and Haukeland Hospital, Bergen. The majority of isolates were tested using the BACTEC (National Institute of Public Health and Ullevål University Hospital) or MGIT systems (National Hospital). All four laboratories participate in an external quality control program organized by the WHO.

Appendix 6
Breakpoints NORM-VET

The following breakpoints for antimicrobial resistance are used in this report. NORM-VET data are categorized by microbiological breakpoints (isolates from feed, animals and food). For details regarding bacteria and antimicrobial panels, see the tables in the text.

Antimicrobials	R (MIC values, mg/L)	*Campylobacter*	*E. coli/Salmonella*	*Staphylococcus*	*Enterococcus*
Oxytetracycline	> 8	■	■	■	■
Chloramphenicol	> 16		■	■	■
Florfenicol	> 16		■		
Ampicillin	> 8				■
	> 16	■	■		
Penicillins	> 0.125			■	
Oxacillin	> 2			■	
Cephalothin	> 1			■	
Cefuroxime	> 16		■		
Ceftiofur	> 2		■		
Trimethoprim	> 8		■	■	
Sulfonamides	> 256		■		
TMS	> 2			■	
Erythromycin	> 4			■	■
	> 16	■			
Clindamycin	> 2			■	
Streptomycin	> 16			■	
	> 32		■		
	> 1024				■
Gentamicin	> 8	■	■	■	
	> 512				■
Kanamycin	> 32		■		
Neomycin	> 8		■		
	> 32			■	
	> 1024				■
Apramycin	> 32		■		
Ciprofloxacin	> 0.5			■	
Enrofloxacin	> 0.25		■		
	> 1	■			
Nalidixic acid	> 16	■	■		
Vancomycin	> 16			■	■
Fucidic acid	> 0.5			■	
Avilamycin	> 8			■	
	> 16				■
Bacitracin	> 32				■
Flavomycin	> 32				■
Virginiamycin	> 4			■	
	> 8				■
Narasin	> 2				■

Appendix 7
Breakpoints NORM

Breakpoints for antimicrobial resistance used in this report. NORM data are categorized according to the breakpoints of the Norwegian Reference Group on Antibiotic Susceptibility Testing – AFA (isolates from humans). For details regarding bacteria and antimicrobial panels, see tables in text.

	MIC values mg/L						
Antimicrobials	S	R	*E. coli/Klebsiella*	*Staphylococcus*	*S. pneumoniae*	*S. pyogenes*	*Enterococcus*
Amoxi./clav.	≤ 0.5	≥ 32	■				
Ampicillin	≤ 1	≥ 32	■				
	≤ 2	≥ 16					■
Cefpirome	≤ 1	≥ 32	■				
Cefotaxime	≤ 0.5	≥ 4			■		
Ceftazidime	≤ 1	≥ 32	■				
Cefuroxime	≤ 0.5	≥ 4			■		
	≤ 1	≥ 32	■				
	≤ 2	≥ 8		■			
Chloramphenicol	≤ 4	≥ 8			■		
Ciprofloxacin	≤ 0.125	≥ 4	■		■		
Clindamycin	≤ 0.25	≥ 4			■	■	
	≤ 1	≥ 4		■			
Doxycycline	≤ 1	≥ 4		■	■	■	
Erythromycin	≤ 0.5	≥ 1			■	■	
	≤ 1	≥ 4		■			
Fucidic acid	≤ 0.5	≥ 1		■			
Gentamicin	≤ 2	≥ 8	■	■			
	≤ 512	≥ 1024					■
Meropenem	≤ 0.5	≥ 4	■				
Oxacillin	≤ 2	≥ 4		■			
Penicillin	≤ 0.064	≥ 0.25		■			
	≤ 0.064	≥ 2			■	■	
	≤ 4	≥ 16					■
Piperacillin/tazo.	≤ 8	≥ 32	■				
Streptomycin	≤ 512	≥ 1024					■
TMS	≤ 0.5	≥ 4			■	■	
	≤ 2	≥ 16	■				
Vancomycin	≤ 2	≥ 8			■		
	≤ 4	≥ 16		■			■

	Breakpoints (mm)	
Antimicrobials (amount in disks)	**S**	**R**
Ampicillin (10 µg)	≥ 24	≤ 12
Ciprofloxacin (10 µg)	≥ 28	≤ 20
Mecillinam (10 µg)	≥ 20	≤ 16
Nalidixic acid (30 µg)	≥ 17	≤ 16
Nitrofurantoin (100 µg)	≥ 19	≤ 18
Sulfonamide (250 µg)	≥ 19	≤ 14
Trimethoprim (5 µg)	≥ 21	≤ 19

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