2001

NORM
NORM-VET

Consumption of Antimicrobial Agents and Occurrence of Antimicrobial Resistance in Norway

ISSN: 1502-2307
Any use of data from NORM/NORM-VET 2001 should include specific reference to this report.
Suggested citation: NORM/NORM-VET 2001. Consumption of Antimicrobial Agents and Occurrence of Resistance in Norway. Tromsø / Oslo 2002. ISSN:1502-2307.
The report is available at www.zoonose.no

CONTRIBUTORS AND PARTICIPANTS

Editors:

Hilde Kruse	NORM-VET, Norwegian Zoonosis Centre
Gunnar Skov Simonsen	NORM, Department of Microbiology, University Hospital of North Norway

Authors:

Hege Salvesen Blix	Norwegian Institute of Public Health
Kari Grave	VETLIS / Norwegian School of Veterinary Science
Einar Heldal	Norwegian Institute of Public Health
Merete Hofshagen	NORM-VET, Norwegian Zoonosis Centre
Hilde Kruse	NORM-VET, Norwegian Zoonosis Centre
Jørgen Lassen	Norwegian Institute of Public Health
Ane Nødtvedt	NORM-VET, Norwegian Zoonosis Centre
Per Sandven	Norwegian Institute of Public Health
Gunnar Skov Simonsen	NORM, Department of Microbiology, University Hospital of North Norway
Martin Steinbakk	NORM, Department of Microbiology, University Hospital of North Norway

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	Gudmund Holstad / Tormod Mørk / Ellen Christensen / Hanne Tharaldsen
Norwegian Zoonosis Centre	Ane Nødtvedt / Hilde Kruse / Merete Hofshagen

Institutions participating in NORM:

Aker University Hospital, Department of Bacteriology	Signe Holta Ringertz / Bitten Rasmussen
Akershus University Hospital, Department of Microbiology	Martin Steinbakk / Siri Haug
Bærum Hospital, Central Laboratory, Section of Microbiology	Fredrik Müller / Merriam Sundberg
Central Hospital of Buskerud, Department of Microbiology	Hjørdis Iveland / Ann-Elise Johansen
Central Hospital of Nordland, Department of Microbiology	Liisa Mortensen / Rannveig M. M. Henriksen
Central Hospital of Nord-Trøndelag, Department of Microbiology	Arne Mehl / Eldbjørg Berg
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 / Herdis Kjelkenes
Central Hospital of Vest-Agder, Department of Microbiology	Ståle Tofteland / Vigdis Landsverk
Central Hospital of Vestfold, Department of Microbiology	Rolf Schøyen / Astrid Lia
County Hospital of Møre og Romsdal, Department of Microbiology	Einar Vik / Margreet B. Sandhaug
Haukeland Hospital, Department of Immunology and Microbiology	Asbjørn Digranes / Berit Riksheim
National Hospital, University of Oslo, Institute of Medical Microbiology	Mette Walberg / Magli Bøvre
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	Turid Mannsåker / Thea Bergheim
University Hospital of North Norway, Department of Microbiology	Gunnar Skov Simonsen / Veronica Olsen
University Hospital of Trondheim, Department of Microbiology	Per Leiv Svarva / Liselotte Buarø

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	Central Hospital of Akershus, 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,

CONTENTS

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. Many programmes focus primarily on human consumption and resistance in human pathogens, but some countries 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 WHO Collaborating Centre for Drug Statistics Methodology at 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 presents the results from NORM and NORM-VET for 2001. The first joint report from these two programmes was issued in 2001 and presented data for the year 2000. In addition to resistance data, the reports present data on the consumption of antimicrobial agents in humans and animals in Norway. The present report, together with last year's report 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 programmess are valuable tools for setting policies, assessing risks and evaluating interventions.

The editors would like to cordially thank all those who contributed to data collection and the writing of this report.

Tromsø / Oslo, August 2002

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 2001 og er den andre 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 5694 kg i 2001. Dette er en reduksjon på 40% siden 1995. 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 36% i 2001. β-laktamase-følsomme penicilliner utgjorde 94% av totalsalget av veterinære penicillinpreparater i 2001. Kombinasjonspreparater av sulfonamider og trimetoprim eller baquiloprim økte sin andel av totalsalget fra 11% i 1995 til 26% i 2001, mens andelen av penicilliner kombinert med aminoglykosider (dihydrostreptomycin) sank fra 35% til 28%. Tetracyklinenes andel av totalsalget sank fra 5% i 1995 til 3% i 2001. Sulfonamidene utgjorde 11% av salget i 1995, mens det i 2001 ikke ble solgt veterinære farmasøytiske spesialpreparater som kun inneholdt sulfonamider. Den gunstige situasjonen kan tilskrives en restriktiv legemiddelpolitikk når det gjelder antibiotika, samt en holdningskampanje for en kritisk holdning til antibiotikabruk innenfor husdyrproduksjonen.

Totalsalget av veterinære antibakterielle midler godkjent for terapeutisk bruk til oppdrettsfisk i Norge var 645 kg i 2001. Kinoloner utgjorde 76% av dette salget. I løpet av de siste 14 årene har forbruket av antibakterielle midler i oppdrettsnæringen blitt redusert med 99% samtidig som produksjonen av oppdrettsfisk er mangedoblet. 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. Husdyrnæringene innførte i 1995 et selvpålagt forbud mot bruk av alle antibakterielle vekstfremmere. Myndighetene forbød vekstfremmeren virginiamycin i 1998. Forbruket av antibakterielle vekstfremmere har vært minimalt etter 1995, og tilnærmet 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 antibiotika til systemisk bruk hos mennesker var 16,8 definerte døgndoser (DDD)/1000 innbyggere/døgn i 2001. Dette er en økning på 3% sammenlignet med 2000. Økningen ble observert for alle grupper av antibiotika unntatt tetracykliner, sulfonamider og trimetoprim. Forbruket av antibiotika til mennesker i Norge er på samme nivå som i Sverige og Danmark og er lavt sammenlignet med syd-europeiske land. Penicilliner var den mest brukte antibiotikagruppen og utgjorde 43% av totalforbruket. Andelen har vært stabil de siste fem årene, men det sees en dreining fra β-laktamase-følsomme penicilliner (31% i 1995 versus 28% i 2001) til bredspektrede penicilliner (10% i 1995 versus 13% i 2001). Tetracykliner utgjorde 19% av totalforbruket, en reduksjon på 34% siden 1993. Makrolider og linkosamider utgjorde 11% av totalforbruket. Dette utgjør en økning på 13% siden 2000. Økningen skyldes hovedsakelig økt forbruk av erytromycin, men en viss økning ble også påvist for klindamycin, azitromycin og klaritromycin.

Sykehusene sto for bare 6,6% av det totale antibiotikaforbruket til systemisk bruk hos mennesker i 2001. Forbruksmønstret var forskjellig på sykehus og i allmennpraksis, sannsynligvis på grunn av en større andel alvorlige infeksjoner blant sykehuspasienter. Forbruket av de bredspektrede antibiotikagruppene cefalosporiner, karbapenemer, aminoglykosider og kinoloner økte i 2001. Cefalosporiner var nest etter penicillin den hyppigst brukte antibiotikagruppen på sykehus, og sykehusene sto for halvparten av det totale cefalosporinforbruket.

Resistens hos indikatorbakterier

Ved undersøkelse av *Escherichia coli* fra hundefôr ble det funnet at 19% av isolatene var resistente mot ett eller flere av de antibiotika som inngikk i undersøkelsen, hyppigst mot henholdsvis tetracyklin, streptomycin, trimetoprim og ampicillin.
En moderat forekomst av resistens ble observert blant *E. coli* fra tarminnhold fra norske slaktegriser. Til sammen 26% av isolatene var resistente mot ett eller flere av de antibiotika som inngikk. Resistens mot streptomycin ble hyppigst observert, etterfulgt av resistens mot henholdsvis sulfonamider, trimetoprim, tetracyklin, og ampicillin. Dette er alle antibiotika som benyttes terapeutisk i norsk slaktegrisproduksjon. Det ble ikke påvist resistens mot fluorokinoloner.
En moderat forekomst av resistens ble observert blant *E. coli* og enterokokker fra tarminnhold og kjøtt fra norsk storfe. Henholdsvis 19% (tarminnhold) og 7% (kjøtt) av *E. coli* var resistente mot ett eller flere av de antibiotika som inngikk. Resistens mot streptomycin ble hyppigst påvist, etterfulgt av resistens mot henholdsvis ampicillin, sulfonamider, tetracyklin, trimetoprim og neomycin. For

E. faecalis fra storfekjøtt var 10% resistente mot ett eller flere av de antibiotika som inngikk. De antibiotika det ble observert resistens mot benyttes terapeutisk til storfe i Norge. Resistens mot fluorokinoloner ble ikke observert.
En lav forekomst av resistens ble observert blant *E. coli* fra fårekjøtt. Kun 3% av isolatene var resistente mot ett eller flere av de antibiotika som inngikk. En moderat forekomst av resistens ble observert blant *E. faecalis* fra fårekjøtt. Til sammen 18% var resistente mot ett eller flere av de antibiotika som inngikk. Det ble hovedsaklig påvist resistens mot antibiotika som brukes terapeutisk til sau i Norge. Resistens mot fluorokinoloner ble ikke observert.

Resultatene fra resistensundersøkelsene av indikator-bakterier fra norske svin, storfe og sau viser at fekale indikatorbakterier fra disse kildene kan være resistente mot ulike typer antibiotika. Generelt ble det hyppigst påvist resistens mot de antibiotika som er blitt mest benyttet i de respektive næringer. Det synes følgelig å være en sammenheng mellom bruk av antibiotika til matproduserende dyr og forekomst av bakterier som uttrykker resistens mot tilsvarende antibiotika i tarminnhold og kjøtt fra slike dyr.

Resistens hos kliniske isolater fra dyr

Forekomsten av resistens blant *Staphylococcus aureus* fra klinisk og subklinisk mastitt hos ku er fortsatt på et lavt nivå. Henholdsvis 92% og 90% av isolatene var følsomme for alle antibiotika som inngikk i undersøkelsen. Det ble hyppigst påvist resistens overfor terapeutisk vanlig brukte antibiotika som penicillin, streptomycin og trimetoprim/sulfa og i mindre grad tetracyklin. Blant koagulase-negative stafylokokker fra mastitt hos ku ble det påvist en betydelig høyere forekomst av resistens sammenlignet med *S. aureus*. Det ble ikke påvist resistens mot kinoloner, cefalosporiner eller oxacillin.

Resistens hos zoonosebakterier og andre næringsmiddelbårne bakterier

I 2001 ble multiresistent *Salmonella* Typhimurium DT104 påvist i to storfebesetninger, henholdsvis i Rogaland og Østfold. Dette var første gang denne fryktede bakterien ble oppdaget blant dyr i Norge. På den ene gården ble samme bakteriestamme isolert fra eieren. Smittekildene er ukjente. På grunn av den lave forekomsten av *Salmonella* blant norske husdyr var få *Salmonella* isolater tilgjengelige for resistens-undersøkelse. Resultatene tyder på at resistens ikke var spesielt utbredt blant endemisk forekommende *S.* Typhimurium i den ville faunaen eller *S. diarizonae* i den norske sauepopulasjonen. Det ble også undersøkt ulike *Salmonella* spp. fra måker, og samtlige var følsomme for alle antibiotika det ble testet for.

For *Salmonella* fra mennesker var resistens mer utbredt blant *S.* Typhimurium enn blant *S.* Enteritidis, et forhold som også rapporteres fra andre undersøkelser. For *S.* Typhimurium var forekomsten av resistens noe høyere blant isolater ervervet utenlands sammenlignet med isolater ervervet i Norge, også når isolater av fagtype DT104 ble ekskludert. Til sammen 86% av isolatene ervervet innenlands (DT104 unntatt) var følsomme for alle antibiotika som inngikk eller resistente mot kun ett antibiotikum, sammenlignet med 69% av isolatene ervervet utenlands. Det ble observert en høyere forekomst av resistens mot henholdsvis nalidiksinsyre, trimetoprim/sulfonamider og tetracykliner i sistnevnte gruppe. Nalidiksinsyreresistens ble kun påvist blant *S.* Typhimurium ervervet utenlands; hos 21% av DT104-isolatene og 5% av isolater av øvrige fagtyper. For DT104-isolatene var resistensmønsteret ganske likt for isolater ervervet innenlands og utenlands, med unntak av at nalidiksinsyreresistens bare ble påvist i sistnevnte gruppe.

Forekomsten av resistens blant *Campylobacter jejuni* fra norsk slaktekylling var lav. Kun 4% av isolatene var resistente mot ett eller flere av de antibiotika som inngikk i undersøkelsen; 2% mot ampicillin, 1% mot nalidiksinsyre og ciprofloxacin, og 2% mot nalidiksinsyre/ciprofloxacin og ampicillin eller tetracyklin. Dette samsvarer med den terapeutiske bruken av antibiotika til norsk slaktekylling.

For *Campylobacter* fra mennesker var forekomsten av resistens betydelig lavere blant *C. jejuni* ervervet innenlands enn blant *C. jejuni* ervervet utenlands. I førstnevnte gruppe var 85% følsomme for alle antibiotika som inngikk i motsetning til 33% i sistnevnte gruppe. Forskjellen skyldes en høyere forekomst av tetracyklinresistens (43% mot 10%) og fluorokinolonresistens (60% mot 7%) blant *C. jejuni* ervervet i utlandet. Resultatene for innenlands ervervet *C. jejuni* samsvarer til en viss grad med resultatene for norsk slaktekylling. Erytromycin-resistens ble imidlertid kun påvist i humane isolater (3%). Alle *C. coli* som inngikk i materialet var ervervet utenlands. Disse isolatene var mer resistente enn *C. jejuni* idet kun 16% av *C. coli* var følsomme for alle antibiotika som inngikk, og 18% var resistente mot fire eller fem antibiotika. Resistens mot erytromycin (29%) og til en viss grad gentamicin (5%) var mer utbredt blant *C. coli.*

Resistens var utbredt blant *Shigella* spp. fra mennesker. Det ble hyppigst påvist resistens mot henholdsvis tetracyklin og trimetoprim/sulfonamider, fulgt av ampicillin og kloramfenikol. Det ble påvist en del nalidixinsyre-resistens og redusert følsomhet for ciprofloxacin hvilket indikerer utvikling av fluorokinolonresistens. Shigellainfeksjoner var i all hovedsak ervervet utenlands.

Resistens hos kliniske isolater fra mennesker

Forekomsten av antibiotikaresistens i humane kliniske isolater var fortsatt meget lav i Norge i 2001. Det ble bare påvist mindre endringer fra 2000 til 2001 for bakterietyper som ble undersøkt begge år. Det ble funnet enkeltisolater av *Klebsiella* spp. med utvidet β-lactamaseproduksjon (3 ESBL blant 260 isolater), methicillinresistente *Staphylococcus aureus* (2 MRSA blant 1339 isolater), *Streptococcus pneumoniae* med nedsatt følsomhet for penicillin (29 PNSP blant 1168

isolater), og multiresistent *Mycobacterium tuberculosis* (2 MDR isolater blant 203 ikke tidligere behandlede og 3 MDR isolater blant 11 tidligere behandlede). De to tilfellene av MRSA-infeksjon og de fem tilfellene av multiresistent tuberkulose var sannsynligvis alle importerte fra utlandet. Det ble ikke påvist enterokokkisolater med overførbar vankomycinresistens.

Det er grunn til bekymring over den høye forekomsten av fucidinresistens blant *S. aureus* fra sårprøver (20,8%). Produsenten av fucidinsalve har nå frarådet bruk av dette preparatet ved behandling av hudinfeksjoner som mistenkes for å være forårsaket av stafylokokker. Den vesentlig lavere forekomsten av fucidinresistens blant *S. aureus* fra blodkultur (5,1%) støtter teorien om at en spesifikk klon er årsak til mange av hudinfeksjonene med gule stafylokokker. Flere forskningsgrupper undersøker nå dette forholdet nærmere.

En annen interessant utvikling ble påvist for *Klebsiella* spp. fra urinvegsinfeksjoner. Andelen av resistente isolater økte i forhold til 2000 for ampicillin (53,1% versus 37,5%), mecillinam (9,3% versus 7,0%), trimetoprim (14,5% versus 3,5%), sulfonamider (9,2% versus 3,5%) og nitrofurantoin (30,7% versus 24,1%). Endringene kan delvis skyldes det lave antallet som ble undersøkt i 2000, men resultatene synliggjør hvor utbredt antibiotikaresistens er blant *Klebsiella* spp. Det er spesielt grunn til å merke seg doblingen av nedsatt følsomhet for ciprofloxacin og femdoblingen av nalidixinsyreresistens. I henhold til norske retningslinjer bør behandling av urinvegsinfeksjoner med kinoloner avgrenses til kompliserte tilfeller med resistente mikrober. Økende kinolonresistens blant vanlige urinvegspatogener er en advarsel til klinikerne om at bruk av denne antibiotikagruppen bør begrenses.

Enterococcus spp. fra blodkultur ble i 2001 inndelt i *E. faecalis* og *E. faecium* for å vise den vesentlig lavere følsomheten for β-laktam-antibiotika blant *E. faecium* sammenlignet med *E. faecalis* (50% versus 95,5% følsomhet for ampicillin (høygradig)). Den høye forekomsten av streptomycinresistens (60% blant *E. faecium* og 12,3% blant *E. faecalis*) har i seg selv liten betydning i og med at streptomycin brukes lite i Norge. Økende streptomycinresistens kan imidlertid være et varsel om mer omfattende aminoglycosidresistens hos enterokokker, selv om mer enn 95% av alle enterokokk-isolater fortsatt er følsomme for gentamicin.

Kun 7% av *Haemophilus influenzae* fra luftveger produserte β-laktamase. I tillegg fikk man i 2001 undersøkt motsigende resultater for doxycyklin-resistens hos *H. influenzae* i NORM 2000. Resultatene av undersøkelsen viser klart nødvendigheten av standardisering av alle ledd i resistensundersøkelsen.

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 matproduksjonen 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 Norway 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 second joint report, presents data for the year 2001. 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 which are not part of the continous monitoring through NORM or NORM-VET.

Use of antimicrobial agents in animals

In 2001, the total sale of antibacterial drugs approved for therapeutic use in animals (excluding fish) in Norway was 5,694 kg. This amount is considered low compared to many other countries and represents a 40% decrease since 1995. Furthermore, the patterns of use can be regarded as favourable. The proportion of the total sale accounted for by pure penicillin preparations increased from 25% in 1995 to 36% in 2001. β-lactamase sensitive penicillins accounted for 94% of the veterinary penicillin preparations sold in 2001. The proportion accounted for by sulfonamides in combination with trimethoprim or baquiloprim increased from 11% in 1995 to 26% in 2001, and the proportion of combined preparations of penicillins and aminoglycosides (dihydrostreptomycin) decreased from 35% to 28%. The proportion of the total sales accounted for by sulfonamides decreased gradually from 11% in 1995 to 0% in 2001, and the proportion of tetracyclines declined from 5% to 3%. This favourable situation is mainly attributed to restrictive antimicrobial drug legislation in Norway as well as a campaign focusing on the prudent use of antimicrobials in food producing animals.

The total sales of veterinary antibacterial drugs for therapeutic use in farmed fish was 645 kg of active substance in 2001. Quinolones accounted for 76% of this. During the past 14 years, the total use of antibacterial drugs in farmed fish has decreased by 99%. In the same period, the total production of fish has increased massively. The decrease in antibacterial consumption 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 the substance was prohibited in 1995. The same year, Norwegian food animal production industries voluntarily abandoned the use of all antibacterial growth promoters. Virginiamycin was prohibited in 1998. Since 1995, the consumption of antibacterial growth promoters in the production of Norwegian food animals has been very low, and since 1998 close to 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 and the use of other ionophores has decreased correspondingly.

Use of antimicrobials in humans

In 2001, the overall consumption of antibacterials for systemic use in humans was 16.8 DDD (defined daily doses)/1,000 inhabitants/day which is a 3% increase compared to 2000. This trend was observed for all subgroups except tetracyclines, sulfonamides, and trimethoprim. The consumption of antimicrobials in Norway is comparable to Sweden and Denmark, but low compared to Southern Europe. Penicillins were most commonly used and accounted for 43% of the total sales in 2001. This proportion has been stable over the past five years, but there has been a shift in use from β-lactamase sensitive penicillins (31% in 1995 versus 28% in 2001) to penicillins with extended spectrum (10% in 1995 versus 13% in 2001). Tetracyclines accounted for 19% of the total use in 2001, a 34% reduction since 1993. Macrolides and lincosamides accounted for 11% of the total use in 2001, a 13% increase compared to 2000. This change is mainly due to increased use of erythromycin, but slight increases were also observed for clindamycin, azitromycin, and clarithromycin.

Hospitals accounted for only 6.6% of the total antimicrobial consumption for systemic use in humans in 2001. The pattern of use in hospitals differed from the usage in general practice due to a higher prevalence of severe infections in hospital settings. The consumption of broad-spectrum antimicrobials such as cephalosporins, carbapenems, aminoglycosides and quinolones increased in 2001. After penicillin, cephalosporins were the most commonly used antimicrobials in hospitals. Half the cephalosporin consumption was in hospitals.

Resistance among indicator bacteria

Nineteen per cent of the *Escherichia coli* isolates from dog food were resistant to one or more of the antimicrobials included in the test panel. Resistance was most frequently observed for tetracycline, streptomycin, trimethoprim and ampicillin.

A moderate occurrence of resistance was observed among faecal *E. coli* from slaughtered pigs. Altogether, 26% of the isolates were resistant to one or more of the antimicrobials included in the test panel. Resistance to streptomycin was most frequently observed, followed by resistance to sulfonamides, trimethoprim, tetracycline and ampicillin. All these antimicrobials are used for therapeutic purposes in Norwegian swine production. No resistance to fluoroquinolones was observed.

A moderate occurrence of resistance was observed for *E. coli* and enterococci from faecal material and meat from Norwegian cattle. For *E. coli*, 19% (faecal material) and 7% (meat) were resistant to one or more of the antimicrobials included in the test panel. Resistance to streptomycin was most frequently observed, followed by ampicillin, sulfonamides, tetracycline, trimethoprim and neomycin. For *E. faecalis* from cattle meat, 10% were resistant to one or more of the antimicrobials included. Fluoroquinolone resistance was not observed.
A low occurrence of resistance was observed in *E. coli* from Norwegian mutton. Only 3% of the isolates were resistant to one or more of the antimicrobials included in the test panel. A moderate occurrence of resistance was observed in *E. faecalis* from mutton. Altogether, 18% were resistant to one or more of the antimicrobials included. Resistance was detected to antimicrobials that are used therapeutically in Norwegian sheep production. Resistance to fluoroquinolones was not observed.

The results show that indicator bacteria from Norwegian swine, cattle and sheep can express resistance to various types of antimicrobials. In general, resistance was most frequently observed to antimicrobials that have been or are still commonly used in the animal production industries concerned. Thus, there appears to be a relationship between the use of antimicrobials in food producing animals and the occurrence of bacteria expressing resistance to the same drugs in faecal material and meat from such animals.

Resistance among animal clinical isolates

The prevalence of resistance among *Staphylococcus aureus* from clinical and subclinical mastitis remained low, 92% and 90%, respectively, being susceptible to all antimicrobials included in the test panel. Resistance was most commonly detected for antimicrobials used for clinical purposes in dairy cattle: penicillin, streptomycin, trimethoprim/sulfonamides and to a lesser degree tetracyclines. Resistance in coagulase negative staphylococci (CNS) from mastitis in cows was considerably more abundant than *S. aureus* isolates. Resistance to quinolones, cephalosporines or oxacillin was not observed.

Resistance among zoonotic and other food-borne bacteria

In 2001, multiresistant *S.* Typhimurium DT104 was detected in two unrelated cattle herds in south-western and south-eastern Norway. This is the first time this particular *Salmonella* variant has been recognized in animals in Norway. At one farm, the same strain was also isolated from the owner. The sources of infection remain unknown. Owing to the low prevalence of *Salmonella* in Norwegian animal husbandry, few isolates from Norwegian animals were examined. However, the results indicate that resistance is not widespread among clones of *S.* Typhimurium which occur endemically among wild birds in Norway, or *S. diarizonae* which occur endemically in Norwegian sheep. Various *Salmonella* spp. from seagulls were also tested, and all the isolates were susceptible to all the antimicrobials included in the test panel.

For *Salmonella* from humans, higher resistance frequencies were observed in *S.* Typhimurium than in *S.* Enteritidis. For *S.* Typhimurium, higher resistance frequencies were observed for isolates acquired abroad than those acquired domestically, also when isolates belonging to phage type DT104 were excluded. When *S.* Typhimurium DT104-isolates were excluded, 86% of domestically acquired isolates were susceptible to all the antimicrobials included in the test panel or they were resistant to only one antimicrobial, as opposed to 69% of the isolates acquired abroad. This is due to the higher frequency of resistance to nalidixic acid, trimethoprim/sulfonamides and tetracyclines in the latter group. Resistance to nalidixic acid was only detected in *S.* Typhimurium acquired abroad: in 21% of DT104 isolates and 5% of isolates belonging to other phage types. The resistance profiles for multiresistant DT104 were similar for isolates acquired in Norway and abroad, except that resistance to nalidixic acid was only detected in the latter category.

The results indicate a low prevalence of resistance among *Campylobacter jejuni* isolates from Norwegian broilers. Only 4% of the isolates were resistant to one or more of the antimicrobials included, 2% to ampicillin, 1% to nalidixic acid and ciprofloxacin, and 2% to nalidixic acid/ciprofloxacin and ampicillin or tetracycline. This corresponds to the usage of antimicrobials in Norwegian poultry production.

For *Campylobacter* from human cases, resistance was more widespread among *C. jejuni* isolates derived from cases infected abroad (33% susceptible to all antimicrobials included) as opposed to *C. jejuni* isolates derived from cases infected in Norway (85% susceptible). These discrepancies were explained by the widespread resistance to nalidixic acid/ciprofloxacin (60% versus 7%) and to tetracycline (43% versus 10%) among *C. jejuni* acquired abroad. The resistance frequencies for domestically acquired isolates were to some degree in accordance with data from Norwegian poultry. However, resistance to erythromycin was only detected among isolates from humans (3%). All *C. coli* included were acquired outside Norway. The resistance prevalences were higher than in *C. jejuni* acquired abroad; only 16% of the isolates were susceptible to all and 18% were resistant to four or five of the antimicrobials included in the test panel. Resistance to erythromycin (29%) and gentamicin (5%) was more common in *C. coli* than in *C. jejuni*.

Resistance was widespread among *Shigella* spp. isolates from humans. The resistance frequencies were particularly high for tetracycline and trimethpoprim/sulfonamides followed by ampicillin and chloramphenicol. Some isolates were resistant to nalidixic acid and showed intermediate susceptibility to ciprofloxacin indicating that fluoroquinolone resistance could be developing. The vast majority of *Shigella* infections were acquired abroad.

Resistance among clinical isolates from humans

The overall prevalence of antimicrobial resistance in human clinical isolates was still very low in Norway in 2001. Only minor changes were observed from 2000 to 2001. A few isolates were detected of *Klebsiella* spp. producing extended spectrum β-lactamases (3 ESBL out of 260 isolates), methicillin resistant *Staphylococcus aureus* (2 MRSA out of 1,339 isolates), *Streptococcus pneumoniae* not susceptible to penicillin (29 PNSP out of 1,168 isolates), and multiresistant *Mycobacterium tuberculosis* (2 MDR isolates among 203 cases not previously treated and 3 MDR among 11 cases previously treated). All the MRSA and MDR patients had probably acquired their infections abroad. No enterococcal isolates harbouring transferable vancomycin resistance were detected.

The high prevalence of resistance to fucidic acid among *S. aureus* from wound specimens (20.8%) is of concern and led the manufacturer of a topical preparation to discourage its use for the treatment of suspected staphylococcal skin infections (impetigo). The considerably lower prevalence of resistance to fucidic acid among *S. aureus* blood culture isolates (5.1%) strengthens the hypothesis of a specific clone of *S. aureus* causing skin infections. Several research groups are currently investigating this issue.

Another interesting development was seen in *Klebsiella* spp. urinary tract isolates. The proportion of resistant isolates increased in 2001 compared to 2000 for ampicillin (53.1% versus 37.5%), mecillinam (9.3% versus 7.0%), trimethoprim (14.5% versus 3.5%), sulfonamides (9.2% versus 3.5%) and nitrofurantoin (30.7% versus 24.1%). Some of these changes may be due to a small sample size in 2000, but nevertheless demonstrate the high prevalence of resistance among *Klebsiella* spp. The two-fold increase of intermediate susceptibility to ciprofloxacin and the five-fold increase of resistance to nalidixic acid require attention. In Norway, quinolone treatment of urinary tract infections is generally restricted to complicated cases involving resistant isolates and troublesome species. A reduced susceptibility to quinolones in ordinary urinary pathogens is a warning to clinicians that expanded use of this class of antimicrobials should be avoided.

Blood culture isolates of *Enterococcus* spp. were speciated as *E. faecalis* and *E. faecium* in 2001, thus demonstrating the much higher prevalence of β-lactamase resistance in *E. faecium* (50% ampicillin susceptibility) than in *E. faecalis* (95.5% ampicillin susceptibility). The prevalence of high-level resistance to streptomycin (60% in *E. faecium* and 12.3% in *E. faecalis*) may indicate future problems with aminoglycoside-resistant enterococci, even though the prevalence of gentamicin susceptibility still exceeds 95% in both species.

Only 7% of *Haemophilus influenzae* from respiratory tract specimens produced β-lactamase. Earlier discrepancies in doxycycline resistance in *H. influenzae* were resolved by a comparative study of different media used for susceptibility testing. The results demonstrated the importance of standardization of laboratory methods for susceptibility testing.

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 resistant clones are imported from abroad. A continual 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 each table.

TABLE 1. Human population in Norway as of 1 January 2001. Statistics Norway.

Age group	All	Males	Females
0 to 4 years	300 954	154 424	146 530
5 to 14 years	601 477	308 837	292 640
15 to 24 years	540 896	276 109	264 787
25 to 44 years	1 330 914	678 557	652 357
45 to 64 years	1 050 369	531 129	519 240
65 years and older	678 826	282 245	396 581
All age groups	4 503 436	2 231 301	2 272 135

TABLE 2. Livestock population in Norway as of 1 January 2001. Statistics Norway.

Animal category	Animals (No.)	Herds (No.)
Cattle, total	979 274	27 571
Dairy cows (incl. in above total)	298 709	20 378
Beef cows	40 167	5 610
Goats, total	68 600	1 327
Dairy goats (incl. in above total)	50 700	675
Sheep, winterfed	1 112 738	21 308
Pigs, total	626 600	4 920
Breeding animals > 6 months	89 900	2 768
Egg- laying hens > 20 weeks of age	3 188 920	3 572
Broilers		532
Ostrich	1 300*	70*
Turkeys	144 400*	80*
Ducks and geese	11 800*	140*

*Register of Production Subsidies, updated to 31 July 2001

TABLE 3. Number of slaughtered animals approved for human consumption in 2001. Statistics Norway (terrestrial animals) and Directorate of Fisheries (fish).

Animal category	Slaughtered animals
Horses	2 416
Cattle	349 625
Goats	21 196
Sheep	1 203 974
Pigs	1 325 955
Poultry	38 335 296
Ostrich	300
Farmed salmon*	422 400
Farmed trout*	72 800

* Amount in metric tons, ungutted fish

TABLE 4. Live animals (excluding fish) imported to Norway in 2001. Norwegian Animal Health Authority.

Animal species	Individuals	Consignments
Cattle	14	1
Sheep/goats	0	0
Pigs	1	1
Reindeer*	9 400	28
Fur animals	2 002	20
Gallus gallus - day old chicks	> 60 000	12
Gallus gallus - eggs	Not specified	2
Turkeys	13 500	7
Ducks and geese	1 327	7
Ostrich	6	1

* 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 1995–2001.

The glycopeptide avoparcin was licensed for the Norwegian market as a growth promoter in poultry 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 the production of Norwegian food 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, whereas 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 1995-2001.

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

* 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. The figures therfore 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 kilograms of active substance) in 2001 of veterinary antibacterial drugs approved for therapeutic use in domestic animals in Norway. The data were collected from wholesalers and are organized according to the main groups of substances (ATCvet) and show the use for the various routes of administration. The total sale of veterinary antibacterial drugs is given in Figure 1, and 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 1995–2001.

TABLE 6. Sales in 2001 (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		3			
	QJ01AA02	Doxycycline			< 0.1		
	QJ01AA06	Oxytetracycline			96	91	
β-lactam	QJ01CA01	Ampicillin			21		
antibacterials	QJ01CA04	Amoxycillin			57	53	
	QJ01CE09	Procaine penicillin*			1 945		
	QJ01CE90/ QJ51CE90	Penethamate hydroiodide*			9		
	QJ01CR02/ QJ51RV01	Amoxicillin and clavulanic acid			105		6
	QJ51CA51	Ampicillin and cloxacillin					3
Sulfonamides and	QJ01EQ10	Sulfadiazine and trimethoprim			1 205		
trimethoprim or	QJ01EQ13	Sulfadoxine and trimethoprim			110		
baquiloprim	QJ01EQ15	Sulfamethoxypyridazine			7		
Lincosamides	QJ01FF02	Lincomycin			9		
Aminoglycosides	QA07AA01	Neomycin	34				
	QA07AA90	Dihydrostreptomycin (DHS)	164				
Quinolones	QJ01MA90	Enrofloxacin			19		
Other antibacterials	QJ01XX92	Tiamulin			6	156	
Combinations of antibacterials	QG01AE99	Sulfadimidine and procaine penicillin* and DHS		219			
	QJ01RA01	Procaine penicillin* and DHS			606		
	QJ01RA01	Spiramycin and metronidazole			8		
	QJ51RC23	Procaine penicillin* and DHS					669
	QJ51RC25	Penethamate hydroiodide*and DHS					93
Total per route of administration			**198**	**222**	**4 203**	**300**	**771**
Total							**5 694**

*Calculated as benzylpenicillin

In 2001, the sales of veterinary antibacterials approved for therapeutic use in animals in Norway amounted to 5,694 kg of active substance. This represents a 40% decrease since 1995. The proportion of pure penicillin preparations rose from 25% in 1995 to 36% in 2000. As much as 94% of the veterinary penicillin preparations sold in 2001 were β-lactamase-sensitive penicillins. From 1995 to 2001, the sale of sulfonamides in combination with trimethoprim or baquiloprim increased from 11% to 26%, whereas combination preparations of penicillins and aminoglycosides decreased from 35% to 28%. The proportion of sulfonamides decreased gradually from 11% in 1995 to 0% in 2001, and the proportion of tetracyclines declined from 5% to 3%.

TABLE 7. Total sales (in kilograms of active substance) of veterinary antibacterial drugs for therapeutic use in farmed fish in Norway in 1995-2001. Data were obtained from Norwegian drug wholesalers and feed mills.

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

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.

In 2001, 645 kg of veterinary antibacterial drugs were sold in Norway for therapeutic use in farmed fish. Quinolones accounted for 76% of the total use in fish. The annual use of antibacterial drugs for fish declined by 99% during the period 1987-2001. In the same period, the total production of farmed fish increased massively. This decrease in the use of antibacterial drugs in aquaculture is mainly attributed to the introduction of effective vaccines and to improved health management.

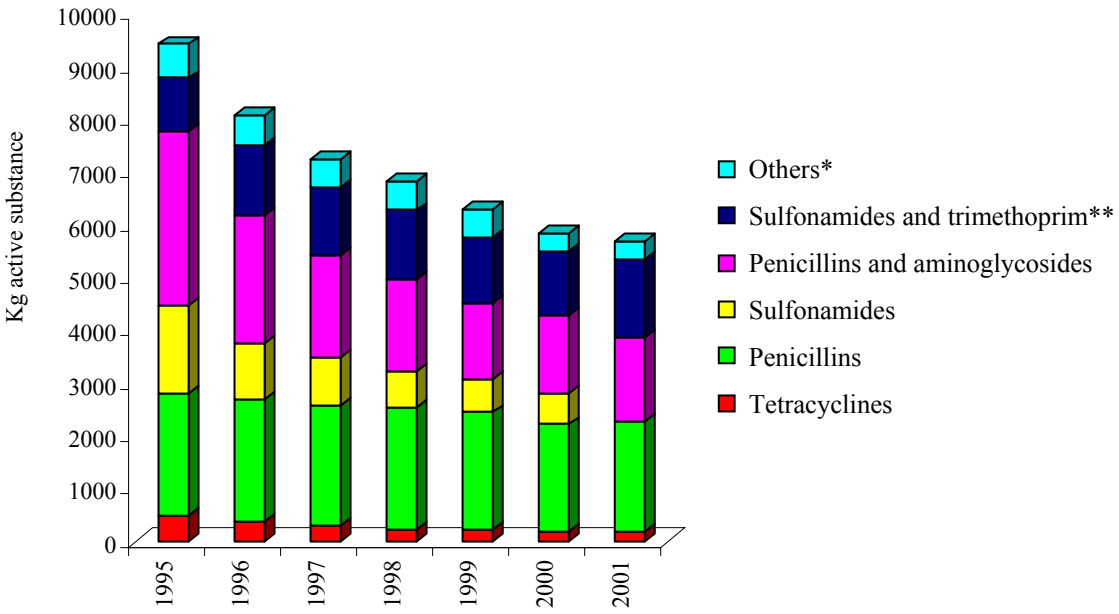


FIGURE 1. Sales (in kilograms of active substance) of veterinary antibacterial drugs (QA07AA, QG01AA, QG01AE, QJ01, QJ51) for therapeutic use in Norway in 1995–2001, fish not included.
*Macrolides, lincosamides, pleuromutilines, quinolones, and imidazoles. ** Includes small amounts of baquiloprim.

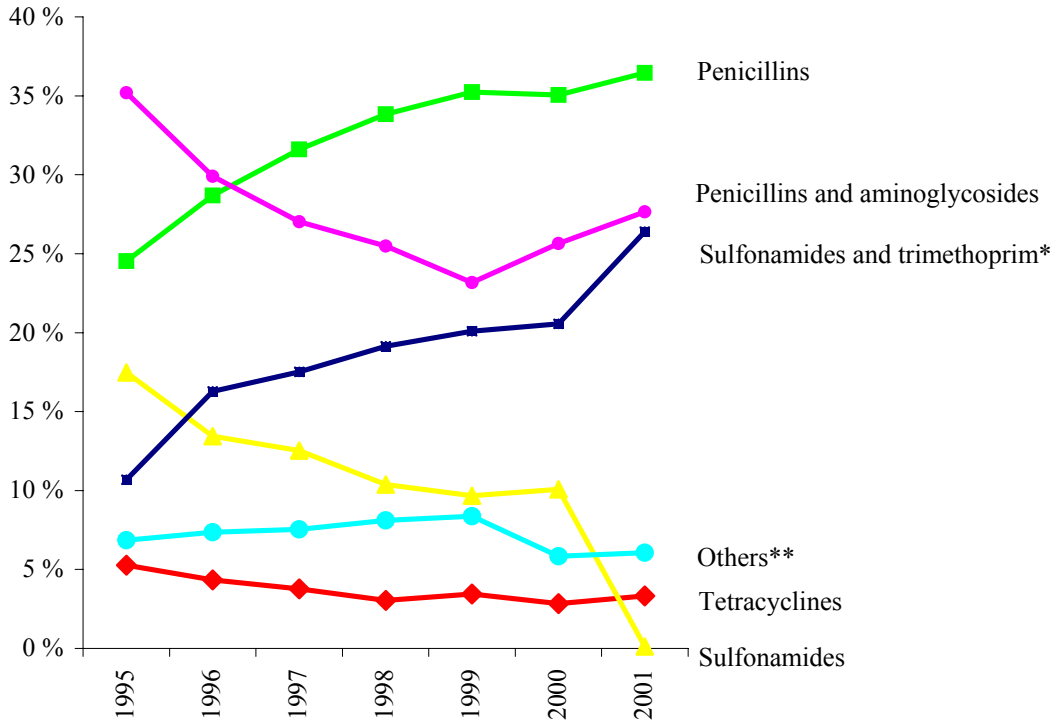


FIGURE 2. Sales (as percentage of total sales) of veterinary antibacterial drugs (QA07AA, QG01AA, QG01AE, QJ01, QJ51) in Norway in 1995–2001, fish not included.
*Includes small amounts of baquiloprim. **Macrolides, lincosamides, pleuromutilines, quinolones and imidazoles.

B. HUMAN CONSUMPTION

The overall consumption of antibacterials for systemic use (ATC group J01) in humans in 2001 was 16.8 defined daily doses (DDD)/1,000 inhabitants/day. The sale of antibacterials has remained stable for many years. The highest total sale of antibacterials ever was registered in 1993 with 17.8 DDD/1,000 inhabitants/day. The sale has decreased since then, but a small increase of 3% was seen in 2001. The increase was observed for all subgroups except tetracyclines (J01A) and sulfonamides and trimethoprim (J01E) (Table 8).

TABLE 8. Human consumption of antibacterial agents in Norway 1995-2001 by ATC groups. The consumption is presented as DDD/1,000 inhabitants/day and percentage change in 1995-2001. Appendix 2 describes how the data were collected.

ATC	Groups of substances	1995	1996	1997	1998	1999	2000	2001	Change (%) 1995-2001
J01A	Tetracyclines	4.14	3.66	3.55	3.37	3.19	3.17	3.11	- 25
J01B	Amphenicols	0.01	0.01	0.01	0.00	0.01	0.00	0.00	
J01CA	Penicillins with extended spectrum	1.72	1.73	1.87	1.90	1.96	2.01	2.10	+ 22
J01CE	β-lactamase sensitive penicillins	5.41	5.08	5.32	5.12	5.01	4.66	4.68	- 14
J01CF	β-lactamase resistant penicillins	0.19	0.21	0.24	0.27	0.32	0.35	0.41	+ 120
J01CR	Combination of penicillins	< 0.01	0.01	0.02	0.01	0.01	0.01	0.01	
J01D	Cephalosporins, monobactams and carbapenems	0.45	0.44	0.42	0.44	0.47	0.52	0.55	+ 22
J01E	Sulfonamides and trimethoprim	1.80	1.57	1.45	1.34	1.26	1.17	1.16	- 35
J01F	Macrolides, lincosamides and streptogramins	1.58	1.50	1.58	1.61	1.59	1.59	1.80	+ 14
J01G	Aminoglycosides	0.05	0.05	0.05	0.05	0.05	0.04	0.06	
J01M	Quinolones	0.27	0.28	0.28	0.30	0.33	0.35	0.40	+ 48
J01X	Other antibacterials	1.75	1.90	2.06	2.20	2.34	2.39	2.55	+ 46
	Total	**17.4**	**16.4**	**16.8**	**16.6**	**16.6**	**16.3**	**16.8**	**- 3**

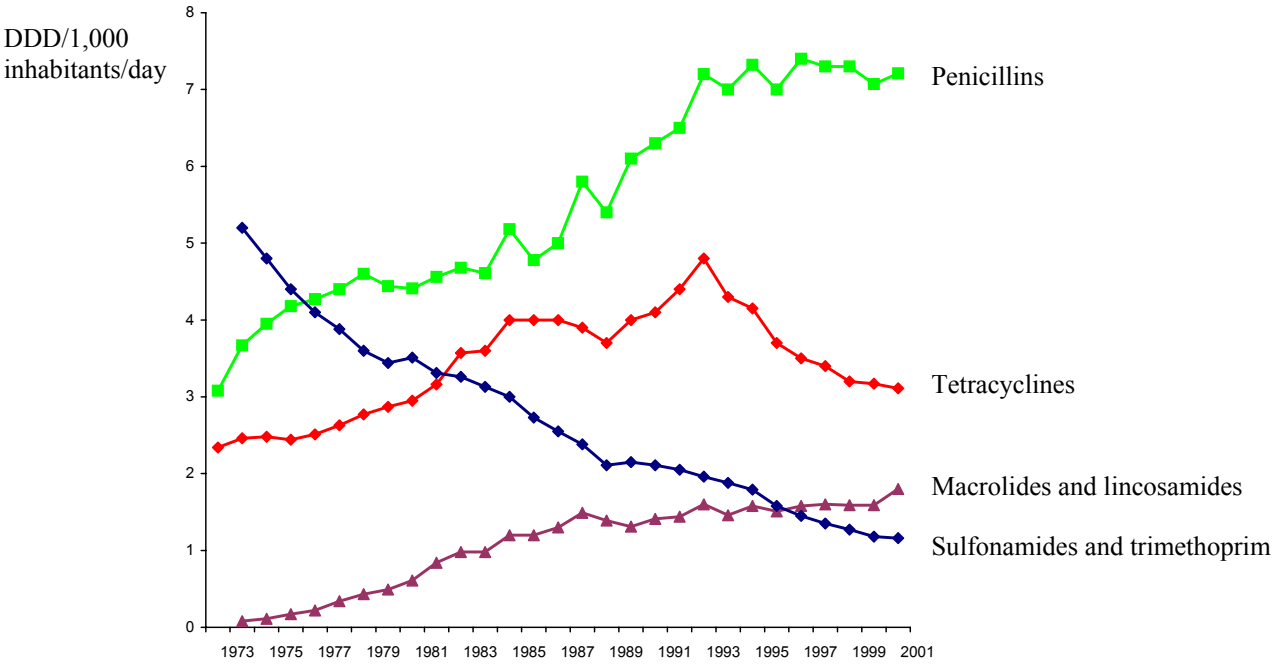


FIGURE 3. Sales of penicillins (J01C), tetracyclines (J01A), macrolides and lincosamides (J01F) and sulfonamides and trimethoprim (J01E) in DDD/1,000 inhabitants/day in Norway in 1973-2001.

The penicillins (ATC group J01C) accounted for 43% of the total use of antimicrobial drugs in Norway in 2001 (Figure 4). In 1995, they accounted for 42%. The β-lactamase sensitive penicillins (J01CE) and penicillins with extended spectrum (J01CA) accounted for 28% and 13%, respectively, as they did in 2000. The sale of penicillins has been stable over the past 5 years, but there has been a shift in use from the β-lactamase sensitive penicillins (31% of J01 in 1995 to 28% in 2001) to extended-spectrum penicillins (10% and 13%, respectively).
Tetracyclines (J01A) accounted for 19% of the total use, and their sale has decreased by 34% since 1993.

Macrolides (J01FA) accounted for 11% of the total use in 2001 and their sale has been fairly stable for some years. However, in 2001 an increase of 13% compared to 2000 was found. This may be due to an ongoing outbreak of pertussis which could lead doctors to prescribe macrolides for upper respiratory infections. Azitromycin treatment of *Chlamydia pneumoniae* may be another reason for the increased use of macrolides. The increase of ATC group J01X was mainly due to the urinary prophylactic agent methenamine (12.5% of the total use). Its sale has risen by 50% since 1995.

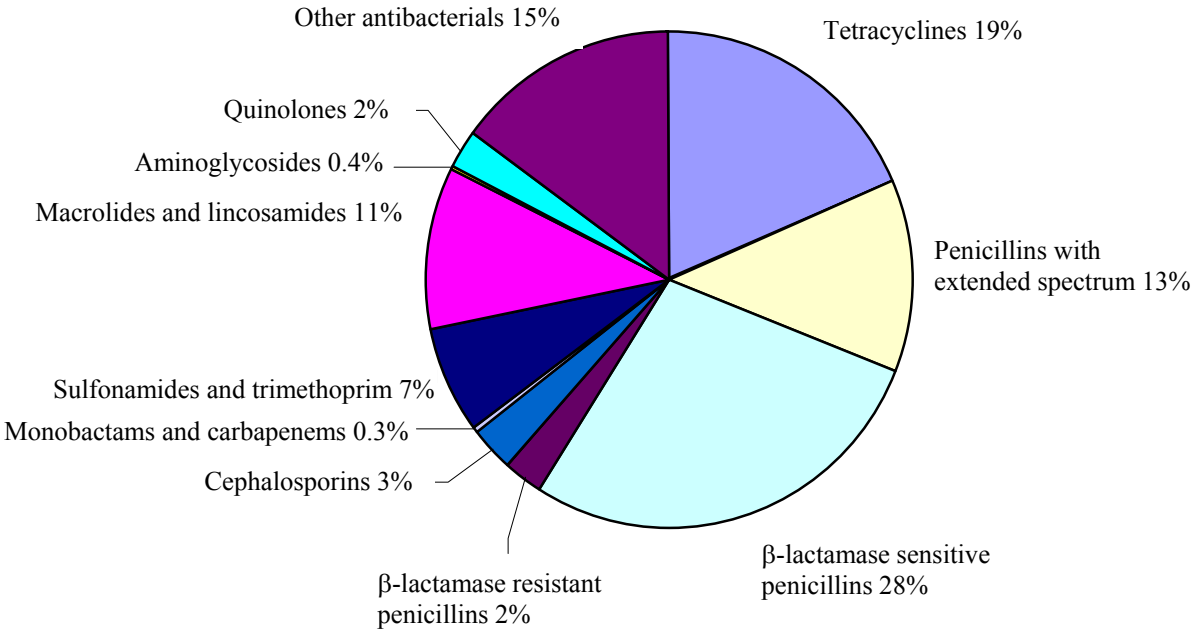


FIGURE 4. Relative amount of antibacterial agents sold for systemic use in Norway in 2001 as DDD/1,000 inhabitants/day. Groups of antibacterials are represented by ATC groups as follows: tetracyclines (J01A), penicillins with extended spectrum (J01CA), β-lactamase sensitive penicillins (J01CE), β-lactamase resistant penicillins (J01CF), cephalosporins (J01D), sulfonamides and trimethoprim (J01E), macrolides and lincosamides (J01F), quinolones (J01M), and all other antibacterials combined.

The sale of cephalosporins, although limited, has increased and currently accounts for 3% of the total sales of antibacterials. Around half the amount was used in hospitals. The sales of sulfonamides and trimethoprim have decreased by 35% since 1995. There has been a small but stable increase in quinolone use over the years. This group accounts for only a small fraction (2%) of the total sale of antibacterial drugs, but the increase has been 56% since 1995.
The pattern of antibacterial use in hospitals differs from the sales related to general practice (Figure 5). Sales to hospitals accounted 6.6% of the total sales in 2001.

Penicillins (J01C) accounted for around half the use in both hospitals and general practice. The most important groups in used general practice were tetracyclines (20%), macrolides (11%) and methenamine (13%). Cephalosporins (J01D) were the second most commonly used group in hospitals.
As much as 93.4% of the antimicrobial drugs sold for use by people were prescribed in general practice. Therapy traditions in this part of the health-care system may thus have a great impact on the total use of antimicrobials and the occurrence of resistance in society.

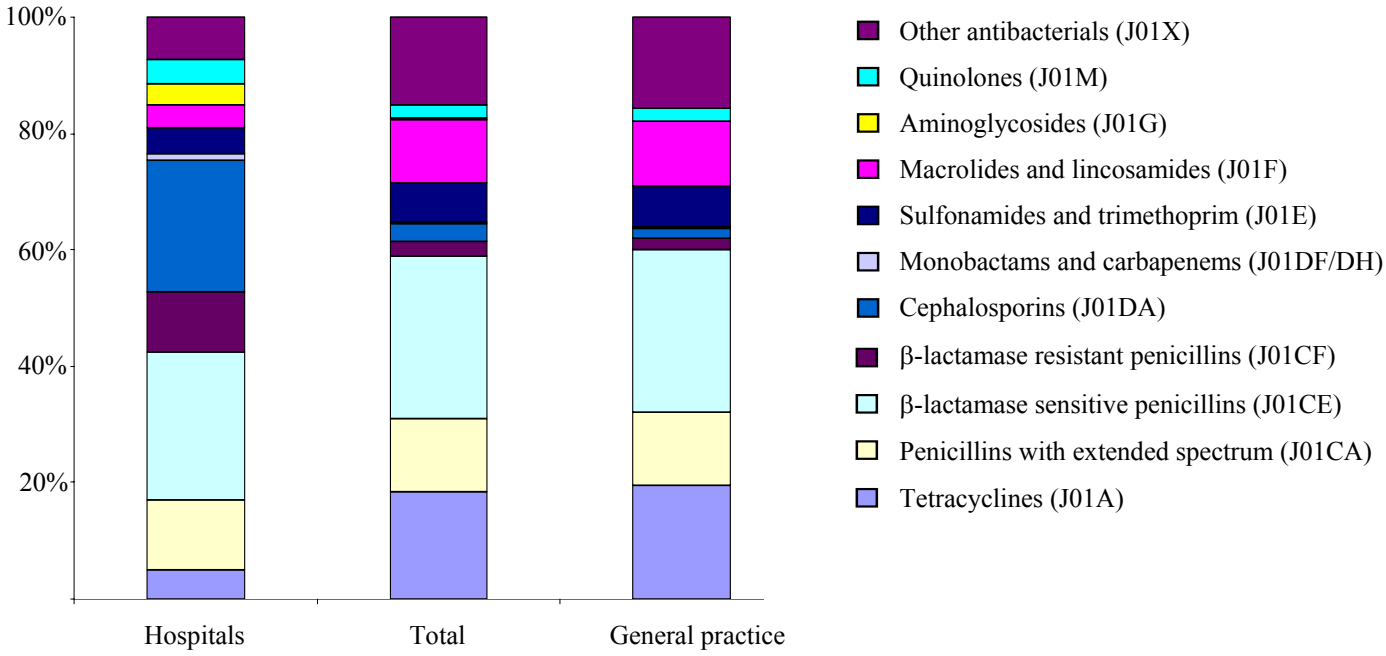


FIGURE 5. Proportions of antibacterial agents for systemic use in hospitals (left) and general practice (right) in Norway in 2001. Consumption is measured as DDD/1,000 inhabitants/year.

TABLE 9. Human consumption of antibacterial agents for systemic use in Norway in 2001. Sales given as DDD/1,000 inhabitants/day. Appendix 2 describes how the data on human consumption of antibacterial agents were collected.

ATC	Substance	1995	1996	1997	1998	1999	2000	2001
A07AA09	Vancomycin	0.001	0.001	0.001	0.001	0.001	0.001	0.001
J01A A02	Doxycycline	2.82	2.49	2.47	2.34	2.20	2.10	2.10
J01A A04	Lymecycline	0.14	0.11	0.10	0.09	0.09	0.14	0.19
J01A A06	Oxytetracycline	0.43	0.36	0.30	0.27	0.25	0.24	0.22
J01A A07	Tetracycline	0.75	0.70	0.68	0.67	0.65	0.69	0.64
J01B A01	Chloramphenicol	0.005	0.005	0.005	0.004	0.005	0.004	0.003
J01C A01	Ampicillin	0.09	0.09	0.09	0,09	0.09	0.09	0.08
J01C A02	Pivampicillin	0.24	0.20	0.17	0.15	0.14	0.13	0.11
J01C A04	Amoxicillin	0.79	0.75	0.85	0.85	0.87	0.83	0.89
J01C A08	Pivmecillinam	0.60	0.69	0.75	0.81	0.86	0.96	1.00
J01C A09	Azlocillin	0.0001	0.0001	0.0001				
J01C A11	Mecillinam	0.002	0.003	0.003	0.003	0.004	0.004	0.005
J01C E01	Benzylpenicillin	0.20	0.19	0.19	0.21	0.23	0.21	0.23
J01C E02	Phenoxymethylpenicillin	5.21	4.89	5.13	4.91	4.78	4.45	4.45
J01C F01	Dicloxacillin	0.08	0.13	0.16	0.19	0.22	0.25	0.31
J01C F02	Cloxacillin	0.10	0.08	0.08	0.08	0.10	0.10	0.09
J01C R02	Amoxicillin and enzyme inhibitor	0.004	0.01	0.02	0.01	0.01	0.01	0.01
J01C R05	Piperacillin and enzyme inhibitor						0.0001	0.0006
J01D A01	Cefalexin	0.26	0.25	0.22	0.22	0.22	0.26	0.27

continued ...

ATC	Substance	1995	1996	1997	1998	1999	2000	2001
J01D A03	Cefalotin	0.04	0.04	0.04	0.04	0.05	0.05	0.05
J01D A05	Cefoxitin	0.0005	0.0004	0.0004	0.0004	0.0004	0.0004	0.0003
J01D A06	Cefuroxim	0.11	0.11	0.11	0.12	0.13	0.13	0.14
J01D A10	Cefotaxim	0.01	0.01	0.02	0.03	0.04	0.04	0.05
J01D A11	Ceftazidim	0.02	0.02	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
J01D A63	Ceftriaxone with lidocain		0.00003	0.0001	0.0001	0.0001		
J01D F01	Aztreonam	0.0008	0.0008	0.0007	0.0005	0.0008	0.001	0.001
J01D H02	Meropenem			0.002	0.004	0.008	0.012	0.014
J01D H51	Imipenem and enzyme inhibitor	0.007	0.006	0.007	0.007	0.006	0.006	0.005
J01E A01	Trimethoprim	0.99	0.93	0.90	0.87	0.84	0.79	0.80
J01E B02	Sulfamethizole	0.005	0.001		0.0002	0.001	0.002	0.002
J01E C20	Sulfonamides, combinations	0.001	0.003	0.003	0.003	0.0004		
J01E E01	Sulfamethoxazol and trimethoprim	0.80	0.64	0.55	0.47	0.42	0.38	0.36
J01F A01	Erythromycin	1.18	1.03	1.04	1.06	1.01	1.00	1.13
J01F A02	Spiramycin	0.09	0.06	0.05	0.04	0.03	0.02	0.02
J01F A09	Clarithromycin	0.06	0.17	0.22	0.24	0.26	0.26	0.30
J01F A10	Azithromycin	0.14	0.14	0.17	0.17	0.18	0.19	0.21
J01F F01	Clindamycin	0.09	0.10	0.10	0.11	0.11	0.12	0.14
J01F F02	Lincomycin	0.003	0.001					
J01G B01	Tobramycin	0.03	0.02	0.03	0.03	0.03	0.02	0.03
J01G B03	Gentamicin	0.006	0.007	0.006	0.006	0.006	0.006	0.008
J01G B07	Netilmicin	0.02	0.02	0.02	0.02	0.02	0.02	0.02
J01M A01	Ofloxacin	0.07	0.07	0.07	0.06	0.06	0.05	0.05
J01M A02	Ciprofloxacin	0.18	0.19	0.20	0.23	0.26	0.29	0.34
J01M B02	Nalidixic acid	0.02	0.02	0.01	0.01	0.01	0.01	0.01
J01X A01	Vancomycin	0.005	0.005	0.005	0.005	0.004	0.005	0.005
J01X A02	Teicoplanin	0.0002	0.0009	0.0009	0.001	0.0007	0.0012	0.0013
J01X B01	Colistin	0.002	0.002	0.004	0.003	0.003	0.003	0.003
J01X C01	Fusidic acid	0.002	0.003	0.003	0.003	0.003	0.003	0.01
J01X D01	Metronidazole	0.052	0.052	0.056	0.056	0.060	0.063	0.065
J01X D02	Tinidazole	0.002	0.001					
J01X E01	Nitrofurantoin	0.39	0.39	0.38	0.38	0.37	0.37	0.36
J01X X05	Methenamin	1.29	1.44	1.61	1.75	1.91	1.95	2.08
P01AB01	Metronidazole	0.20	0.20	0.18	0.18	0.18	0.18	0.18

The sale of antimycobacterials used in the treatment of tuberculosis has been stable. The total amount of antimycobacterials is only available for the last three years due to data collection problems. The sales measured in DDD/1,000 inhabitants/day were 0.11, 0.19 and 0.12 for 1999, 2000 and 2001, respectively. There has been an increased use of combination products to ease the compliance with treatment. Rifampicin is always part of these combinations and can therefore be used as an indicator for the treatment of tuberculosis.

VI. OCCURRENCE OF ANTIMICROBIAL RESISTANCE

A. INDICATOR BACTERIA FROM FEED, ANIMALS AND FOOD

Escherichia coli

TABLE 10. *Escherichia coli* isolates from dog food (n=120). Sampling, laboratory methods and data processing are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)			MIC_{50}	MIC_{90}
	S	R	S	I	R					
Tetracycline	≤ 4	≥ 16	89.2	0.0	10.8	1	-	≥ 256	1	64
Chloramphenicol	≤ 8	≥ 32	99.2	0.0	0.8	0.064	-	32	4	8
Ampicillin	≤ 8	≥ 32	95.8	0.0	4.2	1	-	≥ 256	4	8
Cefuroxime	≤ 8	≥ 32	99.2	0.0	0.8	1	-	64	2	4
Trimethoprim	≤ 8	≥ 16	95.0	-	5.0	0.25	-	≥ 32	1	2
Streptomycin	≤ 32	≥ 64	92.5	-	7.5	1	-	≥ 256	2	32
Gentamicin	≤ 4	≥ 16	100.0	-	0.0	0.5	-	4	1	1
Kanamycin	≤ 16	≥ 64	99.2	-	0.8	1	-	≥ 256	4	4
Enrofloxacin	≤ 0.25	≥ 2	98.3	0.8	0.8	0.016	-	4	0.064	0.125
Nalidixic acid	≤ 16	≥ 32	100.0	0.0	0.0	1	-	16	2	4

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

TABLE 11. *Escherichia coli* isolates from dog food (n=120). Distribution (%) 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
Tetracycline							77	13				1	3	3	6
Chloramphenicol			1					5	76	17		1			
Ampicillin							1	15	73	8					4
Cefuroxime							3	50	47						
Trimethoprim					12	23	44	17		1		5			
Streptomycin							1	53	28	4	3	6	5	3	1
Gentamicin						9	88	3	1						
Kanamycin							1	39	54	5					1
Enrofloxacin	3	13	75	9		1			1						
Nalidixic acid							2	57	39	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.

COMMENTS

The isolates included were from various kinds of dog food of either imported or Norwegian origin, frozen offal products, hide chewing bones and dried abbatoir leftovers such as pigs´ ears and ox penises.

A total of 81% of the isolates were susceptible to all the antimicrobials included in the study. Furthermore, 13% of the isolates were resistant to one of the antimicrobials tested, 3% to two, and 3% to three or more.

Resistance to tetracyclines was most frequently observed, followed by resistance to streptomycin, trimethoprim and ampicillin. All these drugs have been and/or are still commonly used for clinical purposes in food producing animals in Norway and elsewhere.

TABLE 12. *Escherichia coli* isolates from porcine faecal samples (n=93). Sampling, laboratory methods and data processing are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Oxytetracycline	≤ 4	≥ 16	93.5	0.0	6.5	0.5 - ≥ 128	2	2
Chloramphenicol	≤ 8	≥ 32	97.8	1.1	1.1	2 - ≥ 32	4	8
Florfenicol	≤ 16	≥ 32	100.0	-	0.0	2 - 16	8	8
Ampicillin	≤ 8	≥ 32	95.7	0.0	4.3	1 - ≥ 64	2	4
Amoxi./clav.**	≤ 8	≥ 32	94.6	1.1	4.3	2 - ≥ 32	4	8
Ceftiofur	≤ 2	≥ 8	100.0	0.0	0.0	0.25 - 2	0.25	0.5
Trimethoprim	≤ 8	≥ 16	92.5	-	7.5	0.12 - ≥ 32	0.5	1
Sulfamethoxazole	≤ 256	≥ 512	89.2	-	10.8	64 - ≥ 512	64	1024
Streptomycin	≤ 32	≥ 64	81.7	-	18.3	2 - 256	8	128
Gentamicin	≤ 4	≥ 16	100.0	0.0	0.0	0.5 - 4	2	4
Neomycin	≤ 32	≥ 64	100.0	-	0.0	1 - 4	2	4
Apramycin	≤ 32	≥ 64	100.0	-	0.0	4 - 32	8	16
Enrofloxacin	≤ 0.25	≥ 2	100.0	0.0	0.0	0.03 - 0.25	0.064	0.064
Nalidixic acid	≤ 16	≥ 32	100.0	-	0.0	2 - 8	4	8

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
** Amoxi./clav.=Amoxicillin/clavulanic acid.

TABLE 13. *Escherichia coli* isolates from porcine faecal samples (n=93). Distribution (%) of MICs (mg/L).*

	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline					2	45	46						7		
Chloramphenicol							4	63	30	1	1				
Florfenicol							1	36	62	1					
Ampicillin						10	44	42				4			
Amoxi./clav.**							14	68	13	1	4				
Ceftiofur				51	46	2	1								
Trimethoprim			9	15	60	8	1			1	7				
Sulfamethoxazole												89			11
Streptomycin							1	23	43	10	5	7	7	5	
Gentamicin					2	31	52	15							
Neomycin						23	65	13							
Apramycin								26	58	15	1				
Enrofloxacin	48	51		1											
Nalidixic acid							2	62	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.
**Amoxi./clav.=Amoxicillin/clavulanic acid.

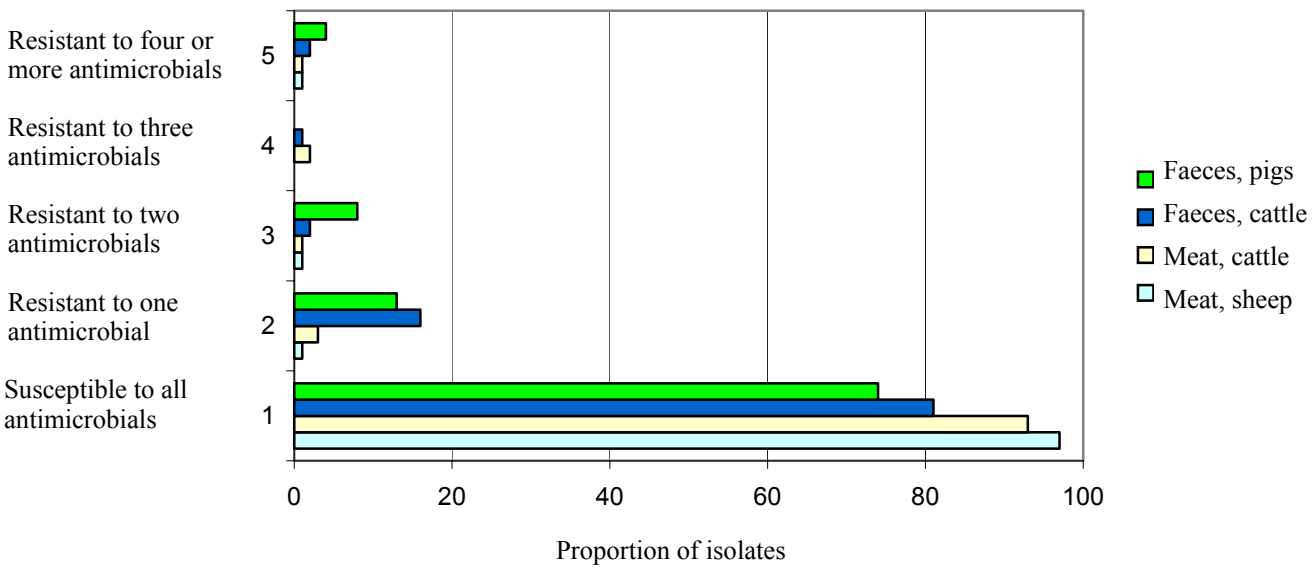


FIGURE 6. Antimicrobial resistance profiles for *Escherichia coli* isolates from porcine faecal samples (n=93), bovine faecal (n=173) and meat (n=100) samples, and ovine meat (n=100) samples. Proportion of isolates fully susceptible to all antimicrobials or resistant to one, two, three, or four or more of the antimicrobials tested for.

COMMENTS

The data indicate a moderate occurrence of resistance among faecal *E. coli* from a representative sample of Norwegian slaughter pigs. Figure 6 illustrates that 74% were susceptible to all antimicrobials included in the test panel, 13% were resistant to one antimicrobial (predominantly streptomycin), 9% to two, 3% to four, and 1% to five antimicrobials. Resistance to streptomycin was most frequent, followed by resistance to sulfonamides, trimethoprim, and ampicillin. All these antimicrobials are commonly used for clinical purposes in swine production (sulfonamides and trimethoprim in combination).

One isolate was resistant to chloramphenicol. Veterinary drugs containing chloramphenicol were withdrawn from the Norwegian market in 1992. However, various studies have shown that *E. coli* with reduced susceptibility to chloramphenicol can still be isolated from pigs.

No quinolone resistance was observed. The use of fluoroquinolones in animals in Norway is very limited.

No resistance to ceftiofur and gentamicin was observed. No veterinary preparations containing cephalosporins or the aminoglycoside gentamicin have been approved in Norway.

The results obtained are comparable with the results off surveys of Norwegian pork in 1997-98 and with data from NORM-VET 2000.

TABLE 14. *Escherichia coli* isolates from bovine faecal samples (n=173). Sampling, laboratory methods and data processing are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Oxytetracycline	≤ 4	≥ 16	97.7	0.0	2.3	0.5 - ≥ 128	2	2
Chloramphenicol	≤ 8	≥ 32	99.4	0.6	0.0	2 - 16	4	8
Florfenicol	≤ 16	≥ 32	100.0	-	0.0	2 - 16	8	8
Ampicillin	≤ 8	≥ 32	93.1	1.2	5.8	1 - ≥ 64	4	4
Amoxi./clav.**	≤ 8	≥ 32	94.2	1.2	4.6	2 - ≥ 32	4	8
Ceftiofur	≤ 2	≥ 8	100.0	0.0	0.0	0.25 - 2	0.5	0.5
Trimethoprim	≤ 8	≥ 16	98.8	-	1.2	0.12 - ≥ 32	0.5	1
Sulfamethoxazole	≤ 256	≥ 512	96.0	-	4.0	4 - ≥ 512	64	64
Streptomycin	≤ 32	≥ 64	86.7	-	13.3	2 - ≥ 512	8	128
Gentamicin	≤ 4	≥ 16	98.8	1.2	0.0	0.5 - 8	2	4
Neomycin	≤ 32	≥ 64	99.4	-	0.6	1 - 128	2	2
Apramycin	≤ 32	≥ 64	100.0	-	0.0	2 - 32	8	8
Enrofloxacin	≤ 0.25	≥ 2	100.0	0.0	0.0	0.03 - 4	0.064	0.064
Nalidixic acid	≤ 16	≥ 32	99.4	-	0.6	1 - 32	4	8

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
** Amoxi./clav.=Amoxicillin/clavulanic acid.

TABLE 15. *Escherichia coli* isolates from bovine faecal samples (n=173). Distribution (%) of MICs (mg/L).*

	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline					3	46	46	4					2		
Chloramphenicol							11	51	37	1					
Florfenicol							8	40	51	1					
Ampicillin						8	40	45	1	1	1	5			
Amoxi./clav.**							9	61	24	1	5				
Ceftiofur				38	56	4	2								
Trimethoprim			8	28	49	11	1	2		1	1				
Sulfamethoxazole								1				95			4
Streptomycin							3	25	50	8		2	4	7	1
Gentamicin					2	36	49	13	1						
Neomycin						25	70	4	1				1		
Apramycin							3	20	69	8	1				
Enrofloxacin	47	51		1				1							
Nalidixic acid						3	14	58	25		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.
**Amoxi./clav.=Amoxicillin/clavulanic acid.

TABLE 16. *Escherichia coli* isolates from bovine meat samples (n=100). Sampling, laboratory methods and data processing are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Oxytetracycline	≤ 4	≥ 16	99.0	0.0	1.0	0.5 - ≥ 128	1	2
Chloramphenicol	≤ 8	≥ 32	99.0	0.0	1.0	2 - ≥ 32	4	8
Florfenicol	≤ 16	≥ 32	100.0	-	0.0	2 - 16	8	8
Ampicillin	≤ 8	≥ 32	97.0	0.0	3.0	1 - ≥ 64	4	4
Amoxi./clav.**	≤ 8	≥ 32	97.0	0.0	3.0	2 - ≥ 32	4	8
Ceftiofur	≤ 2	≥ 8	100.0	0.0	0.0	0.25 - 1	0.5	0.5
Trimethoprim	≤ 8	≥ 16	99.0	-	1.0	0.125 - ≥ 32	0.5	0.5
Sulfamethoxazole	≤ 256	≥ 512	96.0	-	4.0	64 - ≥ 512	64	64
Streptomycin	≤ 32	≥ 64	93.0	-	7.0	4 - 256	8	16
Gentamicin	≤ 4	≥ 16	100.0	0.0	0.0	1 - 4	2	4
Neomycin	≤ 32	≥ 64	100.0	-	0.0	1 - 32	2	4
Apramycin	≤ 32	≥ 64	100.0	-	0.0	4 - 32	8	16
Enrofloxacin	≤ 0.25	≥ 2	100.0	0.0	0.0	0.03 - 0.125	0.064	0.064
Nalidixic acid	≤ 16	≥ 32	100.0	-	0.0	2 - 16	4	8

*S=Susceptible, I=Intermediately susceptible, R=Resistant. ** Amoxi./clav.=Amoxicillin/clavulanic acid.

TABLE 17. *Escerichia coli* isolates from bovine meat samples (n=100). Distribution (%) of MICs (mg/L).*

	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline					1	55	42	1					1		
Chloramphenicol							12	52	35		1				
Florfenicol							4	34	57	5					
Ampicillin						8	39	48	2			3			
Amoxi./clav.**							13	59	25		3				
Ceftiofur				43	55	2									
Trimethoprim			7	12	71	6	3				1				
Sulfamethoxazole												96			4
Streptomycin								21	61	11			4	3	
Gentamicin						26	57	17							
Neomycin						17	67	15			1				
Apramycin								22	60	17	1				
Enrofloxacin	44	54	2												
Nalidixic acid							6	61	32	1					

*/** Footnotes, see Table 15.

COMMENTS

The data indicate a moderate occurrence of resistance among *E. coli* from faecal and meat samples from a representative group of Norwegian cattle presented for slaughter. In total, 81% and 93%, respectively, were susceptible to all antimicrobials included in the test panel: 16% and 3% were resistant to one antimicrobial (predominantly streptomycin), 2% and 1% to two antimicrobials, 1% and 2% to three antimicrobials, and 2% and 1% to four or more antimicrobials. Figure 6 illustrates the proportion of *E. coli* of porcine, bovine and ovine origin that were resistant to none, one, two, three, or four or more of the antimicrobials included. The occurrence of resistance was slightly higher for the porcine isolates than the bovine isolates, which in turn were slightly more resistant than the ovine isolates.

For *E. coli* from cattle, resistance to streptomycin was most frequent, followed by ampicillin, sulfonamides, tetracycline and trimethoprim. All these antimicrobials are commonly used for clinical purposes in cattle (sulfonamides and trimethoprim in combination). One faecal isolate was resistant to neomycin. The aminoglycocide neomycin is approved for treatment of diarrhoea in calves. Two isolates, one from faeces and one from meat, were intermediately resistant to chloramphenicol. Veterinary drugs containing chloramphenicol were withdrawn from the Norwegian market in 1992.

No resistance to the fluoroquinolone enrofloxacin was observed, but one faecal isolate was resistant to the quinolone nalidixic acid. The usage of fluoroquinolones in animals in Norway is very limited. However,

resistance to nalidixic acid indicates that fluoroquinolone resistance may be developing. No resistance to ceftiofur or gentamicin was observed. No preparations containing cephalosporins or the aminoglycoside gentamicin have been approved for veterinary use in Norway.

TABLE 18. *Escherichia coli* isolates from ovine meat samples (n=100). Sampling, laboratory methods and data processing are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Oxytetracycline	≤ 4	≥ 16	99.0	0.0	1.0	1 - ≥ 128	2	2
Chloramphenicol	≤ 8	≥ 32	99.0	1.0	0.0	2 - 16	4	8
Florfenicol	≤ 16	≥ 32	100.0	-	0.0	4 - 16	8	8
Ampicillin	≤ 8	≥ 32	98.0	0.0	2.0	1 - ≥ 64	4	4
Amoxi./clav.**	≤ 8	≥ 32	97.0	1.0	2.0	2 - ≥ 32	4	8
Ceftiofur	≤ 2	≥ 8	100.0	0.0	0.0	0.25 - 1	0.5	0.5
Trimethoprim	≤ 8	≥ 16	100.0	-	0.0	0.125 - 1	0.5	1
Sulfamethoxazole	≤ 256	≥ 512	98.0	-	2.0	64 - ≥ 512	64	64
Streptomycin	≤ 32	≥ 64	98.0	-	2.0	4 - 256	8	8
Gentamicin	≤ 4	≥ 16	100.0	0.0	0.0	0.5 - 4	2	2
Neomycin	≤ 32	≥ 64	100.0	-	0.0	1 - 4	2	2
Apramycin	≤ 32	≥ 64	100.0	-	0.0	4 - 16	8	16
Enrofloxacin	≤ 0.25	≥ 2	100.0	0.0	0.0	0.03 - 0.125	0.064	0.064
Nalidixic acid	≤ 16	≥ 32	100.0	-	0.0	2 - 16	4	8

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
** Amoxi./clav.=Amoxicillin/clavulanic acid.

TABLE 19. *Escherichia coli* isolates from ovine meat samples (n=100). Distribution (%) of MICs (mg/L).*

	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline						33	62	4					1		
Chloramphenicol							1	50	48	1					
Florfenicol								31	66	3					
Ampicillin						2	31	64	1			2			
Amoxi./clav.**							2	79	16	1	2				
Ceftiofur				26	71	3									
Trimethoprim			8	21	60	11									
Sulfamethoxazole												98			2
Streptomycin								39	54	4	1		1	1	
Gentamicin					1	27	65	7							
Neomycin						18	74	8							
Apramycin								30	57	13					
Enrofloxacin	30	67	3												
Nalidixic acid							3	54	41	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.
**Amoxi./clav.=Amoxicillin/clavulanic acid.

COMMENTS

The data indicate a low occurrence of resistance among faecal *E. coli* from a representative sample of Norwegian slaughter sheep. The resistance frequencies were slightly lower than for *E. coli* from Norwegian pigs and cattle (Figure 6). A total of 97% of the isolates were susceptible to all the antimicrobials included in the test panel, 1% were resistant to one antimicrobial (ampicillin), 1% to two (streptomycin and sulfonamides), and 1% to four (ampicillin, streptomycin, sulfonamides, and tetra-cycline). All these antimicrobials may be used for clinical purposes in sheep production. No resistance to ceftiofur, gentamicin, chloramphenicol, enrofloxacin, or nalidixic acid was observed.

Lambs slaughtered at an age of about six months account for approximately 85% of the group of slaughtered sheep. Lamb production in Norway is very extensive and the lambs spend a large part of their lives roaming freely on rough, upland grazing.

Enterococcus spp.

TABLE 20. *Enterococcus faecalis* isolates from bovine meat samples (n=108). Sampling, laboratory methods and data processing are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Oxytetracycline	≤ 4	≥ 16	92.6	0.0	7.4	0.5 - 32	0.5	2
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	0.0	2 - 8	8	8
Ampicillin	≤ 8	≥ 16	100.0	-	0.0	0.25 - 4	1	2
Erythromycin	≤ 4	≥ 8	100.0	-	0.0	0.5 - 4	2	4
Streptomycin	≤ 512	≥ 1024	91.7	-	8.3	4 - ≥ 2048	64	128
Gentamicin	≤ 512	≥ 1024	100.0	-	0.0	4 - 512	8	16
Neomycin	≤ 1024	≥ 2048	100.0	-	0.0	8 - 1024	32	64
Vancomycin	≤ 4	≥ 32	100.0	0.0	0.0	1 - 4	2	2
Bacitracin	≤ 32	≥ 64	100.0	-	0.0	0.5 - 32	8	16
Avilamycin	≤ 8	≥ 16	100.0	-	0.0	0.5 - 8	2	4
Virginiamycin	≤ 4	≥ 8	12.0	-	88.0	1 - 16	8	16
Flavomycin	≤ 32	≥ 64	99.1	-	0.9	2 - ≥ 256	4	8
Narasin	≤ 2	≥ 4	100.0	-	0.0	0.12 - 1	0.25	0.5

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

TABLE 21. *Enterococcus faecalis* isolates from bovine meat samples (n=108). Distribution (%) of MICs (mg/L).*

	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	≥ 2048
Oxytetracycline			56	33	4			3	5						
Chloramphenicol					4	45	51								
Ampicillin		7	30	51	9	4									
Erythromycin			12	17	38	33									
Streptomycin						1		1	12	43	35			3	6
Gentamicin						20	47	27	5				1		
Neomycin							1	24	39	31	5			1	
Vancomycin				27	68	6									
Bacitracin			1	1	6	12	47	32	2						
Avilamycin			1	27	33	38	1								
Virginiamycin				1	6	6	45	43							
Flavomycin					28	57	14	1				1			
Narasin	15	65	19	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.

TABLE 22. *Enterococcus faecalis* isolates from ovine meat samples (n=78). Sampling, laboratory methods and data processing are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Oxytetracycline	≤ 4	≥ 16	85.9	0.0	14.1	0.25 - ≥ 128	1	32
Chloramphenicol	≤ 8	≥ 32	97.4	2.6	0.0	2 - 16	8	8
Ampicillin	≤ 8	≥ 16	100.0	-	0.0	0.25 - 4	1	2
Erythromycin	≤ 4	≥ 8	100.0	-	0.0	0.5 - 4	2	4
Streptomycin	≤ 512	≥ 1024	98.7	-	1.3	32 - ≥ 2048	128	128
Gentamicin	≤ 512	≥ 1024	100.0	-	0.0	2 - 32	16	32
Neomycin	≤ 1024	≥ 2048	100.0	-	0.0	8 - 128	64	128
Vancomycin	≤ 4	≥ 32	100.0	0.0	0.0	1 - 4	2	4
Bacitracin	≤ 32	≥ 64	100.0	-	0.0	2 - 16	16	16
Avilamycin	≤ 8	≥ 16	100.0	-	0.0	0.5 - 8	4	4
Virginiamycin	≤ 4	≥ 8	11.5	-	88.5	0.5 - 32	8	16
Flavomycin	≤ 32	≥ 64	98.7	-	1.3	2 - ≥ 256	4	8
Narasin	≤ 2	≥ 4	100.0	-	0.0	0.12 - 1	0.25	0.5

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

TABLE 23. *Enterococcus faecalis* isolates from ovine meat samples (n=78). Distribution (%) of MICs (mg/L).*

	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	≥ 2048
Oxytetracycline		1	46	30	9				5	8	1				
Chloramphenicol					4	37	56	3							
Ampicillin		5	9	72	10	4									
Erythromycin			12	23	34	31									
Streptomycin									6	39	54				1
Gentamicin					3	5	36	41	15						
Neomycin							1	6	19	47	26				
Vancomycin				12	76	13									
Bacitracin					1		39	60							
Avilamycin			3	14	28	47	8								
Virginiamycin			3		4	5	56	31	1						
Flavomycin					23	63	13					1			
Narasin	12	53	32	4											

* 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 24. *Enterococcus faecalis* isolates from bovine faecal samples (n=9) and *Enterococcus faecium* isolates from bovine faecal samples (n=12), bovine meat samples (n=14) and ovine meat samples (n=9). Sampling, laboratory methods and data processing are described in Appendix 3.

					E. faecalis Cattle, faeces Isolates (n=9)*			*E. faecium* Cattle, faeces Isolates (n=12)*			*E. faecium* Cattle, meat Isolates (n=14)*			*E. faecium* Sheep, meat Isolates (n=9)*		
	Breakpoints (mg/L)				S	I	R	S	I	R	S	I	R	S	I	R
		S		R												
Oxytetracycline	≤	4	≥	16	9	0	0	10	0	2	14	0	0	7	0	2
Chloramphenicol	≤	8	≥	32	9	0	0	12	0	0	14	0	0	9	0	0
Ampicillin	≤	8	≥	16	9	-	0	12	-	0	14	-	0	9	-	0
Erythromycin	≤	4	≥	8	9	-	0	11	-	1	14	-	0	9	-	0
Streptomycin	≤	512	≥	1024	9	-	0	10	-	2	14	-	0	9	-	0
Gentamicin	≤	512	≥	1024	9	-	0	12	-	0	14	-	0	9	-	0
Neomycin	≤	1024	≥	2048	9	-	0	10	-	2	14	-	0	9	-	0
Vancomycin	≤	4	≥	32	9	0	0	12	0	0	14	0	0	9	0	0
Bacitracin	≤	32	≥	64	9	-	0	11	-	1	13	-	1	7	-	2
Avilamycin	≤	8	≥	16	9	-	0	11	-	1	14	-	0	7	-	2
Virginiamycin	≤	4	≥	8	0	-	9	12	-	0	14	-	0	9	-	0
Flavomycin	≤	32	≥	64	9	-	0	0	-	12	0	-	14	0	-	9
Narasin	≤	2	≥	4	9	-	0	12	-	0	14	-	0	8	-	1

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

COMMENTS

E. faecalis is reported to be inherently resistant to the streptogramin virginiamycin, while *E. faecium* is reported to be fully susceptible to this antimicrobial. The situation is reversed for flavomycin. The use of virginiamycin in animal production in Norway has been negligible, and the substance was banned in 1998. Flavomycin has never been approved in Norway. Resistance to virginiamycin and flavomycin is not included in the following discussion.

Of the 108 *E. faecalis* isolates from bovine meat samples, 90% were susceptible to the antimicrobials included in the test panel, 5% were resistant to one antimicrobial (streptomycin (high-level) or tetracycline) and 6% were resistant to two antimicrobials (tetracycline and streptomycin (high-level)). Some tetracycline and streptomycin are used for clinical purposes in Norwegian cattle. All *E. faecalis* from cattle faeces (n=9) were susceptible to the antimicrobials included.

The *E. faecium* isolates from bovine meat samples (n=14) were susceptible to the antimicrobials included except for one which was resistant to bacitracin. Resistance to tetracycline, neomycin, streptomycin (high-level), erythromycin, bacitracin and avilamycin was observed in *E. faecium* from cattle faeces (n=12),. The first three drugs are used for clinical purposes in Norwegian cattle. Spiramycin was approved for use in cattle in the 1990s, and spiramycin resistance can confer cross-resistance to erythromycin.

Of the 78 *E. faecalis* isolates from ovine meat samples, 82% were susceptible to the antimicrobials included in the test panel. A total of 17% were classified as resistant to one antimicrobial (the majority to tetracycline) and one isolate (1%) was resistant to two antimicrobials (tetracycline and streptomycin (high-level)). Some tetracycline and streptomycin are used for clinical purposes in Norwegian sheep. In *E. faecium* from mutton (n=9), resistance to tetracycline, avilamycin and bacitracin was observed.

Avilamycin has never been approved for use in animals in Norway. Bacitracin has never been used as a growth promoter in ruminants in Norway. During the 1990s, the use of bacitracin as a growth promoter in Norwegian animal production was negligible, and no such use has been recorded since 1997.

Vancomycin resistant enterococci (VRE) in Norway

Avoparcin was approved as a feed additive for broilers and turkeys in Norway in 1986. It was banned from 1 June 1995 due to a reported association between its use and the occurrence of vancomycin-resistant enterococci (VRE) in animal husbandry. A study conducted in Norway between June 1995 and March 1997 confirmed a statistically significant association between the former use of avoparcin and the occurrence of VRE in Norwegian poultry production[1,5]. Vancomycin resistance was of the VanA high-level type (MIC ≥ 256 mg/L) mediated by the *vanA* gene cluster. VRE could only be isolated from 1% of faecal samples from Norwegian pig herds.

A study conducted in 1998 revealed that VRE were still prevalent in Norwegian poultry production three years after avoparcin was banned[3]. VRE were isolated by direct culture on selective media from 99% of faecal samples from farms previously exposed to avoparcin as opposed to 11% of farms where avoparcin had never been used. VRE were also isolated from 30% of broiler carcasses[6]. Moreover, VRE were isolated from 18% of farmers on poultry farms previously exposed to avoparcin, as opposed to 1% on farms without known avoparcin exposure. This study reconfirmed the association between avoparcin use and VRE occurrence, and showed that there had been no detectable decrease in the prevalence of VRE in Norwegian poultry production in the three-year period since the use of avoparcin was discontinued in June 1995. A follow-up study on five farms positive for VRE revealed persisting reservoirs of VRE in the farm environment and showed that the chickens were VRE-free upon arrival on the farm, but were colonized within three weeks of their arrival[4]. A genetic linkage of *vanA* and *erm*(B) genes in a poultry *Enterococcus hirae* isolate suggests that co-selection may play a role in the maintenance of VRE in the farm environment[8]. Furthermore, laboratory studies of bacterial fitness of isogenic vancomycin susceptible and resistant enterococcal strains demonstrated a low metabolic cost of possessing vancomycin resistance compared to the benefits of environmental adaptation[11]. Thus, several mechanisms can explain the observed persistence of VRE in the farm environment.

A molecular study of corresponding VRE from poultry flocks and their farmers showed that the *vanA* elements were indistinguishable when analysed by RFLP[2]. At one farm, human and poultry isolates had very similar PFGE-patterns. A recent study has revealed extensive heterogeneity among and between human and animal VRE on the strain level, indicating dynamic and separate reservoirs[10]. However, Tn*1546*-junction fragment analysis suggested the presence of identical plasmids and/or parts of a common replicon present in genomically diverse animal and human VRE. A study comparing Norwegian poultry VRE with VRE from various sources in the Netherlands and the UK using AFLP showed that vancomycin resistant *E. faecium* (VREF) from Norwegian poultry clustered with VREF isolates of poultry origin from the UK and the Netherlands[7].

So far, no data indicate that the reservoir of VRE in Norwegian poultry production has created a public health problem. VRE is currently not a problem in Norwegian hospitals. In a large study conducted in 1997, no VanA VRE were detected among 616 intensive care unit patients in seven hospitals[9]. This may be due to the limited usage of vancomycin in Norwegian hospitals. Although the public health significance of a large agricultural reservoir of VRE remains to be elucidated, such a reservoir may represent a risk to public health as a source of VRE and/or *vanA* genes that can be transferred to the hospital environment.

References on the Norwegian VRE situation

1. Kruse, H., B.K. Johansen, L.M. Rørvik, and G. Schaller. 1999. The use of avoparcin as a growth promoter and the occurrence of vancomycin resistant *Enterococcus* species (VRE) in Norwegian poultry and swine production. Microb. Drug Res. 5:135-139.
2. Simonsen, G.S., H. Haaheim, K.H. Dahl, A. Løvseth, H. Kruse, Ø. Olsvik, and A. Sundsfjord. 1998. Transmission of VanA-type vancomycin resistant enterococci and *vanA* resistance elements between chicken and humans at avoparcin-exposed farms. Microb. Drug Res. 4:313-318.
3. Borgen, K., G.S. Simonsen, A. Sundsfjord, Y. Wasteson, Ø. Olsvik, and H. Kruse. 2000. Continuing high prevalence of VanA-type vancomycin-resistant enterococci on Norwegian poultry farms three years after avoparcin was banned. J. Appl. Microbiol. 89:478-485.
4. Borgen, K., M. Sørum, H. Kruse, and Y. Wasteson. 2000. Persistence of Vancomycin-Resistant Enterococci (VRE) on Norwegian Broiler Farms. FEMS Microbiol. Lett. 191 (2):255-258.
5. Aarestrup, F.M., H. Kruse, E. Tast, A. M. Hammerun, and L. B. Jensen. 2000. Associations between the use of antimicrobial agents for growth promotion and the occurrence of resistance among *Enterococcus faecium* from broilers and pigs in Denmark, Finland and Norway. Microb. Drug Res. 6:63-70.
6. Borgen, K., M. Sørum, Y. Wasteson, and H. Kruse. 2001. VanA-type vancomycin resistant enterococci (VRE) remain prevalent in poultry carcasses 3 years after avoparcin was banned. Int. J. Food Microbiol. 64:89-94.
7. Borgen, K., Y. Wasteson, H. Kruse, and R.J.L. Willems. 2002. Vancomycin-resistant *Enterococcus faecium* (VREF) from Norwegian poultry production cluster with poultry VREF from UK and the Netherlands by AFLP. Appl. Environ. Microbiol. 68: 3133-3137.
8. Borgen, K., M. Sørum, Y. Wasteson, H. Kruse, and H. Oppegaard. Genetic linkage of *erm*(B) and Tn*1546* in *Enterococcus hirae* of poultry origin. Microb Drug Res. In press.
9. Simonsen G.S., B.M. Andersen, A. Digranes, S. Harthug, T. Jakobsen, N. Langeland, E. Lingaas, O.B. Natås, Ø. Olsvik, S.H. Ringertz, A. Skulberg, G. Syversen, and A. Sundsfjord A. 1998. Low Faecal Carriage of Vancomycin Resistant Enterococci in Norwegian Hospitals. Scand J Infect Dis. 30: 465-468.
10. Johnsen, P.J., G.S. Simonsen, J.I. Østerhus, M. Sørum, H. Kruse, A. Sundsfjord. Persistence of animal and human VanA glycopeptide resistant *Enterococcus faecium* strains from an avoparcin exposed Norwegian poultry farm: Characterization of strains and *vanA* containing plasmids. 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC, 42nd), San Diego, California, USA, September 27-30, 2002.
11. Johnsen, P.J., G.S. Simonsen, Ø. Olsvik, T. Midtvedt, A. Sundsfjord. Stability, persistence and evolution of plasmid-encoded VanA glycopeptide resistance in enterococci in the absence of antibiotic selection *in vitro* and in gnotobiotic mice. Microbial Drug Resistance 2002 (in press).

B. ANIMAL CLINICAL ISOLATES

Staphylococcus spp.

TABLE 25. *Staphylococcus aureus* isolates from clinical mastitis in dairy cows (n=108). Sampling, laboratory methods and data processing are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)		MIC_{50}	MIC_{90}
	S	R	S	I	R				
Oxytetracycline	≤ 4	≥ 16	100.0	0.0	0.0	0.5	- 1	0.5	0.5
Chloramphenicol	≤ 8	≥ 32	99.1	0.9	0.0	4	- 16	8	8
Penicillin	≤ 0.125	≥ 0.25	93.5	-	6.5	0.06	- ≥ 16	0.064	0.125
Oxacillin	≤ 2	≥ 4	100.0	-	0.0	0.5	- 2	0.5	1
β-lactamase	Neg	Pos	93.5	-	6.5				
Cephalothin	≤ 8	≥ 32	100.0	0.0	0.0	0.125	- 0.5	0.25	0.5
Trimethoprim	≤ 8	≥ 16	100.0	-	0.0	0.5	- 2	1	2
TMS**	≤ 2	≥ 4	100.0	-	0.0	0.25	- 1	0.25	0.25
Erythromycin	≤ 0.5	≥ 8	52.8	47.2	0.0	0.25	- 2	0.5	1
Spiramycin	≤ 32	≥ 64	100.0	-	0.0	8	- 32	16	16
Clindamycin	≤ 1	≥ 4	100.0	0.0	0.0	1	- 1	1	1
Streptomycin	≤ 32	≥ 64	95.4	-	4.6	2	- ≥ 512	8	16
Gentamicin	≤ 4	≥ 16	100.0	0.0	0.0	0.5	- 2	1	1
Neomycin	≤ 32	≥ 64	100.0	-	0.0	1	- 2	1	1
Ciprofloxacin	≤ 1	≥ 4	100.0	0.0	0.0	0.064	- 0.25	0.125	0.25
Vancomycin	≤ 4	≥ 32	100.0	0.0	0.0	1	- 2	1	1
Fucidic acid	≤ 0.5	≥ 1	98.1	-	1.9	0.064	- 64	0.25	0.25
Avilamycin	≤ 16	≥ 32	100.0	-	0.0	2	- 16	4	8
Virginiamycin	≤ 2	≥ 8	100.0	0.0	0.0	0.25	- 1	0.5	1

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

TABLE 26. *Staphylococcus aureus* isolates from clinical mastitis in dairy cows (n=108). Distribution of MICs (mg/L).*

	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥512
Oxytetracycline					96	4									
Chloramphenicol								19	80	1					
Penicillin		80	14			2			1	4					
Oxacillin					52	44	5								
Cephalothin			7	79	15										
Trimethoprim					18	70	12								
TMS**				99		1									
Erythromycin				2	51	46	1								
Spiramycin									14	83	3				
Clindamycin						100									
Streptomycin							1	39	45	9	1	1		2	2
Gentamicin					48	45	7								
Neomycin						92	8								
Ciprofloxacin		1	77	23											
Vancomycin						97	3								
Fucidic acid		5	31	62					1			1			
Avilamycin							10	61	27	2					
Virginiamycin				1	80	19									

*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. **See footnote to Table 25.

TABLE 27. *Staphylococcus aureus* isolates from subclinical mastitis in dairy cows (n=108). Sampling, laboratory methods and data processing are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Oxytetracycline	≤ 4	≥ 16	98.1	0.0	1.9	0.5 - 64	0.5	0.5
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	0.0	4 - 8	8	8
Penicillin	≤ 0.125	≥ 0.25	93.5	-	6.5	0.06 - ≥ 16	0.064	0.125
Oxacillin	≤ 2	≥ 4	100.0	-	0.0	0.5 - 1	0.5	1
β-lactamase	Neg	Pos	93.5	-	6.5			
Cephalothin	≤ 8	≥ 32	100.0	0.0	0.0	0.125 - 0.5	0.25	0.25
Trimethoprim	≤ 8	≥ 16	100.0	-	0.0	0.5 - 2	1	1
TMS**	≤ 2	≥ 4	100.0	-	0.0	0.25 - 0.25	0.25	0.25
Erythromycin	≤ 0.5	≥ 8	63.0	37.0	0.0	0.25 - 1	0.5	1
Spiramycin	≤ 32	≥ 64	100.0	-	0.0	4 - 32	16	16
Clindamycin	≤ 1	≥ 4	99.1	0.9	0.0	1 - 2	1	1
Streptomycin	≤ 32	≥ 64	98.1	-	1.9	2 - ≥ 512	8	16
Gentamicin	≤ 4	≥ 16	100.0	0.0	0.0	0.25 - 2	0.5	1
Neomycin	≤ 32	≥ 64	100.0	-	0.0	1 - 2	1	1
Ciprofloxacin	≤ 1	≥ 4	100.0	0.0	0.0	0.064 - 0.5	0.125	0.25
Vancomycin	≤ 4	≥ 32	100.0	0.0	0.0	1 - 2	1	1
Fucidic acid	≤ 0.5	≥ 1	97.2	-	2.8	0.125 - 12	0.25	0.25
Avilamycin	≤ 16	≥ 32	100.0	-	0.0	1 - 8	4	8
Virginiamycin	≤ 2	≥ 8	100.0	0.0	0.0	0.5 - 2	0.5	1

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

TABLE 28. *Staphylococcus aureus* isolates from subclinical mastitis in dairy cows (n=108). Distribution (%) of MICs (mg/L)*.

	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline					97		1				1	1			
Chloramphenicol								21	79						
Penicillin		86	7				1		2	4					
Oxacillin					72	28									
Cephalothin			13	81	7										
Trimethoprim					19	73	8								
TMS*				100											
Erythromycin				3	60	37									
Spiramycin								1	9	86	4				
Clindamycin						99	1								
Streptomycin							3	32	45	17	1			1	1
Gentamicin				2	54	38	7								
Neomycin						92	8								
Ciprofloxacin		1	83	16	1										
Vancomycin						98	2								
Fucidic acid			42	55	1			1	1	1					
Avilamycin						1		79	20						
Virginiamycin					69	30		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.
**TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 29. Coagulase negative staphylococci (CNS) isolates from mastitis in dairy cows (n=108). Sampling, laboratory methods and data processing are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)			MIC_{50}	MIC_{90}
	S	R	S	I	R					
Oxytetracycline	≤ 4	≥ 16	98.1	0.0	1.9	0.5	-	64	0.5	1
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	0.0	2	-	8	4	8
Penicillin	≤ 0.125	≥ 0.25	75.9	-	24.1	0.06	-	≥ 16	0.064	4
Oxacillin	≤ 2	≥ 4	100.0	-	0.0	0.5	-	1	0.5	1
β-lactamase	Neg	Pos	76.9	-	23.1					
Cephalothin	≤ 8	≥ 32	100.0	0.0	0.0	0.125	-	1	0.25	0.5
Trimethoprim	≤ 8	≥ 16	57.4	-	42.6	0.25	-	≥ 32	8	64
TMS*	≤ 2	≥ 4	100.0	-	0.0	0.25	-	0.5	0.25	0.5
Erythromycin	≤ 0.5	≥ 8	83.3	15.6	0.8	0.25	-	32	0.5	1
Spiramycin	≤ 32	≥ 64	100.0	-	0.0	4	-	32	16	16
Clindamycin	≤ 1	≥ 4	100.0	0.0	0.0	1	-	1	1	1
Streptomycin	≤ 32	≥ 64	87.0	-	13.0	2	-	≥ 512	4	64
Gentamicin	≤ 4	≥ 16	100.0	0.0	0.0	0.25	-	2	0.25	0.5
Neomycin	≤ 32	≥ 64	100.0	-	0.0	1	-	4	1	1
Ciprofloxacin	≤ 1	≥ 4	100.0	0.0	0.0	0.032	-	0.25	0.125	0.125
Vancomycin	≤ 4	≥ 32	100.0	0.0	0.0	1	-	2	1	1
Fucidic acid	≤ 0.5	≥ 1	90.7	-	9.3	0.032	-	8	0.25	0.5
Avilamycin	≤ 16	≥ 32	97.2	-	2.8	1	-	64	4	16
Virginiamycin	≤ 2	≥ 8	99.1	0.9	0.0	0.5	-	4	0.5	1

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

TABLE 30. Coagulase negative staphylococci (CNS) isolates from mastitis in dairy cows (n=108). 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					88	10					1	1			
Chloramphenicol							7	57	36						
Penicillin		68	8	3	2	3	6	7	3	1					
Oxacillin					69	31									
Cephalothin			19	55	24	2									
Trimethoprim				3	10	21	10	6	9	7	36				
TMS**				69	32										
Erythromycin				16	68	14	2				1				
Spiramycin								6	32	54	8				
Clindamycin						100									
Streptomycin							37	32	12	4	2	4	5	3	2
Gentamicin				62	34	3	1								
Neomycin						99		1							
Ciprofloxacin	1	40	51	8											
Vancomycin						93	7								
Fucidic acid	1	11	28	35	16	5		2	3						
Avilamycin						1	25	31	20	20	2	1			
Virginiamycin					82	14	3	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.
**TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 31. Number of isolates per species in coagulase negative staphylococci from bovine milk samples (n=108).

Species	Number of isolates
Staphylococcus auricularis	1
Staphylococcus capitis ss. capitis	1
Staphylococcus chromogenes	12
Staphylococcus cohnii	2
Staphylococcus epidermidis	9
Staphylococcus haemolyticus	10
Staphylococcus hyicus	15
Staphylococcus sciuri	1
Staphylococcus simulans	43
Staphylococcus warneri	3
Staphylococcus xylosus	2
Staphylococcus spp. various coagulase negative	9

COMMENTS

The prevalence of resistance among *S. aureus* isolates remained at the same level during the 1990s, and this also applies to the data for 2000 and 2001. However, the inclusion criteria for isolates applied in 2000 and 2001 differed from previous years. Before 2000, the prevalence of antimicrobial resistance in staphylococci isolated from cases of mastitis was estimated using all isolates submitted to the diagnostic laboratories. In NORM-VET 2000 and 2001, only one isolate per herd was included to avoid the effect of clustering at the herd level due to frequent submissions from "problem herds".

In 2001, the occurrence of resistance among *S. aureus* from clinical and subclinical mastitis in cows was low, 92% and 90% of the isolates being susceptible to all antimicrobials included in the test panel. In the case of clinical mastitis isolates, 5% were resistant to one antimicrobial (penicillin or streptomycin), 3% to two (penicillin and fucidic acid or streptomycin) and 1% to three antimicrobials (penicillin, streptomycin and fucidic acid). In the case of subclinical mastitis isolates, 8% were resistant to one antimicrobial (penicillin, fucidic acid, streptomycin or tetracycline), 1% to two (fucidic acid and penicillin), and 1% to three antimicrobials (penicillin, fucidic acid, and tetracycline).

The resistance prevalences for the specific antimicrobials were very similar for *S. aureus* from the two categories. The resistance frequencies for the various antimicrobial agents reflect thier usage, penicillin, streptomycin, trimethoprim/sulfonamides and to a lesser degree, tetracycline being commonly used for clinical purposes in dairy cattle.

Resistance in coagulase negative staphylococci (CNS) isolates from mastitis in cows was considerably more abundant than in isolates of *S. aureus.* Only 30% of the isolates were susceptible to all the antimicrobials included. Altogether, 54% of the isolates were resistant to one antimicrobial, 11% to two and 6% to three or more antimicrobials. The occurrence of penicillin resistance in CNS remained at the same level throughout the 1990s, and in 2000 and 2001.

Fluoroquinolones have so far been little used in veterinary practice in Norway, and no cephalosporins are approved for use in animals in Norway. This is reflected by the high prevalence of susceptibility to these classes of antimicrobials in the data presented here. No resistance to oxacillin was observed.

C. ZOONOTIC AND OTHER FOOD-BORNE ENTERIC BACTERIA

Salmonella from animals

Since the prevalence of *Salmonella* in Norwegian animal husbandry is low, only a few isolates were examined. However, strains of *S.* Typhimurium occur endemically in wildlife and *S. enterica* ss. *diarizonae* endemically in Norwegian sheep. Seagulls may also harbour various *Salmonella* serovars.

In 2001, multiresistant *S.* Typhimurium DT104 was detected in two unrelated cattle herds in south-western and south-eastern Norway. This was the first detection ever in animals in Norway of this particular *Salmonella* variant. At one farm, the same strain was also isolated from the farmer. The sources of infection remain unknown.

TABLE 32. *Salmonella* Typhimurium isolates from wild birds (n=10) and a hedgehog (n=1). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mg/L)		Number of isolates*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Oxytetracycline	≤ 4	≥ 16	11	0	0	2 - 2	2	2
Chloramphenicol	≤ 8	≥ 32	11	0	0	1 - 8	4	8
Florfenicol	≤ 16	≥ 32	11	-	0	4 - 4	4	4
Ampicillin	≤ 8	≥ 32	11	0	0	1 - 4	1	2
Amoxi./clav.**	≤ 8	≥ 32	11	0	0	2 - 4	2	4
Ceftiofur	≤ 2	≥ 8	11	0	0	0.5 - 1	1	1
Trimethoprim	≤ 8	≥ 16	11	-	0	0.12 - 0.5	0.5	0.5
Sulfamethoxazole	≤ 256	≥ 512	10	-	1	64 - > 512	64	128
Streptomycin	≤ 32	≥ 64	10	-	1	8 - 128	16	32
Gentamicin	≤ 4	≥ 16	11	0	0	0.5 - 4	1	4
Neomycin	≤ 32	≥ 64	11	-	0	1 - 4	2	2
Apramycin	≤ 32	≥ 64	11	-	0	4 - 8	8	8
Enrofloxacin	≤ 0.25	≥ 2	11	0	0	0.06 - 0.25	0.064	0.125
Nalidixic acid	≤ 16	≥ 32	11	-	0	4 - 16	8	8

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**Amoxi./clav.= Amoxicillin/clavulanic acid

TABLE 33. *Salmonella* Typhimurium isolates from wild birds (n=10) and a hedgehog (n=1). Distribution (No.) of MICs (mg/L).*

	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline						11								
Chloramphenicol					1		8	2						
Florfenicol							11							
Ampicillin					8	2	1							
Amoxi./clav.**						5	6							
Ceftiofur				5	6									
Trimethoprim		2	3	6										
Sulfamethoxazole											7	3		1
Streptomycin								1	8	1		1		
Gentamicin				1	5	3	2							
Neomycin					4	6	1							
Apramycin							4	7						
Enrofloxacin	7	3	1											
Nalidixic acid							3	7	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.
**Amoxi./clav.=Amoxicillin/clavulanic acid.

TABLE 34. *Salmonella* spp. isolates from seagulls. *S.* Agona (n=3), *S.* Montevideo (n=1), *S.* Typhimurium (n=1) and *S.* Senftenberg (n=11). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mg/L)		Number of isolates*			MIC range (mg/L)		MIC_{50}	MIC_{90}
	S	R	S	I	R				
Oxytetracycline	≤ 4	≥ 16	16	0	0	1	- 2	2	2
Chloramphenicol	≤ 8	≥ 32	15	1	0	4	- 16	8	8
Florfenicol	≤ 16	≥ 32	16	-	0	4	- 16	8	8
Ampicillin	≤ 8	≥ 32	16	0	0	0.5	- 2	1	2
Amoxi./clav.**	≤ 8	≥ 32	16	0	0	2	- 4	2	4
Ceftiofur	≤ 2	≥ 8	16	0	0	0.5	- 1	1	1
Trimethoprim	≤ 8	≥ 16	16	-	0	0.25	- 0.5	0.5	0.5
Sulfamethoxazole	≤ 256	≥ 512	16	-	0	64	- 64	64	64
Streptomycin	≤ 32	≥ 64	16	-	0	8	- 16	16	16
Gentamicin	≤ 4	≥ 16	16	0	0	0.5	- 1	1	1
Neomycin	≤ 32	≥ 64	16	-	0	1	- 4	1	2
Apramycin	≤ 32	≥ 64	16	-	0	4	- 16	4	8
Enrofloxacin	≤ 0.25	≥ 2	16	0	0	0.06	- 0.12	0.064	0.064
Nalidixic acid	≤ 16	≥ 32	16	-	0	4	- 8	4	8

*S=Susceptible, I=Intermediately susceptible, R=Resistant. ** Amoxi./clav.=Amoxicillin/clavulanic acid.

TABLE 35. *Salmonella* spp. isolates from seagulls. *S.* Agona (n=3), *S.* Montevideo (n=1), *S.* Typhimurium (n=1) and *S.* Senftenberg (n=11). Distribution of MICs (mg/L).*

	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline					3	13								
Chloramphenicol							5	10	1					
Florfenicol							7	7	1					
Ampicillin				4	10	2								
Amoxi./clav.**						14	2							
Ceftiofur				5	10									
Trimethoprim			2	13	1									
Sulfamethoxazole											16			
Streptomycin								2	14					
Gentamicin				5	11									
Neomycin					13	2	1							
Apramycin							9	6	1					
Enrofloxacin	15	1												
Nalidixic acid							11	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.
**Amoxi./clav.=Amoxicillin/clavulanic acid.

TABLE 36. *Salmonella enterica* subsp. *diarizonae* isolates from sheep (n=20). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mg/L)		Number of isolates*			MIC range (mg/L)			MIC_{50}	MIC_{90}
	S	R	S	I	R					
Oxytetracycline	≤ 4	≥ 16	20	0	0	1	-	2	1	2
Chloramphenicol	≤ 8	≥ 32	20	0	0	2	-	4	4	4
Florfenicol	≤ 16	≥ 32	20	-	0	2	-	4	4	4
Ampicillin	≤ 8	≥ 32	20	0	0	0.5	-	1	1	1
Amoxi./clav.**	≤ 8	≥ 32	20	0	0	2	-	4	2	2
Ceftiofur	≤ 2	≥ 8	20	0	0	0.25	-	1	0.5	0.5
Trimethoprim	≤ 8	≥ 16	20	-	0	0.25	-	0.5	0.5	0.5
Sulfamethoxazole	≤ 256	≥ 512	20	-	0	64	-	64	64	64
Streptomycin	≤ 32	≥ 64	20	-	0	16	-	32	16	32
Gentamicin	≤ 4	≥ 16	20	0	0	0.5	-	1	0.5	1
Neomycin	≤ 32	≥ 64	20	-	0	1	-	2	1	1
Apramycin	≤ 32	≥ 64	20	-	0	2	-	4	2	4
Enrofloxacin	≤ 0.25	≥ 2	20	0	0	0.06	-	0.06	0.064	0.064
Nalidixic acid	≤ 16	≥ 32	20	-	0	4	-	16	8	8

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
** Amoxi./clav.=Amoxicillin/clavulanic acid.

TABLE 37. *Salmonella enterica* subsp. *diarizonae* isolates from sheep (n=20). Distribution of MICs (mg/L).*

	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline					11	9								
Chloramphenicol						6	14							
Florfenicol						9	11							
Ampicillin				5	15									
Amoxi./clav.**						18	2							
Ceftiofur			2	16	2									
Trimethoprim			6	14										
Sulfa											20			
Streptomycin									10	10				
Gentamicin				12	8									
Neomycin					18	2								
Apramycin						11	9							
Enrofloxacin	20													
Nalidixic acid							5	14	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.
**Amoxi./clav.=Amoxicillin/clavulanic acid.

COMMENTS

The data, although based on few isolates, indicate that resistance is not widespread among clones of *S.* Typhimurium that occur endemically among wild birds in Norway, or isolates of *S. enterica ss. diarizonae* that occur endemically in the Norwegian sheep population.
All isolates from seagulls, representing different serovars, were susceptible to all the antimicrobials included in the test panel. There is reason to believe that the serovars and resistance profiles for *Salmonella* from seagulls will vary more than *Salmonella* from other sources because seagulls are prone to be exposed to a variety of *Salmonella* that may occur in the environment.

Salmonella from human clinical specimens

TABLE 38. *Salmonella* Typhimurium isolates from patients infected in Norway (n=92). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	14.1	47.8	38.0	6 - 30
Chloramphenicol	≥ 32	≤ 24	0.0	53.3	46.7	6 - 28
Ampicillin	≥ 25	≤ 8	55.4	6.5	38.0	6 - 31
TMS**	≥ 26	≤ 15	95.7	1.1	3.3	6 - ≥ 36
Ciprofloxacin	≥ 29	≤ 17	98.9	1.1	0.0	26 - ≥ 36
Nalidixic acid	≥ 14	≤ 13	100.0	-	0.0	22 - 34

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 39. *Salmonella* Typhimurium isolates from patients infected in Norway (n=92). Distribution (%) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline	4	2	7	8	13	3							1			
Chloramph.	33															
Ampicillin	38										1					1
TMS**	3															
Ciprofloxacin																
Nalidixic acid																

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	≥ 36
Tetracycline	1	5	10	9	17	5	11	1	2						
Chloramph.		1	13	22	13	10	9								
Ampicillin	1	2	1	3	5	4	21	8	13	1					
TMS**				1	3	2	7	8	15	3	19	10	20	2	8
Ciprofloxacin					1				1	1	2	1	8	12	74
Nalidixic acid	1	7	14	14	39	12	8	2	2				1		

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue).
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 40. *Salmonella* Typhimurium isolates from patients infected outside Norway (n=114). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	9.6	43.9	46.5	6 - 30
Chloramphenicol	≥ 32	≤ 24	0.9	64.0	35.1	6 - ≥ 36
Ampicillin	≥ 25	≤ 8	61.4	2.6	36.0	6 - 32
TMS**	≥ 26	≤ 15	87.7	1.8	10.5	6 - ≥ 36
Ciprofloxacin	≥ 29	≤ 17	93.0	7.0	0.0	23 - ≥ 36
Nalidixic acid	≥ 14	≤ 13	92.1	-	7.9	6 - 34

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 41. *Salmonella* Typhimurium isolates from patients infected outside Norway (n=114). Distribution (%) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline	21	2	2	7	9	2	1		1	1					1	1
Chloramph.	25		1													
Ampicillin	36															
TMS**	11															
Ciprofloxacin																
Nalidixic acid	8														1	1

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	≥ 36
Tetracycline	3	2	4	11	17	9	6		4						
Chloramph.			9	24	20	12	5	1	2						1
Ampicillin		1	2	4	7	8	18	5	18		1				
TMS**			1	1	3	3	5	4	14	3	13	5	14	7	18
Ciprofloxacin		1			1	3	3	1	3	1		1	9	9	70
Nalidixic acid	1	3	9	21	32	11	11	4					1		

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue).
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 42. *Salmonella* Typhimurium DT104 isolates from patients infected in Norway and abroad (n=46). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	0.0	4.3	95.7	7 - 25
Chloramphenicol	≥ 32	≤ 24	0.0	4.3	95.7	6 - 25
Ampicillin	≥ 25	≤ 8	4.3	0.0	95.7	6 - 28
TMS**	≥ 26	≤ 15	97.8	2.2	0.0	25 - 34
Ciprofloxacin	≥ 29	≤ 17	93.5	6.5	0.0	27 - ≥ 36
Nalidixic acid	≥ 14	≤ 13	91.3	-	8.7	6 - 30

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 43. *Salmonella* Typhimurium DT104 isolates from patients infected in Norway and abroad (n=46). Distribution (%) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline		4	13	33	39	7										
Chloramph.	96															
Ampicillin	96															
TMS**																
Ciprofloxacin																
Nalidixic acid	9															

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	≥ 36
Tetracycline				4											
Chloramph.				4											
Ampicillin						2	2								
TMS**				2	7	4	17	20	37	4	7		2		
Ciprofloxacin						4	2		2	2			11	11	67
Nalidixic acid		2	9	7	37	15	13	7	2						

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue).
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 44. *Salmonella* Typhimurium, excluding DT104, isolates from patients infected in Norway (n=65). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	20.0	64.6	15.4	6 - 30
Chloramphenicol	≥ 32	≤ 24	0.0	72.3	27.7	6 - 28
Ampicillin	≥ 25	≤ 8	75.4	9.2	15.4	6 - 31
TMS**	≥ 26	≤ 15	95.4	0.0	4.6	6 - ≥ 36
Ciprofloxacin	≥ 29	≤ 17	98.5	1.5	0.0	26 - ≥ 36
Nalidixic acid	≥ 14	≤ 13	100.0	-	0.0	22 - 34

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 45. *Salmonella* Typhimurium, excluding DT104, isolates from patients infected in Norway (n=65). Distribution (%) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline	6	2			5	2							2			
Chloramph.	8															
Ampicillin	15										2					2
TMS**	5															
Ciprofloxacin																
Nalidixic acid																

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	≥ 36
Tetracycline	2	8	14	9	25	8	15	2	3						
Chloramph.		2	19	28	19	14	12								
Ampicillin	2	3	2	5	8	5	28	11	19	2					
TMS**					2		3	2	6	5	25	14	26	3	11
Ciprofloxacin					2				2		3	2	5	12	75
Nalidixic acid	2	8	15	20	35	9	6	2	2				2		

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue).
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 46. *Salmonella* Typhimurium, excluding DT104, isolates from patients infected outside Norway (n=95). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	11.6	52.6	35.8	6 - 30
Chloramphenicol	≥ 32	≤ 24	1.1	76.8	22.1	6 - ≥ 36
Ampicillin	≥ 25	≤ 8	73.7	3.2	23.2	6 - 32
TMS**	≥ 26	≤ 15	85.3	2.1	12.6	6 - ≥ 36
Ciprofloxacin	≥ 29	≤ 17	94.7	5.3	0.0	23 - ≥ 36
Nalidixic acid	≥ 14	≤ 13	94.7	-	5.3	5 - 34

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 47. *Salmonella* Typhimurium, excluding DT104, isolates from patients infected outside Norway (n=95). Distribution (%) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline	25	1	2		1	1	1		1	1					1	1
Chloramph.	11		1													
Ampicillin	23															
TMS**	13															
Ciprofloxacin																
Nalidixic acid	5														1	1

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	≥ 36
Tetracycline	3	2	4	13	20	11	7		4						
Chloramph.			11	28	24	15	6	1	2						1
Ampicillin		1	2	4	8	10	22	6	22		1				
TMS**			1	1	2	3	2	1	10	1	14	6	17	8	21
Ciprofloxacin		1			1	1	2	1	2	1		1	10	8	72
Nalidixic acid	1	3	10	22	34	11	10	2					1		

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue).
**TMS=Trimethoprim/sulfamethoxazole.

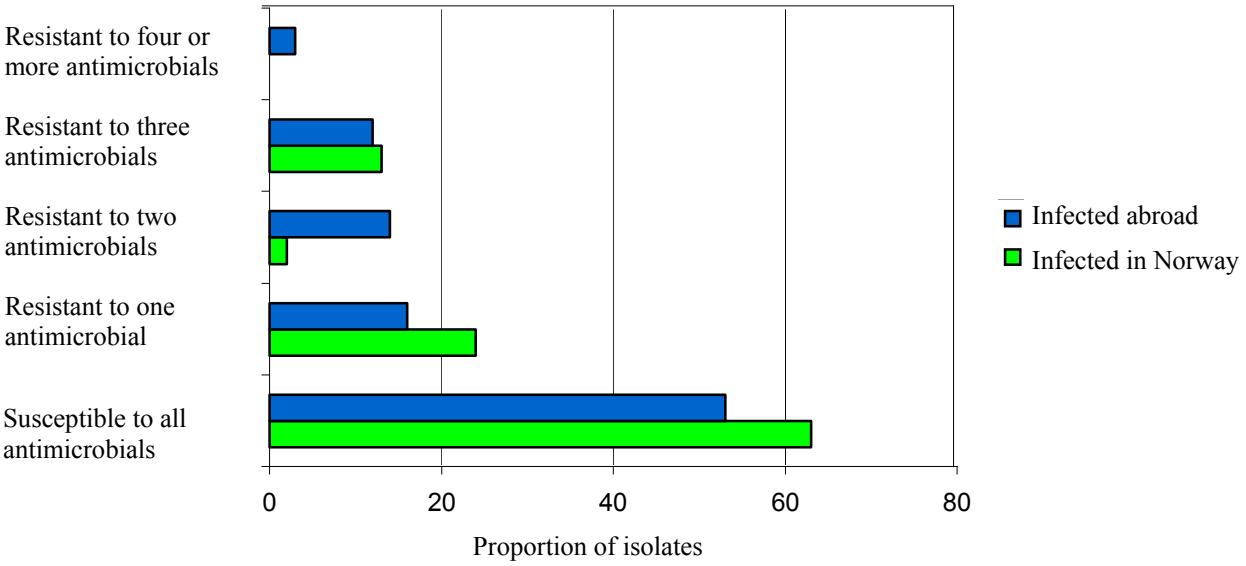


FIGURE 7. Antimicrobial resistance profiles for human *Salmonella* Typhimurium isolates excluding DT104, from Norway (n=65) or abroad (n=95). Proportion of isolates fully susceptible, resistant to one, two, three or four or more of the antimicrobials tested for.

TABLE 48. *Salmonella* Enteritidis isolates from patients infected outside Norway, or where country of infection is unknown (n=169). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	46.7	46.2	7.1	6 - 34
Chloramphenicol	≥ 32	≤ 24	1.2	87.6	11.2	20 - 38
Ampicillin	≥ 25	≤ 8	89.9	7.1	3.0	6 - 32
TMS**	≥ 26	≤ 15	97.6	1.2	1.2	6 - 38
Ciprofloxacin	≥ 29	≤ 17	89.9	10.1	0.0	21 - 40
Nalidixic acid	≥ 14	≤ 13	79.9	-	20.1	6 - 31

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 49. *Salmonella* Enteritidis isolates from patients infected outside Norway, or where origin of infection is unknown (n=169). Distribution (%) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline	5	1	1												1	1
Chloramph.															1	
Ampicillin	3														1	
TMS**	1															
Ciprofloxacin																1
Nalidixic acid	20														1	1

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	≥ 36
Tetracycline	2	1	4	10	15	15	27	7	12		1		1		
Chloramph.	1	1	9	14	27	15	24	4	4				1		1
Ampicillin	1	1	5	4	13	18	28	7	17	1	1				
TMS**				1		4	1	1	7	10	13	15	26	8	13
Ciprofloxacin				1	1	4	5	3	8	2	4	3	5	7	58
Nalidixic acid	3	4	13	21	23	9	6	1		1					

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue).
**TMS=Trimethoprim/sulfamethoxazole.

COMMENTS

In 2001, 1,899 human cases of salmonellosis were recorded in Norway. In 79% of the cases, the infection was acquired abroad. For *S.* Enteritidis, this proportion was 88%, which is due to the absence of this pathogen in Norwegian food producing animals. Only 50% of the patients with *S.* Typhimurium had acquired the infection abroad, 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 in Norway. The most likely sources 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.

Two domestic outbreaks of *S.* Typhimurium infections occurred in Norway in 2001, 26 confirmed cases associated with contact with hedgehogs and 28 confirmed cases infected with multiresistant DT104 due to a contaminated sweet (helva) imported from Turkey.

Of the *S.* Typhimurium acquired domestically, 29% of the isolates were caused by multiresistant DT104, as opposed to 17% for those acquired abroad. Of the total number of multiresistant DT104 isolates, 41% were acquired in Norway. The resistance profiles for the multiresistant DT104 isolates were quite similar for isolates acquired in Norway and those acquired abroad. The isolates were generally resistant to ampicillin, tetracycline, streptomycin, sulfonamides and chloramphenicol. However, four were resistant to nalidixic acid, and three of these were also resistant to ciprofloxacin. These four isolates were acquired abroad. Thus, 21% of the DT104 isolates acquired abroad were resistant to nalidixic acid, as opposed to none of the domestically acquired isolates.

The occurrence of resistance was lower among domestically acquired *S.* Typhimurium than those acquired abroad, due to the lower prevalence of resistance to nalidixic acid, trimethoprim/sulfonamides and tetracycline in the first group.

The proportion of *S.* Typhimurium isolates (excluding DT104) susceptible to all antimicrobials was slightly higher for the category "infected in Norway" (63%) than the "infected abroad" category (53%) (Figure 7). For the category "infected in Norway" (excluding DT104), 23% of the isolates were resistant to one antimicrobial (predominantly chloramphenicol), 2% to two (tetracycline and ampicillin), and 12% to three antimicrobials (tetracycline, ampicillin and chloramphenicol or the combination sulfonamides/ trimethoprim). For the category "infected abroad" (excluding DT104), 16% of the isolates were resistant to one antimicrobial (mostly tetracycline or chloramphenicol), 14% to two antimicrobials (mostly tetracycline and ampicillin), 12% to three (mostly tetracycline, ampicillin and chloramphenicol), 1% to four (tetracycline, ampicillin, chloramphenicol and nalidixic acid), and 2% to five antimicrobials (tetracycline, ampicillin, chloramphenicol, the trimethoprim/ sulfonamides combination and nalidixic acid). The proportion of isolates classified as resistant to tetracycline, ampicillin or the combination trimethoprim/sulfonamides was slightly higher in the category "infected abroad". A discrepancy for the two categories was observed for nalidixic acid and ciprofloxacin as 5% in the category "infected abroad" were resistant to nalidixic acid as opposed to none among those "infected in Norway" (excluding DT104). Most of the isolates classified as resistant to nalidixic acid also expressed reduced susceptibility to ciprofloxacin indicating that resistance could be developing. It is emphasized that the use of

fluoroquinolones in Norway is limited in both human and veterinary medicine.

All the included isolates of *S.* Enteritidis had been acquired abroad. The occurrence of resistance was moderate compared with isolates of *S.* Typhimurium (including those acquired within Norway). The proportion of isolates resistant to tetracycline, chloramphenicol and ampicillin was considerably lower for *S.* Enteritidis. The occurrence of resistance to the combination trimethoprim/sulphonamides was much lower for *S.* Enteritidis than for *S.* Typhimurium isolates acquired outside Norway. It was noticed that a considerable proportion of *S.* Enteritidis isolates were resistant to nalidixic acid. Many of these also showed reduced susceptibility to ciprofloxacin indicating that fluoroquinolone resistance could be developing.

In general, a high proportion of *Salmonella* isolates were classified as intermediately susceptible to chloramphenicol. This is a result of breakpoints being set on the basis of insufficient population data. The AFA has suggested increasing the breakpoint for resistance from 8 mg/L (24 mm) to 16 mg/L (20 mm).

In addition to the *S.* Typhimurium and *S.* Enteritidis isolates, ten isolates of the "typhoid/paratyphoid" group were tested for antimicrobial susceptibility. All these infections had been acquired outside Norway. In this group, some resistance to ampicillin, chloramphenicol, tetracycline and trimethoprim/sulfonamides was observed. One *S.* Typhi isolate was resistant to nalidixic acid and showed reduced susceptibility to ciprofloxacin.

Campylobacter jejuni from broilers

TABLE 50. *Campylobacter jejuni* isolates from broiler cloacal samples (n=113). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Tetracycline	≤ 4	≥ 16	99.1	0.0	0.9	0.032 - 16	0.063	0.125
Ampicillin	≤ 8	≥ 32	96.5	0.9	2.7	1 - 64	2	4
Erythromycin	≤ 1	≥ 4	97.3	2.7	0.0	0.25 - 2	0.5	1
Streptomycin	≤ 8	≥ 16	100.0	-	0.0	0.5 - 8	2	4
Gentamicin	≤ 2	≥ 8	100.0	0.0	0.0	0.125 - 2	1	2
Ciprofloxacin	≤ 0.125	≥ 4	83.2	14.2	2.7	0.032 - ≥ 32	0.125	0.25
Nalidixic acid	≤ 16	≥ 32	97.3	-	2.7	0.25 - ≥ 256	1	2

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

TABLE 51. *Campylobacter jejuni* isolates from broiler cloacal samples (n=113). Distribution (%) of MICs (mg/L).*

	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256
Tetracycline	21	58	18	3						1				
Ampicillin						7	56	33	1	1	1	2		
Erythromycin				8	54	36	3							
Streptomycin					5	24	45	25	2					
Gentamicin			3	11	32	39	16							
Ciprofloxacin	8	39	37	14				1	1		1			
Nalidixic acid				1	9	52	34	2			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.

COMMENTS

The results show that the prevalence of resistance among *C. jejuni* isolates from Norwegian broilers is low. A total of 96% of the isolates tested were susceptible to all the antimicrobials included in the test panel, 2% were resistant to one antimicrobial (ampicillin), 1% to two antimicrobials (nalidixic acid and ciprofloxacin), and 2% to three antimicrobials (nalidixic acid/ciprofloxacin and ampicillin or tetracycline). This corresponds to the usage of antimicrobials in poultry production. Antimicrobials (except coccidiostats) are rarely used, and only for therapeutical purposes. If used, amoxicillin (cross-resistance with ampicillin) and tetracycline are the drugs of choice. No quinolone preparations are licensed for use in poultry in Norway. However, several are approved for use in poultry in the EU, and may therefore perhaps also be used in poultry production in Norway.

Campylobacter spp. from human clinical specimens

TABLE 52. *Campylobacter jejuni* isolates from patients infected in Norway (n=84). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	89.3	1.2	9.5	0.125 - 128	0.25	2
Erythromycin	≤ 1	≥ 4	72.6	22.6	4.8	0.25 - ≥256	1	2
Gentamicin	≤ 2	≥ 8	94.0	6.0	0.0	0.063 - 4	0.5	2
Ciprofloxacin	≤ 0.125	≥ 4	44.0	48.8	7.1	0.125 - ≥ 32	0.25	0.5
Nalidixic acid	≤ 16	≥32	91.7	-	8.3	2 - ≥256	4	8

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

TABLE 53. *Campylobacter jejuni* isolates from patients infected in Norway (n=84). Distribution (%) of MICs (mg/L).*

	≤0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥256
Doxycycline						16	56	13	3	1	1		4	3		1	
Erythromycin							2	11	59	23	2	1					1
Gentamicin					1	6	21	29	25	12	6						
Ciprofloxacin						44	37	11	1					7			
Nalidixic acid										41	42	9	1	1			7

*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 54. *Campylobacter jejuni* isolates from patients infected outside Norway (n=129). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	55.0	1.6	43.4	0.125 - ≥256	0.5	32
Erythromycin	≤ 1	≥ 4	75.2	21.7	3.1	0.25 - 16	1	2
Gentamicin	≤ 2	≥ 8	97.7	1.6	0.8	0.125 - 32	0.5	2
Ciprofloxacin	≤ 0.125	≥ 4	17.8	22.5	59.7	0.125 - ≥ 32	≥ 32	≥ 32
Nalidixic acid	≤ 16	≥32	40.3	-	59.7	2 - ≥256	≥256	≥256

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

TABLE 55. *Campylobacter jejuni* isolates from patients infected outside Norway (n=129). Distribution (%) of MICs (mg/L).*

	≤0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥256
Doxycycline						16	24	14	1	2	4	7	7	18	5	1	2
Erythromycin							1	11	64	22	2		1				
Gentamicin						7	37	22	22	11	2			1			
Ciprofloxacin						18	16	7	1			1	1	59			
Nalidixic acid										17	20	4				2	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 56. *Campylobacter coli* isolates from patients infected outside Norway (n=38). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	50.0	7.9	42.1	0.125 - 128	0.5	64
Erythromycin	≤ 1	≥ 4	44.7	26.3	28.9	0.25 - ≥256	2	≥256
Gentamicin	≤ 2	≥ 8	92.1	2.6	5.3	0.25 - 32	1	2
Ciprofloxacin	≤ 0.125	≥ 4	10.5	23.7	65.8	0.125 - ≥ 32	≥ 32	≥ 32
Nalidixic acid	≤ 16	≥32	31.6	-	68.4	2 - ≥256	≥256	≥256

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

TABLE 57. *Campylobacter coli* isolates from patients infected outside Norway (n=38). Distribution (%) of MIC values (mg/L).*

	≤0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥256
Doxycycline						11	24	16		8	5	5	8	10	10	3	
Erythromycin							10	19	16	27	16						13
Gentamicin							8	37	26	21	3	3		3			
Ciprofloxacin						10	11	8	6			8		58			
Nalidixic acid										3	19	6	5	3		3	63

*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.

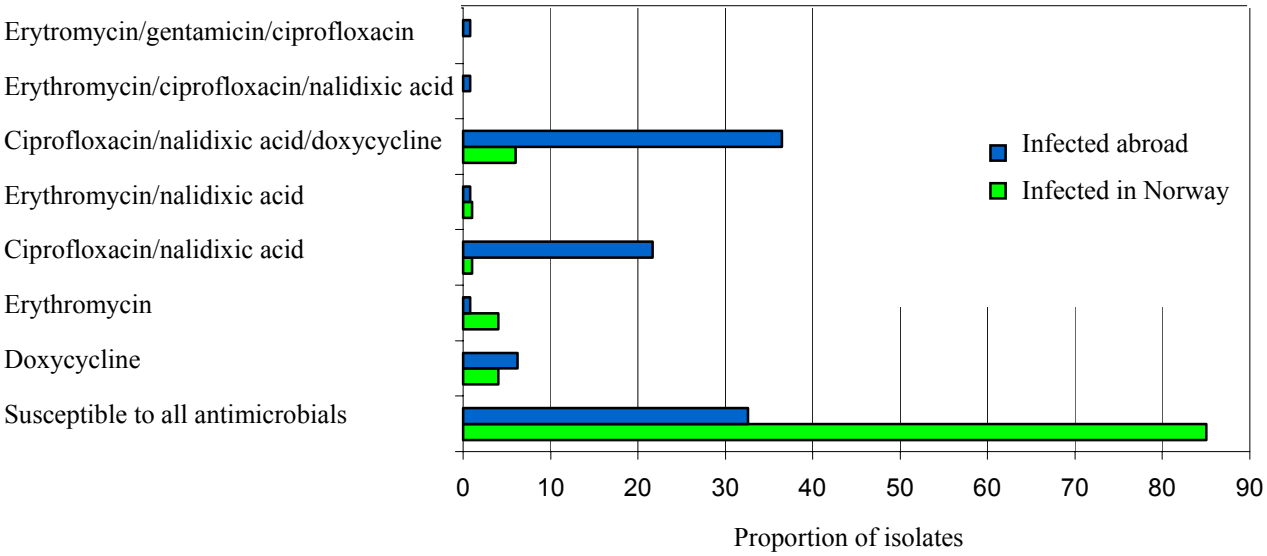


FIGURE 8. Antimicrobial resistance profiles for human *Campylobacter jejuni* isolates acquired in Norway (n=84) and abroad (n=129). Proportion of isolates fully susceptible, or resistant to one, two, or three of the antimicrobials tested for.

COMMENTS

Of the 2,889 human cases of campylobacteriosis recorded in Norway in 2001, 50% were acquired abroad. The vast majority of cases were sporadic. Norwegian case-control studies have revealed that consumption of poultry meat purchased fresh and drinking untreated water are risk factors for domestically acquired campylobacteriosis.

The data show that resistance was more widespread among the *C. jejuni* isolates derived from cases infected abroad (33% susceptible to all antimicrobials included in the test panel) than cases infected in Norway (85% susceptible to all the antimicrobials included). These discrepancies are explained by the widespread resistance to nalidixic acid/ciprofloxacin (60% versus 7%) and to tetracycline (43% versus 10%) in the first category.

The resistance frequencies for domestically acquired isolates are in accordance with data from Norwegian poultry, although they were somewhat higher among the human isolates, and resistance to erythromycin was only detected in the latter category (3%).

All isolates of *C. coli* were acquired outside Norway. Resistance was more common than in *C. jejuni* isolates acquired abroad, only 16% of the isolates being susceptible to all and 18% being resistant to four or five of the antimicrobials included in the test panel. Resistance to erythromycin and gentamicin was more common among the *C. coli* isolates than the *C. jejuni* isolates. *C. coli* is typically associated with pigs and pork.

Yersinia enterocolitica from human clinical specimens

TABLE 58. *Yersinia enterocolitica* serogroup 0:3 isolates from human clinical cases (n=88). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	67.0	31.8	1.1	6 - ≥ 38
Chloramphenicol	≥ 32	≤ 24	19.3	59.1	21.6	6 - ≥ 40
Ampicillin	≥ 25	≤ 8	0.0	30.7	69.3	6 - 14
TMS**	≥ 26	≤ 15	77.3	19.3	3.4	12 - ≥ 40
Ciprofloxacin	≥ 29	≤ 17	85.2	14.8	0.0	18 - ≥ 40
Nalidixic acid	≥ 14	≤ 13	96.6	-	3.4	6 - ≥ 36

*S=Susceptible, I=Intermediately susceptible, R=Resistant. **TMS=Trimethoprim/sulfamethoxazole.

TABLE 59. *Yersinia enterocolitica* serogroup 0:3 isolates (n=88) from human clinical cases. Distribution (%) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline	1															
Chloramph.	10	1												1		1
Ampicillin	32	18	19	10	10	5	2		3							
TMS**							1		1	1	2	2			3	
Ciprofloxacin													1			1
Nalidixic acid	3								1				1		1	1

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	≥ 37
Tetracycline	1	2	6	5	10	8	16	8	22	3	9	3	2		2	1
Chloramph.	3	3	1	2	6	8	13	5	24	2	9		6		2	2
Ampicillin																
TMS**		2	7	2	7	6	14	5	14	6	6	3	8		6	4
Ciprofloxacin	3		2	1	3	1	1	8	11	1	16	3	6	6	6	28
Nalidixic acid	2	5	8	8	5	16	19	3	6	2	10		7		1	

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue).
**TMS=Trimethoprim/sulfamethoxazole.

COMMENTS

Most cases of *Yersinia enterocolitica* infection in Norway were domestically acquired. In 2001, only 29% of the 125 reported cases were classified as imported.
None of the isolates tested were resistant to ciprofloxacin. However, three were classified as resistant to nalidixic acid and 13 were intermediately susceptible to ciprofloxacin. A few isolates were resistant to trimethoprim/sulfonamides and tetracycline, and a considerable proportion were resistant to chloramphenicol. All the isolates showed reduced susceptibility to ampicillin, an intrinsic resistance trait which is governed by the production by serogroup O:3 isolates of two chromosomally mediated β-lactamases, designated A and B.

Shigella spp. from human clinical specimens

TABLE 60. *Shigella sonnei* isolates from human clinical cases (n=119). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	3.4	21.0	75.6	6 - 29
Chloramphenicol	≥ 32	≤ 24	5.0	79.0	16.0	6 - 34
Ampicillin	≥ 25	≤ 8	8.4	78.2	13.4	6 - ≥ 40
TMS**	≥ 26	≤ 15	5.9	10.1	84.0	6 - 36
Ciprofloxacin	≥ 29	≤ 17	95.0	5.0	0.0	22 - ≥ 40
Nalidixic acid	≥ 14	≤ 13	95.0	-	5.0	6 - 36

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 61. *Shigella sonnei* isolates from human clinical cases (n=119). Distribution (%) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline	67	5	2	1		1										
Chloramph.	2														1	
Ampicillin	13											1	2	3	9	7
TMS**	80	1				2		1	1		1	1	2	1	2	
Ciprofloxacin																
Nalidixic acid	3	2							1							

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	≥ 37
Tetracycline		2	2	6	8	3	2	1								
Chloramph.	1	4	8	24	18	8	12	6	10	2	2	2	1			
Ampicillin	23	24	10	4	1	2										2
TMS**	2			1	1				1		1	1	1	1	1	
Ciprofloxacin	1			1		2	2	2	2				4	5	17	66
Nalidixic acid		1		2	3	8	17	13	31	5	8	1	3		1	

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue).
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 62. *Shigella flexneri* isolates from human clinical cases (n=57). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	21.1	0.0	78.9	6 - 34
Chloramphenicol	≥ 32	≤ 24	28.1	0.0	71.9	6 - ≥ 40
Ampicillin	≥ 25	≤ 8	28.1	0.0	71.9	6 - 31
TMS**	≥ 26	≤ 15	28.1	3.5	68.4	6 - 38
Ciprofloxacin	≥ 29	≤ 17	94.7	1.8	3.5	13 - ≥ 40
Nalidixic acid	≥ 14	≤ 13	91.2	-	8.8	6 - 36

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 63. *Shigella flexneri* isolates from human clinical cases (n=57). Distribution (%) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline	75		4													
Chloramph.	63	2	5	2												
Ampicillin	72															
TMS**	68															
Ciprofloxacin								2		2						
Nalidixic acid	5					2		2								

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	≥ 37
Tetracycline							4	2	9		4		4			
Chloramph.											4		9	4	7	6
Ampicillin				2	4	4	11	4	4	2						
TMS**			2	2	2	2						2	2	5	4	13
Ciprofloxacin		2								2	2				7	84
Nalidixic acid						5	14	9	25	16	9	9	2		4	

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue).
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 64. *Shigella boydii* isolates from human clinical cases (n=14). Sampling, laboratory methods and data processing are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	14.3	7.1	78.6	6 - 34
Chloramphenicol	≥ 32	≤ 24	50.0	28.6	21.4	6 - 34
Ampicillin	≥ 25	≤ 8	35.7	14.3	50.0	6 - 31
TMS**	≥ 26	≤ 15	35.7	0.0	64.3	6 - 36
Ciprofloxacin	≥ 29	≤ 17	92.9	7.1	0.0	28 - ≥ 40
Nalidixic acid	≥ 14	≤ 13	100.0	-	0.0	23 - 35

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**TMS=Trimethoprim/sulfamethoxazole.

TABLE 65. *Shigella boydii* isolates from human clinical cases (n=14). Distribution (%) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline	57	7	7												7	
Chloramph.	21															
Ampicillin	50												7			
TMS**	64															
Ciprofloxacin																
Nalidixic acid																

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	≥ 37
Tetracycline					7			7	7							
Chloramph.					7	7			7	7	7		43			
Ampicillin			7	21	7											
TMS**								14	7		7				7	
Ciprofloxacin							7			7					14	70
Nalidixic acid		7			7		14	21	21	14		7		7		

*Shaded areas in each row indicate susceptibility (light blue), intermediate susceptibility (medium blue) and resistance (dark blue).
**TMS=Trimethoprim/sulfamethoxazole.

COMMENTS

It is emphasized that almost all the reported *Shigella* infections in Norway were acquired abroad, mostly in Egypt, Pakistan, and Turkey. In 2001, only 7% of the reported cases were classified as domestically acquired, and all of these were related to a kebab restaurant outbreak (*S. sonnei* infection). Thus, the resistance frequencies reported here predominantly relate to isolates originating in other countries.

The distribution of the *Shigella* species was as follows: *S. sonnei* 119 (62%), *S. flexneri* 57 (30%), *S. boydii* 14 (7%), *S. dysenteriae* 1 (0.5%), and *Shigella* spp. 2 (1%).

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/sulfonamides, 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 most prevalent among *S. flexneri,* followed by *S. boydii*, and less common among *S. sonnei*. Resistance to fluoroquinolones was not common, but the detection of *Shigella* isolates intermediately resistant to ciprofloxacin and resistant to nalidixic acid may indicate that resistance to this class of antimicrobials is developing.

D. BACTERIA FROM HUMAN CLINICAL SPECIMENS

Escherichia coli in blood cultures

TABLE 66. *Escherichia coli* blood culture isolates (n=697). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	2.4	13.5	84.1	0.125 - ≥ 256	8	≥ 256
Ampicillin	≤ 1	≥ 32	3.2	68.7	28.1	0.5 - ≥ 256	4	≥ 256
Amoxi./clav.**	-	-	-	-	-	0.5 - 32	4	8
Cefuroxime	≤ 1	≥ 32	4.3	94.0	1.7	0.125 - ≥ 256	4	4
Ceftazidime	≤ 1	≥ 32	99.1	0.7	0.1	0.016 - 0.5	0.125	0.25
Cefpirome	≤ 1	≥ 32	99.7	0.3	0.0	0.016 - 8	0.063	0.125
Meropenem	≤ 4	≥ 16	100.0	0.0	0.0	0.004 - 0.5	0.016	0.032
TMS***	≤ 2	≥ 16	82.6	0.6	16.8	0.016 - ≥ 32	0.063	≥ 32
Gentamicin	≤ 2	≥ 8	99.1	0.1	0.7	0.016 - ≥ 256	0.5	1
Ciprofloxacin	≤ 0.125	≥ 4	97.0	1.3	1.7	0.002 - ≥ 32	0.016	0.032

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**Amoxi./clav.=Amoxicillin/clavulanic acid. Breakpoints for amoxicillin/clavulanic acid have not been defined by AFA.
***TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 67. *Escherichia coli* blood culture isolates (n=679). Distribution (%) of MICs (mg/L).*

	≤ 0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Doxycycline									3	14	23	24	12	6	2	2	15
Ampicillin								1	2	18	43	4	1				27
Amoxi./Clav.**									3	15	56	20	5				
Cefuroxime								1	3	43	42	5	2	1			1
Ceftazidime				2	10	52	30	4									
Cefpirome			5	42	43	7	2										
Meropenem		5	75	17													
TMS***			1	12	42	18	6	3	1	1				16			
Gentamicin					1	5	29	48	14								
Ciprofloxacin	3	29	53	8	1	2	1							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.
**Amoxi./clav.=Amoxicillin/clavulanic acid. Breakpoints for amoxicillin/clavulanic acid have not been defined by AFA.
***TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS

There were no substantial changes in the prevalence of susceptibility compared to the results from 2000 except for an increase in the proportion of doxycyclin resistance from 66.1% to 84.1%. However, the clinical significance of this change is limited, as tetracyclines are not used therapeutically for *E. coli* infections in Norway. The isolates were generally susceptible to all classes of broad-spectrum antimicrobials, including amino-glycosides (gentamicin), quinolones (ciprofloxacin) and carbapenems (meropenem). Originally, seven isolates were reported to have MIC ≥ 1 mg/L for ceftazidime and/or cefpirome. These isolates were all specifically examined for the presence of extended-spectrum β-lactamase (ESBL) production. None of them produced ESBL. One of the isolates was a misidentified *Citrobacter youngae* which was subsequently excluded from the data base. All the six *E. coli* isolates with elevated MICs for 3rd and/or 4th generation cephalosporins were fully susceptible to ciprofloxacin. Twelve isolates had ciprofloxacin MICs ≥ 4 mg/L and were thus classified as resistant. These strains were all fully susceptible to 3rd and/or 4th generation cephalosporins.

FIGURE 9. Distribution (%) of minimum inhibitory concentrations (MICs) of ampicillin for *E. coli* blood culture isolates. AFA breakpoints are shown in red.

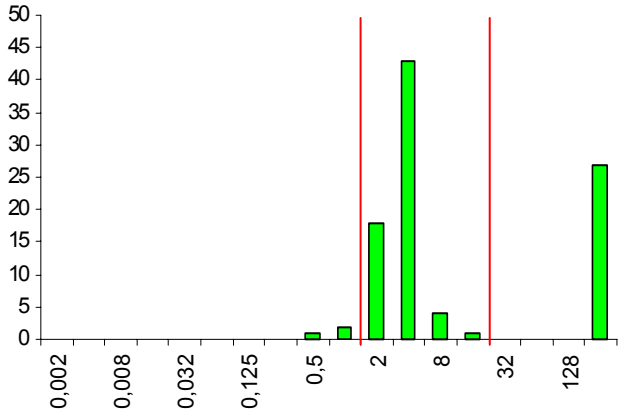
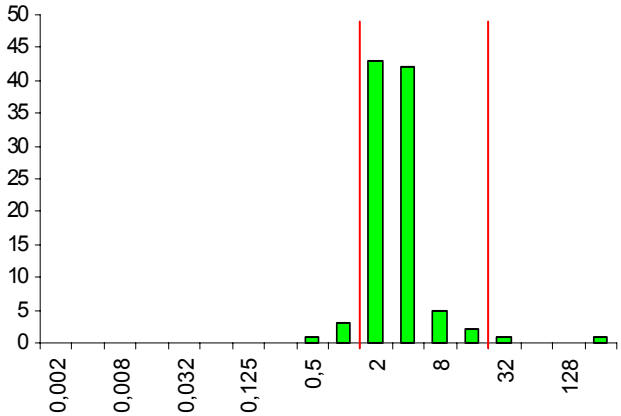


FIGURE 10. Distribution (%) of minimum inhibitory concentrations (MICs) of cefuroxime for *E. coli* blood culture isolates. AFA breakpoints are shown in red.



Klebsiella spp. in blood cultures

TABLE 68. *Klebsiella* spp. blood culture isolates (n=260). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	2.7	15.8	81.5	1 - ≥ 256	32	≥ 256
Ampicillin	≤ 1	≥ 32	0.8	35.8	63.5	1 - ≥ 256	32	≥ 256
Amoxi./Clav.**	-	-	-	-	-	0.5 - 32	2	4
Cefuroxime	≤ 1	≥ 32	23.1	73.1	3.8	0.25 - ≥ 256	2	8
Ceftazidime	≤ 1	≥ 32	97.7	2.3	0.0	0.016 - 4	0.125	0.5
Cefpirome	≤ 1	≥ 32	98.8	0.8	0.4	0.016 - ≥ 256	0.063	0.25
Meropenem	≤ 4	≥ 16	99.6	0.4	0.0	0.004 - 0.125	0.032	0.032
TMS***	≤ 2	≥ 16	97.2	0.4	2.4	0.016 - ≥ 32	0.125	0.5
Gentamicin	≤ 2	≥ 8	98.8	0.4	0.8	0.016 - 32	0.5	1
Ciprofloxacin	≤ 0.125	≥ 4	91.5	7.3	1.2	0.008 - 32	0.032	0.125

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**Amoxi./clav.=Amoxicillin/clavulanic acid. Breakpoints for amoxicillin/clavulanic acid have not been defined by AFA.
***TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 69. *Klebsiella* spp. blood culture isolates (n=260). Distribution (%) of MICs (mg/L).*

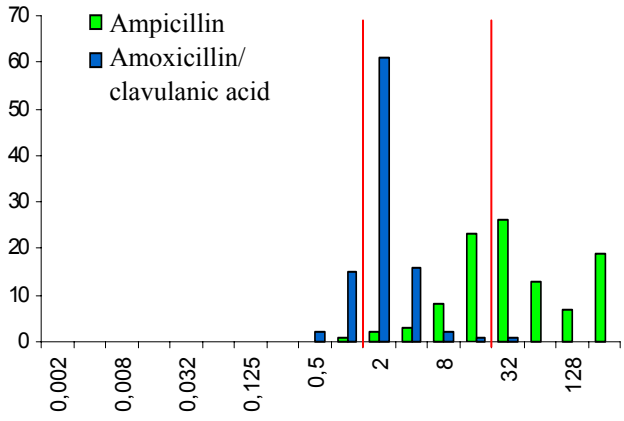
	≤ 0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Doxycycline									3	16	10	12	8	12	9	6	26
Ampicillin									1	2	3	8	23	26	13	7	19
Amoxi./clav.**								2	15	61	16	2	1	1			
Cefuroxime							1	3	19	50	15	5	4		1		2
Ceftazidime			1	6	29	32	19	6	6	2							
Cefpirome			3	37	44	6	7	1	2								
Meropenem			34	64													
TMS***				6	22	40	20	4	3	1				2			
Gentamicin				2		11	34	36	15								
Ciprofloxacin		7	28	35	14	7	6	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.
**Amoxi./clav.=Amoxicillin/clavulanic acid. Breakpoints for amoxicillin/clavulanic acid have not been defined by AFA.
***TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS

The 260 *Klebsiella* spp. blood culture isolates included 138 *K. pneumoniae* ssp. *pneumoniae* and 57 *K. oxytoca*. The remaining 65 isolates were recorded as *Klebsiella* species and most of them were presumably *K. pneumoniae*. The data from 2001 demonstrated the general susceptibility to broad-spectrum antimicrobials of the aminoglycoside (gentamicin), quinolone (ciprofloxacin) and carbapenem (meropenem) classes, which was also seen in 2000. There were no significant changes in resistance patterns except for the occurrence of three quionolone resistant isolates (1%) with ciprofloxacin MIC ≥ 4 mg/L. These isolates were fully susceptible to 3rd and 4th generation cephalosporins. The results for the 138 *K. pneumoniae* ssp. *pneumoniae* were in accordance with the general pattern for *Klebsiella* spp., whereas the 57 *K. oxytoca* had a slightly higher prevalence of resistance to ampicillin (70.2%). However, there were too few isolates to draw any firm conclusion with regard to species-specific levels of resistance.

FIGURE 11. Distribution (%) of minimum inhibitory concentrations (MIC) of ampicillin and amoxicillin/clavulanic acid for *Klebsiella* spp. blood culture isolates. AFA breakpoints for ampicillin are shown in red, AFA breakpoints for amoxicillin/ clavulanic acid have not been defined.



As for *E. coli*, all isolates with MIC ≥ 1 mg/L for ceftazidime and/or cefpirome were specifically examined for the presence of extended-spectrum β-lactamase (ESBL) production by using the ESBL Etest strip. Three out of nine suspected isolates produced ESBL. Two of these were *K. oxytoca* isolates originating in the same hospital. The isolates have not been examined for a possible clonal relationship. The third ESBL producer was a *K. pneumoniae* from another hospital. The nine strains with elevated MICs for 3rd and/or 4th generation cephalosporins were fully susceptible to ciprofloxacin.

Enterococcus spp. in blood cultures

TABLE 70. *Enterococcus* spp. (all species) blood culture isolates (n=191). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints mg/L		Proportion of isolates (%)*			MIC range	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Ampicillin	≤ 1	≥ 32	88.0	9.4	2.6	0.032 - 64	1	2
Penicillin G	≤ 1	≥ 32	30.9	62.8	6.3	0.016 - ≥ 256	2	4
β-lactamase	Neg	Pos	100.0	-	0.0			
TMS**	≤ 2	≥ 16	81.7	0.0	18.3	0.016 - ≥ 32	0.063	≥ 32
Streptomycin	≤ 512	≥ 1024	80.6	-	19.3	0.125 - ≥ 1024	64	≥ 1024
Gentamicin	≤ 512	≥ 1024	95.3	-	4.7	0.125 - ≥ 1024	8	16
Vancomycin	≤ 4	≥ 16	88.5	9.9	1.6	0.5 - 16	4	8
Teicoplanin	≤ 4	≥ 16	100.0	0.0	0.0	0.032 - 4	0.5	2
Vancomycin Agar Screen			99.5	-	0.5			

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

TABLE 71. *Enterococcus* spp. (all species) blood culture isolates (n=191). Distribution (%) of MICs (mg/L).*

	≤ 0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	≥ 1024
Ampicillin				1	18	29	38	6	2		2	2					
Penicillin G	1					8	21	46	14	1	1	2			4		
TMS**	9	35	20	9	4	4						18					
Streptomycin										3	14	29	25	4	2		19
Gentamicin						2	4	10	25	39	11		1		1		4
Vancomycin						2	8	34	46	10	2						
Teicoplanin		1	3	15	25	23	21	10	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.
**TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 72. *Enterococcus faecalis* blood culture isolates (n=155). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints mg/L		Proportion of isolates (%)*			MIC range	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Ampicillin	≤ 1	≥ 32	95.5	4.5	0.0	0.125 - 2	0.5	1
Penicillin G	≤ 1	≥ 32	31.6	68.4	0.0	0.5 - 8	2	4
β-lactamase	Neg	Pos	100.0	-	0.0			
TMS**	≤ 2	≥ 16	86.5	0.0	13.5	0.016 - ≥ 32	0.032	≥ 32
Streptomycin	≤ 512	≥ 1024	87.7	-	12.3	1 - ≥ 1024	64	≥ 1024
Gentamicin	≤ 512	≥ 1024	95.5	-	4.5	0.125 - ≥ 1024	8	16
Vancomycin	≤ 4	≥ 16	86.5	11.6	1.9	0.5 - 16	4	8
Teicoplanin	≤ 4	≥ 16	100.0	0.0	0.0	0.032 - 4	0.5	2
Vancomycin Agar Screen			99.4	-	0.6			

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

TABLE 73. *Enterococcus faecalis* blood culture isolates (n=155). Distribution (%) of MICs (mg/L).*

	≤ 0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	≥ 1024
Ampicillin				1	19	34	43	5									
Penicillin G						8	23	54	13	1							
TMS**	10	42	23	6	2	3	1					14					
Streptomycin							1	1		2	12	35	30	6	3		12
Gentamicin				1		1	1	7	25	45	11	1	2		2	1	4
Vancomycin						1	3	31	51	12	2						
Teicoplanin		1	2	16	27	25	18	9	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.
**TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 74. *Enterococcus faecium* blood culture isolates (n=30). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints mg/L		Proportion of isolates (%)*			MIC range	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Ampicillin	≤ 1	≥ 32	50.0	33.3	16.7	0.032 - 64	1	32
Penicillin G	≤ 1	≥ 32	23.3	40.0	36.7	0.016 - ≥ 256	4	≥ 256
β-lactamase	Neg	Pos	100.0	-	0.0			
TMS**	≤ 2	≥ 16	60.0	0.0	40.0	0.032 - ≥ 32	0.25	≥ 32
Streptomycin	≤ 512	≥ 1024	40.0	-	60.0	0.125 - ≥ 1024	≥ 1024	≥ 1024
Gentamicin	≤ 512	≥ 1024	96.7	-	3.3	0.25 - ≥ 1024	4	16
Vancomycin	≤ 4	≥ 16	96.7	3.3	0.0	0.5 - 8	2	4
Teicoplanin	≤ 4	≥ 16	100.0	0.0	0.0	0.032 - 4	1	2
Vancomycin Agar Screen			99.5	-	0.5			

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

TABLE 75. *Enterococcus faecium* blood culture isolates (n=30). Distribution (%) of MICs (mg/L).*

	≤ 0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	≥ 1024
Ampicillin		6	3	3	10	10	16	10	10		14	14	3				
Penicillin G	7		3			10	3	14	14	6	7	13			23		
TMS**		6	7	27	13	7						40					
Streptomycin				3			3			10	14	3	3	3		3	57
Gentamicin					3	7	17	20	24	13	10	3					3
Vancomycin						10	27	37	23	3							
Teicoplanin		3	3	10	13	17	36	13	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.
**TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS

The data for *Enterococcus* spp. in Tables 70 and 71 are similar to comparable figures from 2000. The vast majority of isolates were susceptible to the traditional combination therapy of ampicillin and an aminoglycoside. High-level resistance to gentamicin has even declined marginally from 7.4% in 2000 to 4.7% in 2001. As pointed out in the NORM/NORM-VET 2000 report, resistance data for enterococci should preferably be specified for *E. faecalis* and *E. faeium* due to species-specific differences in resistance rates. As demonstrated in Tables 72-75 and Figure 12, *E. faecium* is less susceptible to β-lactams than *E. faecalis*. Fifty per cent of the 30 *E. faecium* isolates were intermediately susceptible or resistant to ampicillin, whereas 95.5% of 155 *E. faecalis* isolates were fully susceptible to this agent. Sixty per cent of *E. faecium* isolates displayed high-level resistance to streptomycin in contrast to only 12.3% of *E. faecalis* isolates (Figure 13). It should be noted that *E. faecium* always harbours chromosomally encoded low-level resistance to all aminoglycosides except gentamicin and streptomycin thus precluding a synergistic bactericidal effect with β-lactams. The occurrence of high-level resistance to gentamicin was similar in both enterococcal species and low compared to other countries.

FIGURE 12. Distribution (%) of minimum inhibitory concentrations (MICs) of ampicillin for *E. faecalis* and *E. faecium* blood culture isolates. AFA breakpoints are shown in red.

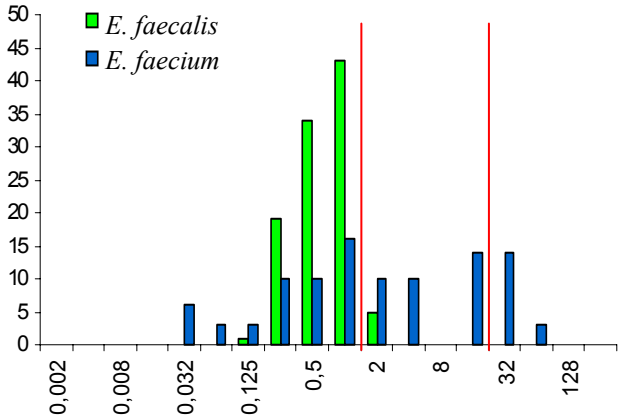
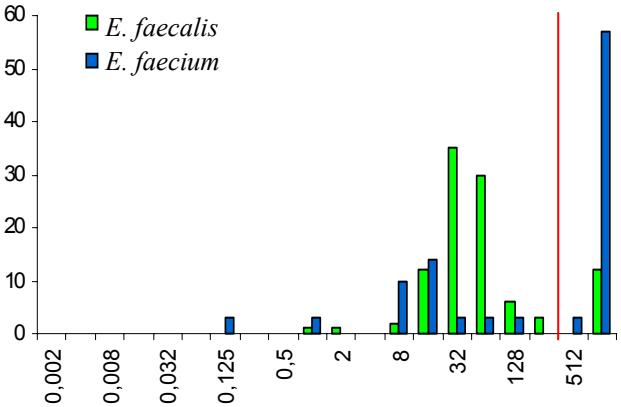


FIGURE 13. Distribution (%) of minimum inhibitory concentrations (MICs) of streptomycin for *E. faecalis* and *E. faecium* blood culture isolates. The AFA breakpoint for high-level resistance is shown in red.



More than 11% of enterococcal isolates were non-susceptible to vancomycin according to the Etest results. The proportion was higher among *E. faecalis* isolates (13.5%) than *E. faceium* isolates (3.3%). As discussed in the NORM/NORM-VET 2000 report, the recommended Etest methodology overestimates the MIC by 1–2 dilution steps. This interpretation was supported when all isolates with vancomycin MIC < 8 mg/L and/or growth on the vancomycin screening agar were examined by PCR analysis of *van* genes. None of the isolates contained genes encoding transferable glycopeptide resistance. Only a single *vanC*2/3 PCR positive *E. casseliflavus* was detected.

Streptococcus pneumoniae in blood cultures

TABLE 76. *Streptococcus pneumoniae* blood culture isolates (n=460). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	98.3	0.2	1.5	0.032 - 16	0.125	0.5
Chloramph.	≤ 2	≥ 8	98.3	0.9	0.9	0.032 - 16	1	2
Penicillin G**	≤ 0.063	≥ 2	96.1	3.5	0.4	0.002 - 8	0.016	0.032
Cefuroxime	≤ 1	≥ 32	99.8	0.2	0.0	0.016 - 2	0.016	0.032
Cefotaxime	≤ 1	≥ 32	100.0	0.0	0.0	0.004 - 1	0.016	0.032
Oxacillin screen	≥ 20 mm	≤ 19 mm	98.8	-	1.2			
TMS***	≤ 2	≥ 16	98.7	0.9	0.4	0.016 - ≥ 32	0.125	0.25
Erythromycin	≤ 1	≥ 4	97.6	0.2	2.2	0.016 - ≥ 256	0.125	0.125
Clindamycin	≤ 1	≥ 4	99.1	0.0	0.9	0.016 - ≥ 256	0.125	0.25
Ciprofloxacin	≤ 0.125	≥ 4	0.9	98.5	0.7	0.125 - 8	1	2
Vancomycin	≤ 4	≥ 16	99.6	0.4	0.0	0.125 - 8	0.5	2

*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.

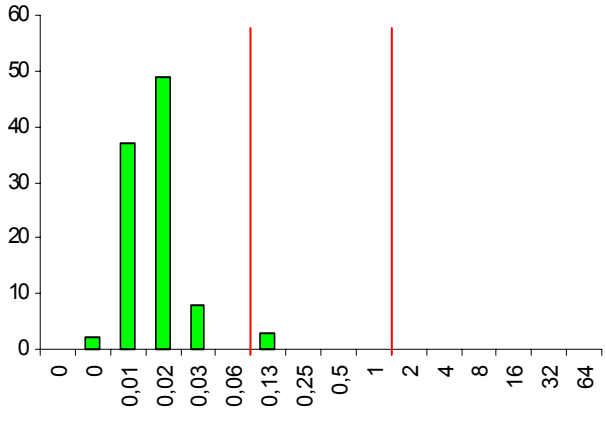
TABLE 77. *Streptococcus pneumoniae* blood culture isolates (n=460). Distribution (%) of MICs (mg/L).*

	≤ 0.002	0.004	0.008	0.016	0.032	0.063	0.125	0,25	0,5	1	2	4	8	16	32	64	≥ 128
Doxycycline					1	4	52	32	8	2				1			
Chloramph.									5	50	42	1					
Penicillin G**		2	37	49	8		3										
Cefuroxime				88	8	2											
Cefotaxime		2	33	54	7	1	2										
TMS***				1	1	6	58	29		1	1	1					
Erythromycin				6	5	37	47	2					1				1
Clindamycin				4	5	31	50	8									1
Ciprofloxacin							1	4	28	52	16						
Vancomycin							1	7	46	32	12	1					

	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	≥ 35
Oxacillin disc			1		2	4	8	9	12	13	8	11	6	9	3	5	6

*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. Breakpoints for the TMS combination are given for the trimethoprim component only.

FIGURE 14. Distibution (%) of minimum inhibitory concentrations (MICs) of penicillin for *S. pneumoniae* blood culture isolates. AFA breakpoints are shown in red.



COMMENTS

Norwegian pneumococcal isolates were generally susceptible to all relevant classes of antimicrobials used for the treatment of localized or systemic infections (Figure 14). Ten *S. pneumoniae* blood culture isolates were non-susceptible to penicillin G, eight were intermediately susceptible with MIC 0.125 – 1 mg/L and two were resistant with MICs of 2 and 8 mg/L, respectively. The oxacillin screening test identified three of these isolates as possibly resistant; these were all intermediately susceptible when the Etest was used. Two were classified as susceptible, one of these being resistant (MIC 8 mg/L) and the other intermediately susceptible using the Etest. No results from the oxacillin screening test were reported for the remaining five cases.

None of the isolates displayed reduced susceptibility to 3rd generation cephalosporins.

Erythromycin resistance was detected in 2.2% of the isolates, which corresponds well with the 2.4% in 2000. The ten resistant isolates from 2001 displayed either low-level resistance (3 isolates MIC 8 mg/L and 3 isolates 16 mg/L) or high-level resistance (4 isolates with MIC ≥ 256 mg/L). The four isolates with high-level resistance were concomitantly highly resistant to clindamycin (MIC ≥ 256) indicating the presence of Erm methylases, whereas the erythromycin low-level resistant isolates were clindamycin susceptible which is compatible with a *mef*-encoded efflux mechanism. Two of the isolates with high-level erythromycin resistance were non-susceptible to penicillin G (MICs of 0.5 and 2 mg/L, respectively).

Staphylococcus aureus in blood cultures

TABLE 78. *Staphylococcus aureus* blood culture isolates (n=510). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	95.7	1.4	3.0	0.032 - ≥ 256	0.125	0.25
Penicillin G**	≤ 0.125	≥ 0.25	28.8	-	71.2	0.008 - ≥ 256	1	4
Oxacillin	≤ 1	≥ 4	98.2	1.2	0.6	0.063 - ≥ 256	0.25	0.5
Cefuroxime	≤ 1	≥ 32	92.2	7.5	0.4	0.125 - 2	1	1
β-lactamase	Neg	Pos	25.9	-	74.1			
Oxacillin screen	≤ 2	≥ 4	99.4	-	0.6			
Erythromycin	≤ 1	≥ 4	97.2	0.6	2.2	0.032 - ≥ 256	0.25	0.5
Clindamycin	≤ 1	≥ 4	99.6	0.0	0.4	0.016 - ≥ 256	0.125	0.125
Gentamicin	≤ 2	≥ 8	99.4	0.0	0.6	0.032 - 16	0.25	0.5
Vancomycin	≤ 4	≥ 16	93.1	6.5	0.4	0.032 - 16	2	4
Fucidic acid	≤ 0.5	≥ 1	94.9	-	5.1	0.016 - ≥ 256	0.125	0.25

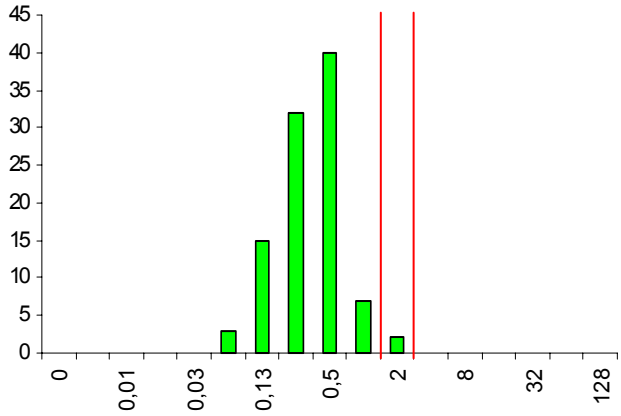
*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**Penicillin G=Benzylpenicillin.

TABLE 79. *Staphylococcus aureus* blood culture isolates (n=510). Distribution (%) of MICs (mg/L).*

	≤ 0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Doxycycline				4	11	40	36	4		1	1						
Penicillin G**			9	14	3	2	5	13	23	17	4	2	2	5			1
Oxacillin					3	15	32	40	7	2							
Cefuroxime						1	2	32	57	8							
Erythromycin				1	10	29	50	7	1								2
Clindamycin				8	38	50	3										
Gentamicin					2	18	38	34	7	1							
Vancomycin								2	41	30	20	6					
Fucidic acid			4	9	27	43	10	2	1	1	1	1	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.

FIGURE 15. Distribution (%) of minimum inhibitory concentrations (MICs) of oxacillin for *S. aureus* blood culture isolates. AFA breakpoints are shown in red.



COMMENTS

A total of 74.1% of *S. aureus* blood culture isolates were β-lactamase producers, compared with 74.5% in 2000. Both β-lactamase positive and β-lactamase negative isolates were generally susceptible to non-β-lactam antimicrobials such as macrolides (erythromycin), lincosamides (clindamycin), aminoglycosides (gentamicin) and glycopeptides (vancomycin). However, there was a tendency for β-lactamase negative isolates to be somewhat more susceptible than the β-lactamase positive ones; 100% versus 96.3% were fully susceptible to erythromycin and 96.8% versus 93.8% were fully susceptible to fucidic acid, respectively. Two isolates were highly resistant (MIC ≥ 256 mg/L) to both erythromycin and clindamycin, whereas six were highly resistant (MIC ≥ 256 mg/L) to erythromycin and susceptible to clindamycin.

Methicillin resistant *S. aureus* (MRSA) are diagnosed by their reduced susceptibility to oxacillin. Resistance to oxacillin indicates resistance to all β-lactam antimicrobials including all penicillins, cephalosporins, monobactams and carbapenems. Only 1.8% of *S. aureus* blood culture isolates displayed oxacillin MIC > 1 mg/L (Figure 15). These nine isolates were specifically examined for oxacillin resistance by phenotypic re-testing and *mecA* PCR when needed. Only two isolates were verified as MRSA corresponding to 0.4% of all *S. aureus* blood culture isolates. These two isolates originated from the same hospital and were both imported cases. No epidemiological link was established between the two patients. Both isolates displayed low-level resistance to erythromycin. The increased incidence of MRSA infections reported by the Norwegian Surveillance System for Communicable Diseases (MSIS) from 67 cases in 2000 to 122 cases in 2001 has consequently not influenced the overall prevalence of MRSA among *S. aureus* blood culture isolates in NORM.

Haemophilus influenzae in respiratory tract specimens

TABLE 80. *Haemophilus influenzae* respiratory tract isolates from all laboratories (n=704). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints mg/L		Proportion of isolates (%)*			MIC range	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	20.5	58.0	21.6	0.25 - 32	2	4
Ampicillin	≤ 2	≥ 8	92.8	0.9	6.4	0.063 - ≥ 256	0.25	1
Penicillin G**	≤ 1	≥ 8	85.1	6.5	8.4	0.125 - ≥ 256	0.5	2
Penicillin V***	≤ 1	≥ 4	14.7	45.7	39.6	0.5 - ≥ 256	2	16
Amoxi./clav.****	≤ 2	≥ 8	98.7	0.3	1.0	0.125 - 32	0.5	1
β-lactamase	Neg	Pos	93.0	-	7.0			
TMS*****	≤ 2	≥ 16	94.5	2.0	3.6	0.004 - ≥ 32	0.063	0.25
Erythromycin	≤ 1	≥ 4	1.1	21.3	77.6	0.125 - ≥ 256	4	8

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**Penicillin G=Benzylpenicillin.
***PenicillinV=Phenoxymethylpenicillin.
****Amoxi./clav.=Amoxicillin/clavulanic acid.
*****TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 81. *Haemophilus influenzae* respiratory tract isolates from all laboratories (n=704). Distribution (%) of MICs (mg/L).*

	≤ 0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Doxycycline							5	16	58	19	2					
Ampicillin					21	57	8	5	1		1	1				4
Penicillin G**					4	28	41	12	6	1	1	1	1			5
Penicillin V***							1	13	45	20	6	3	2	2		6
Amoxi./clav.****					1	14	64	18	3							
TMS*****	1	10	30	36	13	3	1		2	1			4			
Erythromycin								1	21	51	22	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.
***PenicillinV=Phenoxymethylpenicillin.
****Amoxi./clav.=Amoxicillin/clavulanic acid.
*****TMS=Trimethoprim/sulfamethoxazole.

TABLE 82. *Haemophilus influenzae* respiratory tract isolates from six selected laboratories (n=260). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints mg/L		Proportion of isolates (%)*			MIC range			MIC_{50}	MIC_{90}
	S	R	S	I	R					
Doxycycline PDM	≤ 1	≥ 4	13.1	61.9	25.0	1	-	16	2	4
Doxycycline MH	≤ 1	≥ 4	29.6	61.9	8.5	0.5	-	8	2	2
Doxycycline HTM	≤ 1	≥ 4	96.5	3.5	0.0	0.125	-	2	0.5	1
Ampicillin PDM	≤ 2	≥ 8	93.8	1.2	5.0	0.125	-	≥ 256	0.25	1
Ampicillin MH	≤ 2	≥ 8	93.5	1.2	5.4	0.063	-	≥ 256	0.25	1
Ampicillin HTM	≤ 2	≥ 8	94.6	0.8	4.6	0.032	-	≥ 256	0.25	1
Penicillin G**PDM	≤ 1	≥ 8	85.4	7.7	6.9	0.063	-	≥ 256	0.5	2
Penicillin G**HM	≤ 1	≥ 8	82.7	10.0	7.3	0.063	-	≥ 256	0.5	2
Penicillin G**HTM	≤ 1	≥ 8	85.3	8.1	6.6	0.032	-	≥ 256	0.5	2
Penicillin V***PDM	≤ 1	≥ 4	17.4	44.6	38.0	0.063	-	≥ 256	2	32
Penicillin V***MH	≤ 1	≥ 4	5.4	36.3	58.3	0.032	-	≥ 256	4	32
Penicillin V***HTM	≤ 1	≥ 4	18.6	40.7	40.7	0.032	-	≥ 256	2	32
Amoxi./clav.****PDM	≤ 2	≥ 8	97.7	0.8	1.5	0.25	-	16	0.5	1
Amoxi./clav.****MH	≤ 2	≥ 8	95.8	3.1	1.2	0.125	-	≥ 256	0.5	1
Amoxi./clav.****HTM	≤ 2	≥ 8	95.8	3.1	1.2	0.125	-	16	0.5	2
TMS*****PDM	≤ 2	≥ 16	95.0	2.7	2.3	0.008	-	≥ 32	0.063	0.125
TMS*****MH	≤ 2	≥ 16	93.8	1.5	4.6	0.016	-	≥ 32	0.063	1
TMS***** HTM	≤ 2	≥ 16	94.6	0.8	4.6	0.016	-	≥ 32	0.125	0.5
Erythromycin PDM	≤ 1	≥ 4	2.3	20.0	77.7	0.063	-	≥ 256	4	8
Erythromycin MH	≤ 1	≥ 4	1.2	9.6	89.2	0.063	-	≥ 256	8	16
Erythromycin HTM	≤ 1	≥ 4	1.5	10.0	88.4	0.063	-	≥ 256	4	16
β-lactamase	Neg	Pos	95.3	-	4.7					

*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**Penicillin G=Benzylpenicillin.
***PenicillinV=Phenoxymethylpenicillin.
****Amoxi./clav.=Amoxicillin/clavulanic acid.
*****TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 83. *Haemophilus influenzae* respiratory tract isolates from six selected laboratories (n=260). Distribution (%) of MICs (mg/L).*

	≤ 0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Doxycycline PDM								13	62	23	2					
Doxycycline MH							1	29	62	7	1					
Doxycycline HTM						6	50	40	4							
Ampicillin PDM					18	60	10	4	1	1	1					3
Ampicillin MH					13	54	18	7	2	1	1	1				4
Ampicillin HTM					18	48	20	8	1	1		1				3
Penicillin G**PDM					2	29	43	10	7		1		2			3
Penicillin G**MH					1	8	50	22	8	2		1	2			4
Penicillin G**HTM				1	2	21	44	18	7	1	1	1	2			2
Penicillin V***PDM							1	16	45	19	7	2	3	2		5
Penicillin V***MH								5	36	30	11	5	4	2	1	7
Penicillin V***HTM							1	16	40	17	8	5	2	2	1	5
Amoxi./Clav.****PDM						7	66	19	5	1		1				
Amoxi./Clav.****MH						5	52	34	4	3						
Amoxi./Clav.****HTM					1	9	44	35	6	3						
TMS *****PDM	1	16	29	34	10	4	1				1	1	2			
TMS *****MH		3	22	32	20	8	3	4	2		1	1	4			
TMS *****HTM		3	9	24	38	11	8	3					4			
Erythromycin PDM								2	20	44	28	6				
Erythromycin MH									9	38	33	17				
Erythromycin HTM									10	45	31	11				

*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. ***PenicillinV=Phenoxymethylpenicillin. ****Amoxi./clav.=Amoxicillin/clavulanic acid.
*****TMS=Trimethoprim/sulfamethoxazole. Breakpoints for the TMS combination are given for the trimethoprim component only.

FIGURE 16. Distribution (%) of minimum inhibitory concentrations (MICs) of penicillin G (benzylpenicillin) and penicillin V (phenoxymethylpenicillin) for *H. influenzae* respiratory tract isolates. AFA breakpoints are shown in red (lower breakpoint for both penicillins), pink (upper breakpoint for penicillin G) and orange (upper breakpoint for penicillin V).

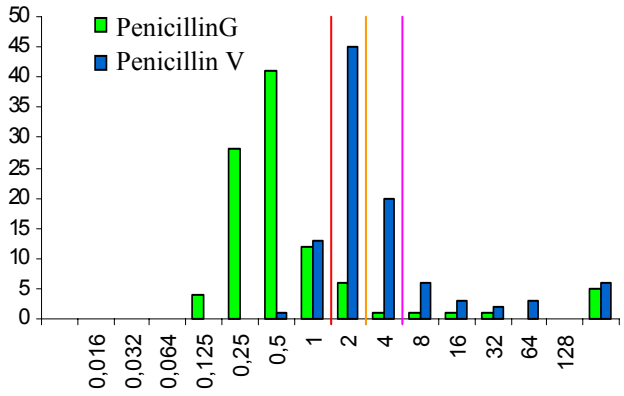
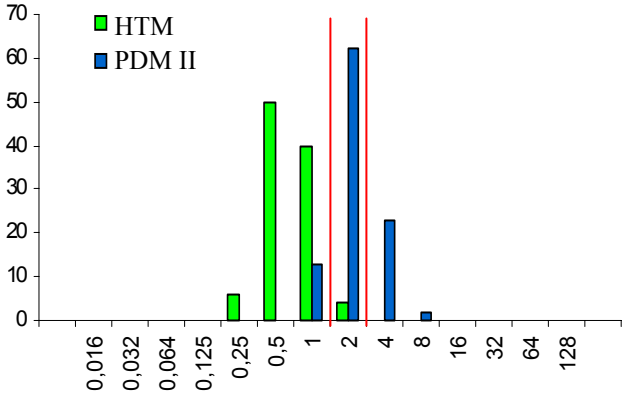


FIGURE 17. Distribution (%) of minimum inhibitory concentrations (MICs) of doxycycline for *H. influenzae* respiratory tract isolates using either HTM or PDM II with defibrinated/lysed horse blood medium for susceptibility testing. AFA breakpoints are shown in red.



COMMENTS

The overall results for respiratory tract *H. influenzae* were in accordance with the results for 2000. The isolates in Tables 80 and 81 were all tested using a PDM II medium. Approximately 7% (range 0-16%) of the isolates produced β-lactamase and were thus resistant to ampicillin, penicillin G and penicillin V. There was a difference of 2-3 dilution steps in the MIC values of penicillin G and penicillin V (MIC_{50}: 0.5 versus 2 mg/L and MIC_{90}: 2 versus 16 mg/L, respectively). The differences in the proportions of isolates categorized as susceptible, intermediately susceptible and resistant were further increased by the lower breakpoint for penicillin V (Figure 16). Both laboratories and clinicians should be aware of these issues with regard to susceptibility testing of *H. influenzae* to penicillins. Almost 99% of isolates were susceptible to the combination of amoxicillin and the β-lactamase inhibitor clavulanic acid. This indicates that resistance to penicillin and ampicillin is predominantly mediated by β-lactamase production and not by altered PBPs. Of the 51 β-lactamase positive isolates, 98% were susceptible to amoxicillin/clavulanic acid. The remaining 2% may be resistant due to structural changes in penicillin-binding proteins. The majority (98.9%) of *H. influenzae* isolates were non-susceptible to erythromycin by AFA criteria; this was also found in 2000.

In 2000, the results for doxycycline varied considerably between laboratories. It is widely recognized that reproducibility may be a problem in susceptibility testing of this organism. It was therefore decided to undertake an evaluation of three different media recommended for susceptibility testing of *H. influenzae*: Paper Disc Medium (PDM) II with hemin and Isovitalex, Mueller Hinton (MH) II with hemin and Isovitalex, and Haemophilus Test Medium (HTM) (Figure 17). Six laboratories participated in this evaluation and 260 isolates were included (Tables 82 and 83). There were large differences for doxycycline MICs with HTM compared to the results for PDM and MH. HTM MICs were approximately two dilution steps lower than for the other two media tested. MIC_{50} was consequenly only 0.5 mg/L for HTM and 2 mg/L for PDM and MH. For β-lactams, the results were comparable for all three media with a tendency for a less distinct distribution peak when HTM was used. This may be due to difficulties in reading Etest results on HTM. The difference between penicillin G and penicillin V was seen for all three media. MICs for trimethoprim/ sulfamethoxazole were slightly lower using PDM. No differences could be detected for erythromycin. The evaluation demonstrated the importance of the test medium used. Reporting of isolates as susceptible, intermediately susceptible and resistant have no meaning if the test method is not standardized and correct breakpoints are used.

Streptococcus pneumoniae in respiratory tract specimens

TABLE 84. *Streptococcus pneumoniae* respiratory tract isolates (n=708). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	95.3	1.1	3.5	0.016 - 32	0.25	0.5
Penicillin G**	≤ 0.063	≥ 2	97.3	2.5	0.1	0.002 - 4	0.016	0.032
Oxacillin screen	≥ 20 mm	≤ 19 mm	96.2	-	3.8			
TMS***	≤ 2	≥ 16	98.0	0.8	1.1	0.002 - ≥ 32	0.125	0.25
Erythromycin	≤ 1	≥ 4	96.8	1.0	2.3	0.016 - ≥ 256	0.063	0.125
Clindamycin	≤ 1	≥ 4	99.2	0.1	0.7	0.016 - ≥ 256	0.125	0.25

*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.

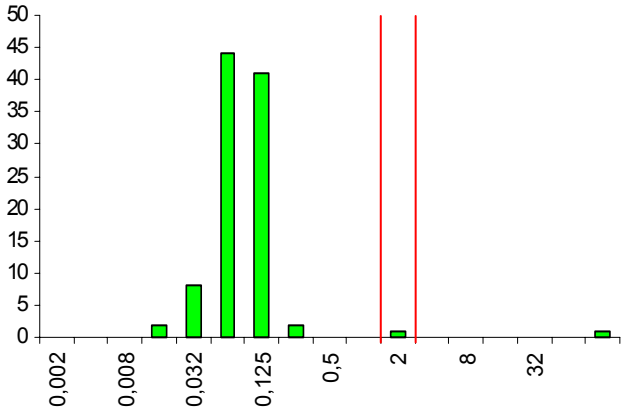
TABLE 85. *Streptococcus pneumoniae* respiratory tract isolates (n=708). Distribution (%) of MIC values (mg/L) and mm (oxacillin) .*

	≤ 0.002	0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	≥ 128
Doxycycline					2	2	44	43	5	1	1	1	1	1			
Penicillin G**	6	3	23	57	9	1	1	1									
TMS***					1	9	46	36	3		1				1		
Erythromycin				2	8	44	41	2			1						1
Clindamycin				2	6	33	46	11									1

	≤ 19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	≥ 35
Oxacillin disc	3	1	1	4	6	6	10	13	13	16	10	8	3	4	1	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.

FIGURE 18. Distribution (%) of minimum inhibitory concentrations (MICs) of erythromycin for *S. pneumoniae* respiratory tract isolates. AFA breakpoints are shown in red.



COMMENTS

The low prevalence of non-susceptibility to penicillin among *S. pneumoniae* respiratory tract isolates corresponds to the blood culture data presented in Tables 76 and 77. Only 19 of 708 (2.7%) were intermediately susceptible (n=18, MIC 0.125 – 1 mg/L) or resistant (n=1, MIC=4) to penicillin. The general situation with respect to penicillin non-susceptibility is unchanged from 2000. The oxacillin screening test identified 15 of the 19 non-susceptible isolates, but failed to detect four isolates categorized as intermediately susceptible to penicillin G by Etest (two isolates with MIC 0.125 mg/L and two isolates with MIC 0.25 mg/L). Conversely, a total of 11 susceptible isolates were categorized as possibly resistant by the oxacillin screening test even though Etest results classified them as susceptible. It is thus prudent to remember that all screening results ≤ 19 mm should be verified by MIC determination due to lack of specificity. Isolates from systemic infectons (especially meningitis) should be subjected to MIC determination due to occasional underestimation of resistance by the screening method.

Sixteen isolates were resistant to macrolides (Figure 18), and 6 of these displayed high-level resistance (MIC erythromycin ≥ 256). Four of them were also highly resistant to lincosamides (clindamycin MIC ≥ 256) thus indicating possible MLS_B resistance encoded by *erm* genes. The remaining 10 macrolide-resistant isolates were either fully or partially susceptible to clindamycin, which is compatible with a macrolide efflux mechanism. Five of the 16 macrolide-resistant isolates were also non-susceptible to penicillin G.

Staphylococcus aureus in wound specimens

TABLE 86. *Staphylococcus aureus* isolates from wound specimens (n=829). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)*			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	95.5	1.6	2.9	0.032 - 64	0.125	0.5
Penicillin V**	≤ 0.125	≥ 0.25	32.1	-	67.9	0.016 - ≥ 256	0.25	2
β-lactamase	Neg	Pos	20.3	-	79.7			
Oxacillin	≤ 1	≥ 4	99.2	0.6	0.2	0.063 - 2	0.5	1
Oxacillin screen	Neg	Pos	99.6	-	0.4			
Erythromycin	≤ 1	≥ 4	96.5	0.1	3.4	0.032 - ≥ 256	0.25	0.25
Clindamycin	≤ 1	≥ 4	99.4	0.0	0.6	0.004 - ≥ 256	0.063	0.125
Vancomycin	≤ 4	≥ 16	95.0	4.0	1.0	0.125 - 16	2	4
Vancomycin Agar Screen	Neg	Pos	99.7	-	0.3			
Fucidic acid	≤ 0.5	≥ 1	79.2	-	20.8	0.016 - ≥ 256	0.125	4

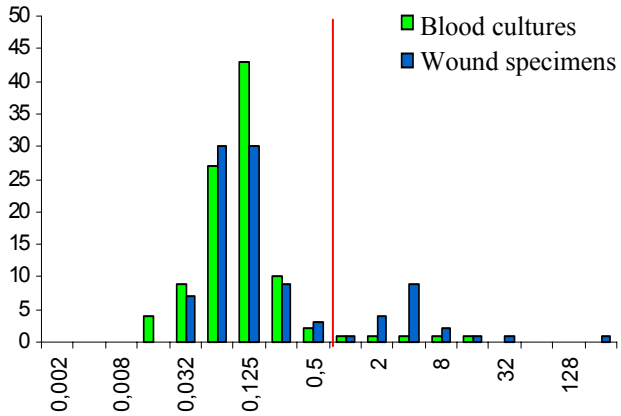
*S=Susceptible, I=Intermediately susceptible, R=Resistant.
**Penicillin V= Phenoxymethylpenicillin.

TABLE 87. *Staphylococcus aureus* isolates from wound specimens (n=829). Distribution (%) of MICs (mg/L).*

	≤ 0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Doxycycline					15	48	22	7	2	1	2	1					
Penicillin V**			13	6	3	9	20	23	15	7	2	1					
Oxacillin					1	10	34	52	11								
Erythromycin					4	45	41	6									3
Clindamycin				3	53	41											1
Vancomycin								2	44	32	17	4	1				
Fucidic acid				7	30	30	9	3	1	4	9	2	1	1			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 V= Phenoxymethylpenicillin.

FIGURE 19. Distribution (%) of minimum inhibitory concentrations (MICs) of fucidic acid for *S. aureus* isolates from blood cultures and wound specimens. The AFA breakpoint is shown in red.



COMMENTS

As *Staphylococcus aureus* isolates from wound specimens were not surveyed by NORM in 2000, there are no Norwegian data comparable to the results presented here. A total of 79.9% of the isolates were β-lactamase producers which is in accordance with NORM 2000 and 2001 blood culture data. The discrepancy between 32.1% penicillin V susceptibility by the Etest and 20.3% susceptibility by the β-lactamase test shows that the epidemiological breakpoint underestimates the prevalence of resistance. It is therefore necessary to perform a specific β-lactamase test to predict the clinical susceptibility of staphylococci in individual cases. Only 0.8% of the isolates were non-susceptible to oxacillin by the Etest and 0.4% grew on the oxacillin 4 mg/L screening agar. None of these isolates were verified as methicillin-resistant *S. aureus* (MRSA) by *mecA* PCR.

The prevalence of resistance to fucidic acid was 20.8%, which is much higher than the 1.9% and 5.1% reported for blood culture isolates in 2000 and 2001, respectively. It has previously been shown that bacterial isolates from localized infections may be more frequently resistant than systemic isolates. This may be due to a selection bias. The probability of diagnostic sampling being performed secondarily to antimicrobial treatment is higher in localized than in systemic infections. The possibility of clonal spread of resistant strains should also be considered. The link between β-lactamase production and resistance to fucidic acid (9.5% fucidic acid resistance among β-lactamase negative isolates and 23.7% fucidic acid among β-lactamase positive isolates) supports this hypothesis. The theory of clonal spread of fucidic acid resistant *S. aureus* in cutaneous infections (impetigo) is presently being investigated in Norway.

Escherichia coli in urine

TABLE 88. *Escherichia coli* urinary tract isolates (n=1268). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Ampicillin	≥ 25	≤ 8	6.8	70.1	23.1	6 - 36
Mecillinam	≥ 24	≤ 13	85.8	11.0	2.2	6 - ≥ 40
Trimethoprim	≥ 22	≤ 16	82.4	0.6	16.9	6 - ≥ 40
Sulfonamide	≥ 26	≤ 11	60.3	15.9	23.8	6 - ≥ 40
Ciprofloxacin	≥ 29	≤ 17	96.7	2.6	0.7	6 - ≥ 40
Nalidixic acid	≥ 14	≤ 13	97.5	-	2.5	6 - 39
Nitrofurantoin	≥ 19	≤ 18	97.1	-	2.9	6 - 36

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

TABLE 89. *Escherichia coli* urinary tract isolates (n=1268). Distribution (%) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Ampicillin	23							1	1	2	3	4	8	9	14
Mecillinam	1							1	1	1	1	1	1	1	2
Trimethoprim	16														
Sulfonamide	24														1
Ciprofloxacin															
Nalidixic acid	2														
Nitrofurantoin													1	1	2

	21	22	23	24	25	26	27	28	29	30	31	32	33	34	≥ 35
Ampicillin	9	9	5	4	2	1	1	1							
Mecillinam	1	2	2	2	3	2	2	4	4	10	10	14	12	9	14
Trimethoprim						2	2	5	7	14	9	12	10	9	12
Sulfonamide	1	2	2	4	6	7	6	8	6	9	5	5	5	4	5
Ciprofloxacin							1	1	1	2	3	6	7	12	66
Nalidixic acid	1	1	3	7	11	12	11	16	11	14	5	2	2		1
Nitrofurantoin	5	6	9	13	17	16	12	8	3	3	1	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.

FIGURE 20. Distribution (%) of disc diffusion diameters (mm) of ampicillin for *E. coli* urinary tract isolates using 30 µg discs. AFA breakpoints are shown in red. A small zone diameter indicates resistance whereas a large zone diameter indicates susceptibility.

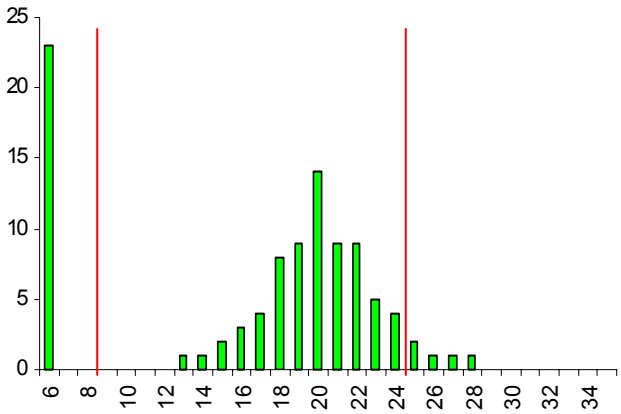
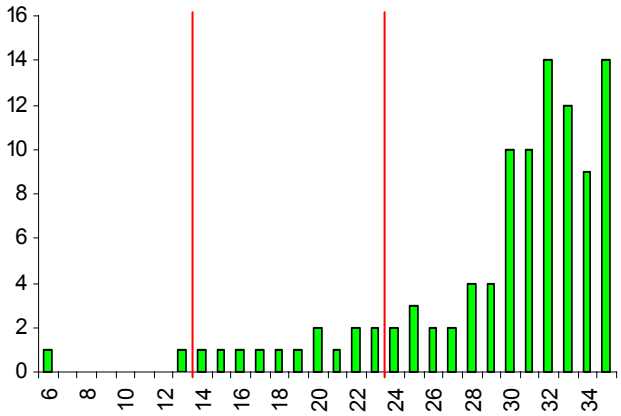


FIGURE 21. Distribution (%) of disk diffusion diameters (mm) of mecillinam for *E. coli* urinary tract isolates using 30 µg disks. AFA breakpoints are shown in red. A small zone diameter indicates resistance whereas a large zone diameter indicates susceptibility.



COMMENTS

According to Norwegian guidelines, uncomplicated infections of the lower urinary tract in adult women should be treated empirically. The data presented here are primarily from complicated infections in adult women and positive cultures from men and children. The majority of isolates represent re-infections or treatment failures, and the prevalence of resistance is probably higher than in uncomplicated infections in adult women. Antimicrobial resistance data may therefore not be suitable for defining primary treatment strategies for uncomplicated cases. A relatively high prevalence of susceptibility was seen for trimethoprim (82.4%), mecillinam (85.8%) and especially nitrofurantoin (97.1%). The results are similar to the findings reported in NORM 2000. The majority of isolates were intermediately susceptible to ampicillin, but distinguishing between susceptible and intermediately susceptible isolates is obviously problematic (Figure 20). It is similarly difficult to define microbiological breakpoints for mecillinam as the population cannot be separated into distinct resistance phenotypes (Figure 21). Most strains (96.7%) were fully susceptible to ciprofloxacin, and the proportion of nalidixic acid resistance (2.5%) was unchanged from 2000. The possible emergence of quinolone resistance in *Klebsiella* spp. urinary tract isolates (see below) was thus not seen in *E. coli*.

Klebsiella spp. in urine

TABLE 90. *Klebsiella* spp. urinary tract isolates (n=675). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Ampicillin	≥ 25	≤ 8	0.6	46.3	53.1	6 - 31
Mecillinam	≥ 24	≤ 13	80.4	10.2	9.3	6 - 38
Trimethoprim	≥ 22	≤ 16	81.8	3.7	14.5	6 - ≥ 40
Sulfonamide	≥ 26	≤ 11	59.2	31.6	9.2	6 - ≥ 40
Ciprofloxacin	≥ 29	≤ 17	81.2	18.6	0.1	15 - ≥ 40
Nalidixic acid	≥ 14	≤ 13	91.3	-	8.7	6 - 33
Nitrofurantoin	≥ 19	≤ 18	69.3	-	30.7	6 - 37

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

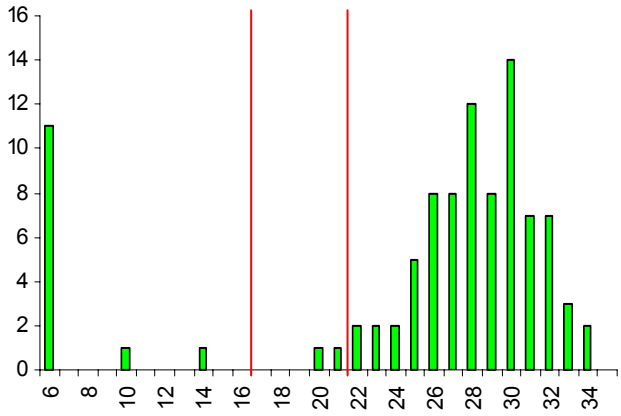
TABLE 91. *Klebsiella* spp. urinary tract isolates (n=675). Distribution (%) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Ampicillin	45	2	6	6	8	8	5	4	3	2	2	2	1	2	1
Mecillinam	8				1				1		1		1	1	2
Trimethoprim	11				1				1						1
Sulfonamide	9									1	1	1	1	1	2
Ciprofloxacin															
Nalidixic acid	6		1		1	1	1		1	1	2	1	2	2	5
Nitrofurantoin	3		1	2	2	2	3	1	2	2	4	3	6	5	8

	21	22	23	24	25	26	27	28	29	30	31	32	33	34	≥ 35
Ampicillin															
Mecillinam	1	2	1	4	5	6	8	10	6	15	6	9	4	4	4
Trimethoprim	1	2	2	2	5	8	8	12	8	14	7	7	3	2	
Sulfonamide	3	5	5	5	6	10	7	11	7	12	4	3	3	2	1
Ciprofloxacin	1	1	2	2	4	2	2	4	4	8	8	13	11	10	26
Nalidixic acid	6	9	11	12	12	12	7	4	2	2		1			
Nitrofurantoin	9	12	6	8	7	4	2	2	2	1	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.

FIGURE 22. Distribution (%) of disk diffusion diameters (mm) ciprofloxacin for *Klebsiella* spp.urinary tract isolates using 5 µg disks. AFA breakpoints are shown in red. A small zone diameter indicates resistance whereas a large zone diameter indicates susceptibility.



COMMENTS

Several changes in the rates of resistance were noted compared to data from NORM 2000, although the number of isolates in 2000 was too low to draw any firm conclusions. The higher prevalence of resistance to ampicillin (53.1% versus 37.5% in 2000), mecillinam (9.3% versus 7.0% in 2000), trimethoprim (14.5% versus 3.5%), sulfonamides (9.2% versus 3.5% in 2000) and nitrofurantoin (30.7% versus 24.1% in 2000) can thus be explained by the small sample size in 2000. The same effect may also be true for the quinolones, but the doubling of intermediate susceptibility to ciprofloxacin and the five-fold increase of resistance to nalidixic acid should be closely monitored. In Norway, quinolone treatment of urinary tract infections is generally restricted to complicated cases involving resistant isolates and troublesome species. An increasing occurrence of non-susceptibility to this class of antimicrobials in ordinary urinary pathogens is a warning to clinicians that further expansion of indications for quinolone use should be avoided. As in 2000, no specific examination of extended-spectrum β-lactamase production (ESBL) was performed on urinary isolates.

Enterococcus spp. in urine

TABLE 92. *Enterococcus* spp. urinary tract isolates (n=794). Sampling, laboratory methods and data processing are described in Appendix 5.

	Breakpoints (mm)		Proportion of isolates (%)*			Range (mm)
	S	R	S	I	R	
Ampicillin	≥ 25	≤ 8	91.8	6.3	1.9	6 - 38
Mecillinam	≥ 24	≤ 13	0.0	0.0	100.0	6 - 6
Trimethoprim	≥ 22	≤ 16	84.8	1.6	13.6	6 - ≥ 40
Sulfonamide	≥ 26	≤ 11	0.	0.0	100.0	6 - 6
Ciprofloxacin	≥ 29	≤ 17	0.8	90.0	9.3	6 - 29
Nalidixic acid	≥ 14	≤ 13	0.0	-	100.0	6 - 6
Nitrofurantoin	≥ 19	≤ 18	99.5	-	0.5	18 - 38

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

TABLE 93. *Enterococcus* spp. urinary tract isolates (n=794). Distribution (%) of zone diameters (mm).*

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Ampicillin	2														
Mecillinam	100														
Trimethoprim	12														
Sulfonamide	100														
Ciprofloxacin	6											2	3	6	14
Nalidixic acid	100														
Nitrofurantoin															1

	21	22	23	24	25	26	27	28	29	30	31	32	33	34	≥ 35
Ampicillin			2	3	9	11	12	16	12	14	6	6	2	1	2
Mecillinam															
Trimethoprim				1	2	3	3	6	5	10	8	12	8	11	13
Sulfonamide															
Ciprofloxacin	16	16	15	10	5	2	2	1							
Nalidixic acid															
Nitrofurantoin	1	1	2	3	9	10	16	14	13	11	5	4	4	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.

COMMENTS

As for *Klebsiella* spp., the number of *Enterococcus* spp. included in NORM 2001 is much higher than in 2000. The prevalences given are consequently more accurate and the value of drawing comparison with NORM 2000 (n=76) is limited. Only 43.5% of enterococcal isolates from the urinary tract were speciated in 2001 (41.7% *E. faecalis* and 1.8% *E. faecium*). The results are therefore presented for *Enterococcus* spp. Ampicillin, nitrofurantoin and to some degree trimethoprim were still useful options for treating most uncomplicated urinary tract infections. Ciprofloxacin resistance (9.3%) was reduced compared with 2000 (15.8%), but the majority of isolates (90%) was still only intermediately susceptible to this agent.

Mycobacterium tuberculosis

A total of 297 cases of tuberculosis were reported to the Norwegian Surveillance System for Communicable Diseases (MSIS) in 2001 (MSIS report 2002 30: 20). 276 of these patients had not previously been treated with antituberculosis drugs (new patients). *Mycobacterium tuberculosis* was isolated and susceptibility tests performed for 203 of these new patients (Table 94).

TABLE 94. Antimicrobial susceptibility of 203 *Mycobacterium tuberculosis* isolates from patients not previously treated for tuberculosis ((MSIS rapport 2002. 30: 27). Sampling, microbiological methods and data processing are described in Appendix 5.

Geographical origin of patients	No. of isolates	Resistance to antimicrobial agents (isolates)				
		Isoniazid	Rifampicin	Ethambutol	Streptomycin*	MDR**
Norway	54	2	0	0	4	0
Europe outside Norway	21	3	1	0	3	1
Asia	53	2	0	1	9	0
Africa	71	9	1	1	7	1
2nd generation immigrants	4	0	0	0	0	0
Total	203	16	2	2	23	2
Proportion of isolates resistant (%)		8	1	1	12	1

*Isolates from 16 patients were not tested for susceptibility to streptomycin.
**MDR=Multidrug resistant isolate (combined resistance to rifampicin and isoniazid).

Susceptibility tests were also performed on *M. tuberculosis* isolates from 11 patients who had previously received antituberculosis drug treatment. Three of these patients had multidrug resistant (MDR) isolates. Five patients were therefore diagnosed with MDR tuberculosis in Norway in 2001. Their country of origin was Russia (3) and Sudan (2).

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 antibacterials 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. Herd or flock treatment of livestock with antibacterial drugs is subject to veterinary prescription, drugs being administered either through the drinking water or in medicated feeds prepared on the farm.

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 1 January 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 can only be legally sold by pharmacies. Drug statistics on consumption of antibacterials for human use are based on sales from drug wholesalers to pharmacies and hospitals in Norway. The data include total sales of antibacterials for humans in Norway. Sales to hospitals accounts for 6.6% of the total use of antibacterials for human use.
The figures presented should be regarded as maximum figures based on the assumption that all medicaments sold from wholesalers are actually consumed. The actual drug consumption is probably somewhat lower.
The data are collected by the WHO Collaborating Centre for Drug Statistics Methodology on behalf of the Ministry of Health and Social Affairs. Data on drug use have been collected since the beginning of the 1970s.

Drug classification system
The data are categorized according to the Anatomical Therapeutical Chemical (ATC) classification system, and Defined Daily Doses (DDDs) are employed as units of measurement. The ATC/ DDD index version 2002 was used.

Unit of measurement
The ATC/DDD system is recommended by the WHO as a tool for drug utilisation research to improve the quality of drug use. The standardized ATC/DDD system can be used to present and compare drug consumption statistics at international and other levels. The use of DDD as a unit of measurement simplifies and improves the evaluation of drug consumption over time both nationally and internationally. The DDD is a theoretical unit of measurement, and does not necessarily correspond to 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 anti-infectives are generally based on their use in infections of moderate severity. Some anti-infectives are only used in severe infections and their DDDs are assigned accordingly. DDD assignments 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.
Antibacterials used in dermatological preparations (ATC group D) and preparations intended for sensory organs (ATC group S) were not included in the material.

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

Sampling

The bacterial isolates included in the NORM-VET monitoring programme were collected from animals at slaughterhouses (*E. coli* and *Enterococcus* spp.) and from diagnostic submissions (*Staphylococcus* spp. from cattle with subclinical or clinical mastisis). In addition, 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. One isolate per herd or product were tested for antimicrobial susceptibility.

Indicator bacteria were isolated from samples of intestinal content (faeces) and abdominal muscles (meat) from healthy animals at slaughterhouses. Faecal samples from fattening pigs, meat samples from sheep and meat and faecal samples from cattle were included. The Municipal Food Control Authorities collected the samples. To obtain a representative random sample from pigs, cattle and sheep, the number of samples collected at each slaughterhouse was determined by the proportion of animals slaughtered there relative to the total number of animals slaughtered in Norway in 2000. Abattoirs that slaughtered fewer than 100 animals of one species annually were excluded. Sampling was performed between September and December 2001.

Milk samples were collected by veterinary practitioners (clinical mastitis) or consultants from the National Production Recording Scheme (subclinical mastitis).

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% washed bovine erythrocytes). 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) containing 5% washed bovine erythrocytes). Colonies were identified as *Enterococcus* spp. by typical appearance and a negative catalase reaction. The enterococci were further speciated by *ddl*-PCR.

***Staphylococcus* spp.**

Isolates were isolated at the National Veterinary Institute or the Mastitis Laboratory in Molde. Secretions (0.01 ml) were plated on blood agar (Heart infusion agar (Difco) containing 5% washed bovine erythrocytes). The plates were incubated in a 5% CO_2 atmosphere at 37°C for 24 and 48 h. If no growth was detected after incubation for 24 h, the original secretion sample was preincubated for 4 h at 37°C, and a larger inoculum (0.05 ml) was cultivated on another blood agar as described above. Species identification was performed at the National Veterinary Institute and was based on the occurrence of haemolytic zones, Gram stain, production of catalase and coagulase, growth on peptone agar with acriflavine, anaerobic fermentation of manitol and the use of the Staph-Zym® system (Rosco).

Susceptibility testing

Bacterial isolates were tested for antimicrobial susceptibility at the National Veterinary Institute. MIC (minimal 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 clover leaf 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; NCCLS breakpoints were used when appropriate (Appendix 6).

Quality assurance systems

The following bacteria were included as quality controls on a weekly basis: *S. aureus* ATCC 29213, *E. coli* ATCC 25922, *E. faecalis* ATCC 29212. The following resistant bacteria were tested on a regular basis: *S. aureus* CCUG 35602 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).

Appendix 4
Sampling, microbiological methods and data processing of zoonotic and other food-borne bacteria

Salmonella **(isolates from animals and humans),** ***Yersinia enterocolitica*** **(isolates from humans) and** ***Shigella*** **spp. (isolates from humans)**

Sampling strategy
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.
All the human clinical isolates were obtained from clinical specimens and were referred to the Reference Laboratory for Enteropathogenic Bacteria at the Norwegian Institute of Public Health.

Isolation and identification of bacteria
Isolation and identification of bacteria from samples from animals were carried out at the National Veterinary Institute according to method number 71 advocated by the Nordic Committee on Food Analyses (NMKL).
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 results for all isolates were verified 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™ microdilution method (Dept. of Antibiotics, National Veterinary Institute, Sweden). Only one isolate of each serovar per incident was included for susceptibility testing.
The isolates from human clinical cases 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). Only one isolate per patient was included.

Campylobacter **spp. (isolates from animals and humans)**

Sampling strategy
Cloacal samples from chickens were collected at slaughterplants as part of the Norwegian action plan against *Campylobacter* in broilers (www.zoonose.no). All broiler flocks that were slaughtered when less than 50 days old were tested for the presence of *Campylobacter*. One isolate per positive farm was submitted for susceptibility testing.

A total of 250 human isolates were obtained from clinical specimens. Five specified laboratories submitted the first five isolates each month to the Reference Laboratory for Enteropathogenic Bacteria at the Norwegian Institute of Public Health.

Isolation and identification of bacteria
Isolation and identification of bacteria from samples from broilers was carried out by the Municipal Food Control Authorities according to the NCoFA (NMKL) method number 119, with minor modifications. The identification results of all isolates were verified at the Norwegian Institute of Public Health.

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).

Susceptibility testing
The isolates were tested for antimicrobial susceptibility (MIC values) using Etest (AB Biodisk). Mueller-Hinton agar plates were used at the National Veterinary Institute (isolates from animals), and PDM agar with 5% defibrinated horse blood at the Norwegian Institute of Public Health (isolates from humans). For animals, only one isolate per farm was included. For humans, only one isolate per patient and infectious episode was included. Breakpoints for antimicrobial resistance are defined by AFA.

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 and are accredited according to the requirements of NS-EN ISO/IEC 17025. *Campylobacter jejuni* subsp. *jejuni* ATCC 33291 was used as quality control at the National Veterinary Institute on a weekly basis. The Norwegian Institute of Public Health participates in the external quality assessment programme for *Salmonella* organized by Enter-Net. 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).

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 processing in NORM

General considerations

NORM is based upon periodic sampling of bacteria from patients with respiratory tract infections, wound infections, urinary tract infections, or septicemia. For enteric infections, see Appendix 4. 2001 was the second year of surveillance, and nineteen laboratories from all over 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 the 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 the bacteria were identified using conventional methods as described in the ASM Manual of Clinical Microbiology (7^{th} ed).

The surveillance period started at 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 2001 were: *E. coli*, *Klebsiella* spp., *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Enterococcus* spp. from blood cultures; *Streptococcus pneumoniae* and *Haemophilus influenzae* from respiratory tract infections, *Staphylococcus aureus* from wound infections and *E. coli*, *Klebsiella* spp. and *Enterococcus* spp. from urinary tract infections.

Blood culture isolates, respiratory tract isolates and isolates from wound specimens were tested using the Etest (AB Biodisk, Solna, Sweden), and 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 as either MICs or mm inhibition zone sizes to enable monitoring of trends in the occurrence of resistance. Suspected MRSA (*S. aureus* with oxacillin MIC $\geq$ 4 mg/L) had to be confirmed by *mecA* PCR, and suspected VRE (enterococci growing on BHI with 6 mg/L vancomycin) had to be confirmed by PCRs for the *van* gene complex.

A computer program (the NORM program) was used to record patient, sample and resistance data. These data were analysed by WHONET5 with the aid of a special program (NORMlink) developed by John Stelling that converts the data base structure of NORM to a single file format. Backlink 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 and October were included in the surveillance. All the isolates were identified to the species level using conventional bacteriological methods. All isolates were tested using the Etest (AB Biodisk). In total, 697 isolates of *E. coli*, 260 isolates of *Klebsiella* spp, 510 isolates of *S. aureus* and 191 isolates of enterococci were tested on PDM agar at 35ºC in ambient air, and the 460 isolates of pneumococci were tested on PDM (AB Biodisk) agar supplemented with 5% lysed horse blood at 35ºC in 5% CO_2.

All the *S. aureus* isolates were tested for production of β-lactamase using either the nitrocefin disc, the acidometric agar plate (3.6 mg/L penicillin G and phenol red) or the clover leaf method.

All the *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 the 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. pneumoniae* and *H. influenzae* from patients with respiratory tract infections were collected in each laboratory from January to March. All the isolates were kept in a freezer and tested in batch using the Etest (AB Biodisk). A total of 708 pneumococci and 704 *H. influenzae* were included in the study.

S. pneumoniae isolates were tested on PDM agar supplemented with 5% lysed horse blood at 35ºC in 5% CO_2. All the pneumococci were screened for penicillin susceptibility using a 1 µg oxacillin disc.

H. influenzae isolates were tested on PDM agar supplemented with 1% haemoglobin and 1% Isovitalex at 35ºC in 5% CO_2. In addition, six selected laboratories tested 260 *H. influenzae* isolates on MH agar supplemented with 1% haemoglobin and 1% Isovitalex and the HTM medium at 35ºC in 5% CO_2.

The following strains were used for quality control:
S. pneumoniae ATCC 49619, and *H. influenzae* ATCC 49247.

Wound specimen isolates

Up to 50 consecutive isolates of *S. aureus* from patients with wound infections were collected in each laboratory from January to March. All the isolates were kept in a freezer and tested in batches using the Etest (AB Biodisk). A total of 829 *S. aureus* were tested on PDM agar at 35ºC in ambient air.

All the *S. aureus* isolates were tested for production of β-lactamase using either the nitrocefin disc, the acidometric agar plate (3.6 mg/L penicillin G and phenol red), or the clover leaf method.

All the *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.

The following strains were used for quality control:
S. aureus ATCC 29213, ATCC 43300 (heterogeneous methicillin resistance) and *S. aureus* CCUG 35600 (homogeneous methicillin resistance).

Urinary tract isolates
Up to 50 consecutive isolates each of *E. coli*, *Klebsiella* spp. and *Enterococcus* spp. from patients with urinary tract infections were collected in each laboratory during January and February. All the isolates were kept on the bench or in a freezer until tested in batches using a disc diffusion method with PDM agar and a paper disc (AB Biodisk) at 35ºC in ambient air. The study included 729 *E. coli* isolates, 675 *Klebsiella* spp. and 794 enterococcal isolates.

The following strains were used for quality control:
E. coli ATCC 25922 and *E. faecalis* ATCC 29212.

Mycobacterium tuberculosis
In 2001, antimicrobial susceptibility testing of *M. tuberculosis* was performed at the following institutions: National Institute of Public Health, Oslo, Ullevål University Hospital, Oslo, the National Hospital, Oslo, and Haukeland Hospital, Bergen. The majority of the 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 programme organized by the WHO.

Appendix 6
Breakpoints

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). 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 the tables in the text.

Antimicrobials	MIC values, mg/L		NORM-VET				NORM					
	S	R	*Campylobacter*	*E. coli / Salmonella*	*Staphylococcus*	*Enterococcus*	*Campylobacter*	*E. coli / Klebsiella*	*Staphylococcus*	*Streptococcus*	*Enterococcus*	*Haemophilus*
Doxycycline	≤ 1	≥ 4					■	■	■	■		■
Oxytetracycline	≤ 4	≥ 16	■	■	■	■						
Chloramphenicol	≤ 2	≥ 8								■		
	≤ 8	≥ 32		■	■	■						
Florfenicol	≤ 16	≥ 32		■								
Ampicillin	≤ 1	≥ 32						■			■	
	≤ 2	≥ 8										■
	≤ 8	≥ 16				■						
	≤ 8	≥ 32	■	■								
Penicillins	≤ 0.125	≥ 0.25			■				■			
	≤ 0.063	≥ 2								■		
	≤ 1	≥ 4										■
	≤ 1	≥ 8									■	■
Oxacillin	≤ 1	≥ 4							■			
	≤ 2	≥ 4			■							
Amoxi./clav.	≤ 2	≥ 8										■
	≤ 8	≥ 32		■								
Cephalothin	≤ 8	≥ 32			■							
Cefuroxime	≤ 1	≥ 32						■	■	■		
	≤ 8	≥ 32		■								
Cefotaxime	≤ 1	≥ 32								■		
Cefrazidime	≤ 1	≥ 32						■				
Cefpirome	≤ 1	≥ 32						■				
Ceftiofur	≤ 2	≥ 8		■								
Meropenem	≤ 4	≥ 16						■				
Trimethoprim	≤ 8	≥ 16		■	■							
Sulfonamides	≤ 256	≥ 512		■	■							
TMS	≤ 2	≥ 4			■							
	≤ 2	≥ 16						■		■	■	■
Erythromycin	≤ 1	≥ 4	■				■		■	■		■
	≤ 0.5	≥ 8			■							
	≤ 4	≥ 8				■						
Streptomycin	≤ 8	≥ 16	■									
	≤ 32	≥ 64		■	■							
	≤ 512	≥ 1024				■					■	
Spiramycin	≤ 32	≥ 64			■							
Clindamycin	≤ 1	≥ 4			■				■	■		
Gentamicin	≤ 2	≥ 8	■				■	■	■			
	≤ 4	≥ 16		■	■							
	≤ 512	≥ 1024				■					■	
Kanamycin	≤ 16	≥ 64		■								
Neomycin	≤ 32	≥ 64		■	■							
	≤ 1024	≥ 2048				■						
Apramycin	≤ 32	≥ 64		■								
Ciprofloxacin	≤ 0.125	≥ 4	■				■	■		■		
	≤ 1	≥ 4			■							
Enrofloxacin	≤ 0.25	≥ 2		■								
Nalidixic acid	≤ 16	≥ 32	■	■			■					
Vancomycin	≤ 4	≥ 16							■	■	■	
	≤ 4	≥ 32			■	■						
Teicoplanin	≤ 4	≥ 16									■	
Fucidic acid	≤ 0.5	≥ 1			■				■			
Avilamycin	≤ 8	≥ 16				■						
	≤ 16	≥ 32			■							
Bacitracin	≤ 32	≥ 64				■						
Flavomycin	≤ 32	≥ 64				■						
Virginiamycin	≤ 2	≥ 8			■							
	≤ 4	≥ 8				■						
Narasin	≤ 2	≥ 4				■						

Antimicrobials (amount in discs)	Breakpoints (mm)		NORM	
	S	R	*Salmonella / Shigella / Yersinia*	*E. coli / Klebsiella / Enterococcus - urine*
Tetracycline (30µg)	≥ 28	≤ 21	■	
Chloramphenicol (30 µg)	≥ 32	≤ 24	■	
Ampicillin (10 µg)	≥ 25	≤ 8	■	■
Mecillinam (10 µg)	≥ 24	≤ 13		■
Trimethoprim (5 µg)	≥ 22	≤ 16		■
Sulfonamide (250 µg)	≥ 26	≤ 11		■
TMS (1.2+23.8 µg)	≥ 26	≤ 15	■	
Ciprofloxacin (10 µg)	≥ 29	≤ 17	■	■
Nalidixic acid (30 µg)	≥ 14	≤ 13	■	■
Nitrofurantoin (100 µg)	≥ 19	≤ 18		■