DANMAP 2001

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DANMAP 2001 - Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, foods and humans in Denmark

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Danish Veterinary and Food Administration
Danish Medicines Agency
Danish Veterinary Institute

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Note to readers

In producing the DANMAP reports we have attempted to provide as much information as possible in the space available. Our written commentary is an attempt to draw attention to trends that we find particularly interesting or to provide additional information pertinent to the interpretation of trends in usage of antimicrobials or in resistance.

This year we have decided to present the MIC distributions for all combinations of bacteria and antimicrobials tested, in addition to the percentage resistant with the appropriate confidence interval. We also included text boxes describing results of antimicrobial residue monitoring as well as a description of veterinary antimicrobial treatment guidelines.

We have highlighted certain trends by illustrating them graphically. The reader will be able to graph other trends by obtaining data from previous years reports. Sufficient data have also been made available to allow the reader to calculate whether differences from one year to the next are statistically significant. Previous DANMAP reports maybe downloaded from the Zoonosis Centre website at: http://www.vetinst.dk.

DANMAP 2001 presents, for the first time, usage data collected by the VetStat programme launched in year 2000. While usage data until now have been collected from the pharmaceutical companies, VetStat data are collected much closer to the point of use, and includes information about target animal species and age group. We have found a discrepancy between usage data from VetStat and reporting from the pharmaceutical industry. This is described in the section about antimicrobial usage and VetStat data collection system in Text box 1.

For technical reasons, data on resistance in bacteria from food were not included in the report for 2000. They may be found in Appendix 3 of the present report.

Sammendrag

DANMAP 2001 er den 6. rapport fra det danske program til overvågning af antibiotikaresistens og antibiotikaforbrug. I år præsenterer vi for første gang antibiotikaforbruget fordelt på dyreart og aldersgruppe, ligesom resultaterne af resistensbestemmelse er vist som MIC-fordelinger, foruden som grafiske fremstillinger af resistensudviklingen.

Forbrug af antibiotika

DANMAP giver en samlet fremstilling af anvendelsen af antibiotika til dyr såvel som til mennesker. Hvad angår mennesker er alle oplysninger om forbrug af receptpligtig medicin hos hver enkelt patient blevet indsamlet af Lægemiddelstyrelsen siden begyndelsen af 1990'erne. Lægemiddelstyrelsen har bidraget med data til denne og tidligere DANMAP rapporter. I 2000 blev det landsdækkende register for receptpligtig veterinærmedicin, VetStat, taget i brug. VetStat giver oplysninger om forbruget af medicin på besætningsniveau, herunder forbruget til de enkelte husdyrarter og aldersgrupper. Fremtidigt vil VetStat opgørelser erstatte de indrapporteringer fra medicinalindustrien, som hidtil har udgjort grundlaget for analyser af forbrugsudviklingen. En sammenligning af de to kilder til forbrugsoplysninger tyder på, at VetStat tegner et mere præcist billede af det totale forbrug end det er tilfældet med indberetningerne fra toppen af distributionskæden.

Forbrug til dyr. Brugen af antibiotiske vækstfremmere blev udfaset i 1999 og det samlede forbrug af antibiotika til dyr er faldet fra 205 tons aktivt stof i 1994 til mindre end 100 tons i 2001. Brug af antibiotika til behandling af dyr er imidlertid steget i de senere år. Stigningen er særligt på den gruppe antibiotika, der bruges til medicinering gennem foder og drikkevand. Stigningstakten fra 2000 til 2001 var dog mindre (20%) end i det foregående år (62%). Samlet er forbruget af antibiotika til produktionsdyr steget med 17% (Tabel 3). I de foregående års rapporter har vi formodet, at den væsentligste del af forbruget af antibiotika blev brugt til smågrise. Oplysningerne fra VetStat har bekræftet dette. Svin tegner sig for 71,2 ton (74%) af det samlede forbrug på 96,2 ton og 41% af al antibiotika til svin blev brugt til smågrise (Tabel 4 og 5). Ved hjælp af VetStat har vi kunnet opgøre forbruget som daglige doser (Animal Daily Dosages, ADD). Denne opgørelse vises i Tabel 6. I 2001 blev der brugt 152 millioner antibiotikadoser til 22,9 millioner smågrise, svarende til 6,6 ADD til hver smågris. Til sammenligning blev brugt 1,6 ADD til slagtesvin, dvs. svin over 35 kg. Til sammenligning blev der i slagtekyllingeproduktionen kun brugt 0,4 ADD til hver kylling, der blev produceret. Langt det højeste forbrug var dog i dambrug, hvor der blev brugt hvad der svarer til 79 mg antibiotikum pr. kg. fisk produceret. Til sammenligning blev der i svineproduktionen brugt hvad der svarer til 41 mg antibiotika pr. kg. produceret svinekød.

Som tidligere nævnt er de antibiotiske vækstfremmere blevet udfaset i Danmark, og det totale forbrug i 2001 var på 14 kg. som fortrinsvis udgjordes af flavomycin.

Forbrug til mennesker. Udskrivning af medicin i almen praksis steg med 5% i 2001. Stigningen lå overvejende på gruppen af penicilliner. Analyser har ikke med sikkerhed kunnet afsløre årsagen til stigningen, men resultaterne tyder på, at den kan skyldes en meningitis epidemi i februar og marts 2001 og de deraf følgende bekymringer for spredning af smitten.

Resistens hos zoonotiske bakterier

I sidste års DANMAP rapport beskrev vi, hvorledes spredning af en nalidixansyre resistent klon af *Salmonella* Enteritidis hos fjerkræ havde en stor betydning for den samlede forekomst af kinolonresistens hos *S.* Enteritidis i 2000. I 2001 blev klonen ikke påvist, sandsynligvis som resultat af den generelle salmonellabekæmpelse i ægproduktionen. Status i 2001 var, at kinolonresistens hos *S*. Enteritidis og *S*. Typhimurium fra produktionsdyr stort set var fraværende (Tabel 15 og 16). Kinolonresistens blev kun fundet hos svin, hvor to *S*. Typhimurium isolater var resistente overfor nalidixansyre og tillige havde nedsat følsomhed for fluorokinoloner. Ingen isolater var resistente overfor cephalosporiner. Blandt *S.* Typhimurium fra mennesker har der været stigende resistensforekomst i de senere år, særligt blandt isolater fra salmonellainfektioner erhvervet i udlandet (Figur 7). Resistens blandt hjemligt erhvervede *S*. Typhimurium tilfælde hos mennesker er generelt højere end blandt isolaterne fra produktionsdyr. Det skyldes blandt andet smitte fra importerede fødevarer, ligesom der kan være en underrapportering af infektioner, der er erhvervet i udlandet. Svin er årsag til mellem 4,8 og 6,4% af *Salmonella* infektioner hos mennesker, herunder især infektioner med *S*. Typhimurium. Siden 1999 synes en stigende forekomst af tetracyklinresistens hos *S.* Typhimurium fra svin at afspejles i en stigning hos mennesker, hvor tetracyklinresistens nåede 31% blandt hjemligt erhvervede infektioner med *S*. Typhimurium tilhørende andre fagtyper end DT104 (Tabel 23).

For *Campylobacter* har vi i lighed med foregående år set, at forekomsten af kinolonresistens tilsyneladende

afspejler brugen af fluorokinoloner. Blandt *Campylobacter jejuni* fra slagtekyllinger er der stigende forekomst af kinolonresistens, medens det falder hos *C. coli* fra svin. I 2001 svarede fluorokinolonforbruget til slagtekyllinger til 2,6 mio. ADD givet som oral medicinering, sammenlignet med mindre end en million til svin givet som injektion. Forbruget til svin har været faldende siden et fluorokinolon til fodermedicinering blev taget af markedet i 1999. Der er en tilsyneladende forskel i resistensforekomst og udviklingstendens hos *C. jejuni* fra mennesker og fra kyllinger (Figur 8). Epidemiologiske undersøgelser har vist, at kyllinger er en vigtig kilde til smitte af mennesker i Danmark. Hos mennesker er der højere resistensforekomst blandt *Campylobacter* isolater, der stammer fra personer der har været på rejse i udlandet (Tabel 27), og det er muligt at den nævnte forskel delvis kan forklares ved at en del rejseassocierede tilfælde fejlagtigt registreres som værende smittet i Danmark. Dertil kommer tilfælde som er smittet i Danmark fra importerede fødevarer.

Resistens hos indikatorbakterier

I DANMAP 2000 beskrev vi, hvorledes en multiresistent *Enterococcus faecium* klon havde stor indflydelse på det samlede resistesniveau hos svin og kvæg. Denne klon var stadig til stede i 2001, men forekomsten var lavere end i 2000. Overordnet var der en god sammenhæng mellem udfasning af brugen af antibiotiske vækstfremmere og resistensudviklingen hos *E. faecium* fra slagtekyllinger og svin, henholdsvis fra kyllingekød og svinekød (Figur 10-15). Den tilsyneladende dårlige overensstemmelse mellem forekomst af visse resistensfænotyper fra produktionsdyr og prøver af kød herfra udtaget i detailleddet skyldes delvis tilfældige variationer på grund af det begrænsede bakterieisolater fra visse fødevarekategorier. Imidlertid er enterokokker i stand til at overleve og formere sig i miljøet i produktionslokaler, som det fremgår af vore fund af enterokokker i fisk i tidligere års DANMAP undersøgelser. Det er derfor muligt, at enterokokker i fødevarer kun delvis afspejler enterokokpopulationerne i de dyr, de pågældende fødevarer stammer fra.

Derimod er der for *Escherichia coli* fra slagtedyr god overensstemmelse med resistensniveauet i de tilsvarende produktkategorier. Generelt er resistensforekomsten lav, lavere end i importerede fødevarer. Ca. 10% af isolaterne fra kyllinger og kyllingekød var resistente overfor nalidixansyre og et enkelt isolat fra kyllingekød af dansk oprindelse var resistent overfor ciprofloxacin. Ingen af isolaterne var resistente overfor cephalosporiner.

I 2002 er der som led i DANMAP overvågningen etableret indsamling af prøver fra raske mennesker med henblik på at overvåge resistensudviklingen hos *E. coli* og enterokokker. Resultaterne vil blive beskrevet i fremtidige DANMAP rapporter.

Resistens i prøver fra diagnostiske indsendelser

Produktionsdyr. En sammenligning af resistensresultater for *E. coli* fra diagnostiske indsendelser (Tabel 37) med resultaterne fra indikator *E. coli* viser, at forekomsten er højest blandt førstnævnte. Medens niveauet blandt *E. coli* fra slagtekyllinger generelt er faldende eller uændret (Figur 17) giver andre af udviklingstendenserne årsag til bekymring. Således har kinolonresistens blandt *E. coli* fra kvæg været næsten uafbrudt stigende siden 1996.

Blandt *E. coli* fra svin er tetracyklinresistens i stigning medens kinolonresistens falder. Dette afspejler formentlig udviklingen af forbruget af de pågældende antibiotikagrupper. I en tidligere DANMAP rapport henledte vi opmærksomheden på, at markedsføring af apramycin til behandling af infektioner hos svin og kalve kunne føre til en stigning i resistens overfor gentamicin. Dette forhold er den mulige årsag til den stigning i gentamicinresistens vi har set hos *E. coli* fra svin og kvæg fra 2000 til 2001, men det skal understreges at det genetiske grundlag for resistensen endnu ikke er undersøgt.

Der er et relativt lavt resistensniveau blandt stafylokokker fra mastitis hos kvæg, herunder resistens overfor penicillin. Ingen isolater var resistente overfor cephalosporiner. For *Staphylococcus hyicus* fra svin gælder at resistenstendenserne er noget variable (Figur 18). Dette kan delvis forklares ved at antallet af isolater er begrænset. Derudover kender vi ikke årsagen hertil.

Mennesker. DANMAP giver en samlet fremstilling af resistensoplysninger for nogle almindeligt forekommende sygdomsfremkaldende bakterier fra mennesker. Elleve ud af 16 amter bidrager nu med resultater. Om end det synes klart at udviklingen overordnet set er meget sammenlignelig i alle egne af landet, betyder forskelle i overvågningsmetoder i de enkelte amter dog, at det ikke er muligt at kombinere resultaterne med henblik på detaljerede analyser af udviklingen i relation til antibiotikaforbruget.

I DANMAP 2000 kommenterede vi udvikling i methicillinresistens hos *Staphylococcus aureus*. Udvikling i methicillinresistens fortsatte med at stige i 2001 og om end forekomsten stadig er lav, er der dog grund til at følge udviklingen nøje.

Summary

DANMAP 2001 is the 6th report from the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme. This year we present data on antimicrobial usage by animal species and age group and the susceptibility data – in addition to resistance trends – are shown as MIC distributions.

Antimicrobial use

DANMAP brings together data on the use of antimicrobials in animals and in humans. Since the early 1990's, usage of all prescription medicines in humans has been monitored at the level of the individual patient. This monitoring has been carried out by the Danish Medicines Agency who has provided data for the usage trends in this and in previous DANMAP reports. In 2000, we initiated a prescription-based monitoring of medicine usage in animals. This programme, VetStat, provides information about usage at herd level, including target animal species and age group. Data from this programme will replace reporting by the pharmaceutical industry of annual sales, the data that have until now formed the basis for usage trends described in DANMAP reports. A comparison of the two reporting systems in this years report indicate that the VetStat programme provides more accurate measures of total usage than does reporting from the top of the distribution pyramid.

Usage in animals. Antimicrobial growth promoters were phased out in Denmark in 1999 and total antimicrobial usage in food animals has been cut in half from 205 tonnes of active compound in 1994 to less than 100 tonnes in 2001. Usage of antimicrobials for therapy has increased in recent years and we saw a further increase in the usage of antimicrobials for oral application in 2001 compared with 2000, although the rate of increase was slower (20%) than in the previous year (62%). Overall usage of antimicrobials for treatment of food animals, increased by 17% (Table 3). In previous reports we have speculated that a significant part of the total usage was in weaner pigs. The point-of-use data provided by VetStat have been able to confirm this: pigs account for 71.2 tonnes of a total of 96.2 tonnes of antimicrobials used for animals in Denmark (74%) and weaner pigs alone account for 41% of antimicrobials used in that species (Tables 4 and 5). In the VetStat system we have calculated usage as Animal Daily Dosages (ADD's). The results are presented in Table 6. In 2001, 152 million ADD's were used in 22.9 million weaner pigs, or 6.6 ADD per weaner pig, compared with 1.6 ADD in slaughter pigs. In contrast to pigs, broilers were given a more modest 0.4 ADD total antimicrobial per bird produced. The highest usage, however, was in aquaculture, with 79 mg antimicrobial per kg fish produced. In comparison, usage in pigs amounted to 41 mg per kg pig slaughtered.

Antimicrobial growth promoters have been phased out in Denmark and total usage in 2001 was 14 kg, mainly flavomycin.

Consumption in humans. In human medicine, consumption of antimicrobials in primary health care increased by 5%, mainly as a result of an increased use of beta-lactamase sensitive penicillins. Analyses indicated that a possible explanation for the increased consumption might be concerns sparked by an outbreak of bacterial meningitis in February and March 2001.

Resistance in zoonotic bacteria

In our previous report we described how the spread of a nalidixic acid resistant clone of *Salmonella* Enteritidis in poultry had a significant effect on the overall level of quinolone resistance in that bacterium in 2000. In 2001, none of the isolates were resistant to nalidixic acid as a result of the general measures to control *Salmonella* in layers. Overall, we have found quinolone resistance in *S*. Enteritidis and *S.* Typhimurium from food animals to be almost absent (Tables 15 and 16). The only finding was in pigs, where two isolates were resistant to nalidixic acid and also had decreased susceptibility to ciprofloxacin. Resistance to cephalosporins was absent in *Salmonella*. Resistance among *S.* Typhimurium from humans has been increasing in recent years, especially in cases associated with foreign travel. (Figure 7). Levels of resistance among domestically acquired human *S*. Typhimurium show that the levels are generally higher than among isolates from food animals. The main reason for this is the contribution from imported food stuffs and some underreporting of travel. Pigs are recognized as the source of between 4.8% to 6.4% of *Salmonella* infections in humans, in particular infections with *S*. Typhimurium. Since 1999, increasing levels of tetracycline resistance in *S*. Typhimurium from pigs appear to be reflected in increases in humans, where tetracycline resistance reached 31% in domestically acquired infections with *S.* Typhimurium phage types other than DT104 (Table 23).

In *Campylobacter* from food animals we have observed as we did in 2000, that the level of quinolone resistance appears to reflect usage: in *C. jejuni* from broilers

resistance, is increasing, while it is decreasing in *C. coli* from pigs. In 2001, fluoroquinolone usage in broilers amounted to 2.6 million ADD's as oral medication, compared with less than a million in pigs as injectables (data not shown). In pigs, usage of fluoroquinolones has decreased since the withdrawal from the market in 1999 of a formulation for oral treatment. The apparent difference in levels of resistance and in trend among *C. jejuni* from humans compared with broilers is interesting (Figure 8). Epidemiological investigations have shown that these animal species constitute important reservoirs for human campylobacteriosis in Denmark. We have found that the levels of resistance are higher in isolates from incidents associated with travel abroad (Table 27), and it is possible that the disparity may be explained by some travel associated cases being misclassified as domestically acquired, in addition to cases that are acquired from imported foods.

Resistance in indicator bacteria

In DANMAP 2000 we reported how a particular multiresistant clone of *Enterococcus faecium* had a significant impact on the overall levels of resistance in pigs and cattle. The clone was still present in 2001 but with a decreased incidence. Overall, we have found a rather good association between the phasing out of antimicrobial growth promoters and resistance trends in E*. faecium* from broilers and pigs as well as from broiler meat and pork (Figures 10-15). The apparent poor agreement seen for some resistance phenotypes between isolates from domestic animals and from the corresponding food product sampled in retail outlets (Tables 32 and 33) is likely to result mainly from random variation, considering the limited number of isolates in some food categories. However, enterococci are able to survive and perhaps proliferate in processing environments, as seen from our finding in previous years of enteroccocci in samples of fish. Enterococci in food animal products may only partly reflect the populations in the animals of origin.

In contrast, among *Escherichia coli* from animals at slaughter there is good agreement with resistance levels in the corresponding products. In general, resistance levels are low, lower than in imported products. About 10% of isolates from broilers and broiler meat were resistant to nalidixic acid and one *E. coli* isolate from Danish broiler meat was resistant to ciprofloxacin. No isolates were resistant to cephalosporins.

In 2002 the DANMAP group has initiated sampling of the healthy human population to recover *E. coli* and enterococci for susceptibility testing. The results will be presented in future DANMAP reports.

Resistance in bacteria from diagnostic submission

Food animals. Comparison of results for *E. coli* from diagnostic submissions (Table 37) with the results for indicator *E. coli* show that resistance levels in the former are the highest. While the trend in *E. coli* from broilers generally is decreasing or the level is stable (Figure 17), some of the trends in isolates from cattle and pigs are a cause for concern. In cattle, quinolone resistance in *E. coli* has – with one exception – been increasing since 1996.

In *E. coli* from pigs, tetracycline resistance is on the increase, while quinolone resistance decreases. These trends appear to be driven by usage trends. In a previous report we have commented that the marketing of apramycin in 1998 for use in pigs and calves might lead to increase in resistance to gentamicin. This is the possible cause of the increase in gentamicin resistance observed in *E. coli* from cattle as well as in pigs from 2000 to 2001, however, the genetic basis for the resistance has not yet been examined.

In staphylococci from cases of mastitis resistance levels are relatively low, including resistance to penicillin. No isolate was resistant to cephalosporins. In *Staphylococcus hyicus* from pigs the resistance trends appear somewhat variable (Figure 18). Part of this may be explained by a relatively small number of isolates. Other than that vi have no explanation for the variation.

Humans. DANMAP brings together resistance data for some common human pathogens. Eleven of 16 Danish counties now contribute their results. While it is apparent that the overall trends are very similar in all parts of the country, differences in surveillance methods still preclude pooling of data and detailed analyses of trends relative to antimicrobial consumption are not yet possible.

In 2000 we commented on an increase in occurrence of methicillin resistant *Staphylococcus aureus*. This increase continued in 2001 and while the incidence is still low, it does represent a cause for concern.

Demographic data

Table 1 shows the production of food animals, meat, milk and fish. From 2000 to 2001, the number of cattle slaughtered decreased by 5.5%, while the number of poultry and pigs slaughtered increased by 2.2% and 2.6% respectively. The proportion of imported meat consumed has been estimated at 36% for beef, 27% for poultry and 10% for pork.
Table 2 provides information on the distribution of the human population and on the health care system in Denmark.

Table 1. Production of food animals and the production of meat, milk and fish, Denmark, 1990-2001

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Year	Poultry		Cattle (slaughtered)		Dairy cows		Pigs		Farmed fish	
									Fresh water	Salt water
	1,000 heads	mio. kg	1,000 heads	mio. kg	1,000 heads	mio. kg. milk	1,000 heads	mio. kg	mio. kg	mio. kg
1990	98,686	126	789	219	753	4,742	16,427	1,260		
1992	111,536	150	862	236	714	4,605	18,559	1,442	35	7
1994	120,349	167	813	210	700	4,642	20,760	1,604	35	7
1996	111,495	165	789	198	701	4,695	20,530	1,592	32	8
1998	129,334	185	733	179	669	4,668	22,873	1,770	32	7
2000	136,934	197	691	171	636	4,720	22,336	1,748	33	7
2001	140,015	a)	653	a)	a)	a)	22,926	a)	31	a)

a) Data on the production of meat and fish, and no. of cows in 2001 was not yet available

Table 2. Distribution of the human population and health care structure by county, Denmark

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County no.	County name	No. inhabitants (1/1/2001)	No. inh./km2 (1/1/2001)	No. inh. /GP c) (2001)	No. bed-days d) (2000, provisional)	No. hospitals (2000)
1	Copenhagen Municipality a)	499,148	5,656	1,569	1,037,000 e)	4
2	Frederiksberg Municipality a)	91,076	10,385	1,602	-	1
3	Copenhagen County b)	615,115	1,170	1,629	597,000	3
4	Frederiksborg	368,116	273	1,512	323,000	4
5	Roskilde	233,212	262	1,631	226,000	2
6	West Zealand	296,875	99	1,540	270,000	4
7	Storstroem	259,691	76	1,515	271,000	5
8	Bornholm	44,126	75	1,300	40,000	1
9	Funen	472,064	135	1,486	529,000	9
10	South Jutland	253,249	64	1,472	216,000	4
11	Ribe	224,446	72	1,537	206,000	4
12	Vejle	349,186	117	1,612	381,000	6
13	Ringkoebing	273,517	56	1,550	256,000	5
14	Aarhus	640,637	140	1,561	701,000	9
15	Viborg	233,921	57	1,562	254,000	3
16	North Jutland	494,833	80	1,544	495,000	7
All	Denmark	5,349,212	124	1,552	5,802,000	71

a) Inner Copenhagen.

b) Outer Copenhagen.

c) GP, general practitioner.

d) Excluding psychiatry, private hospitals and one rehabilitation center.

e) Public hospitals in Copenhagen and Frederiksberg municipalities (inner Copenhagen) represent one single administrative body.

Antimicrobial use

Usage of therapeutics in animals

In previous DANMAP reports we have shown trends in antimicrobial usage based on sales figures reported by the pharmaceutical industry. These data from the top of the supply pyramid have – with some exceptions – not included information on usage in individual target animal species.

In 2000 we initiated a monitoring programme, VetStat, where usage information is collected close to the point of use. These data include information about – among other things - target animal species and age group of the animals. Please refer to Text box 1 for details about VetStat data collection. In this DANMAP report we compare usage data based on these two different types of reporting. In the future, usage data collected by the VetStat programme will replace the returns on annual sales from the pharmaceutical industry.

Reports from pharmaceutical companies. These data are comparable with data from previous years. In our calculation of total quantity of active compound used, we have - as in previous years – excluded antimicrobials used only in companion animals, i.e. mainly antimicrobials formulated as small tablets.

Table 3 compares usage in 2001 with results from 2000 and Figure 1 shows the trend from 1996 to 2001. Overall, the quantity of antimicrobials used in production animals (excluding aquaculture) amounted to 94,200 kg active compound. This represents an increase of 17%, which exceeds the increase in animal production. The increase is mainly in antimicrobials for oral use, in particular tetracyclines, macrolides/lincosamides and extended spectrum penicillins. While we have no hard data on usage in target animal species in these sales returns from pharmaceutical companies, we know from other sources that the major proportion of tetracyclines and macrolides/lincosamides are used in pig production.

In contrast to the increasing usage of oral formulations and injectables, the quantities of antimicrobials for intra-mammary and intra-uterine use have remained rather constant over the past five years (Figure 1). Intra-mammaries are used almost exclusively in dairy cattle, where milk production has been quite stable at around 4,700 million kgs per year during the same period.

Point of use data (VetStat). VetStat usage data are prescription-based and are collected from pharmacies, veterinary practise and from feed mills. Antimicrobials for therapeutic use can be legally obtained only through pharmacies or – on the basis of a prescription from a veterinarian – from a feed mill as medicated feed. Table 4 shows sales from pharmacies in kg active compound by target animal species and age group. For some data

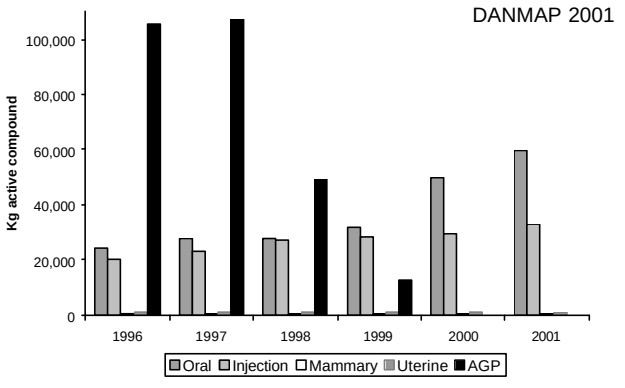


Figure 1.Trend in usage of antimicrobials for treatment of food animals by route of administration and usage of antimicrobial growth promoters (AGPs)1996-2001, Denmark

Table 3. Usage of antimicrobials (kg active compound) for treatment of food animals by route of administration, Denmark

DANMAP 2001

Antimicrobial group a)	Oral		Injection		Intramammary		Intrauterine		Total	
	2000	2001	2000	2001	2000	2001	2000	2001	2000	2001
Tetracyclines	21,200	24,800	2,800	3,200	<25	0	0	<25	24,000	27,900
Extended Spectrum Penicillins	4,500	5,600	3,000	3,500	150	150	0	0	7,600	9,300
Narrow Spectrum Penicillins	0	0	14,700	17,000	100	100	50	50	14,800	17,100
Cephalosporins	0	0	50	50	<25	50	0	0	50	100
Sulfonamides	0	0	0	0	0	0	1,000	800	1,000	800
Sulfonamides + trimethoprim	3,500	4,000	3,500	3,400	50	<25	0	0	7,000 b)	7,400 b)
Macrolides + lincosamides	9,200	11,900	1,800	2,000	<25	0	0	0	11,100	14,300
Aminoglycosides	7,300	8,400	2,800	3,200	100	150	150	100	10,400	11,900
Fluoroquinolones	50	50	100	150	0	0	0	0	150	200
Others	4,200	4,900	300	300	<25	<25	0	0	4,500	5,200
Total	50,000	59,600	29,100	32,900	400	500	1,200	950	80,600	94,200

a) For a description of individual compounds included in each group, please refer to Text box 5
b) Does not include consumption in aquaculture

Text box 1

Collection of data on antimicrobial usage at the point of use
The VetStat programme

Background

One of the key recommendations of the 'Antimicrobial Threat' invitational conference held in Copenhagen in 1998 was that usage of antimicrobials in animal production should be monitored. While Denmark had for some time monitored such usage on the basis of information provided from the top of the distribution system (i.e. by the pharmaceutical industry), the Danish government decided to develop and implement monitoring of usage of all prescription medicines closer to the point of use. The programme, VetStat, started data collection in mid-2000. From 2001 the data were of sufficient quality to permit publication of monthly usage statistics. These data are available at the Danish Zoonosis Centre homepage at www.vetinst.dk.

VetStat collects data on usage of all prescription medicines prescribed or used by veterinarians, including human medicines. VetStat also collects data on usage of antimicrobial growth promoters and coccidiostats.

Description of data collection

All antimicrobials for treatment of disease are prescription-only medicines and available only through pharmacies. Antimicrobials obtained by veterinarians for use in practise or for re-selling to clients must also be purchased through pharmacies. The only exception to this is pre-mixes for use in medicated feed produced at licensed feed mills. A farmer may obtain such feed on the basis of a veterinarian's prescription, however, the feed mill may obtain the pre-mix direct from a medical wholesaler or a pharmaceutical company. Coccidiostats approved by the EU as feed additives are freely available.

Data in VetStat originates from three sources: pharmacies, large animal practices and feed mills.

Pharmacies. Information for use in VetStat is extracted automatically during electronic processing of sales at the pharmacy, be it medicine ordered by a veterinarian for use in practice or a sale based on a veterinary prescription redeemed by an animal owner. The data record describing each sale includes a numerical code unequivocally identifying the type of medicine, including its formulation, strength and size of pack; the quantity sold of each pack; codes for target animal species, age group and disease entity as stated on the prescription (the two latter for production animals only); where applicable, a code identifying the farm where the medicine will be used; codes identifying the prescribing veterinarian, the date of sale, as well as other items of information. For medicines sold for use in practice, the type and quantity of medicine as well as the receiving practice is identified.

The data are sent electronically on a monthly basis to the Danish Medicines Agency which forwards them to the central VetStat database.

Veterinary practise. Veterinarians are required by law to report to VetStat the use of all prescription medicines in production animals. The information to be reported includes the identity and quantity of medicine, target animal species, age group and disease entity, farm ID, as well as information identifying the veterinarian and the practice. Veterinarians are not presently required to report usage of medicines in companion animals and horses.

For data collection, most practices use software that automatically extracts the information required by VetStat during the billing procedure. In this case, there is no special data entry required.

Veterinarians also have the option of recording usage directly into the VetStat database, which can be accessed via the internet.

Feed mills. Feed mills record sales of medicated feed directly into the database via the internet. The information recorded includes a code identifying the active ingredient, its concentration, the quantity of

Text box 1 continued ...

feed, as well as information identifying target animal species, age group, the farm, and the prescriber. For coccidiostats, records identifying the type of coccidiostat, the concentration, the quantity of feed sold, and the identity of the farm receiving it. The records are sent electronically to the VetStat database once a month.

The database

The VetStat database is a relational database on an Oracle platform and is part of the so-called GLR/ CHR register, operated by LEC a/s on behalf of the Ministry of Food, Agriculture and Fisheries. The Danish Zoonosis Centre is responsible for VetStat, however, its development and implementation has taken place in close collaboration with the Danish Veterinary and Food Administration. VetStat is integrated with a number of other databases, among them the central farm register which contains, among other data, information about the number and species of animals at each holding.

Access to data

Veterinarians and farmers may access their data via a secure connection to the VetStat homepage on the internet. Their access is restricted by password to registrations concerning their own clients or herds, respectively. However, for comparative purposes they have access to standardised outputs showing mean usage on other farms on a regional and national level. In order to make such comparisons meaningful we have defined Animal Daily Dosages (ADD) for each combination of antimicrobial product and animal species/age group. An ADD is, for any formulation, the daily dosage required to treat an animal of a certain weight. We have used the manufacturers recommended dosages and when these have been given as a range we have chosen the median value. We have also, for each species and age group chosen a standard weight for each animal. So, for a given antimicrobial, we take the total quantity active compound recorded as used for a species and age group and divide by the median dosage in mg per kilogram and divide again with the standard weight chosen.

records with a valid code for animal species, information about age group was not available and for some records there was a valid farm code, but no information about target animal species. These have separate entries in the table. Furthermore, a substantial part of the total quantity has been sold for use in veterinary practise. Information about the animal species in which this has been used is incomplete, however, the major proportion is used in cattle, with most of the remainder in companion animals. The VetStat data also include human antibiotics prescribed for use in companion animals, however this quantity is small and amounted to 275 kg active compound in 2001.

Table 5 shows sales of antimicrobials in medicated feed. More than half of the total sales were for use in aquaculture with the rest being used in pigs. The quantity used in poultry amounted to less than 0.5 kg.

It is clear from these data that 74% of all antimicrobials are used in pig production, while broilers, at the other extreme, were responsible for less than 0.5% of the total usage. Relative to production figures (2000 data), usage of antimicrobials in pig production amounted to 41 mg/ kg and in broilers to 0.8 mg/kg of meat produced.

In Table 6 we present usage as Animal Defined Dosages (ADD) based on prescription information. An ADD is – for any formulation – the daily dosage required to treat an animal of a certain weight. For calculation of ADD's, please refer to Text box 1. When evaluating the data in Table 6, one must remember that it is based on pharmacy data only. Usage in cattle to a large extent consists on medicine purchased by the veterinarian for use in practice. The data in Table 6 therefore underestimates usage in cattle to a considerable degree as information about usage by age group in this species relies on information reported by veterinary practitioners. This reporting was not complete in 2001. Furthermore, as will be clear from an examination of Tables 4 and 5, usage in aquaculture is largely by feed medication. For this reason we have excluded usage in aquaculture from the pharmacy-based information in Table 6 as the figure would be quite misleading. For pigs and poultry, however, the pharmacy records are fairly complete.

It is clear from Table 6 that in pig production by far the most intensive usage is in weaner pigs. In 2001 152 million dosages were used in weaners, or 6.6 ADD per pig produced, compared with 0.4 ADD per broiler.

Comparison of pharmaceutical industry data with VetStat. In 2001 the total quantity of antimicrobials reported by pharmaceutical companies amounted to 97,400 kgs, including use in aquaculture but excluding preparations obviously intended for use in pets. In contrast, sales from pharmacies and feed mills amounted to only 96,200 kg, a difference of 1,200 kg. We have been able to establish that the reason for some of this discrepancy was that one pharmaceutical company erroneously reporting some antimicrobials as having been sold for domestic use, even though they were in fact exported.

Coccidiostats

Table 7 shows usage of coccidiostats in poultry production. In contrast to previous years where usage information was provided by the Danish Plant Directorate, for 2001 the data were obtained using VetStat. Reporting of feed additive use in VetStat has not been subject to final validation, however, the overall usage information as presented in Table 7 is reasonably correct. Nevertheless, the data should be interpreted with some caution. It is clear from the table that almost all coccidiostats used belong to the ionophore group of compounds.

Antimicrobial growth promoters

Following the official ban on the growth promoter virginiamycin in January 1998, the Danish food animal industries decided to discontinue all further use of growth promoting antimicrobials. This became effective in broilers, slaughter pigs and cattle in February and

Table 4. Antimicrobials sold from pharmacies in Denmark in 2001 (kg active compound) by animal species and age group. Usage has been rounded to the nearest kg

DANMAP 2001

Animal species	Age group	Amcol a)	Amglc	Ceph	FQ	Quinol	Linco	Macrol	Pen-sim	Pen-ext	Sulfa/TMP	Tet	Others	Total
Pigs	Breeders and suckling pigs	1	2,431	20	52	0	516	1,574	5,852	2,343	2,922	2,904	1	18,617
	Weaners	0	5,880	2	26	0	657	5,919	787	1,934	1,367	11,341	4	27,919
	Slaughter pigs	0	636	2	14	0	1,002	5,815	3,202	1,362	201	9,794	0	22,028
	Age not given	0	75	0	2	0	25	188	93	78	45	346	0	854
Cattle	Cows, bulls	0	8	1	0	0	3	12	35	16	17	19	0	112
	Calves < 12 months	31	270	1	8	0	8	29	480	100	157	249	0	1,333
	Heifers, steers	1	2	0	0	0	0	2	9	5	1	10	0	29
	Age not given	2	9	0	0	0	2	12	5	4	4	26	0	64
Small ruminants	> 12 mdr.	0	2	0	0	0	1	1	2	1	4	1	0	11
	< 12 mdr.	0	0	0	0	0	0	0	0	0	0	1	0	1
	Age not given	0	0	0	0	0	0	2	2	0	0	2	0	6
Poultry	Broilers	0	0	0	5	0	0	4	0	145	5	2	0	160
	Layers	0	0	0	2	0	0	4	0	20	2	1	0	29
	Rearing flocks	0	3	0	2	0	1	23	0	40	38	8	0	116
	Age not given	0	0	0	3	0	0	2	0	10	7	1	0	23
Aquaculture		1	0	0	0	110	0	0	0	47	110	4	0	273
Horses		0	17	0	0	0	0	1	19	2	103	2	0	144
Other production animals		1	34	5	1	0	3	13	38	38	31	10	1	176
Mink		0	166	0	1	0	34	65	0	341	33	19	0	659
Use in practise or species not given		56	1,807	206	51	156	162	966	5,385	1,991	2,939	1,494	35	15,246
Farm identified		3	429	2	12	7	106	668	478	455	311	875	0	3,346
Pets		1	110	62	4	0	9	21	32	81	90	29	13	453
		98	11,880	302	183	273	2,530	15,324	16,420	9,010	8,391	27,135	54	91,602

a) Amcol: amphenicols; Amglc: aminoglycosides; Ceph: cephalosporins; FQ: fluoroquinolones; Quinol: quinolones; Linco: lincosamides; Macrol: macrolides; Pen-sim: simple penicillins; Pen-ext: penicillins with extended spectrum; Sulfa/TMP: sulfonamide and sulfonamide-trimethoprim combinatin; Tet: tetracycline. For a description of individual compounds included in each group, please refer to Text box 6

Table 5. Sales of antimicrobials as medicated feed in kg active compound by animal species and age group, Denmark

DANMAP 2001

Animal species	Age group	Amcol a)	Amglc	Quinol	Linco	Macrol	Sul/TMP	Tet	Total
Pigs	Breeders, sucklers	0	1	0	3	56	25	61	145
Pigs	Weaners	0	3	0	3	306	32	1,133	1,476
Pigs	Slaughter pigs	0	1	0	6	56	0	77	141
Poultry		0	0	0	0	0	0	0	0
Aquaculture		96	0	266	0	0	2,521	0	2,883
Total		96	4	266	12	419	2,577	1,271	4,646

a) For abbreviation, please refer to Table 4

March of that year and in weaner pigs during 1999. In 2000 antimicrobial growth promoters were not used. However, in 2001 reporting through the VetStat programme showed the use of very small quantities of flavomycin (11 kg) and avilamycin (3 kg), both among the four growth promoters still approved by the EU (Table 8).

Table 6. Usage of antimicrobials given as Animal Defined Dosages (ADD's), based on sales from pharmacies to animal owners, Denmark

DANMAP 2001

Animal species	Age group	Standard weight (kg)	Kg antimicrobial	ADD (1000's)	Kg animal treated (1000's)
Pigs	Breeders and suckling pigs	200	18,617	6,787	-
	Weaners	15	27,918	151,740	-
	Slaughter pigs	50	22,028	37,371	-
	Age not given	-	854	-	71,230
Cattle	Cows, bulls	600	112	30	-
	Calves < 12 months	100	1,333	946	-
	Heifers, steers	300	29	9	-
	Age not given	-	64	-	4,219
Small ruminants	> 12 mdr.	50	11	12	-
	< 12 mdr.	20	1	2	-
	Age not given	-	6	-	185
Poultry	Broilers	0.2	161	56,764	-
	Layers	1	29	1,698	-
	Rearing flocks	1	116	3,640	-
	Age not given	-	23	-	1,132
Horses		-	144	9	-
Mink		1	659	36,604	-
Total kg antimicrobial		-	72,380	-	-

Table 7. Usage of coccidiostats in poultry (kg active compound), Denmark

DANMAP 2001

Coccidiostats	1990	1992	1994	1996	1998	1999	2000	2001
Amprolium/Ethopabat	3,562	2,716	2,342	1,339	275	839	-	13
Dimetridazol	-	-	-	38	-	106	-	-
DOT	-	-	300	-	-	13	-	-
Monensin	-	108	1,016	3,405	3,709	8,664	3,962	1,361
Robenidin	33	295	858	293	367	85	-	2
Metichlorpindol/ Methylbenzoat	89	1,503	3,360	4,857	930	155	-	-
Lasalocid	75	-	5	773	1,677	895	606	872
Halofuginon	-	-	19	8	-	2	-	-
Narasin	1,588	5,157	6,370	3,905	3,177	5,806	5,073	2,687
Salinomycin	7,783	10,298	6,018	4,531	7,884	8,812	6,338	12,801
Nicarbazin	-	-	-	115	36	4	-	-
Narasin/Nicarbazin	-	-	-	-	-	32	20	1
Nifursol	-	395	-	146	234	79	-	-
Diclazuril	-	-	18	34	3	1	-	2
Total	13,569	20,472	20,306	19,444	18,292	25,493	15,999	17,739

Table 8. Usage of antimicrobial growth promoters (kg active compound), Denmark

DANMAP 2001

Antibiotic group	Growth promoter	1990	1992	1994	1996	1998	1999	2000	2001
Bacitracin	Bacitracin	3,983	5,657	13,689	8,399	3,945	63	-	-
Flavofosfolipol	Flavomycin	494	1,299	77	18	6	665	-	11
Glycopeptide	Avoparcin	13,718	17,210	24,117	-	-	-	-	-
Ionophore	Monensin	2,381	3,700	4,755	4,741	935	-	-	-
	Salinomycin	12	-	213	759	113	-	-	-
Macrolides	Spiramycin	-[a)]	-	95	15	0.3	-	-	-
	Tylosin	42,632	26,980	37,111	68,350	13,148	1,827	-	-
Oligosaccharides	Avilamycin	10	853	433	2,740	7	91	-	3
Quinoxalines	Carbadox	850	7,221	10,012	1,985	1,803	293	-	-
	Olaquindox	11,391	21,193	22,483	13,486	28,445	9,344	-	-
Streptogramins	Virginiamycin	3,837	15,537	2,801	5,055	892	-	-	-
Total		79,308	99,650	115,786	105,548	49,294	12,283	-	14

a) - indicates that the compound was not used

Text box 2

Few antimicrobial residues in slaughtered animals, eggs and milk

For almost 15 years between January 1987 and April 2001 the Danish Veterinary and Food Administration has carried out intensive surveillance of the antimicrobial residues in slaughter animals, eggs and milk. The sampling scheme was stratified random and included samples from 0.1% of the annual production of fattening pigs, 1.0% of the sows slaughtered, 0.5% of the adult cattle and 0.2% of the fattening calves. The analytical method used was the official EU reference microbiological test, which was sufficiently sensitive for most but not all of the relevant substances. The risk of false negative results was estimated by aid of specific chemical methods of analysis (see below).

On the basis of examination of approximately 200,000 slaughter pigs over the 15-year period, it was concluded that the frequency of violations of residue limits was 0.02% which is extremely low by international standards. For this reason, the frequency of sampling was drastically reduced in May 2001.

In recent years positive screening results were verified by quantitative chemical methods. In cases where the latter showed that the residue was less than the EU defined Maximum Residue Level (MRL), the screening result was declared false positive and the final result as negative.

In 2001, a total of 9,339 randomly selected slaughter pigs were analysed with no positives. Likewise, 1,064 cattle, 12 sheep and 3 horses were analysed with no positives. We also found no violations in 334 samples of poultry, 98 samples of fish from aquaculture, 256 samples of milk taken by the official inspectors, 140 samples of eggs, 10 samples of farmed game and 34 samples of honey. However, we found 2 violations in samples from 1,424 sows, corresponding to 0.14%, a level similar to that found in sows in recent years.

Milk samples are also collected by non-official staff on all dairy farms 13 times a year. During the period 1993 - 1999, we found violations of MRLs in 0.04% of the samples. In 2000 and 2001, the total number of samples was 242,173. Seventy-one of the samples corresponding to 0.03% had higher residues than permitted. The most frequently detected antimicrobial residues were simple penicillins, including benzylpenicillin, with less frequent findings of sulfamethazine, cloxacillin and ampicillin residues. Residues of sulfadiazin, amoxicillin and oxytetracycline were very rarely found.

The application of the official EU reference microbiological test was chosen on the basis of a cost-benefit analysis since the analysis of huge numbers of samples was economically affordable only in this case. In order to evaluate the performance of the test with respect to the frequency of false negative results we have recently implemented the use of specific methods of analysis for those substances which are not sufficiently detected by the microbiological method. In 2001, these tests found no violations in 779 porcine and 99 bovine samples that comprise the vast majority of slaughter animals.

Comparison with other European Member States should be done with great caution since information on risk groups (for instance the proportion of sows and boars versus fattening pigs) and the applied analytical methods is often lacking. For example, in Denmark kidney tissue is analysed, because most of the antibiotics are concentrated there, whereas other countries analyse muscle tissue.

Annual reports in Danish on monitoring residues in food are made available on the Internet under 'Publikationer' at the homepage of the Danish Veterinary and Food Administration.

Further information on the monitoring of residues in Denmark and Europe can be obtained from Senior Scientific Adviser Flemming Kæreby (FK@FDIR.DK).

Text box 3

Veterinary antimicrobial treatment guidelines

The use of antimicrobial agents for treatment of food animals implies a risk of selection for antimicrobial resistant bacteria. The Danish Veterinary Institute introduced a veterinary antibiotic policy for prudent use of antimicrobial agents in 1997. This policy takes into account the need to treat animals efficiently and at the same time to minimize possible negative impact on human health by the emergence of resistance. General guidelines for veterinary use of antimicrobials may be valuable as part of an overall strategy for limiting the emergence and spread of antimicrobial resistance. However, to be useful on a daily basis the policy has to include guidelines for choice of antimicrobial agents for specific infections. The Danish veterinary antibiotic policy is based on knowledge of the resistance patterns in Denmark. Such knowledge is a prerequisite for the development of an operational policy.

Main principles for prudent use of antimicrobial agents for treatment of food animals

Prudent use of antimicrobial agents in veterinary medicine is important to ensure efficacious treatment of diseased animals, but also to limit the negative consequences as much as possible. The implementation of antimicrobial treatment must be based on an aetiological diagnosis. This may be based on clinical signs. However, in many cases a laboratory diagnosis is necessary. For some bacterial species the susceptibility can be predicted with great certainty. This includes e.g. *Erysipelotrix rhusiopathiae* and beta-haemolytic streptococci. For other species, such as *E. coli*, *Salmonella* and staphylococci, the susceptibility patterns vary. It is the veterinarians' responsibility to have thorough knowledge of the susceptibility patterns in the different herds under his/her care. The effect of empirically initiated treatment should be monitored and evaluated. The choice of antimicrobial treatment should be adjusted if indicated by the susceptibility test or lack of effect. In Denmark, all antimicrobial agents used for treatment of animals are prescription-only medicine.

Choice of antimicrobial agent

For the most common bacterial infectious diseases among food animals in Denmark, suggestions for choice of antimicrobial treatment are given as 1st, 2nd and 3rd priority. If prophylaxis using vaccination is most appropriate, no antimicrobial agent is recommended. These recommendations are revised once annually and published in the "Users manual" of The Danish Veterinary Institute.
Concerning the choice of antimicrobial agents for individual infections the following points have been taken into consideration:

- Narrow spectrum antimicrobials (penicillin) are given first priority
- General occurrence of resistance to the given bacterial species
- Expected clinical effect
- Mode of administration

Only antimicrobial agents that are approved for treatment of the given food animal species, are included. First priority antimicrobials are suggested as the drug of choice for a specific infection. Second priority antimicrobials can be used when occurrence of resistance or mode of administration exclude the 1st priority antimicrobials. Third priority antimicrobials should only be used after susceptibility testing, and when specific circumstances exclude 1st and 2nd priority antimicrobials. All antimicrobial agents where more than 70% of the bacteria are resistant are excluded from the recommendations, and antimicrobials where more than 40% are resistant are not given higher than 3rd priority.

Text box 3 continued ...

Exclusion or downgrading of certain antimicrobial agents

For precautionary reasons and to protect human health, certain antimicrobial agents are given low priority. In Denmark, the occurrence of antimicrobial resistance is generally low, and it is often possible to exclude certain antimicrobial agents from the list without limiting the possibilities to treat animals.

Fluoroquinolones and gentamicin are important antimicrobials in the treatment of gastrointestinal infections, septicaemia and meningitis in humans. Methicillin is important in the treatment of infections caused by staphylococci in humans. Thus, quinolones, gentamicin, cloxacillin and nafcillin are totally excluded from the list of suggested antimicrobial agents.

A number of other antimicrobial agents have been downgraded. These are ceftiofur, cefoperazone, tetracycline and lincospectin. Ceftiofur and cefoperazone are downgraded because, as third generation cephalosporins, they may select for broadspectrum penicillin resistance. Tetracyclines are downgraded because this group of antimicrobials can select for multiple resistance. Lincospectin is downgraded because it is not suitable to use combination treatment when a single drug can be used.

Further information on the veterinary antimicrobial treatment guidelines can be obtained from Veterinary Consultant Sven Erik Lind Jorsal (sej@vetinst.dk).

Human consumption

Overall

In 2001, overall consumption of antibacterials for systemic use (ATC Group J01, 2001 definition) in humans in Denmark amounted to 27.9 million DDDs or 14.3 DDD/1,000 inhabitant-days. To allow comparison with consumption in food animals, we also present data as kilograms of active compounds (Table 9). In 2001, approximately 42 tonnes of antibacterials were used in humans in Denmark, which represents an increase as compared to 2000.

Primary health care sector

Table 10 presents the consumption of antibacterials for systemic use in primary health care from 1997 to 2001 calculated using the 2001 update of the ATC classification (includes nitrofurantoin and methenamine). As for previous years, beta-lactamase sensitive penicillins (mostly phenoxy-methylpenicillin) represented 38% of total antimicrobial use in 2001. Other frequently used antimicrobials were penicillins with extended spectrum (mostly amoxicillin, pivampicillin and pivmecillinam) and macrolides, each representing approximately 19% and 16%, respectively. Detailed data on the consumption of the various macrolides is presented in Figure 2. Finally, in 2001, fluoroquinolones, combinations of penicillins including beta-lactamase inhibitors (essentially amoxicillin + clavulanate) and cephalosporins only represented 1.3%, 0.2% and 0.2% of the total consumption in primary health care, respectively.

Total consumption in primary health care showed a 5% increase between 2000 and 2001. Beta-lactamase sensitive penicillins, penicillins with extended spectrum and macrolides were responsible for more than 75% of this increase. Further analyses revealed that excessive use was mainly observed in March and April and to a lesser extent in October 2001 (Figure 3). This excess occurred at the same time in all Danish counties (Figure 4), there were differences in the overall level of consumption consistent with what has been observed in past years. Among penicillins with extended spectrum, the pattern of peaks in March and October was not seen for pivmecillinam, which is only used to treat urinary tract infections. Additionally, the pattern was not seen for other classes of antibacterials that are not used to treat

Table 9. Consumption of antibacterials for systemic use in humans (kg active compound), Denmark. These data must only be used for comparison with consumption in food animals. For monitoring in human primary health care and hospitals, the correct way of expressing consumption is to use DDDs per population-days (see Tables 10 and 11). Consumption in kg active compound has been recalculated from original data expressed as a number of DDDs and includes both primary health care and hospitals. These data therefore represent an estimate of consumption expressed as a number of kg active compound

DANMAP 2001

ATC group a)	Therapeutic group	Year					
		1997	1998	1999	2000	2001	(low est.-high est.) b)
J01AA	Tetracyclines	1,692	1,692	1,590	1,701	1,705	
J01B	Amphenicols	1	1	0	1	0	
J01CA	Penicillins with extended spectrum	5,513	5,467	5,181	5,135	5,371	
J01CE	Beta-lactamase sensitive penicillins	18,813	19,947	18,790	19,782	20,715	
J01CF	Beta-lactamase resistant penicillins	1,913	2,115	2,416	2,654	3,225	
J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	48	55	51	51	144	
J01D	Cephalosporins and related substances	660	657	685	727	785	(364-1,205)
J01EA	Trimethoprim and derivatives	245	256	258	263	280	
J01EB	Short-acting sulfonamides	3,498	3,493	3,289	3,148	3,111	
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	337	322	279	285	283	
J01FA	Macrolides	4,227	4,536	4,147	4,040	4,089	(2,966-5,212)
J01FF	Lincosamides	28	38	33	33	42	(34-51)
J01G	Aminoglycosides	32	31	32	32	28	
J01MA	Fluoroquinolones	320	343	321	290	335	(236-434)
J01MB	Other quinolones	15	17	16	0	0	
J01XA	Glycopeptides	25	27	32	37	36	
J01XC	Steroid antibacterials (fusidic acid)	74	73	78	70	59	
J01XD	Imidazoles	128	127	140	154	168	
J01XE	Nitrofuran derivatives	137	141	141	149	152	
J01XX	Other antibacterials (methenamine)	2,233	2,132	1,956	1,792	1,637	(1,309-1964)
J01	Antibacterials for systemic use (Total) c)	39,938	41,469	39,436	40,344	42,163	(40,185-44,142)

a) From the 2001 edition of the Anatomical Therapeutic Chemical (ATC) classification system
b) When 2 different DDDs existed for different presentations, e.g. oral and parenteral, of an antimicrobial, i.e. for cefuroxime, erythromycin, clindamycin, ciprofloxacin and methenamine, an average DDD was used. For 2001, extremes values, i.e. estimates using the lowest and the highest DDD, are given in parentheses
c) Does not include polymyxins

Table 10. Consumption of antibacterials for systemic use in primary health care (DDD/1,000 inhabitant-days), Denmark

DANMAP 2001

ATC group a)	Therapeutic group	Year				
		1997	1998	1999	2000	2001
J01AA	Tetracyclines	0.98	0.98	0.93	0.98	0.99
J01CA	Penicillins with extended spectrum	2.39	2.39	2.29	2.30	2.47
J01CE	Beta-lactamase sensitive penicillins	4.57	4.81	4.48	4.70	4.91
J01CF	Beta-lactamase resistant penicillins	0.34	0.40	0.48	0.52	0.65
J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	0.02	0.03	0.02	0.02	0.03
J01DA	Cephalosporins and related substances	0.02	0.03	0.02	0.02	0.03
J01EA	Trimethoprim and derivatives	0.30	0.32	0.32	0.33	0.35
J01EB	Short-acting sulfonamides	0.41	0.41	0.38	0.37	0.36
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	0.08	0.04	0.03	0.03	0.04
J01FA	Macrolides	2.03	2.28	2.17	2.02	2.10
J01FF	Lincosamides	0.01	0.01	0.01	0.01	0.01
J01MA	Fluoroquinolones	0.22	0.23	0.20	0.15	0.17
J01XB	Polymyxins	0.03	0.02	0.03	0.03	0.02
J01XC	Steroid antibacterials (fusidic acid)	0.02	0.02	0.02	0.02	0.01
J01XE	Nitrofuran derivatives (nitrofurantoin)	0.35	0.36	0.36	0.38	0.39
J01XX	Other antibacterials (methenamine)	0.46	0.43	0.40	0.36	0.33
J01	Antibacterials for systemic use (Total)	12.24	12.76	12.14	12.25	12.85

a) From the 2001 edition of the Anatomical Therapeutic Chemical (ATC) classification system

respiratory tract infections, such as sulfonamides, trimethoprim or fluoroquinolones. These findings suggest a link with outbreaks of respiratory tract infections. In 2001, there was marked peak of influenza activity in February, i.e. a few weeks before the increase in antimicrobial use. Additionally, we identified, in February and March 2001, a clearly increased frequency of articles on bacterial meningitis published in the major Danish newspapers. These articles were commenting on an outbreak of meningococcal meningitis in Denmark, including reports on the death of a patient following misidentification of disease, and could well have resulted in more concern about meningitis among parents and general practioners, and thus in more prescriptions of antimicrobials. Nevertheless, the reason for the overall increase in antimicrobial use in primary health care in 2001 remains unexplained.

In the DANMAP 2000 report, we presented the decrease in consumption of fluoroquinolones following removal of their subsidisation in May 1999. Despite a slowly increasing trend somewhat parallel to the one that was observed before the change in reimbursement, the reduction in fluoroquinolone consumption achieved by the change in subsidisation has been maintained in 2001 (Figure 5). The latest change in subsidisation of antimicrobials took place on 1st March 2000 when a new policy started to be applied to all subsidised medicines including those antimicrobials that were still subsidised, i.e. penicillins, sulfonamides, trimethoprim, macrolides, fusidic acid and nitrofurantoin. In short, adults must have purchased 500 DKK worth of prescription medicines during the past year before the insurance system started subsidising 50% of the price. This rule does not apply to children below 18 years of age that receive 50% subsidisation. Additionally, higher percentages of subsidisation are applied to annual purchases over 1,200 DKK and again over 2,800 DKK for both adults and children. As of now, this change does not seem to have had an impact on total consumption of antibacterials in primary health care (Figure 6).

Hospitals

Table 11 presents the consumption of antibacterials for systemic use in hospitals from 1997 to 2001. Total consumption in hospitals was 457 DDD/1,000 bed-days in 2000 and estimated to be approximately 484 DDD/ 1,000 bed-days in 2001. Use in hospitals may comprise small amounts of antibacterials given to outpatients, whereas the number of bed-days does not include outpatient care. Therefore, hospital consumption data in this report are likely to be slightly overestimated.

DANMAP 2001

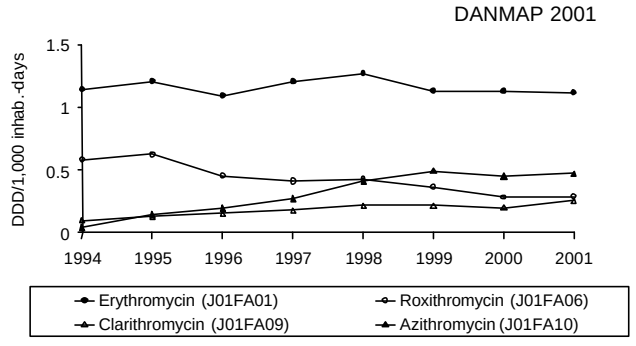


Figure 2. Consumption of macrolides (J01FA) for systemic use in primary health care, Denmark, 1994-2001

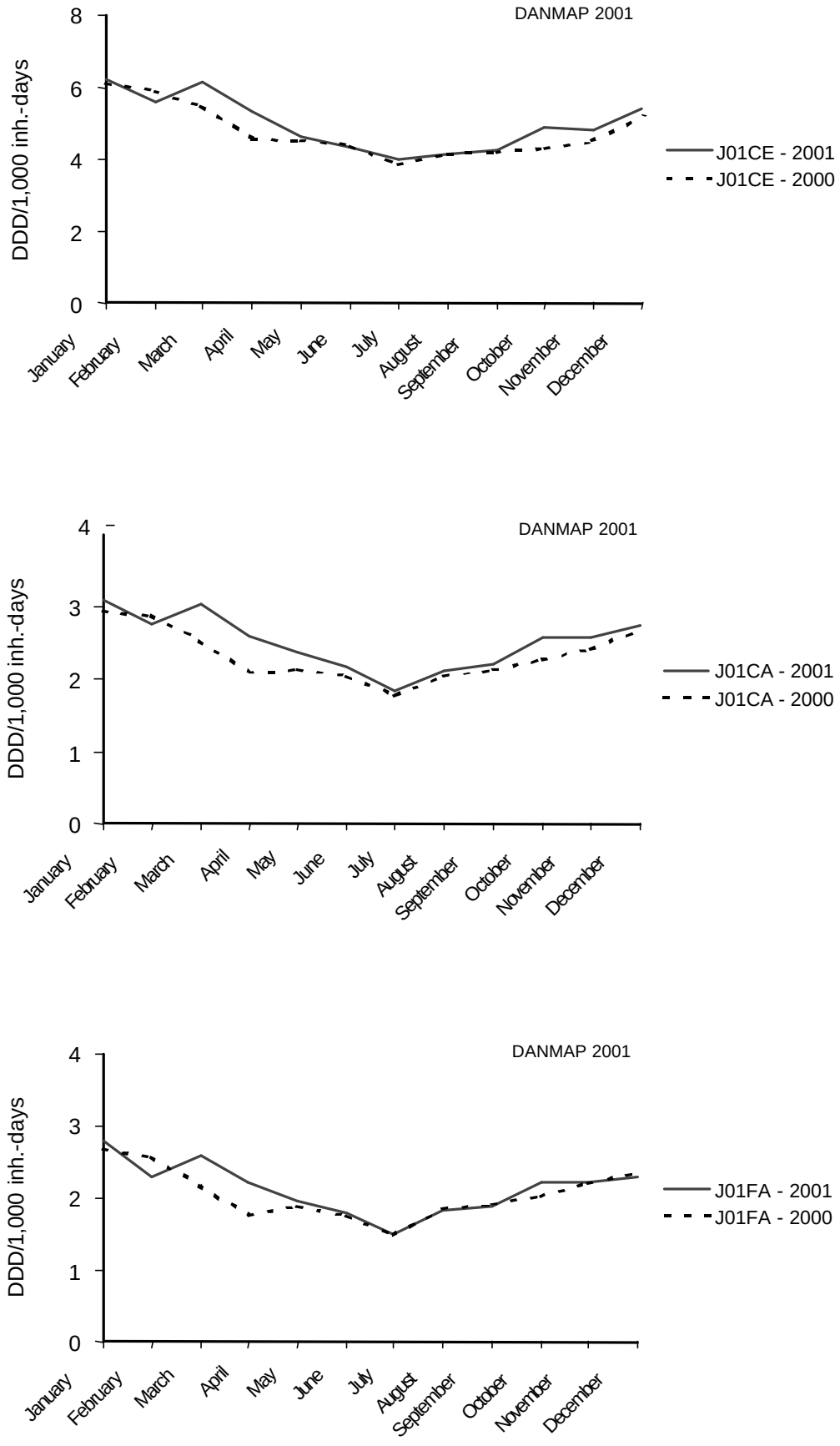


Figure 3. Monthly consumption of beta-lactamase sensitive penicillins (J01CE), penicillins with extended spectrum (J01CA) and macrolides (J01FA) in primary health care, Denmark, 2000-2001

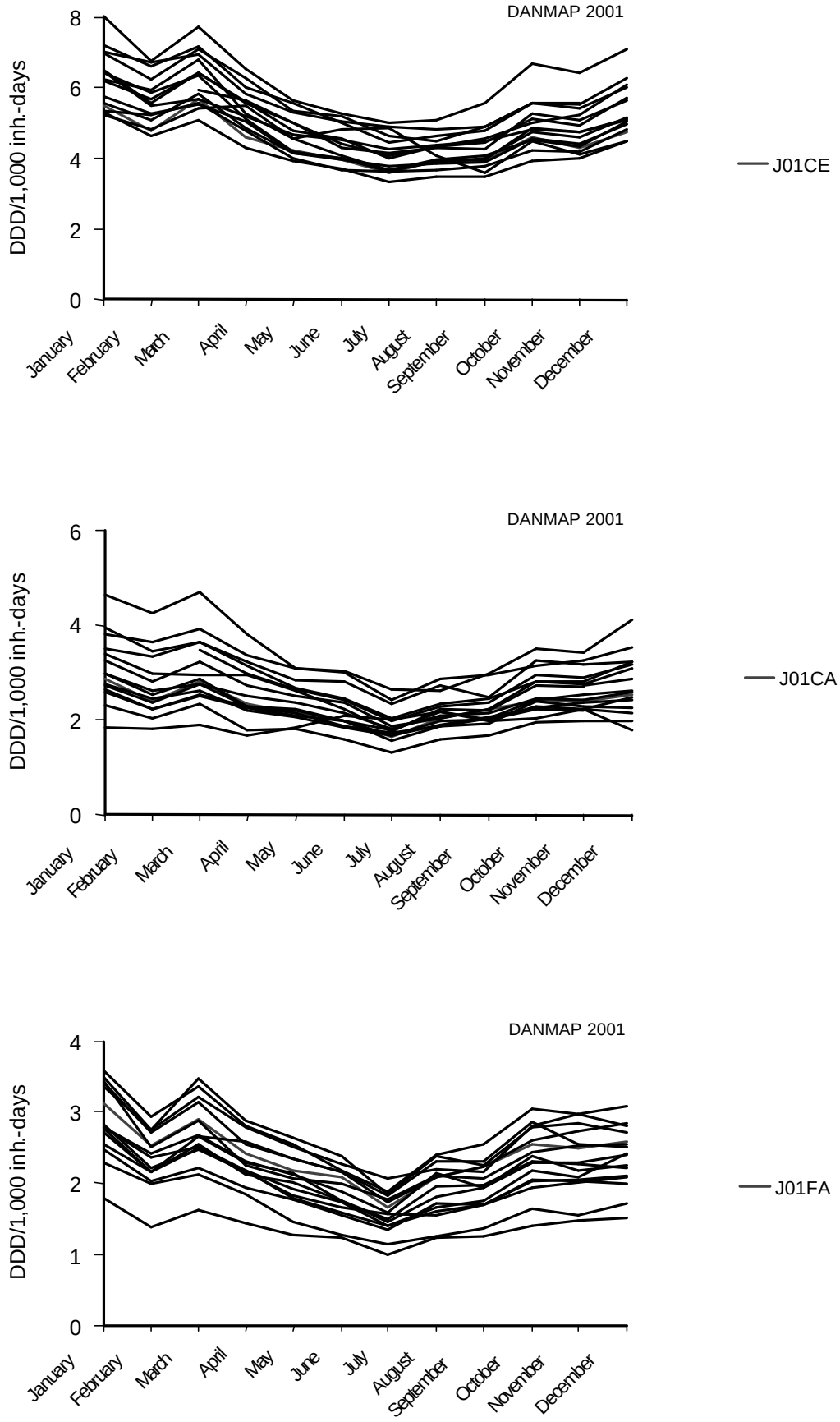


Figure 4. Monthly consumption of beta-lactamase sensitive penicillins (J01CE), penicillins with extended spectrum (J01CA) and macrolides (J01FA) in primary health care, by county, Denmark, 2001

Nevertheless, comparison with those few data available from other countries show that antimicrobial consumption in Danish hospitals is among the lowest. In 2001, all penicillins combined represented almost 60% of hospital antimicrobial use in Denmark. Cephalosporins (mainly cefuroxime) and fluoroquinolones (mainly ciprofloxacin) only represented 12.1% and 6% of total hospital use, respectively. Tetracyclines, combinations of penicillins incl. beta-lactamase inhibitors, carbapenems and glycopeptides each represented less than 1% of total hospital use.

Although the prescription of antimicrobials in Danish hospitals can be described as conservative, there has been a steady increase in hospital antimicrobial consumption overall and for specific classes including cephalosporins, fluoroquinolones and combinations of penicillins incl. beta-lactamase inhibitors (Table 11). This increase was mainly due to a 13% increase in the number of DDDs of antimicrobials registered by hospital pharmacies (numerator) from approximately 2.3 million DDDs in 1997 to 2.7 million DDDs in 2000, while there was only a 3% decrease in the total number of hospital

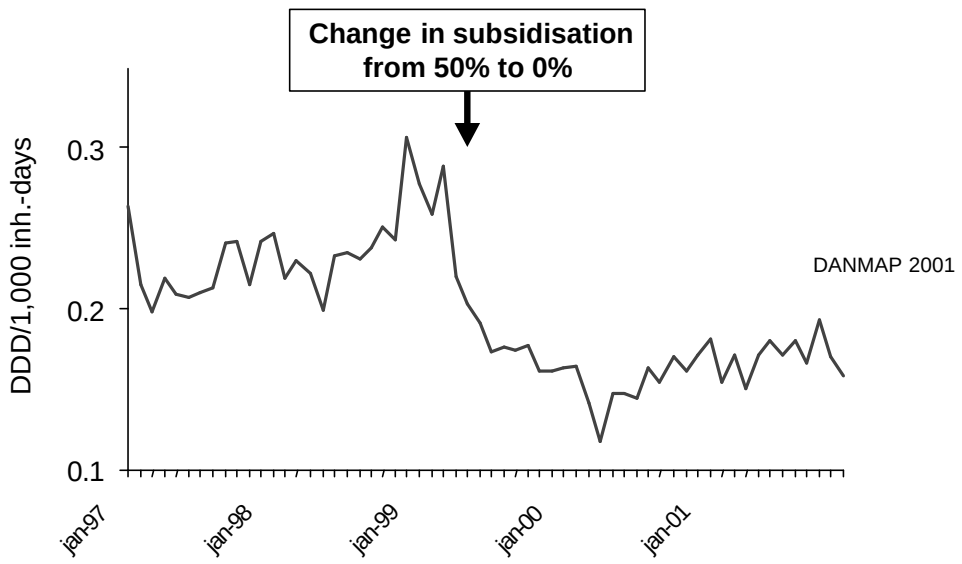


Figure 5. Monthly consumption of fluoroquinolones (J01MA) in primary health care, Denmark, January 1997 - December 2001

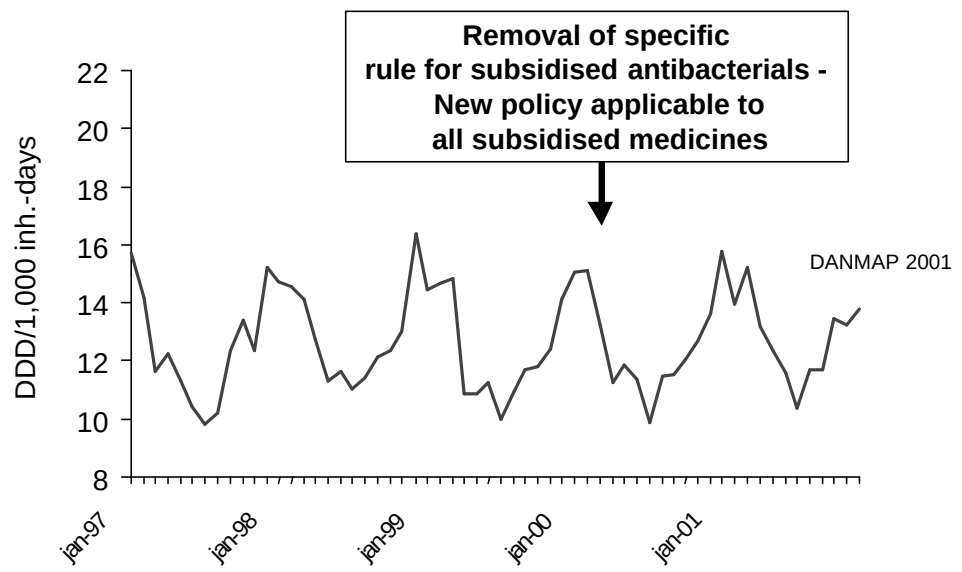


Figure 6. Monthly consumption of antibacterials for systemic use (J01, 2001 definition) in primary health care, Denmark, January 1997 - December 2001

bed-days registered in Denmark (denominator) between 1997 and 2000. However, the average length of stay in Danish hospitals decreased from 5.7 days in 1997 to 5.2 days in 2000. An explanation for the increase in hospital antimicrobial consumption could therefore be that, as a result of earlier discharge, bed-days registered by hospitals may now originate from sicker patients. It could also be that to expedite discharges patients now receive more intensive treatment. Nevertheless, and because it concerns so-called “broad-spectrum” antimicrobials, this increase is of concern and deserves close surveillance.

Table 11. Consumption of antibacterials for systemic use in hospitals (DDD/1,000 bed-days). This represented more than 98% of the total DDDs used in hospitals in Denmark in 2001. Psychiatric hospitals, private hospitals and one rehabilitation center were excluded.

DANMAP 2001

ATC group a)	Therapeutic group	Year				
		1997	1998	1999	2000	*2001 b)*
J01AA	Tetracyclines	3.3	3.2	2.7	2.8	*2.8*
J01CA	Penicillins with extended spectrum	108.6	109.6	108.1	112.5	*114.4*
J01CE	Beta-lactamase sensitive penicillins	77.2	85.9	91.7	98.4	*105.4*
J01CF	Beta-lactamase resistant penicillins	43.2	44.4	46.8	52.4	*59.6*
J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	0.3	0.4	0.4	0.9	*1.7*
J01DA	Cephalosporins	44.7	46.5	49.9	53.7	*58.8*
J01DF	Monobactams	0.6	0.1	0.1	0.2	*0.1*
J01DH	Carbapenems	3.6	2.4	3.2	3.9	*4.2*
J01EA	Trimethoprim and derivatives	4.0	4.2	3.6	3.6	*4.3*
J01EB	Short-acting sulfonamides	12.4	12.7	12.3	12.0	*12.3*
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	4.4	12.9	13.6	13.9	*13.4*
J01FA	Macrolides	33.7	34.0	32.1	32.0	*32.4*
J01FF	Lincosamides	1.3	1.8	1.4	1.6	*1.7*
J01GB	Aminoglycosides	19.5	19.5	20.2	21.0	*18.4*
J01MA	Fluoroquinolones	14.3	15.1	18.4	22.7	*27.9*
J01XA	Glycopeptides	2.1	2.3	2.8	3.2	*3.2*
J01XB	Polymyxins	0.4	0.2	0.3	0.4	*0.3*
J01XC	Steroid antibacterials (fusidic acid)	2.5	2.4	2.6	2.3	*2.0*
J01XD	Imidazoles	13.9	14.0	15.8	17.6	*19.6*
J01XE	Nitrofuran derivatives	0.6	0.5	0.3	0.4	*0.3*
J01XX	Other antibacterials (methenamine)	1.7	1.8	1.5	1.4	*1.3*
J01	Antibacterials for systemic use (Total)	392.4	413.9	428.0	457.1	*484.0*

a) From the 2001 edition of the Anatomical Therapeutic Chemical (ATC) classification system.
b) Estimated consumption using the exact number of DDDs and an estimate of the number of bed-days in 2001 based on past trends.

Resistance in zoonotic bacteria

Salmonella

Table 12 shows the *Salmonella* serotype distribution of isolates from food animals, food and humans. The phage type distributions of *Salmonella* Typhimurium and *Salmonella* Enteritidis are presented in Tables 13 and 14.

Salmonella from food animals

Salmonella isolates from pigs and poultry (broilers and layers) were mainly from subclinical infections, while the majority of isolates from cattle were from clinical cases of salmonellosis. Only one isolate of each serotype per farm was included in this report.

Table 12. Distribution (%) of Salmonella *serotypes isolated from animals, foods and humans among the isolates selected for susceptibility testing, Denmark* DANMAP 2001

Serotypes	Poultry	Broiler meat	Cattle	Beef	Pigs	Pork	Humans
Agona	3	1			<1		5
Derby	1		1	2	11	18	1
Dublin			51	67	<1	4	<1
Enteritidis	34	11	1		<1		49
Hadar	3	7				1	2
Infantis	9	5			7	8	<1
Newport		9					1
Senftenberg	1	<1			<1		<1
Typhimurium	20	2	35	7	65	14	20
Virchow		6					1
Others incl. not typable	28	59	11	24	16	54	17
Number of isolates	74	161	88	42	338	76	2,918

Table 13. Distribution (%) of Salmonella *Typhimurium phages types from animals, food and humans among the isolates selected for susceptibility testing, Denmark* DANMAP 2001

Phage type	Poultry	Cattle	Pigs	Pork	Humans
1			<1		3
3			<1		4
12	40	23	38	9	20
17		10		9	4
66		3	6		1
104/104a/104b	7	10	6	18	15
120		16	2		7
135		3	<1		2
170		26	10	9	3
193			5	18	5
Others incl. not typable	53	10	31	36	37
Number of isolates	15	31	218	11	569

Due to the high number of *Salmonella* isolates from pigs a representative subsample was randomly selected among all *Salmonella* pig isolates that were serotyped at the Danish Veterinary Institute in 2001. In contrast, the *Salmonella* samples from cattle and poultry consisted of one isolate from all farms where *Salmonella* was detected.

Tables 15 and 16 show the MIC distribution and the occurrence of resistance in *S.* Enteritidis from poultry and in *S.* Typhimurium from poultry, cattle and pigs in 2001.

When comparing the results from Table 15 with the corresponding results from 2000 the resistance levels among *S*. Enteritidis have remained almost unchanged. In contrast to previous years none of the *S.* Enteritidis isolates from poultry were resistant to nalidixic acid. Among *S.* Typhimurium isolates from cattle, resistance to tetracycline, sulfamethoxazole and streptomycin remained unchanged in 2001 despite a reduction in the percentage of pentaresistant DT104 isolates, from 35% in 2000 to 10% in 2001. Among non-DT104 phage types from cattle, resistance to tetracycline, sulfonamide and streptomycin increased from 17% [6.6; 33.7], 20% [8.4; 36.9] and 17% [6.6; 33.7] to 36% [18.6; 55.9], 36% [18.6; 55.9] and 39% [21.5; 59,4], respectively from 2000 to 2001. With a sample size of 35 isolates in 2000 and 28 isolates in 2001, these differences were statistically non-significant.

From 1996 to 1999, the level of tetracycline resistance in *S*. Typhimurium isolates from pigs was almost unchanged. We have seen a significant increase in

Table 14. Distribution (%) of Salmonella *Enteritidis phages types from animals, food and humans among the isolates selected for susceptibility testing, Denmark* DANMAP 2001

Phage type	Poultry	Broiler meat	Humans
1b	12		<1
1		18	5
4	8	59	24
6	12	6	4
6a		18	2
8	32		30
21/21b	8		4
34	4		12
Others incl. not typable	24		19
Number of isolates	25	17	637

Table 15. Distribution of MICs and occurrence of resistance among Salmonella *Enteritidis from poultry (n=25), Denmark*

DANMAP 2001

Compound	% Resistant [95% Confidence interval]		Distribution (%) of MICs <=0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512
Tetracycline	4	[0.1-20.4]							96.0					4.0 a)			
Chloramphenicol	0	[0.0-13.7]								52.0	48.0						
Florfenicol	0	[0.0-13.7]								96.0	4.0						
Ampicillin	4	[0.1-20.4]						76.0	20.0					4.0			
Ceftiofur	0	[0.0-13.7]					44.0	56.0									
Sulfonamide	0	[0.0-13.7]											52.0	44.0	4.0		
Trimethoprim	0	[0.0-13.7]								100							
Apramycin	0	[0.0-13.7]								96.0	4.0						
Gentamicin	0	[0.0-13.7]						100									
Neomycin	0	[0.0-13.7]							100								
Spectinomycin	0	[0.0-13.7]										36.0	64.0				
Streptomycin	0	[0.0-13.7]								92.0	8.0						
Ciprofloxacin	0	[0.0-13.7]	88.0	12.0													
Nalidixic acid	0	[0.0-13.7]								88.0	12.0						
Colistin	0	[0.0-13.7]								96.0	4.0						

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

resistance to tetracycline from 14% in 1999 to 25% in 2000 and 30% in 2001 (Figure 7). This is not explained by increased occurrence of *S.* Typhimurium DT104 among the isolates. The increase in tetracycline resistance, however, coincided with a 72% increase in usage of tetracycline in pigs during the same period. We consider it likely that the increase in resistance is a reflection of increased usage. Two *S*. Typhimurium isolates from pigs had ciprofloxacin MIC values of 0.25 and 1, respectively, (Table 16) and were resistant to nalidixic acid. According to NCCLS guidelines, these isolates are susceptible to ciprofloxacin, however clinical experience shows that in humans the response of such isolates to treatment with ciprofloxacin is considerably reduced.

Salmonella from food

In 2001, a total of 279 isolates were included in this report, 161 isolates originated from broiler meat, 42 from beef and 76 from pork. Tables 17 and 18 show the MIC distribution and the occurrence of resistance in *S.* Enteritidis from broiler meat and in *S.* Typhimurium from pork. All 18 *S*. Enteritidis isolates were isolated from imported products. Eight of the 11 *S.* Typhimurium isolates were from Danish pork and the remaining 3 from imported products. Due to the low number of isolates in each food category it is not possible to determine if there has been a change in resistance over time.

Salmonella from humans

In 2001, 2,918 human infections with zoonotic *Salmonella* serotypes were registered in Denmark, an increase from 43.3 cases per 100,000 inhabitants in 2000 to 54.5 in 2001.

Antimicrobial resistance among human *S.* Enteritidis isolates remained low in 2001 (Table 19). When comparing the isolates associated with travel abroad with domestically acquired isolates, no difference was detected in the level of antimicrobial resistance (Table 19).

Among *S*. Typhimurium isolates, however, antimicrobial resistance was in general higher in isolates from cases associated with travel abroad than in isolates from domestic cases (Table 20, Figure 7). From 1996 to 1999, resistance to ampicillin, sulfonamide, tetracycline and chloramphenicol increased among *S*. Typhimurium from domestic human cases (Figure 7). These increases are mainly explained by an increase in the proportion of *S.* Typhimurium DT104 and related phage types among the *S.* Typhimurium isolates. Since 1999, the proportion of DT104 isolates among domestic *S*. Typhimurium isolates has decreased. In the same period, we have observed a significant increase in tetracycline, sulfonamide and streptomycin resistance among *S*. Typhimurium phage types other than DT104 and related phage types (DTU302, DT104a, DT104b). From 1997 to 2001, only a few human *S*. Typhimurium cases acquired domestically were resistant to nalidixic acid. The only exception was a small increase in 1998, due to an outbreak with a nalidixic acid resistant *S*. Typhimurium DT104 strain. In contrast, nalidixic acid resistance has increased since 1997 among isolates of *S.* Typhimurium from cases with a history of travel abroad.

Table 16. Distribution of MICs and occurrence of resistance among Salmonella *Typhimurium from broilers (n=15), cattle (n=31) and pigs (n=218), Denmark*

DANMAP 2001

Compound	Animal species	% Resistant [95% Confidence interval]		Distribution (%) of MICs																
				<=0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Tetracycline	Poultry	20	[4.3-48.1]							73.3	6.7			13.3	6.7 a)				
	Cattle	42	[24.6-60.9]							54.8	3.2			9.7	32.3				
	Pigs	30	[23.8-36.4]							67.0	3.2		0.5	6.9	22.5				
Chloramphenicol	Poultry	7	[0.2-32.0]							6.7	66.7	20.0				6.7			
	Cattle	10	[2.0-25.8]							16.1	38.7	35.5				9.7			
	Pigs	7	[3.9-11.1]							12.4	55.5	23.4	1.8		2.3	4.6			
Florfenicol	Poultry	7	[0.2-32.0]							13.3	73.3	6.7		6.7					
	Cattle	10	[2.0-25.8]							9.7	80.6			9.7					
	Pigs	4	[1.6-7.1]							7.8	81.7	5.5	1.4	3.2	0.5				
Ampicillin	Poultry	13	[1.7-40.5]						80.0	6.7					13.3				
	Cattle	26	[11.9-44.6]						58.1	16.1					25.8				
	Pigs	11	[7.2-15.9]						71.1	16.5	1.4				11.0				
Ceftiofur	Poultry	0	[0.0-21.8]					73.3	26.7										
	Cattle	0	[0.0-11.2]					74.2	25.8										
	Pigs	0	[0.0-1.7]					73.9	24.8	1.4									
Sulfonamide	Poultry	13	[1.7-40.5]											33.3	46.7	6.7			13.3
	Cattle	42	[24.6-60.9]											54.8	3.2				41.9
	Pigs	30	[24.3-36.8]											58.7	11.0				30.3
Trimethoprim	Poultry	0	[0.0-21.8]								100								
	Cattle	0	[0.0-11.2]								100								
	Pigs	9	[5.7-13.8]								90.8				9.2				
Apramycin	Poultry	0	[0.0-21.8]								93.3	6.7							
	Cattle	0	[0.0-11.2]								96.8	3.2							
	Pigs	<1	[0.01-2.5]								99.5					0.5			
Gentamicin	Poultry	0	[0.0-21.8]						100										
	Cattle	0	[0.0-11.2]						96.8	3.2									
	Pigs	<1	[0.01-2.5]						98.6	0.9				0.5					
Neomycin	Poultry	7	[0.2-32.0]							93.3					6.7				
	Cattle	0	[0.0-11.2]							100									
	Pigs	7	[4.3-11.7]							92.2	0.5				7.3				
Spectinomycin	Poultry	7	[0.2-32.0]										20.0	66.7	6.7		6.7		
	Cattle	13	[3.6-29.8]										3.2	83.9			12.9		
	Pigs	13	[8.7-18.0]										1.4	84.9	0.9	0.9	11.9		
Streptomycin	Poultry	13	[1.7-40.5]								6.7	26.7	53.3		6.7	6.7			
	Cattle	45	[27.3-64.0]								3.2	35.5	16.1		3.2	41.9			
	Pigs	24	[18.4-30.1]								0.9	65.6	9.6	1.4	6.0	16.5			
Ciprofloxacin	Poultry	0	[0.0-21.8]	100															
	Cattle	0	[0.0-11.2]	100															
	Pigs	0	[0.0-1.7]	96.3	2.3	0.5	0.5		0.5										
Nalidixic acid	Poultry	0	[0.0-21.8]								93.3		6.7						
	Cattle	0	[0.0-11.2]								100								
	Pigs	<1	[0.1-3.3]								93.1	6.0					0.9		
Colistin	Poultry	0	[0.0-21.8]								100								
	Cattle	0	[0.0-11.2]								100								
	Pigs	0	[0.0-1.7]								100								

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

Farm to table

Although *S*. Enteritidis was the predominant serotype in layers in Denmark, it was rare in broiler production, and hardly isolated from other animal species. Table 21 presents a comparison of resistance among *S*. Enteritidis from Danish poultry, imported broiler meat and isolates from human cases acquired domestically and abroad. The resistance levels among *S*. Enteritidis isolates from Danish poultry (mainly layers) and domestically acquired human cases were not significantly different. In contrast, significantly higher levels of nalidixic acid resistance were found in isolates from imported broiler meat. National estimates of sources of human salmonellosis (Annual Report on Zoonosis in Denmark) showed that imported poultry accounted for 7% of human Salmonella cases in 2001, while domestically produced table eggs accounted for 29%. This is consistent with the observed levels of nalidixic acid resistance in domestically acquired human cases.

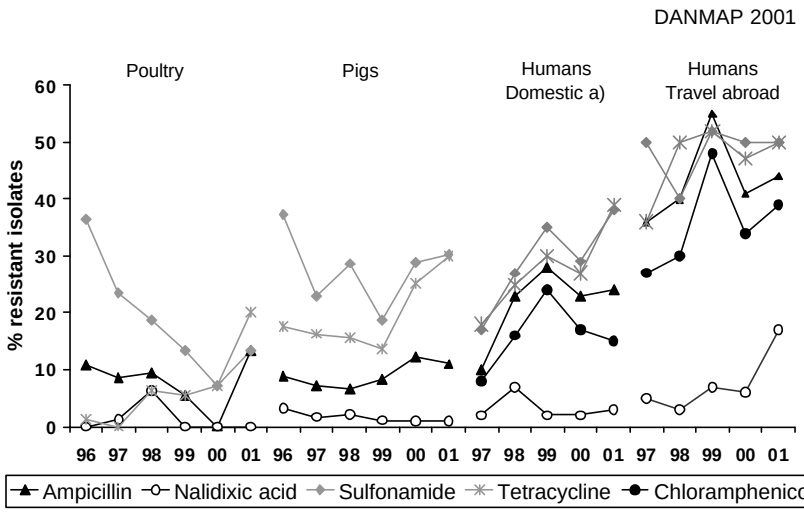


Figure 7. Trends in resistance to some selected antimicrobials among Salmonella *Typhimurium isolated from poultry and pigs and from human cases, Denmark*

a) Includes cases where origin of infection is non-documented and may therefore include some isolates acquired abroad but not documented as such.

Table 17. Distribution of MICs and occurrence of resistance in Salmonella *Enteritidis from imported broiler meat (n=18), Denmark*

DANMAP 2001

Compound	% Resistant	[95% Confidence interval]	Distribution (%) of MICs															
			<=0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Tetracycline	17	[3.6-41.4]							83.3					16.7 a)				
Chloramphenicol	0	[0.0-18.5]							11.1	83.3	5.6							
Florfenicol	0	[0.0-18.5]							27.8	66.7	5.6							
Ampicillin	6	[0.1-27.3]						83.3	5.6	5.6				5.6				
Ceftiofur	0	[0.0-18.5]					94.4		5.6									
Sulfonamide	0	[0.0-18.5]											5.6	88.9	5.6			
Trimethoprim	0	[0.0-18.5]								100								
Apramycin	0	[0.0-18.5]								100								
Gentamicin	0	[0.0-18.5]						100										
Neomycin	17	[3.6-41.4]							83.3			5.6	5.6	5.6				
Spectinomycin	0	[0.0-18.5]										100						
Streptomycin	0	[0.0-18.5]								94.4	5.6							
Ciprofloxacin	0	[0.0-18.5]	61.1			33.3	5.6											
Nalidixic acid	39	[17.3-64.3]								61.1						38.9		
Colistin	0	[0.0-18.5]								94.4	5.6							

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

Table 18. Distribution of MICs and occurrence of resistance in Salmonella *Typhimurium from pork (n=11), Denmark*

DANMAP 2001

Compound	% Resistant	[95% Confidence interval]	Distribution (%) of MICs															
			<=0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Tetracycline	45	[16.7-76.6]							54.5				9.1	36.4 a)				
Chloramphenicol	9	[0.2-41.3]							9.1	45.5	36.4				9.0			
Florfenicol	9	[0.2-41.3]							9.1	81.8			9.1					
Ampicillin	27	[6.0-61.0]						27.3	45.5					27.3				
Ceftiofur	0	[0.0-28.5]					54.5	45.5										
Sulfonamide	45	[16.7-76.6]											45.5	9.1				45.5
Trimethoprim	18	[2.3-51.8]								81.8				18.2				
Apramycin	0	[0.0-28.5]								100								
Gentamicin	0	[0.0-28.5]						100										
Neomycin	18	[2.3-51.8]							81.8					18.2				
Spectinomycin	9	[0.2-41.3]											90.9			9.1		
Streptomycin	36	[10.9-69.2]									63.6			9.1	27.3			
Ciprofloxacin	0	[0.0-28.5]	100															
Nalidixic acid	0	[0.0-28.5]								100								
Colistin	0	[0.0-28.5]								100								

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

Table 19. Occurrence of resistance (%) among Salmonella *Enteritidis isolated from humans by origin of infection, Denmark*

DANMAP 2001

Compound	Travel abroad		Domestic a)	
	% Resistant	[95% Confidence interval]	% Resistant	[95% Confidence interval]
Tetracycline	3	[0.7-9.9]	3	[1.7-4.5]
Chloramphenicol	0	[0.0-4.2]	0	[0.0-0.6]
Ampicillin	1	[0.03-6.3]	1	[0.5-2.4]
Ceftiofur	0	[0.0-4.2]	0	[0.0-0.6]
Sulfonamide	1	[0.03-6.3]	1	[0.4-2.2]
Trimethoprim	1	[0.03-6.3]	1	[0.6-2.6]
Apramycin	0	[0.0-4.2]	<1	[0.04-1.2]
Gentamicin	0	[0.0-4.2]	0	[0.0-0.6]
Kanamycin	1	[0.03-6.3]	<1	[0.04-1.2]
Spectinomycin	0	[0.0-4.2]	0	[0.0-0.6]
Streptomycin	0	[0.0-4.2]	<1	[0.0-0.9]
Nalidixic acid	8	[3.3-16.1]	5	[3.1-6.7]
Colistin	0	[0.0-4.2]	0	[0.0-0.6]
Number of isolates	86		598	

a) Includes cases where origin of infection is non-documented and may therefore include some isolates acquired abroad but not documented as such

Table 20. Occurrence of resistance (%) among Salmonella *Typhimurium isolated from humans by origin of infection, Denmark*

DANMAP 2001

Compound	Travel abroad		Domestic a)	
	% Resistant	[95% Confidence interval]	% Resistant	[95% Confidence interval]
Tetracycline	50	[32.9-67.1]	39	[34.5-42.8]
Chloramphenicol	39	[23.1-56.5]	15	[11.8-17.9]
Ampicillin	44	[27.9-61.9]	24	[20.3-27.6]
Ceftiofur	3	[0.1-14.5]	0	[0.0-0.7]
Sulfonamide	50	[32.9-67.1]	38	[33.9-42.2]
Trimethoprim	11	[3.1-26.1]	10	[7.2-12.3]
Apramycin	3	[0.1-14.5]	<1	[0.0-1.0]
Gentamicin	3	[0.1-14.5]	<1	[0.3-2.1]
Kanamycin	0	[0.0-9.7]	3	[1.7-4.7]
Spectinomycin	31	[16.4-48.1]	15	[11.8-17.9]
Streptomycin	47	[30.4-64.5]	34	[30.0-38.1]
Nalidixic acid	17	[6.4-32.8]	3	[1.7-4.7]
Colistin	0	[0.0-9.7]	0	[0.0-0.7]
Number of isolates	36		547	

a) Includes cases where origin of infection is non-documented and may therefore include some isolates acquired abroad but not documented as such

S. Dublin is the predominant *Salmonella* serotype in both cattle and beef (Table 12). In humans, 0.9% of all *Salmonella* infections in 2001 were caused by *S*. Dublin. In 2001, 45 *S*. Dublin isolates from cattle were included in this report. In general, the isolates were susceptible to most antimicrobials. One (2%) isolate was resistant to nalidixic acid. This level is not different from previous years. All *S*. Dublin isolates from beef and humans were susceptibel to all antimicrobials in the test panel.

The comparison of resistance levels among *S*. Typhimurium isolates from animals, pork and domestically-acquired human cases is presented in Table 22. The frequency of pentaresistent *S*. Typhimurium DT104 in the samples has a strong

Table 21. Comparison of resistance (%) among Salmonella *Enteritidis from food animals, imported food and human cases acquired domestically or associated with travel abroad, Denmark.*

DANMAP 2001

Compound	Poultry	Broiler meat	Humans	
	Danish	Imported	Domestic a)	Travel abroad
	%	%	%	%
Tetracyclines	4	17	3	3
Chloramphenicol	0	0	0	0
Ampicillin	4	6	1	1
Ceftiofur	0	0	0	0
Sulfonamide	0	0	1	1
Trimethoprim	0	0	1	1
Apramycin	0	0	<1	0
Gentamicin	0	0	0	0
Spectinomycin	0	0	0	0
Streptomycin	0	0	<1	0
Nalidixic acid	0	39	5	8
Colistin	0	0	0	0
Number of isolates	25	18	598	86

a) Includes cases where origin of infection is non-documented and may therefore include some isolates acquired abroad but not documented as such

influence on the resistance levels. Therefore comparison of resistance levels among *S.* Typhimurium phage types other than DT104 and related phage types (DT104b, DTU302) from food animals, pork and domestically acquired human cases were made; the results are presented in Table 23. The similar levels of resistance presented in Tables 22 and 23 show that pentaresistant **DT104 only account for a small proportion of all** *S.* Typhimurium isolates. The observed increase in tetracycline resistance in domestically acquired *S.* Typhimurium isolates from humans is likely to be associated with consumption of Danish pork.

Table 22. Comparison of resistance (%) among Salmonella *Typhimurium from food animals, food of Danish origin, imported food and human cases acquired domestically or associated with travel abroad, Denmark*

DANMAP 2001

Compound	Poultry	Cattle	Pigs	Pork	Humans	
	Danish %	Danish %	Danish %	a) %	Domestic b) %	Travel abroad %
Tetracycline	20	42	30	45	39	50
Chloramphenicol	7	10	7	9	15	39
Ampicillin	13	26	11	27	24	44
Ceftiofur	0	0	0	0	0	3
Sulfonamide	13	42	30	45	38	50
Trimethoprim	0	0	9	18	10	11
Apramycin	0	0	<1	0	<1	3
Gentamicin	0	0	<1	0	<1	3
Spectinomycin	7	13	13	9	15	31
Streptomycin	13	45	24	36	34	47
Nalidixic acid	0	0	<1	0	3	17
Colistin	0	0	0	0	0	0
Number of isolates	15	31	218	11	547	36

a) 8 isolates originated from Danish pork and 3 isolates from imported pork
b) Includes cases where origin of infection is non-documented and may therefore include some isolates acquired abroad but not documented as such.

Table 23. Comparison of resistance (%) among Salmonella *Typhimurium other than DT104, DT104a, DT104b and DTU302 from food animals, pork and human cases acquired domestically, Denmark*

DANMAP 2001

Compound	Poultry	Cattle	Pigs	Pork	Humans
	Danish %	Danish %	Danish %	a) %	Domestic b) %
Tetracyclines	14	36	27	44	31
Chloramphenicol	0	0	3	0	3
Ampicillin	7	18	7	22	14
Ceftiofur	0	0	0	0	0
Sulfonamide	7	36	28	44	30
Trimethoprim	0	0	10	11	10
Apramycin	0	0	0	0	0
Gentamicin	0	0	0	0	<1
Spectinomycin	0	4	10	0	3
Streptomycin	7	39	20	33	26
Nalidixic acid	0	0	1	0	2
Colistin	0	0	0	0	0
Number of isolates	14	28	205	9	468

a) 7 isolates originated from Danish pork and 2 isolates from imported pork
b) Includes cases where origin of infection is non-documented and may therefore include some isolates acquired abroad but not documented as such.

Campylobacter

With 86.4 cases per 100,000 inhabitants, campylobacteriosis is the most common foodborne zoonosis in Denmark. *Campylobacter jejuni* is estimated to be responsible for 90-95% of all human *Campylobacter* infections while *C. coli* is the second most common species. Approximately 80% of the human cases are acquired in Denmark.

Campylobacter from food animals

Tables 24 and 25 present the MIC distributions and occurrence of antimicrobial resistance among *C. jejuni* from cattle and broilers and *C. coli* from pigs and broilers in 2001. Trends in resistance to selected antimicrobials among *C. jejuni* and *C. coli* during 1996-2001 are presented in Figures 8 and 9, respectively. Among *Campylobacter* spp., resistance to nalidixic acid often results in simultaneous resistance to ciprofloxacin. In 2001 the breakpoint for ciprofloxacin was adjusted from >1 to >2 (Table A1). Applying this breakpoint retrospectively did not alter the proportion of resistant isolates from 1997-2001 (Figures 8 and 9).
Nalidixic acid resistance was still low in *C. jejuni* from broilers; however, the steady increase observed during the past years is a cause for concern (Figure 8). In contrast, resistance to nalidixic acid decreased from 17% to 5% in *C. coli* from pigs between 1998 and 2001 (Figure 9). This decrease coincided with withdrawal from the market of an oral fluoroquinolone formulation for pigs.

Macrolide resistance in *C. coli* from pigs has remained at a high level in 2000 and 2001 (Figure 9). The macrolide tylosin was the most widely used antimicrobial growth promoter (AGP) in the pig production until 1999 where all AGPs were withdrawn. However, macrolides are still used for treatment of infections in pigs. In 2000 and 2001, 8,900 kg and 10,835 kg tylosin, respectively were used for this indication. Because *C. coli* is rarely isolated from broilers (only 12 isolates in 2001), it is difficult to analyse trends in resistance for this bacteria. Nevertheless, erythromycin resistance in *C. coli* remained at a relatively high level during 1996-2001. This is probably due to the use of the AGP virginiamycin until 1998 (Figure 9).

Campylobacter from food

Campylobacter spp. were isolated from Danish and imported poultry meat samples collected at retail outlets. A new semi-quantitative method for the analysis of thermophilic *Campylobacter* spp. in foods was introduced in 2000 (Appendix 1). In 2001, the prevalence of thermophilic *Campylobacter* spp. was 35.3% (387/1,096) in raw broiler meat and 22.1% (177/800) in raw turkey meat (Annual Report on Zoonosis in Denmark 2001). Among these, a random subsample of

Table 24. Distribution of MICs and occurrence of resistance among Campylobacter jejuni *from broilers (n=79 isolates) and cattle (n=38 isolates), Denmark*

DANMAP 2001

Compound	Animal species	% Resistant	[95% Confidence Interval]	Distribution (%) of MICs															
				0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024
Tetracycline	Broilers	1	[0.03-6.9]					94.9	2.5	1.3				1.3 a)					
	Cattle	8	[1.7-21.4]					81.6	2.6	5.3	2.6		2.6	2.6	2.6				
Chloramphenicol	Broilers	0	[0.0-4.6]						8.9	67.1	20.3	3.8							
	Cattle	8	[1.7-21.4]							71.1	18.4	2.6				7.9			
Sulfonamide	Broilers	0	[0.0-4.6]									25.3	31.6	24.1	11.4	6.3	1.3		
	Cattle	0	[0.0-9.3]									39.5	10.5	21.1	23.7	5.3			
Erythromycin	Broilers	0 b)	[0.0-4.6]				11.5	25.6	55.1	5.1	2.6								
	Cattle	8	[1.7-21.4]				2.6	31.6	44.7	13.2					7.9				
Gentamicin	Broilers	0	[0.0-4.6]					67.1	30.4	2.5									
	Cattle	0	[0.0-9.3]					44.7	52.6	2.6									
Neomycin	Broilers	0	[0.0-4.6]						43.0	49.4	7.6								
	Cattle	0	[0.0-9.3]						31.6	57.9	7.9	2.6							
Streptomycin	Broilers	3	[0.3-8.9]						7.6	68.4	21.5					2.5			
	Cattle	13	[4.4-28.1]						5.3	60.5	21.1			5.3		7.9			
Ciprofloxacin	Broilers	6	[2.1-14.2]	2.5		1.3	58.2	30.4	1.3				1.3	5.1					
	Cattle	8	[1.7-21.4]			2.6	52.6	36.8			2.6			5.3					
Nalidixic acid	Broilers	8	[2.8-15.8]							1.3	24.1	64.6	2.5		2.5	3.8	1.3		
	Cattle	8	[1.7-21.4]								18.4	60.5	7.9	5.3	2.6		5.3		
Colistin	Broilers	0	[0.0-4.6]					2.5	1.3	7.6	19.0	38.0	29.1	2.5					
	Cattle	0	[0.0-9.3]					7.9	5.3	15.8	10.5	39.5	15.8	5.3					

Lines indicate breakpoints for resistance
a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration
b) Only 78 isolates were tested against erythromycin.

Table 25. Distribution of MICs and occurrence of resistance among Campylobacter coli *from broilers (n=12 isolates) and pigs (n=94 isolates), Denmark*

DANMAP 2001

Compound	Animal species	% Resistant	[95% Confidence Interval]	Distribution (%) of MICs															
				0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024
Tetracycline	Broilers	0 a)	[0.0-28.5]					100 b)											
	Pigs	1	[0.03-5.8]					88.3	6.4	3.2	1.1				1.1				
Chloramphenicol	Broilers	0	[0.0-26.5]							50.0	50.0								
	Pigs	1	[0.03-5.8]						7.4	24.5	48.9	12.8	5.3		1.1				
Sulfonamide	Broilers	0	[0.0-26.5]									33.3	33.3	25.0	8.3				
	Pigs	1 c)	[0.03-5.9]									44.1	31.2	11.8	9.7	2.2			1.1
Erythromycin	Broilers	27 a)	[6.0-61.0]					9.1	45.5	18.2					27.3				
	Pigs	30	[20.8-40.1]				5.3	7.4	13.8	18.1	16.0	8.5	1.1		29.8				
Gentamicin	Broilers	0	[0.0-26.5]					33.3	58.3	8.3									
	Pigs	0	[0.0-3.9]					13.8	51.1	34.0	1.1								
Neomycin	Broilers	0	[0.0-26.5]						33.3	50.0	16.7								
	Pigs	0	[0.0-3.9]						6.4	34.0	54.3	5.3							
Streptomycin	Broilers	17	[2.1-48.4]						8.3	41.7	33.3					16.7			
	Pigs	48	[37.5-58.4]						1.1	12.8	26.6	11.7	1.1	5.3	5.3	36.2			
Ciprofloxacin	Broilers	0	[0.0-26.5]	8.3	8.3	33.3	41.7	8.3											
	Pigs	5	[1.8-12.0]	3.2	10.6	31.9	29.8	11.7	3.2	4.3		1.1	3.2	1.1					
Nalidixic acid	Broilers	0 a)	[0.0-28.5]								9.1	81.8	9.1						
	Pigs	5 c)	[1.8-12.1]						2.2	4.3	9.7	48.4	22.6	7.5	4.3	1.1			
Colistin	Broilers	0	[0.0-26.5]					16.7	8.3	33.3	8.3	16.7	8.3	8.3					
	Pigs	1	[0.03-5.8]					27.7	31.9	14.9	16.0	3.2	4.3	1.1		1.1			

Lines indicate breakpoints for resistance

a) Only 11 isolates were tested against tetracycline, erythromycin and nalidixic acid.

b) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

c) Only 93 isolates were tested against sulfamethoxazole and nalidixic acid.

DANMAP 2001

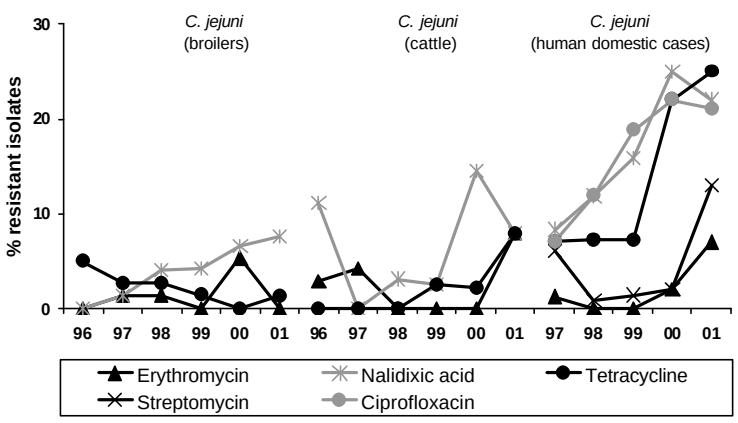


Figure 8. Trends in resistance to selected antimicrobials among Campylobacter jejuni *from broilers, cattle and human domestic cases, Denmark*

DANMAP 2001

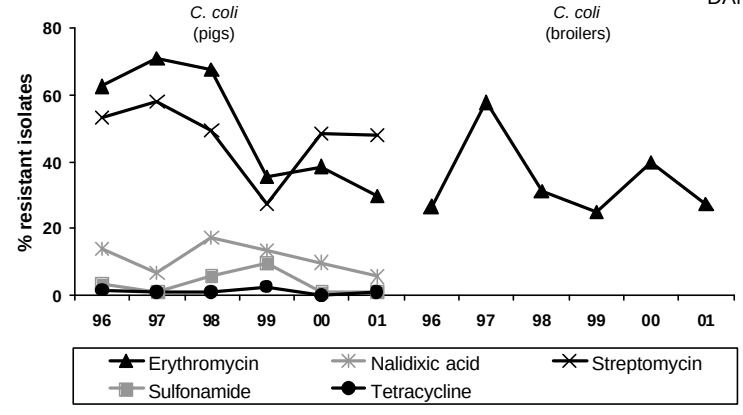


Figure 9. Trends in resistance to selected antimicrobials among Campylobacter coli *from pigs and broilers, Denmark*

117 *C. jejuni* isolates from broiler and turkey meat was tested for antimicrobial susceptibility.
Table 26 presents the MIC distributions and occurrence of antimicrobial resistance among *C. jejuni* from broiler and turkey meat samples in 2001. Resistance to tetracycline was significantly higher in isolates from turkey meat than from broiler meat.

Campylobacter from humans

Resistance in *C. jejuni* from human clinical samples stratified among domestic and travel-associated cases is presented in Table 27. Resistance to tetracycline and quinolones was higher among *C. jejuni* associated with travel. Additionally, 5-year trends in resistance to selected antimicrobials among human *C. jejuni* isolates acquired in Denmark are presented in Figure 8. This analysis showed that the increase in tetracycline and quinolone resistance observed seems to have levelled out in 2001. Resistance data on *C. coli* isolated from humans are not presented because of the much lower frequency of this species in human *Campylobacter* infections as compared to *C. jejuni.*

Farm to table

A comparison of resistance levels among *C. jejuni* from Danish food animals, food of Danish and imported origin and domestically acquired human cases are presented in Table 27. In general the resistance levels were comparable. The exception was a significantly lower level of tetracycline resistance in *C. jejuni* from broilers and Danish broiler meat compared to *C. jejuni* from domestically acquired human cases.
Epidemiological studies have shown that broilers/broiler meat are important host risk factors for *C. jejuni* infections in humans but also that previous antibiotic treatment was a risk factor. Thus, humans taking antibiotics are more likely to get *Campylobacter* infections. This and infections aquired from imported broiler products may influence the occurrence of resistance among *Campylobacter* isolates from humans.

Table 26. Distribution of MICs and occurrence of resistance among Campylobacter jejuni *from broiler meat (n=74 isolates) and turkey meat (n=43 isolates), Denmark* DANMAP 2001

Compound	Food type	% Resistant	[95% Confidence Interval]	Distribution (%) of MICs															
				<=0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Tetracycline	Broiler meat	3	[0.3-9.4]					86.5	1.4	5.4		4.1		1.4	1.4 a)				
	Turkey meat	26	[13.5-41.2]					69.8	4.7				2.3	7.0	16.3				
Erythromycin	Broiler meat	1	[0.0-7.3]					24.3	6.8	20.3	18.9	25.7	2.7	1.4					
	Turkey meat	2 b)	[0.1-12.9]					34.1		4.9	41.5	14.6	2.4		2.4				
Gentamicin	Broiler meat	0	[0.0-4.9]					86.5	12.2	1.4									
	Turkey meat	0	[0.0-8.2]					76.7	20.9	2.3									
Streptomycin	Broiler meat	7	[2.2-15.1]						79.7	5.4	2.7	5.4	4.1	1.4	1.4				
	Turkey meat	7	[1.5-19.1]						79.1	14.0					7.0				
Ciprofloxacin	Broiler meat	11	[4.8-20.2]	81.1	2.7	2.7	1.4			1.4	8.1		2.7						
	Turkey meat	0	[0.0-8.2]	90.7		4.7	2.3	2.3											
Nalidixic acid	Broiler meat	11	[4.8-20.2]						29.7	5.4	37.8	13.5	1.4	1.4	8.1	1.4	1.4		
	Turkey meat	0	[0.0-8.2]						37.2		25.6	32.6	4.7						

Lines indicate breakpoints for resistance
a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration
b) Only 41 isolates from turkey meat were tested against erythromycin.

Table 27. Resistance (%) among Campylobacter jejuni *from Danish food animals, food of Danish origin and imported food, and human cases acquired domestically or associated with travel* DANMAP 2001

Compound	Cattle	Broilers	Broiler meat		Turkey meat		Humans	
	Danish %	Danish %	Danish %	Imported %	Danish %	Imported %	Domestic %	Travel associated %
Tetracycline	8	1	2	8	16	39	25	33
Chloramphenicol	8	0	NT a)	NT a)	NT a)	NT a)	10	7
Erythromycin	8	0	2	0	0 b)	6	7	0
Gentamicin	0	0	0	0	0	0	21 c)	20 c)
Streptomycin	13	3	8	0	8	6	13	0
Ciprofloxacin	8	6	13	0	0	0	21	53
Nalidixic acid	8	8	13	0	0	0	22	53
Number of isolate	38	79	61	13	25	18	72	15

a) NT, not tested.
b) Only 23 isolates were tested against erythromycin.
c) Resistance to gentamicin in these isolates may be attributable to a methodological problem as indicated by evaluation of population histograms. This problem had no impact on susceptibility to other antimicrobials.

Resistance in indicator bacteria

Enterococci from food animals

The indicator bacteria from food animals were isolated from faecal samples from cattle and pigs and cloacal swabs from broilers. The samples were collected at slaughter.

The MIC distribution and the occurrence of resistance among enterococci are shown in Tables 28 and 29.

Among *Enterococcus faecium* from broilers, virginiamycin resistance decreased from 39.2% in 1999

Table 28. Distribution of MICs and occurrence of resistance among Enterococcus faecium *from broilers (n=131), cattle (n=18) and pigs (n=175), Denmark* DANMAP 2001

Compound	Animal species	% Resistant	[95% Confidence interval]	Distribution (%) of MICs													
				<=0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048
Tetracycline	Broilers	2	[0.5-6.6]		97.7				0.8	0.8	0.8 a)						
	Cattle	11	[1.4-34.7]		88.9					5.6	5.6						
	Pigs	52	[44.3-59.6]		46.9	0.6		0.6	1.7	5.7	44.6						
Chloramphenicol	Broilers	0	[0.0-2.8]			9.2	32.8	58.0									
	Cattle	0	[0.0-18.5]				33.3	66.7									
	Pigs	<1	[0.01-3.1]			2.9	29.7	66.3	0.6	0.6							
Florfenicol	Broilers	0	[0.0-2.8]			34.4	65.6										
	Cattle	0	[0.0-18.5]			22.2	77.8										
	Pigs	0	[0.0-2.1]			38.3	61.7										
Penicillin	Broilers	57	[48.3-65.9]			29.8	6.9	6.1	9.9	46.6	0.8						
	Cattle	0	[0.0-18.5]			55.6	27.8	16.7									
	Pigs	36	[28.9-43.6]			28.6	25.1	10.3	34.3	1.7							
Erythromycin	Broilers	15	[9.6-22.6]		76.3	5.3	3.1	2.3	2.3	2.3	8.4						
	Cattle	11	[1.4-34.7]		27.8	44.4	16.7	11.1									
	Pigs	26	[19.9-33.5]		20.0	30.3	23.4	2.3		0.6	23.4						
Gentamicin	Broilers	0	[0.0-2.8]									100					
	Cattle	0	[0.0-18.5]									100					
	Pigs	0	[0.0-2.1]									99.4	0.6				
Kanamycin	Broilers	<1	[0.02-4.2]									26.7	60.3	9.2	3.1		0.8
	Cattle	0	[0.0-18.5]									38.9	50.0	5.6	5.6		
	Pigs	16	[10.9-22.3]									35.4	37.7	10.3	0.6	1.1	14.9
Streptomycin	Broilers	<1	[0.02-4.2]									98.5	0.8				0.8
	Cattle	0	[0.0-18.5]									88.9	11.1				
	Pigs	18	[12.9-24.8]									74.3	2.3	2.3	2.9	9.1	9.1
Vancomycin	Broilers	3	[0.8-7.6]		91.6	3.8	1.5				3.1						
	Cattle	0	[0.0-18.5]		66.7	33.3											
	Pigs	3	[1.3-7.3]		80.6	12.0	0.6	3.4			3.4						
Virginiamycin	Broilers	27	[20.1-36.0]	25.2	39.7	4.6	3.1	25.2	2.3								
	Cattle	0 b)	[0.0-19.5]	29.4	58.8	5.9	5.9										
	Pigs	6	[3.2-11.0]	21.7	41.7	23.4	6.9	6.3									
Quinupristin/dalfopristin	Broilers	31	[22.8-39.2]	19.8	22.9	26.7	22.9	6.9	0.8								
	Cattle	6	[0.1-27.3]	22.2	11.1	61.1		5.6									
	Pigs	9	[4.9-13.7]	21.7	9.7	60.0	6.3	2.3									
Avilamycin	Broilers	5	[2.2-10.7]		19.8	29.0	38.2	7.6	4.6		0.8						
	Cattle	0	[0.0-18.5]		5.6	61.1	33.3										
	Pigs	0	[0.0-2.1]		17.7	73.1	9.1										
Bacitracin	Broilers	84	[76.6-89.8]					9.9	3.1	2.3	0.8	16.0	5.3	62.6			
	Cattle	78	[52.4-93.6]							5.6	16.7	44.4	16.7	16.7			
	Pigs	63	[55.8-70.6]					13.7	2.3	3.4	17.1	30.9	14.3	18.3			
Nitrofurantoin	Broilers	11	[6.6-18.2]								88.5	11.5					
	Cattle	0	[0.0-18.5]								100						
	Pigs	11	[6.7-16.4]								89.1	10.9					
Salinomycin	Broilers	0	[0.0-2.8]		12.2		16.8	71.0									
	Cattle	0	[0.0-18.5]		77.8	22.2											
	Pigs	0	[0.0-2.1]		88.6	10.9		0.6									

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

b) n=17 isolates

to 27.7% in 2001 (Figure 10). In 2001, the combination of resistance to penicillin and streptogramin was still prevalent among *E. faecium* from broilers, while only a few isolates had the macrolide/streptogramin resistance combination. Virginiamycin has not been used in Denmark since January 1998. Instead, it is possible that the use of penicillin for treatment of disease has selected for penicillin/streptogramin resistant isolates so that virginiamycin resistance remained at a high level. Data from the VetStat programme showed that penicillin was the most common antimicrobial used for treatment of broilers in Denmark in 2001.

After the withdrawal of antimicrobial growth promoters, the occurrence of resistance to avoparcin and avilamycin has decreased markedly among *E. faecium* from broilers and has remained at the same low level from 2000 to 2001 (Figures 11 and 12). Resistance to bacitracin has remained unchanged at >80% in broilers and >50% in pigs despite the withdrawal.

In 2000, an *E. faecium* clone resistant to erythromycin, kanamycin, streptomycin, quinupristin/dalfopristin, virginiamycin and tetracycline emerged among isolates from cattle. In 2001, only 18 *E. faecium* isolates were collected from cattle compared to 48 isolates in 2000 and none of the 18 isolates shared this specific resistance profile.

The resistance profile was also observed in pigs in 2000. In 2001, it was still present in pigs but had become less prevalent. The result has been a significant decrease in resistance to virginiamycin, erythromycin (figures 13 and 14), nitrofurantoin, quinupristin/dalfopristin and tetracycline among *E. faecium* from pigs from 2000 to 2001. The reason why the specific resistance profile is less prevalent in pigs, and perhaps also in cattle, in 2001 compared to 2000 is not known. From 2000 to 2001, resistance to vancomycin (avoparcin) among *E. faecium* from broilers and pigs has remained unchanged (Figure 15).

Table 29. Distribution of MICs and occurrence of resistance among Enterococcus faecalis *from broilers (n=82) and pigs (n=184), Denmark*

DANMAP 2001

Compound	Animal species	% Resistant	[95% Confidence interval]	Distribution (%) of MICs												
				<=0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048
Tetracycline	Broilers	43	[31.8-54.1]		57.3				7.3	8.5	26.8 a)						
	Pigs	85	[78.8-89.6]		14.1			1.1	11.4	16.8	56.5						
Chloramphenicol	Broilers	1	[0.03-6.6]			4.9	57.3	36.6			1.2						
	Pigs	3	[1.2-7.0]				8.7	81.5	6.5		2.2	1.1					
Florfenicol	Broilers	0	[0.0-4.4]			69.5	30.5										
	Pigs	0	[0.0-2.0]			23.4	76.1	0.5									
Penicillin	Broilers	0	[0.0-4.4]			78.0	20.7	1.2									
	Pigs	0	[0.0-2.0]			38.0	62.0										
Erythromycin	Broilers	22	[13.6-32.5]		35.4	40.2	2.4	3.7	7.3	2.4	8.5						
	Pigs	32	[25.4-39.3]		59.8	7.6	0.5				32.1						
Gentamicin	Broilers	0	[0.0-4.4]									100					
	Pigs	3	[1.2-7.0]									96.7				2.2	1.1
Kanamycin	Broilers	0	[0.0-4.4]									92.7	7.3				
	Pigs	14	[9.4-20.0]									84.2	1.1	0.5			14.1
Streptomycin	Broilers	6	[2.0-13.7]									91.5	2.4			1.2	4.9
	Pigs	29	[22.4-35.9]									57.6	13.0		0.5	1.6	27.2
Vancomycin	Broilers	0	[0.0-4.4]		81.7	18.3											
	Pigs	0	[0.0-2.0]		75.5	23.4	1.1										
Avilamycin	Broilers	0	[0.0-4.4]		31.7	68.3											
	Pigs	1	[0.1-3.9]		28.3	68.5	2.2				1.1						
Bacitracin	Broilers	63	[52.1-73.8]					8.5	4.9	6.1	17.1	23.2	4.9	35.4			
	Pigs	40	[32.6-47.1]					2.7	7.6	15.8	34.2	29.9	7.1	2.7			
Flavomycin	Broilers	11	[5.1-19.8]	2.4	29.3	53.7	3.7				11.0						
	Pigs	<1	[0.01-3.0]	21.2	66.3	10.9	1.1				0.5						
Nitrofurantoin	Broilers	1	[0.03-6.6]								98.8	1.2					
	Pigs	0	[0.0-2.0]								100						
Salinomycin	Broilers	0	[0.0-4.4]		69.5	6.1	24.4										
	Pigs	0	[0.0-2.0]		93.5	6.5											

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

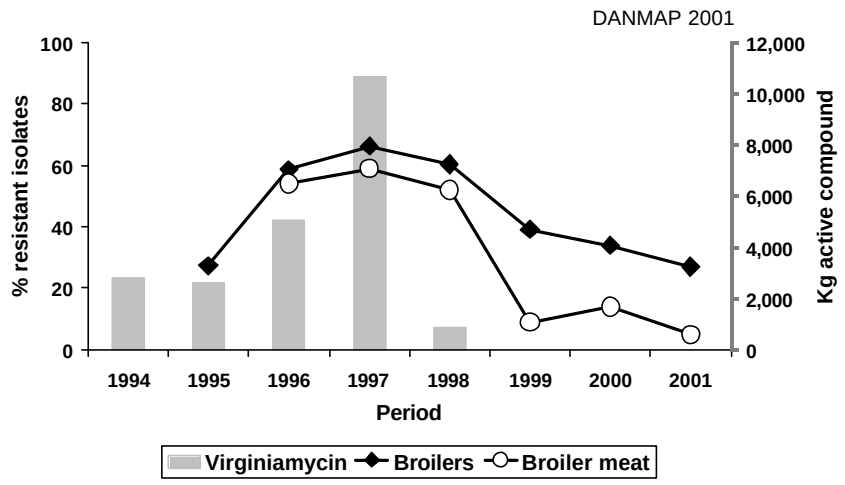


Figure 10. Trend in virginiamycin resistance among Enterococcus faecium *from broilers and broiler meat and the usage of the growth promoter virginiamycin, Denmark*

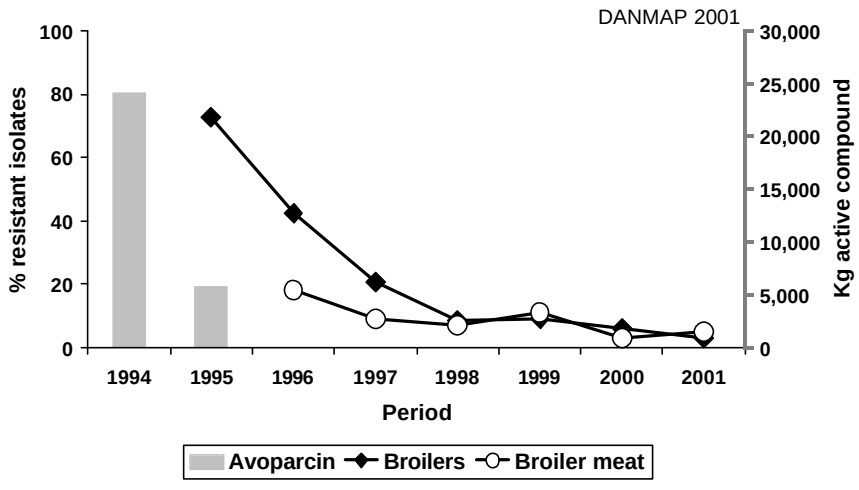


Figure 11. Trend in avoparcin resistance among Enterococcus faecium *from broilers and broiler meat and the usage of the growth promoter avoparcin, Denmark*

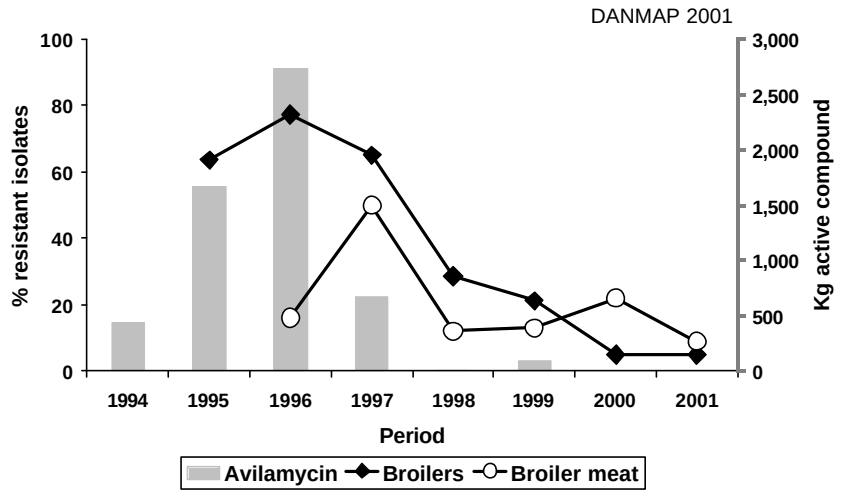


Figure 12. Trend in avilamycin resistance among Enterococcus faecium *from broilers and broiler meat and the usage of the growth promoter avilamycin, Denmark*

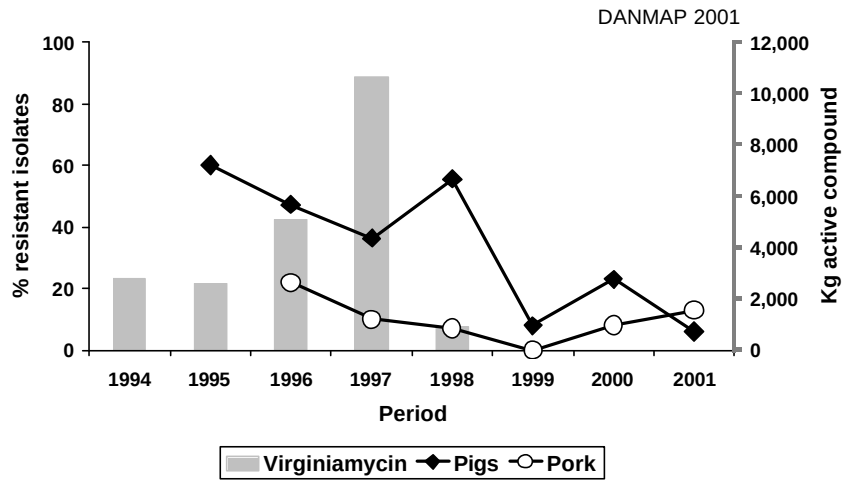


Figure 13. Trend in virginiamycin resistance among Enterococcus faecium *from pigs and pork and the usage of the growth promoter virginiamycin, Denmark*

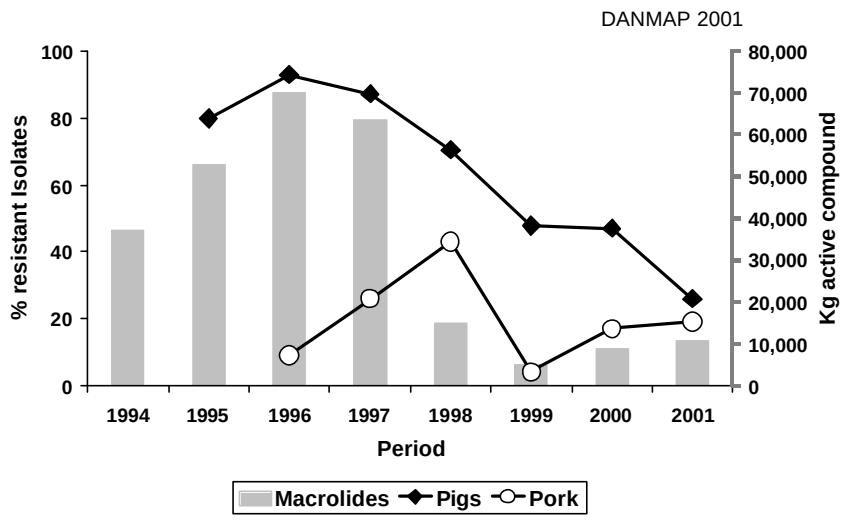


Figure 14. Trend in erythromycin resistance among Enterococcus faecium *from pigs and pork and the total usage of macrolides, both as growth promoters and therapeutics, Denmark*

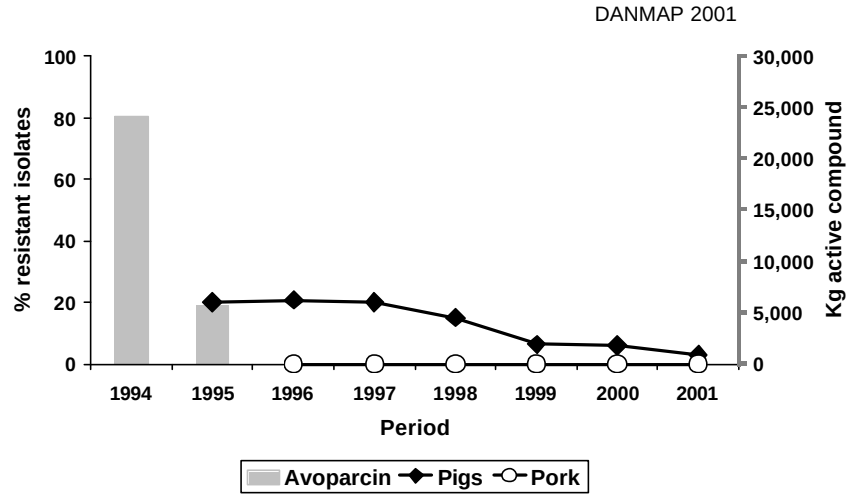


Figure 15. Trend in avoparcin resistance among Enterococcus faecium *from pigs and pork and the usage of the growth promoter avoparcin, Denmark*

Table 30. Distribution of MICs and occurrence of resistance among Enterococcus faecium *from turkey meat (n=21), broiler meat (n=44), beef (n=45) and pork (n=16), Denmark* DANMAP 2001

Compound	Food type	% Resistant	[95% Confidence interval]	Distribution (%) of MICs													
				<=0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048
Tetracycline	Turkey meat	43	[21.8-66.0]		52.4	4.8				9.5	33.3 a)						
	Broiler meat	41	[26.3-56.8]		56.8	2.3			4.5	6.8	29.5						
	Beef	18	[8.0-32.1]		77.8			4.4	2.2	6.7	8.9						
	Pork	13	[1.6-38.4]		87.5						12.5						
Chloramphenicol	Turkey meat	0	[0.0-16.1]			38.1	33.3	9.5	19.0								
	Broiler meat	0	[0.0-8.0]			40.9	43.2	9.1	6.8								
	Beef	0	[0.0-7.9]			31.1	46.7	17.8	4.4								
	Pork	0	[0.0-20.6]			56.3	37.5		6.3								
Florfenicol	Turkey meat	0	[0.0-16.1]			85.7	14.3										
	Broiler meat	0	[0.0-8.0}			90.9	9.1										
	Beef	0	[0.0-7.9]			100											
	Pork	0	[0.0-20.6]			93.8		6.3									
Penicillin	Turkey meat	0	[0.0-16.1]			81.0		19.0									
	Broiler meat	7	[1.4-18.7]			61.4	15.9	15.9	6.8								
	Beef	0	[0.0-7.9]			88.9	11.1										
	Pork	0	[0.0-20.6]			93.8	6.3										
Erythromycin	Turkey meat	71	[47.8-88.7]		4.8	9.5	14.3	38.1			33.3						
	Broiler meat	30	[16.8-45.2]		47.7	15.9	6.8	11.4	2.3	4.5	11.4						
	Beef	22	[11.2-37.1]		37.8	22.2	17.8	13.3	2.2	2.2	4.4						
	Pork	19	[4.1-45.7]		62.5	6.3	12.5	12.5			6.3						
Gentamicin	Turkey meat	0	[0.0-16.1]									100					
	Broiler meat	0	[0.0-8.0]									100					
	Beef	0	[0.0-7.9]									100					
	Pork	0	[0.0-20.6]									100					
Kanamycin	Turkey meat	14	[3.1-36.3]									47.6	33.3	4.8			14.3
	Broiler meat	2	[0.1-12.0]									63.6	29.5	4.5			2.3
	Beef	0	[0.0-7.9]									60.0	26.7	13.3			
	Pork	0	[0.0-20.6]									68.8	31.3				
Streptomycin	Turkey meat	14	[3.1-36.3]									81.0		4.8		9.5	4.8
	Broiler meat	2	[0.1-12.0]									95.5			2.3		2.3
	Beef	9	[2.5-21.2]									86.7			4.4	6.7	2.2
	Pork	0	[0.0-20.6]									93.8		6.3			
Vancomycin	Turkey meat	0	[0.0-16.1]		100												
	Broiler meat	5	[0.6-15.5]		81.8	13.6					4.5						
	Beef	0	[0.0-7.9]		93.3	6.7											
	Pork	0	[0.0-20.6]		68.8	31.3											
Virginiamycin	Turkey meat	10	[1.2-30.4]	33.3	42.9	14.3				4.8	4.8						
	Broiler meat	5	[0.6-15.5]	45.5	31.8	11.4	6.8	2.3		2.3							
	Beef	4	[0.5-15.2]	55.6	22.2	11.1	6.7	4.4									
	Pork	13	[1.6-38.4]	18.8	56.3	6.3	6.3	12.5									
Quinupristin/dalfopristin	Turkey meat	14	[3.1-36.3]	9.5	38.1	38.1		4.8		9.5							
	Broiler meat	9	[2.5-21.7]	38.6	20.5	31.8	4.5	2.3		2.3							
	Beef	16	[6.5-29.5]	40.0	15.6	28.9	11.1	2.2	2.2								
	Pork	13	[1.6-38.4]	25.0	12.5	50.0	6.3	6.3									
Avilamycin	Turkey meat	14	[3.1-36.3]		28.6	57.1					14.3						
	Broiler meat	9	[2.5-21.7]		29.5	52.3	6.8	2.3			9.1						
	Beef	0	[0.0-7.9]		48.9	46.7	4.4										
	Pork	0	[0.0-20.6]		68.8	31.3											
Bacitracin	Turkey meat	29	[11.3-52.2]					19.0	4.8	19.0	28.6			28.6			
	Broiler meat	43	[28.4-59.0]					20.5	9.1	11.4	15.9	4.5	4.5	34.1			
	Beef	18	[8.0-32.1]					31.1	8.9	13.3	28.9	13.3		4.4			
	Pork	6	[0.2-30.2]					37.5	12.5	18.8	25.0			6.3			
Nitrofurantoin	Turkey meat	0	[0.0-16.1]								100						
	Broiler meat	0	[0.0-8.0]								100						
	Beef	0	[0.0-7.9]								100						
	Pork	0	[0.0-20.6]								100						
Salinomycin	Turkey meat	0	[0.0-16.1]		71.4	14.3	14.3										
	Broiler meat	0	[0.0-8.0]		50.0	9.1	36.4	4.5									
	Beef	0	[0.0-7.9]		100												
	Pork	0	[0.0-20.6]		100												

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

Table 31. Distribution of MICs and occurrence of resistance among Enterococcus faecalis *from turkey meat (n=21), broiler meat (n=22), beef (n=32) and pork (n=33), Denmark* DANMAP 2001

Compound	Food type	% Resistant	[95% Confidence interval]	Distribution (%) of MICs												
				<=0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048
Tetracycline	Turkey meat	57	[34.0-78.1]		38.1			4.8	4.8	4.8	47.6 a)						
	Broiler meat	41	[20.7-63.7]		45.5	13.6			4.5	13.6	22.7						
	Beef	16	[5.2-32.8]		81.3			3.1	3.1		12.5						
	Pork	24	[11.1-42.2]		75.8					9.1	15.2						
Chloramphenicol	Turkey meat	10	[1.6-30.4]			14.3	47.1	29.1			9.5						
	Broiler meat	0	[0.0-15.4]			22.7	54.5	22.7									
	Beef	0	[0.0-10.9]			15.6	65.6	18.8									
	Pork	3	0.1-15.8			30.3	39.4	27.3			3.0						
Florfenicol	Turkey meat	0	[0.0-16.1]			71.4	28.6										
	Broiler meat	0	[0.0-15.4]			86.4	13.6										
	Beef	0	[0.0-10.9]			90.6	9.4										
	Pork	0	[0.0-10.6]			87.9	12.1										
Penicillin	Turkey meat	0	[0.0-16.1]			90.5	9.5										
	Broiler meat	0	[0.0-15.4]			95.5	4.5										
	Beef	0	[0.0-10.9]			75.0	21.9	3.1									
	Pork	0	[0.0-10.6]			84.8	15.2										
Erythromycin	Turkey meat	29	[11.2-52.2]		47.6	23.8					28.6						
	Broiler meat	32	[13.9-54.9]		45.5	22.7			18.2		13.6						
	Beef	6	[0.8-20.8]		56.3	34.4	3.1	3.1			3.1						
	Pork	9	[1.9-24.3]		57.6	33.3					9.1						
Gentamicin	Turkey meat	0	[0.0-16.1]									100					
	Broiler meat	0	[0.0-15.4]									100					
	Beef	0	[0.0-10.9]									100					
	Pork	0	[0.0-10.6]									100					
Kanamycin	Turkey meat	0	[0.0-16.1]									100					
	Broiler meat	0	[0.0-15.4]									100					
	Beef	3	[0.1-16.2]									96.9					3.1
	Pork	3	[0.1-15.8]									97.0					3.0
Streptomycin	Turkey meat	19	[5.5-41.9]									76.2		4.8			19.0
	Broiler meat	14	[2.9-34.9]									86.4			4.5		9.1
	Beef	6	[0.8-20.8]									87.5	3.1	3.1			6.3
	Pork	6	[0.8-20.2]									93.9					6.1
Vancomycin	Turkey meat	0	[0.0-16.1]			47.6	52.4										
	Broiler meat	0	[0.0-15.4]			77.3	22.7										
	Beef	0	[0.0-10.9]			71.9	25.0	3.1									
	Pork	0	[0.0-10.6]			69.7	30.3										
Avilamycin	Turkey meat	5	[0.1-23.9]			47.6	47.6				4.8						
	Broiler meat	0	[0.0-15.4]			59.1	40.9										
	Beef	0	[0.0-10.9]			56.3	43.8										
	Pork	0	[0.0-10.6]			51.5	45.5	3.0									
Bacitracin	Turkey meat	19	[5.5-41.9]					52.4	19.0	9.5				19.0			
	Broiler meat	18	[5.2-40.3]					54.5	18.2	9.1				18.2			
	Beef	6	[0.8-20.8]					68.8	12.5	12.5				6.3			
	Pork	6	[0.8-20.2]					81.8	6.1	3.0	3.0			6.1			
Flavomycin	Turkey meat	5	[0.1-23.8]	9.5	42.9	42.9					4.8						
	Broiler meat	5	[0.1-22.8]	54.5	18.2	22.7			4.5								
	Beef	3	[0.1-16.2]	43.8	37.5	9.4	6.3				3.1						
	Pork	3	[0.1-15.8]	42.4	36.4	12.1	6.1				3.0						
Nitrofurantoin	Turkey meat	0	[0.0-16.1]								100						
	Broiler meat	0	[0.0-15.4]								100						
	Beef	0	[0.0-10.9]								100						
	Pork	0	[0.0-10.6]								100						
Salinomycin	Turkey meat	0	[0.0-16.1]		100												
	Broiler meat	0	[0.0-15.4]		77.3	18.2	4.5										
	Beef	0	[0.0-10.9]		90.6	6.3	3.1										
	Pork	0	[0.0-10.6]		100												

Lines indicate breakpoints of resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

Table 32. Occurrence of resistance (%) among Enterococcus faecium *from food animals and foods of Danish and imported origin* DANMAP 2001

Compound	Pigs	Pork	Cattle	Beef		Broilers	Broiler meat	
	Danish %	Danish %	Danish %	Danish %	Imported %	Danish %	Danish %	Imported %
Tetracycline	52	13	11	20	15	2	20	68
Chloramphenicol	<1	0	0	0	0	0	0	0
Florfenicol	0	0	0	0	0	0	0	0
Penicillin	36	0	0	0	0	57	8	5
Erythromycin	26	19	11	28	15	15	32	26
Gentamicin	0	0	0	0	0	0	0	0
Kanamycin	16	0	0	0	0	<1	0	5
Streptomycin	18	0	0	16	0	<1	0	5
Vancomycin	3	0	0	0	0	3	4	5
Virginiamycin	6	13	0	4	5	27	4	5
Quinupristin/dalfopristin	9	13	6	20	10	31	12	5
Avilamycin	0	0	0	0	0	5	4	16
Bacitracin	63	6	78	20	15	84	44	42
Nitrofurantoin	11	0	0	0	0	11	0	0
Salinomycin	0	0	0	0	0	0	0	0
Number of isolates	176	16	18	25	20	131	25	19

Table 33. Occurrence of resistance (%) among Enterococcus faecalis *from food animals and foods of Danish origin* DANMAP 2001

Compound	Pigs	Pork	Broilers	Broiler meat
	Danish %	Danish %	Danish %	Danish %
Tetracycline	85	23	43	40
Chloramphenicol	3	3	1	0
Florfenicol	0	0	0	0
Penicillin	0	0	0	0
Erythromycin	32	10	22	33
Gentamicin	3	0	0	0
Kanamycin	14	3	0	0
Streptomycin	29	6	6	20
Vancomycin	0	0	0	0
Avilamycin	1	0	0	0
Bacitracin	40	6	63	20
Flavomycin	<1	3	11	7
Nitrofurantoin	0	0	1	0
Salinomycin	0	0	0	0
Number of isolates	184	31	82	15

Among *E. faecalis* isolates from broilers we saw no significant changes in 2001 compared to 2000, whereas among *E. faecalis* isolates from pigs there was a significant increase in the proportion of isolates resistant to bacitracin. It should be noted that most of the failures in the performance test were in testing susceptibility of enterococci to bacitracin.

Enterococci from food

The examination of samples from broiler meat, turkey meat, beef and pork at retail outlets resulted in 126 isolates of *E. faecium* and 108 isolates of *E. faecalis*. Resistance towards tetracycline, macrolides, streptomycin and bacitracin were most frequent.

The MIC distribution and the occurrence of resistance are shown in Tables 30 and 31. Three out of 44 isolates of *E. faecium* from broiler meat (7%) exhibited penicillin resistance.

Vancomycin resistance was observed in two *E. faecium* isolates from broiler meat, one originated from a Danish product and one from an imported broiler meat product.

Enterococci from farm to table

The trends in resistance presented in Figures 10-15 showed that after the withdrawal of growth promoters a decrease in resistance to avoparcin, avilamycin, erythromycin and virginiamycin was observed among *E. faecium* from animals and some categories of meat products.

A comparison of resistance among enterococci from Danish food animals and foods of Danish and imported origin are presented in Tables 32 and 33. The occurrence of resistance in *E. faecium* from cattle/beef seems to be comparable except for bacitracin. However, in the comparison of pigs/pork and broilers/broiler meat different resistance levels were found for tetracycline, penicillin and bacitracin. In previous years, differences between pigs/pork and broilers/broiler meat were also observed.

Escherichia coli from food animals

Table 34 presents the MIC distribution and occurrence of resistance in *E. coli* from animals at slaughter (indicator *E. coli*).

When comparing the results from Table 34 with the corresponding results from 2000, the resistance levels among indicator *E. coli* have remained almost unchanged. Even though the consumption of tetracycline in weaner pigs increased markedly between 1999 and 2001, this has resulted in no change in the level of tetracycline resistance among *E. coli* from pigs at slaughter (Figure 16). The *E. coli* serotypes causing diarrhoea in weaner pigs are different from the serotypes that predominate in older pigs. In 2001, only minor quantities of the total amounts of aminoglycosides and sulfonamides used in pigs were administrated to slaughter pigs. In spite of this, streptomycin and sulfonamide resistance was common among indicator *E. coli* from slaughter pigs. Streptomycin and sulfonamide resistance are often seen in combination with tetracycline resistance and use of tetracycline may have co-selected for streptomycin and sulfonamide resistance.

Table 34. Distribution of MICs and occurrence of resistance among Escherichia coli *from broilers (n=134), cattle (n=85) and pigs (n=304), Denmark* DANMAP 2001

Compound	Animal species	% Resistant	[95% Confidence interval]	Distribution (%) of MICs														
				<=0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Tetracycline	Broilers	12	[7.0-18.7]							87.3	0.7		2.2		9.7 a)				
	Cattle	5	[1.3-11.6]							95.3				1.2	3.5				
	Pigs	25	[19.9-29.9]							72.0	3.3			1.3	23.4				
Chloramphenicol	Broilers	0	[0.0-2.7]							2.2	50.7	45.5	1.5						
	Cattle	0	[0.0-4.3]							9.4	48.2	41.2	1.2						
	Pigs	3	[1.6-6.0]							6.9	53.9	34.9	1.0	2.0	0.3	1.0			
Florfenicol	Broilers	0	[0.0-2.7]							6.0	60.4	32.1	1.5						
	Cattle	0	[0.0-4.3]							7.1	51.8	41.2							
	Pigs	0	[0.0-1.2]							5.9	59.5	33.6	1.0						
Ampicillin	Broilers	16	[10.0-23.0]						16.4	46.3	20.9	0.7		1.5	14.2				
	Cattle	0	[0.0-4.3]						15.3	58.8	24.7	1.2							
	Pigs	10	[6.5-13.4]						15.1	50.0	24.7	0.7		0.3	9.2				
Ceftiofur	Broilers	0	[0.0-2.7]					97.8	2.2										
	Cattle	0	[0.0-4.3]					100											
	Pigs	0	[0.0-1.2]					99.0	1.0										
Sulfonamide	Broilers	25	[17.6-32.8]											74.6	0.7				24.6
	Cattle	4	[0.7-10.0]											92.9	3.5				3.5
	Pigs	27	[22.1-32.3]											71.7	1.3				27.0
Trimethoprim	Broilers	4	[1.7-9.5]								94.8	0.7			4.5				
	Cattle	0	[0.0-4.3]								100								
	Pigs	7	[4.1-10.0]								93.1	0.3			6.6				
Apramycin	Broilers	1	[0.2-5.3]								53.0	45.5	1.5						
	Cattle	0	[0.0-4.3]								84.7	15.3							
	Pigs	<1	[0.01-1.8]								88.2	11.5	0.3						
Gentamicin	Broilers	0	[0.0-2.7]						97.0	3.0									
	Cattle	0	[0.0-4.3]						100										
	Pigs	0	[0.0-1.2]						97.7	2.3									
Neomycin	Broilers	0	[0.0-2.7]							100									
	Cattle	0	[0.0-4.3]							98.8	1.2								
	Pigs	4	[1.8-6.4]							95.7	0.7		0.3	1.0	2.3				
Spectinomycin	Broilers	2	[0.5-6.4]									1.5	73.9	19.4	3.0	2.2			
	Cattle	0	[0.0-4.3]									1.2	81.2	17.6					
	Pigs	31	[25.8-36.5]								0.3	1.3	54.9	8.2	4.3	11.5	19.4		
Streptomycin	Broilers	7	[3.6-13.3]								5.2	71.6	15.7	1.5	4.5	1.5			
	Cattle	4	[0.7-10.0]								18.8	71.8	5.9	2.4	1.2				
	Pigs	40	[34.3-45.6]								21.4	32.2	6.6	10.2	15.8	13.8			
Ciprofloxacin	Broilers	0	[0.0-2.7]	87.3	2.2	3.0	6.7	0.7											
	Cattle	0	[0.0-4.3]	100															
	Pigs	0	[0.0-1.2]	98.0	0.3	1.3	0.3												
Nalidixic acid	Broilers	10	[5.3-16.0]								89.6		0.7	0.7	3.0	3.7	2.2		
	Cattle	0	[0.0-4.3]								97.6	2.4							
	Pigs	2	[0.5-3.8]								98.4			0.3	0.3	0.7	0.3		
Colistin	Broilers	0	[0.0-2.7]								99.3	0.7							
	Cattle	0	[0.0-4.3]								100								
	Pigs	0	[0.0-1.2]								100								

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

According to VetStat figures from 2001, 86% of the total fluoroquinolone consumption in pigs was administrated to piglets and weaner pigs and only 14% to older pigs. This distribution of usage among age groups may explain the low level of nalidixic acid resistance among indicator *E. coli* from pigs at slaughter. No indicator *E. coli* isolates were ciprofloxacin resistant but 14 and 5 isolates from broilers and pigs, respectively had ciprofloxacin MIC-values between 0.12 and 1.0. Seventeen of the 19 isolates were resistant to nalidixic acid. According to NCCLS guidelines these isolates are susceptible to ciprofloxacin, however clinical experiences shows that in humans the response of such isolates to treatment with ciprofloxacin is considerably reduced.

In 2001, ampicillin, nalidixic acid, sulfonamide and tetracycline were the most commonly observed resistance phenotypes among indicator *E. coli* from broilers (Table 34 and Figure 16). This reflects quite well the consumption of antimicrobials in poultry where penicillins, sulfonamides, and fluoroquinolones were the most commonly used antimicrobials (Table 4). There was little use of tetracycline in broilers and the presence of tetracycline resistance may be a result of co-selection by other compounds.

Escherichia coli from food

A total of 362 isolates of *E. coli* were collected from broiler meat, other poultry meat (predominantly turkey meat), beef and pork at retail outlets. One hundred and six of the isolates (29%) originated from imported foods. Table 35 presents the MIC distribution and occurrence of resistance. Resistance against ampicillin, tetracycline, sulfonamide, trimethoprim and streptomycin were the most frequent. Compared to results from previous years, the resistance level in *E. coli* from foods has remained almost constant.

Escherichia coli from farm to table

A comparison of resistance levels in food animals and food is given in Table 36**.**
In general, the resistance levels in *E. coli* from Danish animals and food of Danish origin were similar, while the resistance levels found in *E. coli* from imported broiler meat products was higher than the levels found in Danish products.

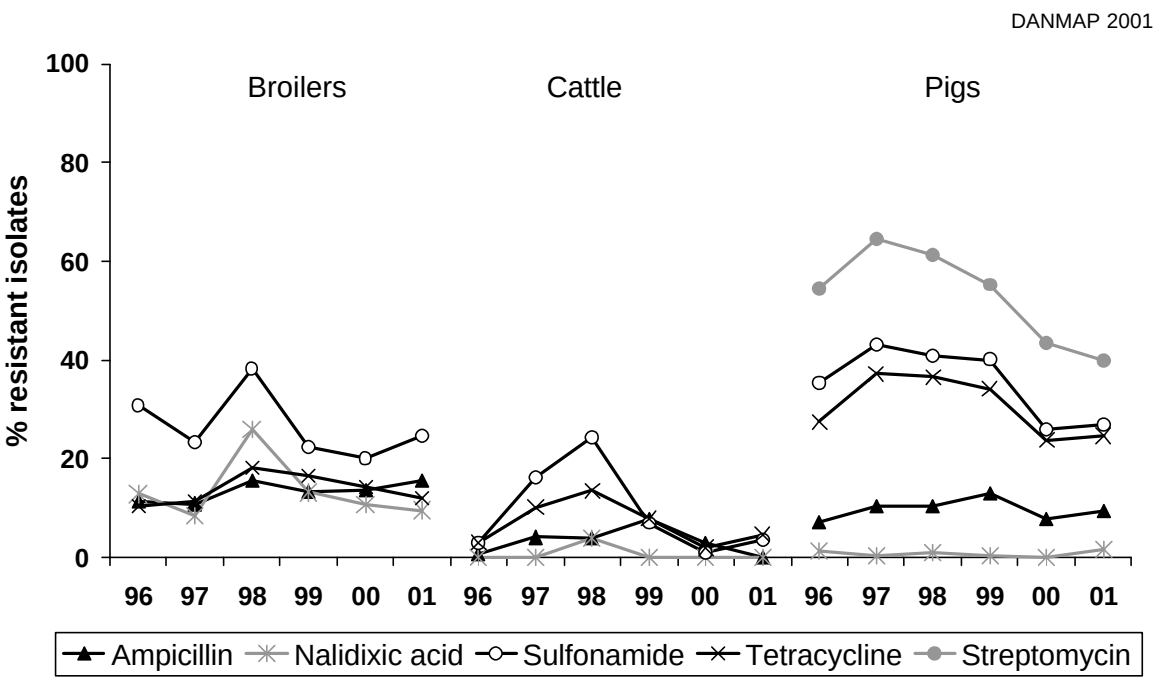


Figure 16. Trends in resistance to some selected antimicrobials among Escherichia coli *from food animals, Denmark*

Table 35. Distribution of MICs and occurrence of resistance among Escherichia coli *from beef (n=94), pork (n=48), broiler meat (n=122), and other poultry meat (n=98), Denmark* DANMAP 2001

Compound	Food type	% Resistant [95% Confidence interval]		Distribution (%) of MICs															
				<=0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Tetracycline	Beef	6	[2.4-13.4]							91.5	1.1	1.1	1.1	2.1	3.2 a)				
	Pork	38	[24.0-52.7]							58.3	2.1	2.1		14.6	22.9				
	Broiler meat	31	[23.1-40.2]							67.2	1.6		2.5	6.6	22.1				
	Other poultry meat	63	[53.0-72.8]							36.7			2.0	20.4	40.8				
Chloramphenicol	Beef	1	[0.0-5.8]							2.1	45.7	50.0	1.1			1.1			
	Pork	4	[0.5-14.3]							6.3	37.5	52.1				4.2			
	Broiler meat	2	[0.2-5.8]							4.9	56.6	35.2	1.6	0.8	0.8				
	Other poultry meat	11	[5.7-19.2]							2.0	51.0	34.7	1.0		1.0	10.2			
Florfenicol	Beef	0	[0.0-3.5]							4.3	54.3	40.4	1.1						
	Pork	0	[0.0-7.4]							4.2	60.4	35.4							
	Broiler meat	0	[0.0-3.0]							7.4	75.4	16.4	0.8						
	Other poultry meat	0	[0.0-3.7]							3.1	76.5	20.4							
Ampicillin	Beef	12	[6.0-20.0]						7.4	48.9	30.9	1.1			11.7				
	Pork	23	[12.0-37.3]						12.5	37.5	27.1				22.9				
	Broiler meat	20	[13.0-27.8]						21.3	43.4	15.6				19.7				
	Other poultry meat	43	[32.9-53.3]						13.3	31.6	12.2				42.9				
Ceftiofur	Beef	0	[0.0-3.5]					98.9	1.1										
	Pork	0	[0.0-7.4]					97.9	2.1										
	Broiler meat	0	[0.0-3.0]					97.5	1.6	0.8									
	Other poultry meat	0	[0.0-3.7]					95.9	4.1										
Sulfonamide	Beef	9	[3.8-16.1]											89.4	2.1				8.5
	Pork	25	[13.6-39.6]											75.0					25.0
	Broiler meat	32	[23.8-41.0]											62.3	5.7			1.6	30.3
	Other poultry meat	52	[41.7-62.2]											48.0				1.0	51.0
Trimethoprim	Beef	5	[1.8-12.0]								94.7				5.3				
	Pork	10	[3.8-22.7]								89.6				10.4				
	Broiler meat	18	[11.7-26.0]								81.1	0.8			18.0				
	Other poultry meat	42	[32.0-52.2]								57.1	1.0			41.8				
Apramycin	Beef	0	[0.0-3.5]								91.5	8.5							
	Pork	0	[0.0-7.4]								100								
	Broiler meat	0	[0.0-3.0]								88.5	11.5							
	Other poultry meat	0	[0.0-3.7]								87.8	12.2							
Gentamicin	Beef	0	[0.0-3.5]						100										
	Pork	0	[0.0-7.4]						100										
	Broiler meat	0	[0.0-3.0]						98.4	1.6									
	Other poultry meat	1	[0.0-5.6]						99.0				1.0						
Neomycin	Beef	2	[0.3-7.5]							97.9				1.1	1.1				
	Pork	8	[2.3-20.0]							91.7			4.2		4.2				
	Broiler meat	6	[2.3-11.5]							93.4		0.8	1.6	1.6	2.5				
	Other poultry meat	3	[0.6-8.7]							92.9	3.1	1.0			3.1				
Spectinomycin	Beef	0	[0.0-3.5]									7.4	81.9	9.6	1.1				
	Pork	13	[4.7-25.3]							2.1		6.3	70.8	4.2	4.2	6.3	6.3		
	Broiler meat	2	[0.5-7.0]									6.6	77.9	10.7	2.5	1.6	0.8		
	Other poultry meat	8	[3.6-15.5]									3.1	67.3	18.4	3.1	3.1	5.1		
Streptomycin	Beef	7	[3.1-14.7]								24.5	61.7	6.4		2.1	5.3			
	Pork	38	[24.0-52.7]								14.6	43.8	4.2	6.3	14.6	16.7			
	Broiler meat	20	[13.0-27.8]								30.3	42.6	7.4	3.3	5.7	10.7			
	Other poultry meat	44	[33.9-54.3]								15.3	37.8	3.1	4.1	8.2	31.6			
Ciprofloxacin	Beef	0	[0.0-3.5]	95.7	1.1		2.1		1.1										
	Pork	0	[0.0-7.4]	95.8			4.2												
	Broiler meat	5	[0.5-7.0]	84.4	0.8	1.6	5.7	2.5			2.5	2.5							
	Other poultry meat	3	[0.6-8.7]	80.6	1.0	1.0	12.2	2.0			1.0	2.0							
Nalidixic acid	Beef	3	[0.7-9.0]								96.8					2.1	1.1		
	Pork	4	[0.5-14.3]								95.8					4.2			
	Broiler meat	16	[9.6-23.3]								83.6	0.8		0.8	2.5	5.7	6.6		
	Other poultry meat	18	[11.3-27.5]								80.6		1.0	1.0	1.0	6.1	10.2		
Colistin	Beef	0	[0.0-3.5]								98.9	1.1							
	Pork	0	[0.0-7.4]								100								
	Broiler meat	0	[0.0-3.0]								99.2	0.8							
	Other poultry meat	0	[0.0-3.7]								100								

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

Table 36. Occurrence of resistance (%) among Escherichia coli *from Danish animals and food of Danish and imported origin*

DANMAP 2001

Compound	Broilers	Broiler meat		Cattle	Beef		Pigs	Pork
	Danish	Danish	Imported	Danish	Danish	Imported	Danish	Danish
	%	%	%	%	%	%	%	%
Tetracycline	12	16	69	5	9	0	25	38
Chloramphenicol	0	1	3	0	1	0	3	4
Florfenicol	0	0	0	0	0	0	0	0
Ampicillin	16	10	43	0	9	20	10	23
Ceftiofur	0	0	0	0	0	0	0	0
Sulfonamide	25	23	54	4	10	4	27	25
Trimethoprim	4	7	46	0	6	4	7	10
Apramycin	1	0	0	0	0	0	<1	0
Gentamicin	0	0	0	0	0	0	0	0
Neomycin	0	2	14	0	1	4	4	8
Spectinomycin	2	2	3	0	0	0	31	13
Streptomycin	7	11	40	4	6	12	40	38
Ciprofloxacin	0	1	6	0	0	0	0	0
Nalidixic acid	10	9	31	0	3	4	2	4
Colistin	0	0	0	0	0	0	0	0
Number of isolates	134	87	35	85	69	25	304	48

Resistance in bacteria from diagnostic submissions

Bacteria from food animals

The DANMAP programme monitors resistance in the following bacterial species isolated from diagnostic submissions from food animals: *Escherichia coli* from poultry, cattle and pigs, coagulase negative staphylococci (CNS) and *Staphylococcus aureus* from cattle, and *Staphylococcus hyicus* from pigs.

Escherichia coli

We have included the serotypes O2 and O78 from poultry, F5 from cattle (young calves) and serotype O149 from weaned pigs.

The MIC distribution and the occurrence of resistance are presented in Table 37. When comparing the results for 2001 with those from 2000, the resistance levels were found to be almost unchanged for most antimicrobials. In 2001, tetracycline and sulfonamide resistance was the most common resistance phenotype among the 17 *E. coli* isolates from poultry. VetStat usage monitoring showed limited use of tetracycline for treatment of poultry in 2001, somewhat less than the use of sulfonamide. Tetracycline resistance occurred only in combination with sulfonamide resistance and it is possible that the use of sulfonamide selected for tetracycline resistance.

Table 37. Distribution of MICs and occurrence of resistance among Escherichia coli *from diagnostic submissions from broilers (n=17), cattle (n=86) and pigs (n=196), Denmark* DANMAP 2001

Compound	Animal species	% Resistant	[95% Confidence interval]	Distribution (%) of MICs															
				<=0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Tetracycline	Broilers	29	[10.3-56.0]							70.6					29.4 a)				
	Cattle	69	[57.7-78.2]							31.4				3.5	65.1				
	Pigs	67	[60.3-73.9]							31.6	1.0		0.5	6.1	60.7				
Chloramphenicol	Broilers	6	[0.2-28.7]							5.9	52.9	35.3				5.9			
	Cattle	8	[3.3-16.1]								31.4	60.5				8.1			
	Pigs	32	[25.7-39.2]							8.2	46.4	12.2	1.0	11.2	2.6	18.4			
Florfenicol	Broilers	0	[0.0-19,5]							5.9	76.5	17.6							
	Cattle	0	[0.0-4.2]								54.7	44.2	1.2						
	Pigs	<1	[0.01-2.8]							14.3	59.7	24.0	1.5	0.5					
Ampicillin	Broilers	6	[0.2-28.7]						5.9	41.2	47.1				5.9				
	Cattle	80	[70.3-88.0]						9.3	8.1	1.2	1.2			80.2				
	Pigs	30	[23.8-37.1]						21.9	41.3	4.6	2.0		1.5	28.6				
Ceftiofur	Broilers	0	[0.0-19,5]					94.1	5.9										
	Cattle	0	[0.0-4.2]					100											
	Pigs	0	[0.0-1.9]					99.5	0.5										
Sulfonamide	Broilers	35	[14.2-61.7]											58.8	5.9				35.3
	Cattle	83	[72.9-89.9]											17.4					82.6
	Pigs	77	[70.0-82.3]											23.0	0.5			0.5	76.0
Trimethoprim	Broilers	12	[1.5-36.4]								88.2				11.8				
	Cattle	56	[44.7-66.5]								44.2				55.8				
	Pigs	37	[30.5-44.4]								62.8				37.2				
Apramycin	Broilers	0	[0.0-19,5]								76.5	23.5							
	Cattle	1	[0.03-6.3]								66.3	32.6		1.2					
	Pigs	10	[6.4-15.3]								86.2	3.6	0.5			9.7			
Gentamicin	Broilers	0	[0.0-19,5]						100										
	Cattle	19	[11.0-28.5]						79.1		2.3		8.1	8.1	2.3				
	Pigs	9	[5.1-13.5]						88.8	0.5		2.0	5.1	1.0	2.6				
Neomycin	Broilers	0	[0.0-19,5]							100									
	Cattle	13	[6.6-21.7]							82.6	3.5	1.2		3.5	9.3				
	Pigs	35	[28.1-41.8}							63.8	1.5		0.5	6.6	27.6				
Spectinomycin	Broilers	0	[0.0-19,5]									17.6	64.7	17.6					
	Cattle	14	[7.4-23.1]										79.1	4.7	2.3	4.7	9.3		
	Pigs	60	[52.5-66.6]									0.5	29.1	4.6	6.1	14.3	45.4		
Streptomycin	Broilers	6	[0.2-28.7]								41.2	52.9				5.9			
	Cattle	74	[63.9-83.2]								1.2	23.3	1.2	3.5	12.8	58.1			
	Pigs	72	[65.1-78.1]								12.2	13.3	2.6	11.2	24.0	36.7			
Ciprofloxacin	Broilers	0	[0.0-19,5]	82.4	5.9	11.8													
	Cattle	1	[0.03-6.3]	77.9				17.4	1.2	2.3		1.2							
	Pigs	1	[0.1-3.6]	83.7	3.6	2.6	8.7		0.5			1.0							
Nalidixic acid	Broilers	12	[1.5-36.4]								88.2					11.8			
	Cattle	22	[13.9-32.3]								77.9					4.7	17.4		
	Pigs	14	[9.3-19.4]								81.6	3.6	1.0	1.0	5.1	6.1	1.5		
Colistin	Broilers	0	[0.0-19,5]								100								
	Cattle	0	[0.0-4.2]								100								
	Pigs	<1	[0.01-2.8]								99.5					0.5			

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

Among *E. coli* F5 from cattle we observed a significant increase in resistance to nalidixic acid from 7% in 2000 to 22% in 2001. From 1996 to 2001, the overall trend in nalidixic acid resistance has been a steady increase (Figure 17).

In 2001, tetracycline was the most widely used antimicrobial for treatment of infections in pigs. Between 1996 and 2001, 50% to 70% of *E. coli* O149 isolates from weaned pigs were resistant to tetracycline - only sulfonamide resistance occurred more frequently (Figure 17). Nalidixic acid resistance has decreased among *E. coli* O149 from 1998 to 2001, reflecting the decreased use of fluoroquinolones for oral medication in pigs (see DANMAP 2000 for analysis of usage trend). However, nalidixic acid resistance remains more frequent among *E. coli* O149 from weaner pigs, compared to indicator *E. coli* (not serotyped) from pigs at slaughter (Figure 16 and Figure 17). This reflects the consumption pattern in pigs where 86% of the fluoroquinolones were used in piglets and weaned pigs while only 14% were administrated to slaughter pigs.

Apramycin was first marketed in Denmark in 1998 and is used for treatment of infections in pigs and calves. Certain apramycin resistance genotypes are cross-resistant to gentamicin. In 2001, we observed for the first time an increase in resistance to gentamicin among *E. coli* from pigs (Figure 17), even though the usage of gentamicin remained unchanged. It is possible that the increase is caused by use of apramycin, however, we have not yet examined the genetic basis for the emerging gentamicin resistance.

Staphylococci

The isolates of CNS and *S. aureus* originated from cases of bovine mastitis while *S. hyicus* originated from skin infections in pigs. Only isolates collected during the first 3 quarters of 2001 are included in this report. The MIC distribution and the occurrence of resistance are presented in Tables 38-40. In general, CNS and *S. aureus* were susceptible to most antimicrobials with little change between 2000 and 2001. Trends in resistance to some selected antimicrobials over a 6 year period (1996-2001) are presented in Figure 18. In general, *S. hyicus* from pigs were more often resistant to antimicrobials in the test panel than were staphylococci from cattle. Tetracycline resistance in *S. hyicus* increased significantly from 21% in 2000 to 47% in 2001 (Figure 18). The tetracycline usage in the pig production also increased during this time. Another explanation for the sudden increase in tetracycline resistance in *S. hyicus* could be the spread of a particular clone, although examination of the resistance profiles have not been able to confirm this.

We observed a decrease in erythromycin resistance in *S. hyicus* after use of tylosin as growth promoter in slaughter pigs was discontinued in March 1998. However, from 1999 to 2001, no further decrease occurred in erythromycin resistance (Figure 18). A likely explanation could be that tylosin remains used for treatment of disease in pigs with increasing usage between 1999 and 2001.

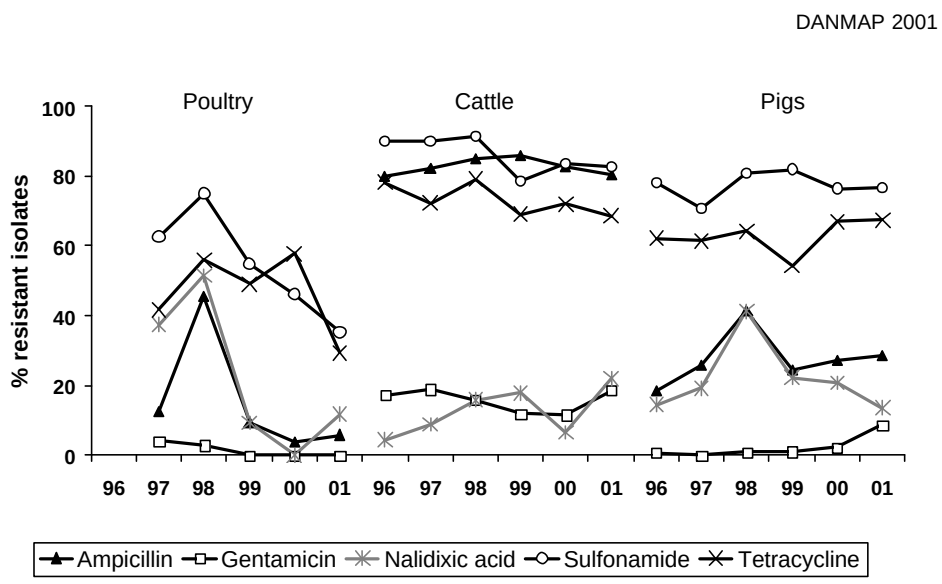


Figure 17. Trends in resistance to some selected antimicrobials among Escherichia coli *from diagnostic submissions from animals, Denmark*

Table 38. Distribution of MICs and occurrence of resistance among coagulase negative staphylococci from cattle (n=59), Denmark

DANMAP 2001

Compound	% Resistant	[95% Confidence interval]	Distribution (%) of MICs														
			<=0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Tetracycline	0	[0.0-6.1]				94.9	1.7	3.4 a)									
Chloramphenicol	0	[0.0-6.1]						3.4	39.0	54.2	3.4						
Florfenicol	0	[0.0-6.1]						52.5	45.8	1.7							
Oxacillin	0	[0.0-6.1]				98.3	1.7										
Penicillin	25	[15.0-38.4]	72.9		1.7	5.1	6.8	5.1	1.7	3.4	1.7	1.7					
Ceftiofur	0	[0.0-6.1]		3.4		25.4	30.5	40.7									
Sulfonamide	5	[1.1-14.2]								8.5	22.0	22.0	16.9	20.3	5.1	1.7	3.4
Trimethoprim	14	[6.0-25.0]					42.4	15.3	10.2	18.6	6.8	1.7	5.1				
Erythromycin	0	[0.0-6.1]			47.5	49.2	3.4										
Gentamicin	0	[0.0-6.1]					100										
Kanamycin	0	[0.0-6.1]						100									
Spectinomycin	2	[0.04-9.1]										13.6	84.7	1.7			
Streptomycin	5	[1.1-14.2]						61.0	22.0	11.9		1.7		3.4			
Ciprofloxacin	2	[0.04-9.1]		78.0	20.3						1.7						
Vancomycin	0	[0.0-6.1]					79.7	18.6	1.7								
Virginiamycin	0	[0.0-6.1]					100										
Quinupristin/dalfopristir	0	[0.0-6.1]					100										
Avilamycin	5	[1.1-14.2]						37.3	44.1	13.6	3.4		1.7				
Bacitracin	24	[13.6-36.6]									47.5	3.4	25.4	16.9	6.8		

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

Table 39. Distribution of MICs and occurrence of resistance among Staphylococcus aureus *from cattle (n=60), Denmark*

DANMAP 2001

Compound	% Resistant	[95% Confidence interval]	Distribution (%) of MICs												
			<=0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512
Tetracycline	0	[0.0-6.0]				100 a)										
Chloramphenicol	0	[0.0-6.0]						3.3	8.3	88.3						
Florfenicol	0	[0.0-6.0]						23.3	76.7							
Oxacillin	0	[0.0-6.0]				100										
Penicillin	18	[9.5-30.4]	81.7		1.7	1.7	5.0	8.3	1.7							
Ceftiofur	0	[0.0-6.0]			5.0	73.3	21.7									
Sulfonamide	0	[0.0-6.0]								10.0	11.7	50.0	25.0	3.3		
Trimethoprim	0	[0.0-6.0]					46.7	38.3	13.3	1.7						
Erythromycin	0	[0.0-6.0]		5.0	55.0	40.0										
Gentamicin	0	[0.0-6.0]					100									
Kanamycin	0	[0.0-6.0]						98.3	1.7							
Spectinomycin	5	[1.0-13.9]										1.7	93.3	5.0		
Streptomycin	0	[0.0-6.0]						5.0	48.3	43.3	3.3					
Ciprofloxacin	0	[0.0-6.0]		51.7	41.7	6.7										
Vancomycin	0	[0.0-6.0]					96.7	3.3								
Virginiamycin	0	[0.0-6.0]					100									
Quinupristin/dalfopristin	0	[0.0-6.0]					100									
Avilamycin	2	[0.04-8.9]						21.7	65.0	11.7	1.7					
Bacitracin	0	[0.0-6.0]									91.7	5.0	3.3			

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

Table 40. Distribution of MICs and occurrence of resistance among Staphylococcus hyicus *from pigs (n=53), Denmark*

DANMAP 2001

Compound	% Resistens [95% Confidence interval]		Distribution (%) of MICs <=0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512
Tetracycline	47	[33.3-61.4]				50.9		1.9			3.8	34.0	9.4 a)			
Chloramphenicol	0	[0.0-6.7]							13.2	86.8						
Florfenicol	0	[0.0-6.7]						58.5	41.5							
Oxacillin	0	[0.0-6.7]				100										
Penicillin	62	[47.9-75.2]	37.7				1.9	3.8	13.2	11.3	11.3	20.8				
Ceftiofur	0	[0.0-6.7]			3.8	62.3	34.0									
Sulfonamide	4	[0.5-13.0]									37.7	43.4	9.4	5.7		3.8
Trimethoprim	21	[10.8-34.1]					5.7	20.8	35.8	17.0			20.8			
Erythromycin	26	[15.3-40.3]			7.5	66.0					1.9	24.5				
Gentamicin	0	[0.0-6.7]					100									
Kanamycin	8	[2.1-18.2]							86.8		5.7			7.5		
Spectinomycin	21	[10.8-34.1]										5.7	73.6			20.8
Streptomycin	43	[29.8-57.7]						7.5	32.1	17.0			9.4	11.3	22.6	
Ciprofloxacin	8	[2.1-18.2]		84.9		7.5			7.5							
Vancomycin	0	[0.0-6.7]					96.2	3.8								
Virginiamycin	4	[0.5-13.0]					86.8	7.5	1.9		3.8					
Quinupristin/dalfopristin	4	[0.5-13.0]					96.2		1.9	1.9						
Avilamycin	0	[0.0-6.7]						7.5	83.0	9.4						
Bacitracin	0	[0.0-6.7]									15.1	49.1	35.8			

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

DANMAP 2001

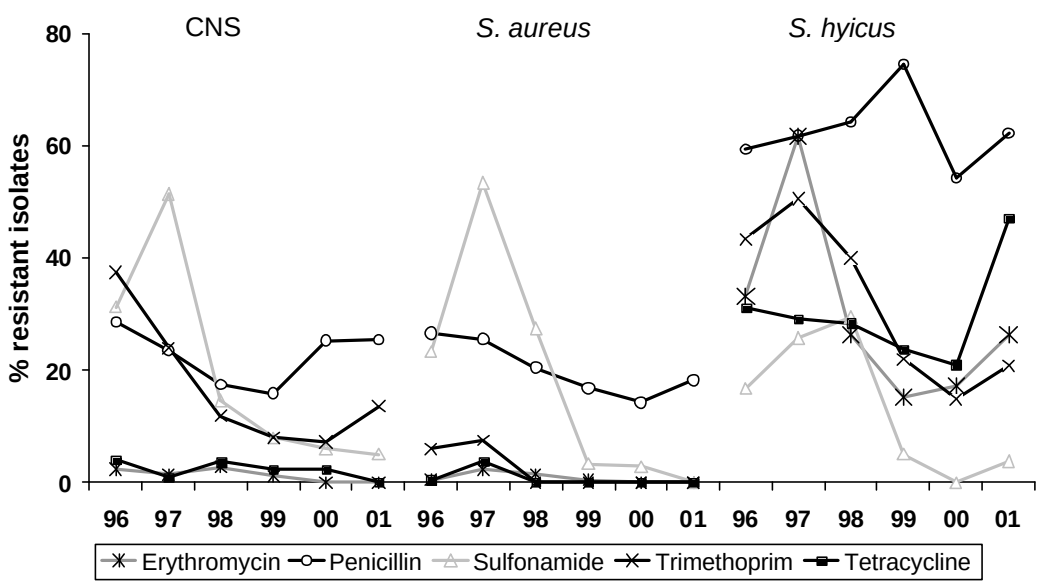


Figure 18. Trends in resistance to some selected antimicrobials among staphylococci from diagnostic submissions from animals, Denmark

Bacteria from humans

For *Salmonella* spp., *Campylobacter* spp., *Streptococcus pneumoniae* and *Staphylococcus aureus*, this report includes data representing the whole country. For *Escherichia coli* and coagulase-negative staphylococci, this report includes data from the clinical microbiology laboratories serving the Copenhagen and Frederiksberg municipalities, which have status of counties, and the counties of Copenhagen, Roskilde, West Zealand, Storstroem, Ribe, Ringkoebing, Aarhus, Viborg and North Jutland, which represent more than 70% of the Danish population. Some of these laboratories did not routinely test for resistance in *Streptococcus pyogenes* and the data for this microorganism cover only 56% of the population. More information on demographics is presented in Table 2, page 10.

Escherichia coli

The results for eleven counties for the period 1995-2001 are presented in Figures 19 and 20. As the number of laboratories that participate in DANMAP increases, it is becoming more difficult to represent and make sense of the data that have been collected since the beginning of the project. However, we still find it too early to pool these data from various origins since standardisation of surveillance methods, e.g. algorithm for removal of duplicate isolates, has not yet been achieved. This stresses the need for a national working group on antimicrobial resistance surveillance to clearly define these methods before a Danish electronic surveillance system is implemented.

Figure 19 shows the level of resistance to selected antimicrobials among *E. coli* blood isolates. As in 2001, and possibly with the exception of one county, data from 2001 confirm that the general increase in ampicillin resistance in *E. coli* blood isolates has stopped and remains at between 30% and 45%. The sharp variations observed in some counties between 2000 and 2001 are likely to be due to the smaller number of isolates tested in these counties. Similarly to what has been reported during the past years, gentamicin and cefuroxime resistance in *E. coli* blood isolates remained low in 2001. Figure 20 shows the level of resistance to selected antimicrobials among *E. coli* urine isolates. The results are presented separately for isolates from primary health care and from hospitals. Despite a resistance level of between 30% and 40%, sulfonamides still represent the drug of choice for treating urinary tract infections in Denmark. One should be aware that, in primary health care, a significant proportion of urine samples is submitted to the laboratory because of treatment failure and therefore represents a selected population. Additionally, one cannot exclude differences in the frequency of sampling among counties which precludes any comparison of resistance levels. However, if each county is considered separately, sulfonamide resistance was always higher in primary health care than in hospitals. This observation is consistent with the fact that sulfonamide use is very low in Danish hospitals (Table 11**,** page 24). Ampicillin resistance in *E. coli* urine isolates ranged between 35% and 45%. Finally, ciprofloxacin resistance in *E. coli* urine isolates remained very low in 2001.

Coagulase-negative staphylococci

Figure 21 shows the level of resistance to selected antimicrobials among coagulase-negative staphylococci blood isolates from eleven counties. As in most other countries, penicillin resistance was almost 80%. Methicillin resistance varied amoung counties from less than 10% to approximately 50%. However, it is possible that differences in the level of resistance were merely the consequences of the procedure for selection of isolates that are submitted for susceptibility testing. For example, the laboratories reporting the highest percentage of methicillin-resistant coagulase-negative staphylococci mentioned that they only perform susceptibility testing in isolates of clinical significance. Caution is therefore warranted when trying to make comparisons of resistance levels among counties. Finally, erythromycin resistance in coagulase-negative staphylococci blood isolates ranged betweem 20% and 40% depending on the county.

Streptococcus pneumoniae

As the national reference centre, the Streptococcus Unit at the Statens Serum Institut performs typing and susceptibility testing on *S. pneumoniae* isolates referred by the Danish local clinical microbiology laboratories. In 2001, susceptibility testing was performed on 981 non duplicate isolates from blood or spinal fluid samples. Resistance to penicillin in *S. pneumoniae* isolates is an increasing problem worldwide. In Denmark, this type of resistance was rare until 1995 when it started to increase reaching a peak at approximately 4% in 1999. In 2000, there was a slight decrease in the percentage of penicillin-non susceptible *S. pneumoniae* and this decrease continued reaching 2% in 2001 (Figure 22).

Resistance to erythromycin has been increasing since 1992 and reached 5% among isolates from blood and spinal fluid in 2000. In 2001, the level of resistance remained at 5% (Figure 22). This was surprising since there has been no major change in overall macrolide consumption, which has remained at about 2 DDD/

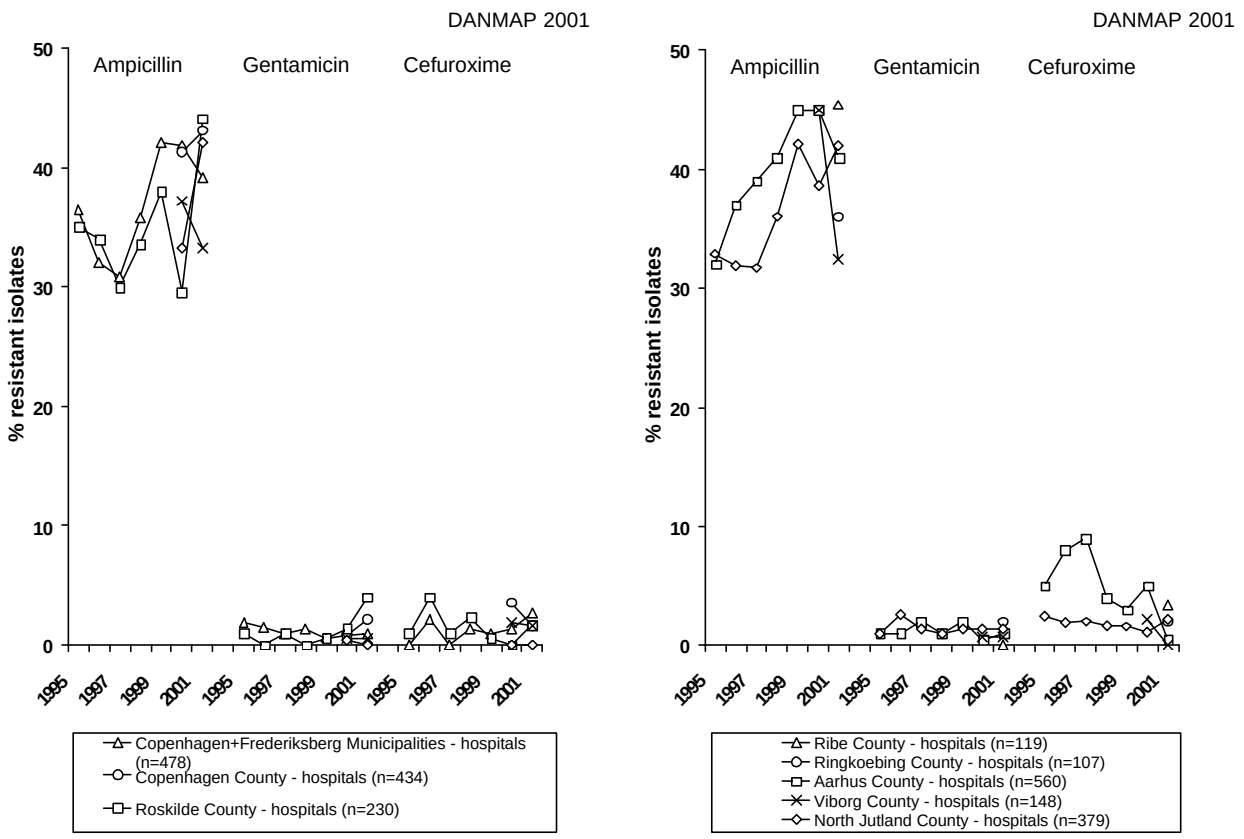


Figure 19. Resistance (%) to selected antimicrobials in Escherichia coli *blood isolates from humans, Denmark. The number n in parentheses represents the number of isolates tested for antimicrobial susceptibility in 2001*

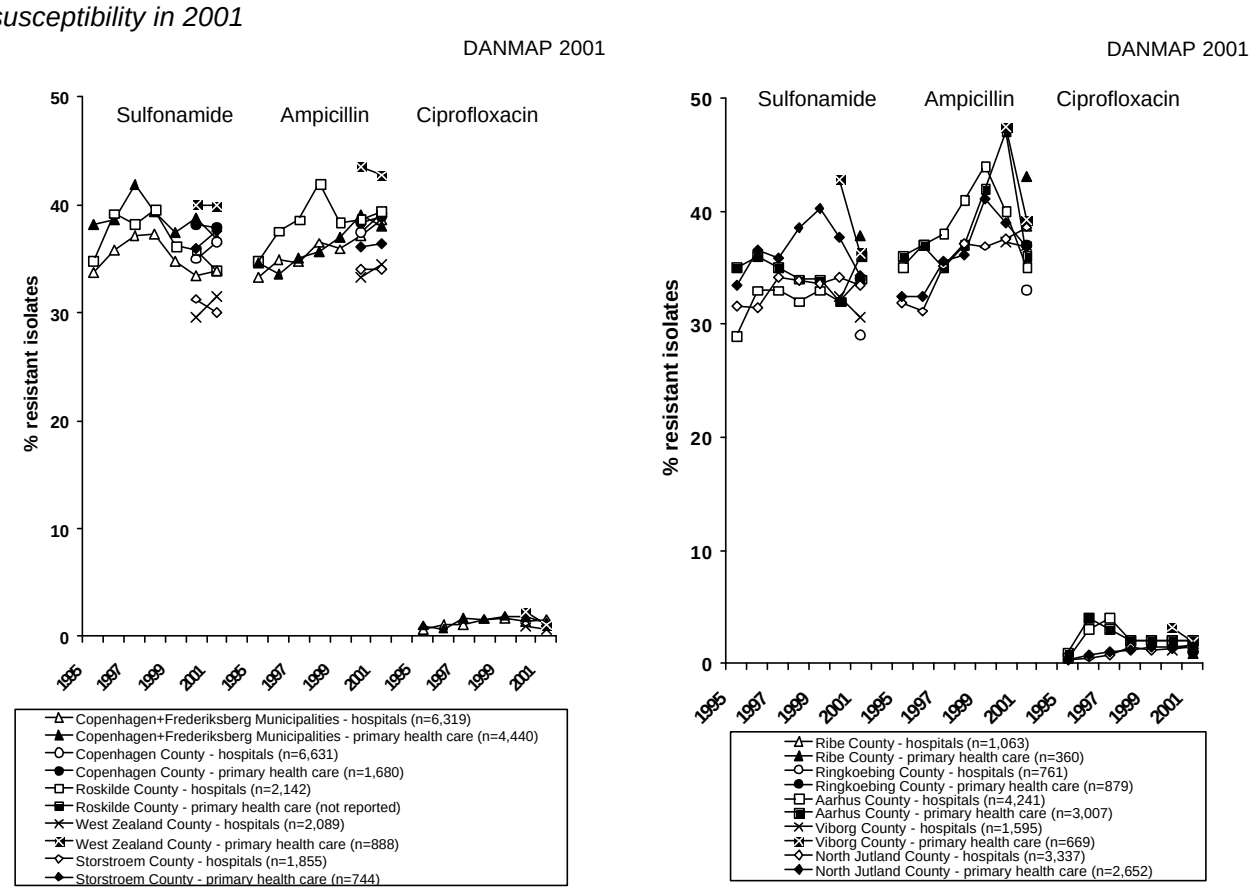


Figure 20. Resistance (%) to selected antimicrobials in Escherichia coli *urine isolates from humans, Denmark. The number* n *in parentheses represents the number of isolates tested for antimicrobial susceptibility in 2001.*

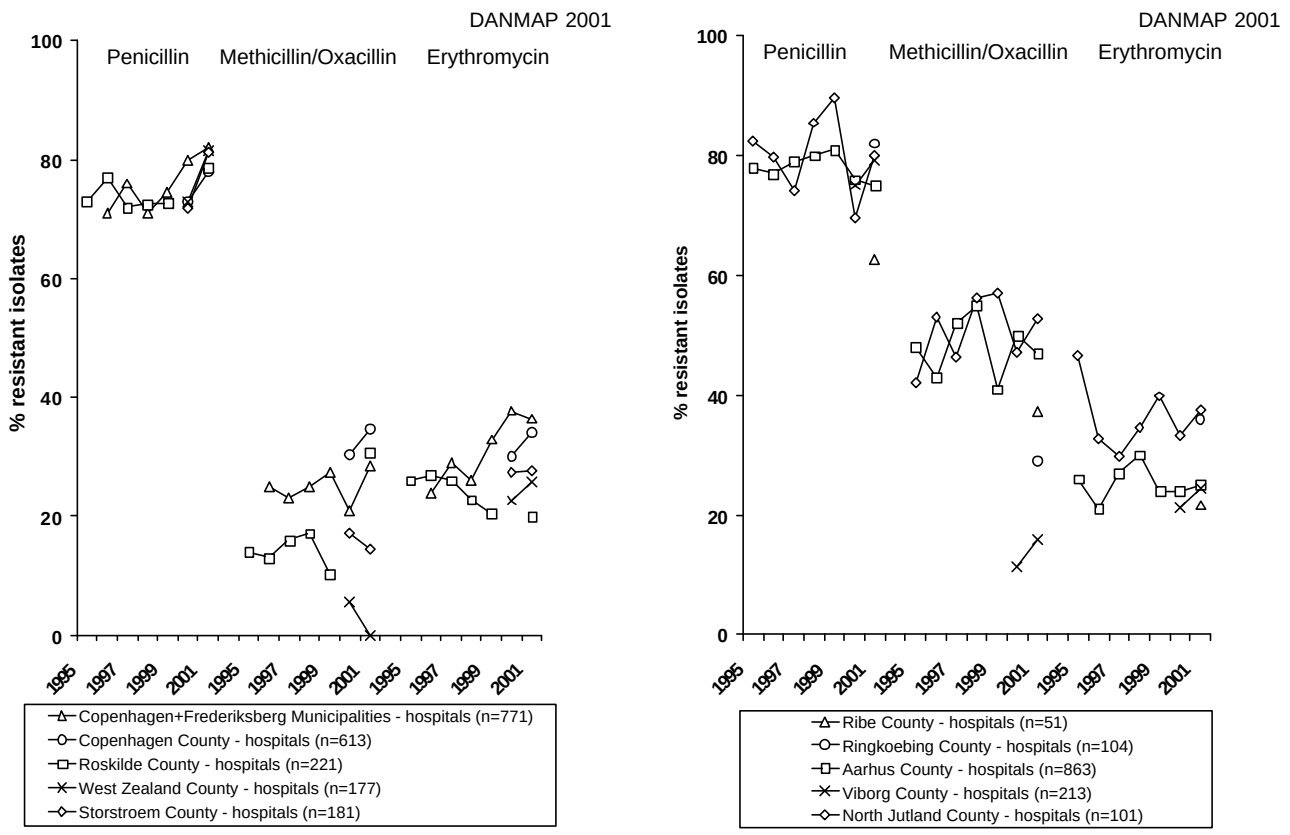


Figure 21. Resistance (%) to selected antimicrobials in coagulase-negative staphylococci blood isolates from humans, Denmark. The number n *in parentheses represents the number of isolates tested for antimicrobial susceptibility in 2001*

1,000 inhabitant-days during the past years (Table 10, page 20). In Denmark, the prevalence of erythromycin-resistant *S. pneumoniae* started to increase following the introduction of azithromycin and then showed a parallel increase to consumption of this macrolide, while during the same period consumption of other macrolides either decreased or remained the same (Figure 2, page 20). Since 1999, there has been no further increase in azithromycin consumption, which could well be the cause for the interruption observed in the increase in erythromycin-resistant *S. pneumoniae*.

Preliminary results from a multivariate model that tested consumption of each individual antimicrobial during 1995-1999 showed that azithromycin consumption was the most powerful independent factor associated with erythromycin resistance in *S. pneumoniae* at the county level. Other preliminary data from typing showed that most erythromycin-resistant *S. pneumoniae* isolated in Denmark during this period corresponded to a single clone (Margit Kaltoft, personal communication). These results suggest that the increase in erythromycin-resistant *S. pneumoniae* in Denmark was due to both person-to-person transmission of a successful clone and pressure due to consumption of macrolides in primary health care. The possible differential effect of antimicrobial pressure due to macrolides with different half-lives is currently under investigation.

Streptococcus pyogenes

In 2001 we introduced surveillance of macrolide resistance in *S. pyogenes* (group A streptococci or GAS). Until now, resistance to macrolides has been considered a minor problem in Denmark, but increasing resistance worldwide has called for closer monitoring. Among a total of 4,875 GAS isolates from various clinical samples in nine counties, resistance to erythromycin was 2.7% [95% C.I.: 2.3-3.2], with county-to-county variations ranging from 0.4% to 4.5%. As for *S. pneumoniae*, both the maintained high level of overall consumption of macrolides and changes in the distribution of the macrolides used could result in an increase in erythromycin-resistant GAS in Denmark as seen in other countries. To monitor a possible increase in erythromycin resistance, DANMAP will now include GAS in its surveillance. Additionally, preliminary reports on the distribution of macrolide resistance genes among GAS isolates found all three genes to be present in Denmark with *ermB* being the most frequent. Typing found 14 different patterns among erythromycin-resistant GAS, thus showing that macrolide resistance in GAS is not a clonal problem as seen for *S. pneumoniae*. Forty-eight percent of the erythromycin-resistant GAS isolates were also resistant to tetracycline.

Staphylococcus aureus

For the past 20 years, methicillin-resistant *S. aureus* (MRSA) represented less than 1% of *S. aureus* blood isolates and more than one half of these MRSA strains had been acquired outside Denmark. Last year, we reported on a slow increase in the overall number of MRSA cases in Denmark. During the past year, we performed a detailed analysis of the MRSA register maintained by the Staphylococcus Unit at the Statens Serum Institut for the period 1999-2001. It was then completed by an analysis of patients' discharge letters and of a database containing the pulsed-field gel electrophoresis (PFGE) profiles of all strains.

Although part of the increase was due to an increasing number in MRSA isolates from active screening samples, there has been an increase in reported MRSA infections from 54 cases in 1999 to 83 in 2001 (Figure 23). The number of MRSA infections imported from other countries showed little variations during 1999-2001. The analysis confirmed that most of the increase observed in 2000 was due to three outbreaks in Danish hospitals involving three different MRSA clones. These outbreaks were quickly controlled. Additionally, there has been a steady increase in reported MRSA infections in primary health care during 1999-2001. About 60% of these community MRSA infections were due to a single clone named EDK97-1 (Figure 23). This clone first started spreading in 1997 in the county of North Jutland and has since been spreading in the rest of the Danish community. In 2001, infections due to this clone were reported from 11 of the 16 Danish counties. Clone EDK97-1 is still very rarely isolated from hospitalised patients with only 1 infection reported in 2000 and 2 infections in 2001. Despite the very low prevalence of MRSA in Denmark, this new trend in the community is worrying. It stresses the importance of maintaining a Danish MRSA register that includes information on patient, location, type of infection and PFGE typing.

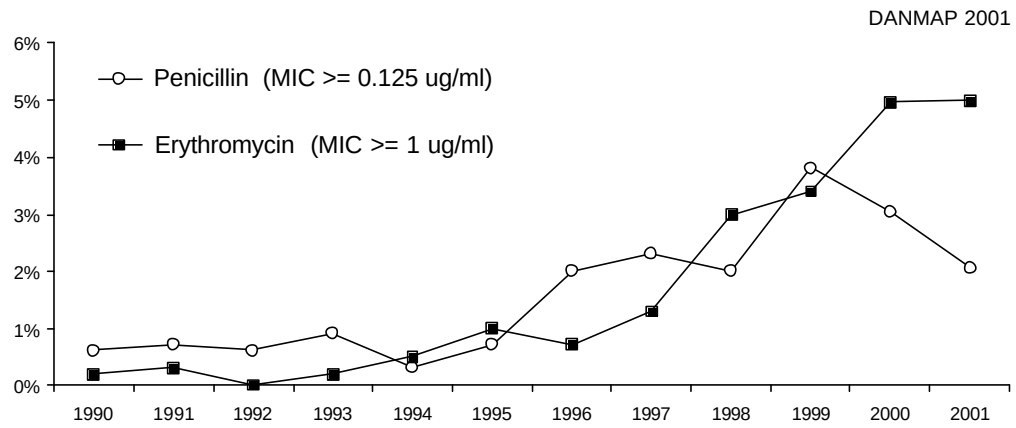


Figure 22. Resistance (%) to selected antimicrobials in Streptococcus pneumoniae *blood and spinal fluid isolates from humans, Denmark*

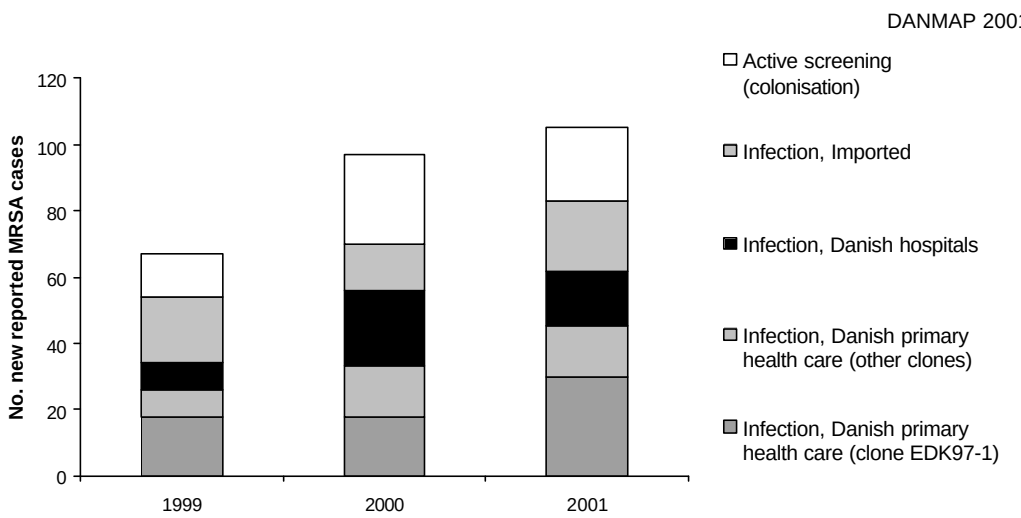


Figure 23. New reported cases of human infection or colonisation by methicillin-resistant Staphylococcus aureus *(MRSA), Denmark*

Text box 4

Epidemiology and antifungal susceptibility of human *Candida* bloodstream isolates in Denmark

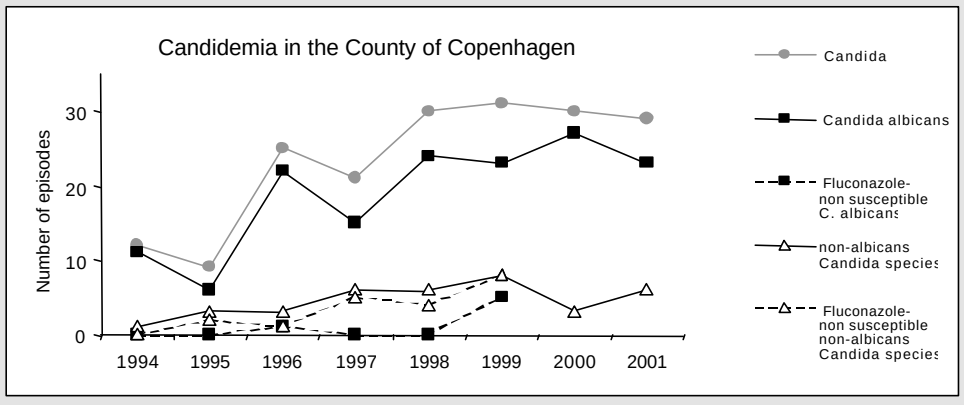
Invasive *Candida* infections are increasing in many countries as a consequence of an increasing number of patients at risk for these infections. Risk factors for infection include indwelling devices, treatment with broad-spectrum antimicrobials and/or immunosuppressive agents and complicated abdominal surgery. In Denmark, information on the epidemiology and antifungal susceptibility of these infections is sparse due to the lack of a surveillance program and to the fact that only a small proportion of *Candida* isolates are tested for susceptibility to antifungals. Indeed, while antimicrobial susceptibility testing of bacteria has been performed on a routine basis for decades, a standardized method for antifungal susceptibility testing of yeasts has only been available for 4 years. Susceptibility patterns vary among *Candida* species. *Candida albicans* is generally susceptible to fluconazole, whereas *C. glabrata* is intrinsically less susceptible and *C. krusei* resistant to this widely used antifungal. Therefore, changes in species distribution are also used as an indirect indicator for changes in susceptibility patterns.

An increase in the number of candidemia cases, and in particular in the number of non-*albicans* *Candida* species, has been observed in Denmark during the last decade. Schønheyder et al. [1] reported an increase in candidemia in the county of North Jutland over a 6-year period, highest among intensive care unit patients in whom incidence rose from 4 to 30 per 1,000 blood culture episodes between 1995-1996 and 1999-2000. *Candida albicans* accounted for 77% of these episodes. A similar increase in the number of candidemia episodes has been observed in Copenhagen County, with a simultaneous increase in episodes due to isolates not fully susceptible to fluconazole (Figure). *Candida albicans* accounted for 85% of the episodes in 1994-1996 and for 81% in 1998-2001 [2, 3]. Finally, 55 cases of candidemia, of which only 47% involved *C. albicans,* were diagnosed during 1987-1997 among patients with underlying haematological diseases admitted at Rigshospitalet, a Copenhagen university hospital that includes a bone marrow transplant unit [4].

In conclusion, there are very few studies on the epidemiology and susceptibility of candidemia in Denmark. However, available data indicates an increasing incidence of candidemia in general and an increase of *Candida* blood isolates with reduced susceptibility to fluconazole in particular.

References:

1. Schønheyder HC. Candidæmi i Nordjyllands amt – en opfølgning. Nyt om Mikrobiologi 2001;(57): 5.
2. Arendrup M, Lundgren B, Jensen IM, Hansen BS, Frimodt-Møller N. Comparison of Etest and a tablet diffusion test with the NCCLS broth microdilution method for fluconazole and amphotericin B susceptibility testing of *Candida* isolates. J Antimicrob Chemother 2001, 47:521-6.
3. Jarløv JO. Dept. of Clinical Microbiology, Herlev Hospital, Denmark. Personal communication.
4. Bruun B, Christensen BE, Ellegård J, et al. Svampeinfektioner. In: Infektioner hos hæmatologiske og onkologiske patienter. Odense Universitets Forlag 2000: 25-31.



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Appendix 1
Materials and methods

Data on consumption of antimicrobials

Antimicrobials in animals

In Denmark, all antimicrobials used in therapy are prescription-only medicines and must be distributed through pharmacies. The pharmacy either sells the medicines to veterinarians for use in practice or for re-sale to farmers, or will sell directly to the animal owner on presentation of a prescription. By law, the profit that veterinarians can make on the sale of medicines is severely limited and thus they have little financial enticement to sell medicines. Accordingly, an estimated 80% of all antimicrobials used for therapy in food animals are sold to farmers by pharmacies on the basis of a veterinary prescription.

In previous DANMAP reports data on antimicrobial usage in animals has been based on sales figures reported by the pharmaceutical industries. In 2000, the VetStat programme was initiated. This programme collects data on antimicrobial usage close to the point of use and is prescription based.

Reports from pharmaceutical companies. All medicines must be given a marketing authorisation by the Danish Medicines Agency (DMA), and importers and manufacturers are required to provide an annual report to the DMA on the quantities sold. These statistics will be affected by changes in the stocks held by wholesalers and pharmacies and provide little information on the food animal species in which the antimicrobials are used. Products and formulations obviously intended for use only in pets have been excluded from the statistics shown in this report.

The results shown in Table 3, page 11 were rounded, so that quantities between 1 and 25 are shown as ”< 25”; quantities between 25 and 1,000 were rounded to the nearest 50, and quantities over 1,000 kg were rounded to the nearest 100.

The Danish Plant Directorate is responsible for the collection of data on the use of antimicrobials for growth promotion and on the use of coccidiostats. The statistic is based on compulsory reporting by companies authorised to produce premixes containing antimicrobials. The system used for collection of data allows us to discriminate between the quantities of, for example tylosin, used for growth promotion and for therapy. From 2001, information on usage of coccidiostats was collected using the VetStat system.

The VetStat programme – Point of use data. For details about data collection in the VetStat system, please refer to the Text box 1 on page 12-13. Antimicrobial groups used when reporting sales on basis of information from pharmaceutical companies and the VetStat prescription database are presented in the Text boxes 5 and 6, respectively.

Antimicrobials in humans

The Danish Medicines Agency (DMA) has the legal responsibility for monitoring the consumption of all medicinal products in humans. This is done by monthly reporting from all pharmacies in Denmark, including hospital pharmacies, to the DMA. Data from the primary health care sector have been collected since 1994, whereas valid data on consumption in hospitals are only available from 1997.

In Denmark, all antimicrobials for use in humans are prescription-only medicines. All antimicrobials are sold by pharmacies in defined packages. Each package is uniquely identified by a code, which can be related to the size of the package (by content and in Defined Daily Doses or DDD), to the code of the antimicrobial in the Anatomical Therapeutic Chemical (ATC) classification system, and to the name of the producer. In addition, the following information is collected for each transaction: social security number (CPR-number) of the patient, code identifying the prescribing physician, date and place (pharmacy, hospital pharmacy, institution) of the transaction, and information regarding reimbursement of cost if applicable. Information on the indication for the prescription is not yet available. The data are transferred monthly to the DMA in an electronic format. On-line transfer of the transactions in real time is being established.

The present report includes data on the consumption of antibacterials for systemic use, or group J01 of the 2001 update of ATC classification system, in primary health care and in hospitals. As recommended by the World Health Organization (WHO), consumption of antimicrobials in primary health care is expressed as a number of DDD per 1,000 inhabitants and per day (DDD/1,000 inhabitant-days) and consumption of antimicrobials in hospitals is expressed as a number of

Text box 5

DANMAP- Antimicrobial groups

Categorisation of antimicrobials used when reporting sales on the basis of information from pharmaceutical companies

DANMAP antimicrobial category	Active antimicrobial included in category
Aminoglycosides	Apramycin, dihydrostreptomycin, framycetin, gentamicin, neomycin, spectinomycin
Cephalosporins	Cefadroxil, cefalexin, cefapirin, cefoperazone, cefquinom, ceftiofur,
Macrolides + lincosamides	Lincomycin, spiramycin, tiamulin, tilmicosin, tylosin,
Penicillins with narrow spectrum	Benzylpenicillins, benethamin penicillin, benzathine penicillin, penethamath hydroiodide
Penicillins with extended spectrum	Amoxycillin, ampicillin, cloxacillin, nafcillin
Fluoroquinolones	Danofloxacin, difloxacin, enrofloxacin, marbofloxacin
Sulfonamides	Sulfadimidine
Sulfonamides + trimethoprim	Baquiloprim, sulfadiazine, sulfadimidine, sulfadoxine, sulfatroxazole, trimethoprim
Tetracyclines	Chlortetracycline, doxycycline, oxytetracycline, tetracycline
Others	Bacitracin, colistin, florphenicol

Text box 6

VetStat - Antimicrobial groups

Categorisation of antimicrobials used when reporting usage on the basis of the VetStat prescription database

Antimicrobial category	VetStat antimicrobial category abbreviation	Antimicrobial agents included in category
Amphenicols	Amcol	Chloramphenicol, florphenicol
Aminoglycosides	Amglc	Apramycin, dihydrostreptomycin, framycetin, gentamicin, neomycin, spectinomycin
Cephalosporins	Ceph	Cefadroxil, cefalexin, cefapirin, cefoperazone, cefquinom, ceftiofur
Fluoroquinolones	FQ	Danofloxacin, difloxacin, enrofloxacin, marbofloxacin
Quinolones	Quinol	Oxolinic acid
Lincosamide	Linco	Lincomycin
Macrolides	Macrol	Azithromycin, clindamycin, erythromycin, spiramycin, tiamulin, tilmicosin, tylosin
Penicillins with narrow spectrum	Pen-sim	Benzyl penicillin, benzyl penicillin procaine, penethamat hydroiodide, pencillin benethamine, phenoxymethyl penicillin
Penicillins with extended spectrum	Pen-ext	Amoxicillin, ampicillin, cloxacillin benzathine, nafcillin
Sulfonamides and sulfonamides with trimethoprim	Sulfa-TMP	Baquiloprim, sulfaclozine, sulfadiazine, sulfadimidine, sulfadoxine, sulfamethizole, sulfamethoxazole, sulfathiazole, sulfatroxazole, trimethoprim
Tetracyclines	Tet	Chlortetracycline, doxycycline, oxytetracycline, tetracycline
Others	Others	Bacitracin, colistin, fusidic acid, metronidazole, polymyxins

DDD per 1,000 beds and per day (DDD/1,000 bed-days). Data on the number of bed-days in each hospital were obtained from the National Board of Health (http://www.sst.dk).

Collection of bacterial isolates

Isolates from animals

Bacterial isolates included in the monitoring programme are collected from animals at slaughter (*E. coli,* enterococci and *Campylobacter)*, as well as from diagnostic submissions *(Staphylococcus hyicus* from pigs and coagulase negative staphylococci and *Staphylococcus aureus* from examination of cattle for mastitis, and *E. coli* from diarrhoea in cattle and pigs and septicaemia in poultry). Finally, *Salmonella* isolates from subclinical infections as well as from cases of clinical salmonellosis are included.

The samples from animals at slaughter are collected by meat inspection staff or company personnel and sent to the Danish Veterinary Institute for examination. The number of samples for each plant has been determined in proportion to the number of animals slaughtered per year. Each sample represents one herd or flock. They are collected once a month (weekly for broilers). The broiler, cattle and pig slaughter plants included in the surveillance programme account for 98%, 80% and 95%, respectively, of the total production of these animal species in Denmark. Accordingly, the bacterial isolates may be regarded as representing a stratified random sample of the respective populations, so that the occurrence of resistance provides an estimate of the true occurrence in the populations.

The *Salmonella* isolates included in DANMAP are selected as a true random sample among isolates serotyped at the Danish Veterinary Institute. The DVI is the national reference laboratory with respect to *Salmonella* in animals, feeding stuffs and food, and receives all such isolates for typing.

Bacterial isolates from diagnostic submissions are selected by a pseudo-random process among isolates from submissions to the DVI, the Cattle Health Laboratory in Ladelund and the laboratory of the Federation of Danish Pig Producers and Slaughterhouses in Kjellerup. Accordingly, the programme achieves nationwide coverage for these pathogens.

Isolates from food

All food samples were collected at wholesale and retail outlets by the Regional Veterinary and Food Control Authorities (RFCA) during the course of routine inspection carried out by the authorities, or on request specifically for the DANMAP surveillance programme. The collection of food samples for analyses of indicator bacteria (enterococci and *E. coli*) was planned and coordinated by the Danish Veterinary and Food Administration (DVFA). The collected material consisted of both Danish and imported foods. The food samples were collected according to the guidelines for microbiological examination of foods from the DVFA (Vejledning om mikrobiologisk kontrol af fødevarer, ISBN: 87-90978-46-3).

Isolates from humans

With the exception of *Salmonella* Typhimurium isolates which are all tested for susceptibility to antimicrobials, *Salmonella* spp. and *Campylobacter* spp. from humans represent a random sample of isolates grown from faeces samples submitted for microbiological diagnostic to the Department of Gastrointestinal Infections at the Statens Serum Institut in 2001.

All *Staphylococcus aureus* blood isolates nationwide are sent to the Staphylococcus reference laboratory at the Statens Serum Institut for confirmation of susceptibility results, phage typing and pulsed-field gel electrophoresis (PFGE) typing.

Similarly, all *Streptococcus pneumoniae* blood and spinal fluid isolates nationwide are sent to the Streptococcus Unit at the Statens Serum Institut for confirmation of susceptibility testing and typing.

Escherichia coli and coagulase-negative staphylococci from humans represent all isolates recorded from either blood or urine samples submitted for microbiological diagnostic at one of the ten participating laboratories serving the Copenhagen and Frederiksberg municipalities, Copenhagen county, Roskilde county, West Zealand county, Storstroem county, Ribe county, Ringkoebing county, Aarhus county, Viborg county and North Jutland county, respectively.

Isolation of bacteria

Examination of samples from animals

***Salmonella*.** Examination of samples from cattle and pigs was done by non-selective pre-enrichment of 22 g

material in 200 ml of BPW and incubated overnight at 37°C. A plate with Modified Semi-solid Rappaport-Vassiliadis medium was inoculated with 100 ml of pre-enrichment broth deposited on the agar as 3 drops. Overnight incubation at 41.5°C was followed by serotyping of suspect colonies by slide agglutination.

Samples from poultry were examined by non-selective pre-enrichment in BPW of paired sock samples, or homogenized organs, at a ratio of 1:9 and incubated at 37°C overnight, followed by selective enrichment by inoculation of 9.9 ml Rappaport-Vassiliadis broth with 0.1 ml pre-enrichment broth and incubation at 41.5°C overnight. The selective broth was inoculated onto Rambach agar. Presumptive *Salmonella* isolates were verified and typed by slide agglutination.

Campylobacter. The samples were examined by direct inoculation of selective agar as well as by selective enrichment. As selective agar we used CCD agar, which was incubated in microaerophilic atmosphere with 3% hydrogen for 1-3 days at 42°C. Selective enrichment was done by inoculation of Preston broth at a ratio of 1:10, followed by incubation in microaerophilic atmosphere for 24 h at 42°C. Ten ml of this enrichment culture was inoculated onto CCD agar and incubated as described above. Campylobacter-like colonies were identified by their catalase activity, by their ability to hydrolyse hippurate and indoxyl acetate, and by their susceptibility to cephalothine.

Escherichia coli. The material was inoculated directly onto Drigalski agar and incubated at 37°C overnight. Yellow colonies that were catalase positive and oxidase negative were identified according to the following standard criteria: indole, citrate, methyl red and Voges-Proskauer reaction.

Enterococci. Enterococci from pigs and cattle were isolated and identified by the following procedure. One drop of faecal material suspended in 2 ml sodium chloride (0.9%) was spread on Slanetz agar and incubated for 2 days at 42°C. Up to three colonies showing a morphology typical of *E. faecalis* and *E. faecium* were re-inoculated on Slanetz agar and incubated for 2 days at 37°C. The isolates were then sub-cultivated onto aesculine agar. Aesculine positive, white colonies were identified according to the following criteria: motility, arginine dihydrolase and the ability to ferment mannitol, ribose, sorbitol, arabinose, raffinose and melibiose.

Enterococci from broilers were isolated and identified as follows. Cloacal swabs were incubated overnight at 42°C in Enterococcus Selective Broth, prepared with a composition identical to that of Enterococcosel broth (Becton Dickinson). Cultures were streaked on Slanetz agar and incubated for 48 h at 37°C. Colonies that morphologically resembled *E. faecium* and *E. faecalis* were identified to species level by using standard biochemical and physiological tests as described above. A subset of all isolates verified as *E. faecium* and *E. faecalis* were subjected to antimicrobial susceptibility testing.

Pathogens. The diagnostic submissions were examined according to the standard procedures employed by the participating laboratories. All bacterial isolates from food animals have been stored at –80°C for further study as required.

Examination of food samples

The isolation of indicator organisms from food samples was performed by the RFCA. Subsequently, the isolates were sub-cultured to standard transport media and shipped to the Danish Veterinary and Food Administration. Verifications of species identity and MIC-determinations were performed by the DVFA. Only one strain of *E. coli* and/or Enterococcus from each food sample was tested for antimicrobial susceptibility.

The isolation method for *E. coli* employed 5 grams of food, which was incubated at 44°C for 18-24 hours in 45 ml of MacConkey- or laurylsulfate-broth. The broth culture was streak-inoculated onto violet red bile agar and incubated for 48 hours at 44°C. Presumptive *E. coli* were sub-cultured onto blood agar, transferred to standard transport medium and shipped to DVFA. The isolates were identified as *E. coli* by standard morphological examinations and biochemical tests, including an api 20E test (bioMérieux, France) or AP80 test (Sensititre).

Analysis for enterococci was carried out by adding 5 g of the sample to 45 ml of azide dextrose broth, which was incubated at 44°C for 18-24 hours, and subsequently streaked onto Slanetz-Bartley agar. After incubation at 44°C for 48 hours the plates were examined for growth, and typical red colonies were sub-cultured on blood agar, then transferred to transport medium and shipped to the DVFA. The isolates were identified by standard morphological examinations and biochemical tests, including an api 20STREP test (bioMérieux, France) or AP90 test (Sensititre). Only *E. faecium* and *E. faecalis* were included in the surveillance.

A few of the *Enterococcus* and *E. coli* strains were isolated in accordance with the Nordic Committee on Food Analysis (NMKL) No. 68, 2nd ed., 1992 (*Enterococcus*) and NMKL No. 125, 3rd ed., 1996 (*E. coli*).

Salmonella isolates were isolated according to NMKL No. 71, 5th ed., 1999. Sero- and phage-typing was performed at DVI.

Thermotolerant *Campylobacter* spp. was isolated by a semi-quantitative method. Twenty-five g food sample was mixed 1:4 with Mueller-Hinton bouillon supplemented with sodium pyrovate 0.25 mg/l, sodium metabisulphite 0.25 mg/l, ferro sulphate 0.25 mg/l, cefaperazone 30 mg/l, and trimethoprim lactate 50 mg/l and the sample was stomachated. Dilutions 1:10 were prepared. One ml from each dilution was enriched under microaerophilic conditions for 24 hours at 42 ºC in 9 ml of Mueller-Hinton bouillon with supplement (as described above). After pre-enrichment 10 µl was striked on mCCDA and further incubated under microaerophilic conditions for 24-48 hours at 42 ºC. mCCDA plates were examined for the presence of *Campylobacter*-like colonies. Suspected colonies were verified by phase-contrast microscopy, positive oxidase reaction, and hydrolysis of hippurate- and indoxyl acetate. Species identification was performed according to NMKL No. 119, 2nd ed., 1990. Only isolates of *C. jejuni* were included in the surveillance.

Examination of samples from humans

Salmonella spp. were isolated from faeces samples using the SSI Enteric Medium (SSI rød plade, SSI Diagnostika, Copenhagen, Denmark) and enrichment using a 0.6% selenite medium (SSI Diagnostika).

Campylobacter spp. were isolated from faeces samples using a modified CCDA medium (SSI Diagnostika).

Other clinical isolates were isolated on various common media used in clinical microbiology laboratories.

Susceptibility testing

Isolates from animals and foods

Plate dilution was used to test the susceptibility of *Campylobacter* isolates to all animicrobials included in the panel.

All other susceptibility testing was done with Sensititre (Trek Diagnostic Systems Ltd.), a commercially available MIC technique using dehydrated antimicrobials

Table A1. Breakpoints and range of dilutions used for testing bacteria from animals and food. Isolates with MIC higher than or equal to the figures shown were considered resistant

DANMAP 2001

Antimicrobial agent	*E. coli, Salmonella*		Staphylococci		Enterococci		*Campylobacter*	
	Breakpoints µg/ml	Range	Breakpoints µg/ml	Range	Breakpoints µg/ml	Range	Breakpoints µg/ml	Range
Ampicillin	32	1-32					32	1-32
Apramycin	16	4-64						
Avilamycin			16	2-32	16	1-32		
Bacitracin			128	16-256	128	8-256		
Ceftiofur	8	0.5-8	8	0.12-16				
Chloramphenicol	32	2-64	32	2-64	32	2-64	32	1-64
Ciprofloxacin	4	0.03-4	4	0.12-8			4	0.03-16
Colistin	16	4-64					64	0.5-64
Erythromycin			8	0.12-16	8	1-32	32	0.25-32
Flavomycin					16	0.5-32		
Florfenicol	32	2-64	32	1-64	32	2-32		
Gentamicin	16	1-32	16	1-32	1,024	128-2,048	16	0.5-32
Kanamycin			64	4-128	2,048	128-2,048		
Nalidixic acid	32	4-128					64	1-128
Neomycin	16	2-32					16	1-64
Nitrofurantoin					128	64 - 256		
Oxacillin + 2% NaCl			4	0.5-8				
Penicillin			0.25	0.06-16	16	2-128		
Salinomycin					16	1-32		
Spectinomycin	128	2-128	128	8-256				
Streptomycin	32	4-64	32	2-128	2,048	128-2,048	16	1-64
Sulfamethoxazole	512	32-512	512	8-512			512	8-512
Quinupristin/dalfopristin a)			4	1-32	4	0.5-32		
Tetracycline	16	2-32	16	0.5-32	16	1-32	16	0.5-32
Trimethoprim	16	4-32	16	1-32				
Vancomycin			32	1-32	32	1-32		
Virginiamycin			8	1-32	8	0.5-32		

a) The trade name is Synercid®

in microtitre wells. The wells were inoculated according to NCCLS guidelines and incubated aerobically at 37°C for 18-22 hours. The MIC was defined as the lowest concentration of antimicrobial with no visible growth. The breakpoints used are shown in Table A1.

The following strains were used for quality control: *Staphylococcus aureus ATCC 29213*, *Escherichia coli ATCC 25922, Pseudomonas aeruginosa ATCC 27853* and *Enterococcus faecalis ATCC 29212*. In Sensititre, weekly quality control was performed by inoculation and incubation of a set of wells with the control stains. The MIC values for the strains were evaluated in accordance to NCCLS guidelines and tests re-done if the values were out of range. With plate dilution, all 4 control strains were included on each plate.

Isolates from humans

Gastrointestinal pathogens. Susceptibility testing for *Salmonella* spp. isolates was performed using the tablet diffusion method (Neo-SensitabsÒ, A/S Rosco, Roskilde, Denmark) on Danish Blood Agar (Resistens-plade, SSI Diagnostika) and the breakpoints defined in Table A2.

Susceptibility testing for *Campylobacter* spp. isolates was performed using the tablet diffusion method (Neo-SensitabsÒ, A/S Rosco) on 5% blood yeast extract-supplemented agar (SSI Diagnostika) and the breakpoints defined in Table A2.

Staphylococcus aureus. The Staphylococcus Unit at the Statens Serum Institut is using the tablet diffusion method (Neo-SensitabsÒ, A/S Rosco) on Danish Blood Agar (Resistensplade, SSI Diagnostika) and the breakpoints defined for this medium by A/S Rosco. Methicillin resistance was confirmed with a 3-h hybridization assay for the detection of the mecA gene (Skov RL, et al. J. Antimicrob. Chemother. 1999; 43: 467-475).

Streptococcus pneumoniae. The Streptococcus Unit at the Statens Serum Institut screens for penicillin-resistant *S. pneumoniae* using a 1 microgram oxacillin tablet (Neo-SensitabsÒ, A/S Rosco) on 10% horse blood agar (SSI Diagnostika). Penicillin MICs are determined using the E-test (AB Biodisk, Solna, Sweden) on Danish Blood Agar (Resistensplade, SSI Diagnostika). The breakpoints used are those defined by the National Committee for Clinical Laboratory Standards (NCCLS).

***Escherichia coli*, coagulase-negative staphylococci and *Streptococcus pyogenes*.** In 2001, the clinical microbiology laboratories serving the Roskilde, Storstroem, Ribe, Ringkoebing and Viborg counties were using the tablet diffusion method (Neo-SensitabsÒ, A/S Rosco) on Danish Blood Agar (Resistensplade, SSI Diagnostika) and the breakpoints defined for this medium by A/S Rosco. The clinical microbiology laboratory serving North Jutland county used the same tablets on Mueller-Hinton II agar (Becton-Dickinson, Franklin Lakes, NJ, USA, and SSI Diagnostika) and the breakpoints defined by the Swedish Reference Group for Antibiotics.

In 2001, the clinical microbiology laboratories serving the Copenhagen and Frederiksberg Municipalities, West Zealand county and Aarhus county were using the disk diffusion method (Oxoid, Basingstoke, UK) on 5% horse blood Iso-Sensitest (ISA) medium (Oxoid). The clinical microbiology laboratory serving Copenhagen county was using the disk diffusion method (AB Biodisk, Solna, Sweden) on 5% horse blood Antibiotic Sensitivity Medium (PDM, AB Biodisk). All laboratories performing the disk diffusion method used the breakpoints defined by the Swedish Reference Group for Antibiotics (Available from: URL: http://www.ltkronoberg.se/ext/raf/ZONTAB/Zontab.htm).

These ten laboratories participate in national and international quality assurance collaborations such as the United Kingdom National External Quality Assessment Schemes (NEQAS).

Table A2. Breakpoints used for gastrointestinal pathogens from humans. Isolates were considered resistant if they had an inhibition zone less than shown in the table

DANMAP 2001

Antimicrobial agent	Species	
	Salmonella enterica	*Campylobacter*
Ampicillin	28 mm	-
Apramycin	20 mm	24 mm
Ceftiofur	20 mm	-
Chloramphenicol	24 mm	33 mm
Colistin	17 mm	18 mm
Ciprofloxacin	- a)	27 mm
Erythromycin	-	27 mm
Gentamicin	22 mm	30 mm
Kanamycin	19 mm	22 mm
Nalidixic acid	24 mm	27 mm
Spectinomycin	21 mm	30 mm
Streptomycin	21 mm	32 mm
Sulfonamide	20 mm	-
Tetracyclin	28 mm	32 mm
Trimethoprim	18 mm	-

a) Resistance to fluoroquinolones is based on susceptibility results for nalidixic acid

Performance test

A performance test was carried out as in previous years to ascertain the comparability of susceptibility tests of the laboratories involved in the presentation of data.

The laboratory in the Department of Gastrointestinal Infections and the Clinical Microbiology Laboratory at the Statens Serum Institute as well as the Danish Veterinary Institute and the Danish Veterinary and Food Administration received 10 *E. coli* strains, 10 *Enterococcus* spp. and 8 *Staphylococcus* spp.

A total of 1,568 antibiotic-bacterium susceptibility tests were performed and the overall results were 2.7% failures (Table A3. Failures were divided into misinterpretations of test results (i.e. with similar MIC´s found), and actual failures, i.e. > 2 fold differences in MIC´s (or zone sizes differing completely from MIC-results). Most failures were in testing the susceptibility of enterococci to bacitracin, or the susceptibility of *E. coli* to sulfonamide. For both tests, performed using the Sensititre microtitre system, failures were due to differences in reading the endpoint. However, an overall agreement of 97.3% was considered excellent.

Data handling

Data on animal isolates

The results of primary examination of slaughterhouse samples for the bacteria of interest – positive as well as negative findings – and of the susceptibility testing were stored in an Oracle database. The susceptibility data were stored as continuous values (MIC) as well as categorised as susceptible or resistant, respectively, as defined by the relevant breakpoint. Each isolate was identified by the bacterial species, including subtype as applicable and by the date and place of sampling and the species of animal. Information on the herd or flock of origin was also recorded. All handling and evaluation of results was carried out using PC SAS, v.8.

Table A3. Results of performance testing (correct results / number of tests performed) among laboratories participating in DANMAP

DANMAP 2001

Antimicrobial agent	*E.coli*		*Staphylococcus aureus*		*Enterococcus* spp.		
	S + I a)	R a)	S + I	R	S + I	R	Total
Penicillin			6/6	18/18	18/18	9/9	
Ampicillin	30/30	20/20					
Amox/clav	34/36	4/4					
Oxacillin			8/8	6/8			
Cefalothin	20/20	17/20					
Ceftiofur	37/40		12/12	4/4			
Erythromycin			15/15	8/9	28/28	8/8	
Lincomycin					4/4	16/16	
Tetracyklin	25/25	25/25	15/15	7/9	15/15	15/15	
Chloramphenicol	32/32	8/8	18/18	6/6	32/32	8/11	
Vancomycin			24/24		28/28	10/12	
Teicoplanin					29/30		
Linezolid					20/20		
Synercid			8/8		21/21	7/9	
Virginiamycin			8/8				
Nalidixic acid	36/36	4/4					
Ciprofloxacin	50/50		18/18	5/6			
Neomycin	40/40						
Streptomycin	20/20	20/20	6/6	8/10	24/24	6/6	
Kanamycin			8/8	7/8	24/24	6/6	
Apramycin	36/36	4/4					
Gentamicin	35/35	14/15					
Spectinomycin	7/7	3/3	12/12	8/8			
Colistin	50/50						
Sulfonamide	21/25	25/25	21/21	2/3			
Trimethoprim	30/30	20/20	21/21	2/3			
Sulfa/trim			14/14	1/2			
Bacitracin			21/24		7/9	17/21	
Tiamulin			8/8				
Florfenicol	40/40		8/8		30/30		
Avilamycin			8/8		30/30		
Flavomycin					15/15	21/21	
Salinomycin					30/30		
Total	543/552	164/168	259/262	82/94	355/358	123/134	1526/1568

a) S+I: susceptible and intermediate; R: resistant

Data on food isolates

Results from the analysis of food samples were reported via the Food Microbiology Database or mailed as written data sheets. For each bacterial isolate information is available on the type of food sample, bacterial species, date of examination of the sample, the RFCA that collected and processed the sample, and an identification number, which makes it possible to obtain further information about the isolate from the Authority. Furthermore, information about the country of origin was recorded whenever possible. This information was stored in a database (Microsoft Access) and the data were combined with the susceptibility results (stored as MIC values) in a resistance database (Microsoft Excel).

Data on human isolates

Data on *Salmonella* spp. and *Campylobacter* spp. infections were exported from the Danish registry on gastro-intestinal infections (Microsoft® Access) maintained by the Department of Gastrointestinal Infections at the Statens Serum Institut. This register includes only one isolate per patient within a window of 6 months. Data on susceptibility testing of gastrointestinal pathogens are stored as zone diameters (mm) in a Microsoft® Excel database in the same department. Using the isolate identification number, this second database was linked to the Danish register on gastro-intestinal infections and data were analysed using Epi Info v. 6.04c.

Data on methicillin-resistant *Staphylococcus aureus* (MRSA) were exported from the Danish MRSA registry (Microsoft® Excel) maintained by the Staphylococcus Unit at the Statens Serum Institut. Patients are only registered in this database the first time they are diagnosed as being infected or colonised by MRSA. Additional information concerning the probable origin of MRSA isolates was obtained by contacting local clinical microbiology laboratories and from careful examination of the patients' discharge letters. MRSA cases were then classified as active screening (surveillance samples to detect nasal or skin colonisation), imported infection (in patients who have been admitted in a foreign hospital, refugees and children adopted from foreign countries), infection acquired in a Danish hospital or infection acquired in the Danish primary health care. Finally, results from PFGE typing were added to the database.

Data on susceptibility testing of *Streptococcus pneumoniae* isolates are stored as MICs in a Microsoft® Access database at the Streptococcus Unit at the Statens Serum Institut. Analysis including selection of isolates from blood and spinal fluid samples and removal of duplicate isolates was performed using this software.

Ten clinical microbiology laboratories provided compiled data on resistance levels in *Escherichia coli* blood and urine isolates and in coagulase-negative staphylococci blood isolates. In nine of these laboratories, data were extracted from the laboratory information system, i.e. ADBakt (Autonik AB, Skoldinge, Sweden) for Copenhagen Municipality (Hvidovre Hospital), Copenhagen county (Herlev Hospital), West Zealand county (Slagelse Hospital) and North Jutland county (Ålborg Hospital), and MADS (Clinical Microbiology Laboratory, Aarhus Kommunehospital, Aarhus, Denmark) for Aarhus county, Storstroem county (Næstved Hospital), Ribe county (Esbjerg Hospital), Ringkoebing county (Herning Hospital) and Viborg county (Viborg Hospital). For Rosklide county, resistance data on *E. coli* and coagulase-negative staphylococci from blood samples were obtained from the laboratory information system at the Statens Serum Institut, and resistance data on *E. coli* from hospital urine samples from the chemical laboratory at Roskilde County Hospital. Laboratories were asked to provide data on the number of isolates tested and the number found to be resistant to selected antimicrobials. Although all laboratories were asked to remove duplicate isolates from the same patient within a window of 30 days, only the laboratories serving the Copenhagen and Frederiksberg municipalities and North Jutland county were able to comply with this rule. Other laboratories removed duplicate isolates using a window of 21 days (Copenhagen and West Zealand counties) or the whole study period, i.e. one year (Storstroem, Ribe, Ringkoebing and Viborg counties). In the two remaining laboratories, removing duplicate isolates would have required too much additional work and was not performed.

Appendix 2

2000

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Appendix 3

Results for food isolates from 2000

For technical reasons data on resistance in bacteria from food were not included in the report from 2000. Instead they are presented here. Please refer to the DANMAP 2000 (available on http://www.vetinst.dk) for the corresponding data from food animals and humans in Denmark 2000.

Table A4. Occurrence of resistance among Salmonella *Enteritidis from broiler meat, Denmark 2000 (n=12) (all isolates from* DANMAP 2001

Compound	% Resistant [95% Confidence interval]	
Tetracycline	0	[0.0-26.5]
Chloramphenicol	0	[0.0-26.5]
Florfenicol	0	[0.0-26.5]
Ampicillin	8	[0.2-38.5]
Ceftiofur	0	[0.0-26.5]
Sulfonamide	0	[0.0-26.5]
Trimethoprim	0	[0.0-26.5]
Apramycin	0	[0.0-26.5]
Gentamicin	0	[0.0-26.5]
Neomycin	0	[0.0-26.5]
Spectinomycin	0	[0.0-26.5]
Streptomycin	8	[0.2-38.5]
Ciprofloxacin	0	[0.0-26.5]
Nalidixic acid	33	[9.9-65.1]
Colistin	0	[0.0-26.5]

Table A5. Occurrence of resistance among Salmonella *Typhimurium from pork, Denmark 2000 (n=18) (danish pork 4 isolates; imported pork 14 isolates).* DANMAP 2001

Compound	% Resistant [95% Confidence interval]	
Tetracycline	72	[46.5-90.3]
Chloramphenicol	44	[21.5-69.2]
Florfenicol	44	[21.5-69.2]
Ampicillin	50	[26.0-74.0]
Ceftiofur	0	[0.0-18.5]
Sulfonamide	72	[46.5-90.3]
Trimethoprim	33	[13.3-59.0]
Apramycin	0	[0.0-18.5]
Gentamicin	0	[0.0-18.5]
Neomycin	6	[0.1-27.3]
Spectinomycin	50	[26.0-74.0]
Streptomycin	50	[26.0-74.0]
Ciprofloxacin	0	[0.0-18.5]
Nalidixic acid	0	[0.0-18.5]
Colistin	0	[0.0-18.5]

Table A6. Distribution of MICS and occurrence of resistance among Campylobacter jejuni *from broiler meat (n=105) Denmark, 2000*

DANMAP 2001

Compound	% Resistant [95% Confidence interval]		Distribution (%) of MICs															
			<=0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Tetracycline	5	[1.6-10.8]					81.9	9.5	1.0	1.0	1.9		4.8 a)					
Chloramphenicol	1	[0.0-5.2]					0.0	62.9	19.0	7.6	9.5		1.0					
Erythromycin	2	[0.2-6.7]					29.5	48.6	17.1	2.9			1.9					
Gentamicin	0	[0.0-3.5]					91.4	7.6		1.0								
Streptomycin	9	[4.0-15.6]						78.1	4.8	1.0	7.6	2.9	5.7					
Ciprofloxacin	10	[4.7-16.8]		2.9	3.8	21.9	46.7	14.3	1.0		1.0	1.0	7.6					
Nalidixic acid	10	[4.7-16.8]						10.5	19.0	39.0	7.6	6.7	7.6	5.7	3.8			

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

Table A7. Distribution of MICs and occurrence of resistance among Enterococcus faecium *from turkey meat (n=10), broiler meat (n=36), beef (n=21) and pork (n=12), Denmark, 2000* DANMAP 2001

Compound	Food type	% Resistant	[95% Confidence interval]	Distribution (%) of MICs													
				<=0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048
Tetracycline	Turkey meat	50	[18.7-81.3]		40.0	10.0					50 a)						
	Broiler meat	50	[32.9-67.1]		50.0					2.8	47.2						
	Beef	19	[5.5-41.9]		71.4	4.8	4.8		4.8		14.3						
	Pork	25	[5.5-57.2]		75.0				8.3		16.7						
Chloramphenicol	Turkey meat	0	[0.0-30.9]			50.0	30.0		20.0								
	Broiler meat	3	[0.1-14.5]			58.3	13.9	22.2	2.8	2.8							
	Beef	0	[0.0-16.1]			57.1	14.3	23.8	4.8								
	Pork	0	[0.0-26.5]			41.7	25.0	33.3									
Florfenicol	Turkey meat	0	[0.0-30.9]			100											
	Broiler meat	0	[0.0-9.7]			91.7	8.3										
	Beef	0	[0.0-16.1]			81.0	19.0										
	Pork	0	[0.0-26.5]			58.3	41.7										
Penicillin	Turkey meat	20	[2.5-55.6]			60.0	20.0		10.0		10.0						
	Broiler meat	31	[16.3-48.1]			55.6	8.3	5.6	8.3	5.6	2.8	8.3	5.6				
	Beef	10	[1.2-30.4]			57.1	9.5	23.8		4.8	4.8						
	Pork	8	[0.2-38.5]			58.3		33.3		8.3							
Erythromycin	Turkey meat	20	[2.5-55.6]		40.0	20.0	20.0				20.0						
	Broiler meat	28	[14.2-45.2]		50.0	16.7	5.6		5.6		22.2						
	Beef	24	[8.2-47.2]		33.3	19.0	23.8	4.8			19.0						
	Pork	17	[2.1-48.4]		41.7	33.3	8.3				16.7						
Gentamicin	Turkey meat	0	[0.0-30.9]									100					
	Broiler meat	0	[0.0-9.7]									97.2	2.8				
	Beef	0	[0.0-16.1]									100					
	Pork	0	[0.0-26.5]									100					
Kanamycin	Turkey meat	0	[0.0-30.9]									70.0	30.0				
	Broiler meat	11	[3.1-26.1]									52.8	30.6	2.8	2.8		11.1
	Beef	10	[1.2-30.4]									76.2	4.8	9.5			9.5
	Pork	0	[0.0-26.5]									66.7		16.7	16.7		
Streptomycin	Turkey meat	10	[0.3-44.5]									70.0		10.0	10.0	10.0	
	Broiler meat	14	[4.7-29.5]									86.1					13.9
	Beef	0	[0.0-16.1]									66.7		33.3			
	Pork	0	[0.0-26.5]									66.7	8.3	16.7	8.3		
Vancomycin	Turkey meat	0	[0.0-30.9]		100												
	Broiler meat	3	[0.1-14.5]		97.2						2.8						
	Beef	0	[0.0-16.1]		95.2	4.8											
	Pork	0	[0.0-26.5]		91.7	8.3											
Virginiamycin	Turkey meat	10	[0.3-44.5]	10.0	60.0	20.0		10.0									
	Broiler meat	14	[4.7-29.5]	38.9	30.6	11.1	5.6	13.9									
	Beef	0	[0.0-16.1]	42.9	14.3	38.1	4.8										
	Pork	8	[0.2-38.5]	66.7		16.7	8.3	8.3									
Quinupristin/dalfopristin	Turkey meat	10	[0.3-44.5]		40.0	50.0		10.0									
	Broiler meat	14	[4.7-29.5]	33.3	36.1	16.7	8.3	2.8			2.8						
	Beef	0	[0.0-16.1]	28.6	33.3	38.1											
	Pork	8	[0.2-38.5]	25.0	41.7	25.0	8.3										
Avilamycin	Turkey meat	20	[2.5-55.6]		60.0	10.0	10.0				20.0						
	Broiler meat	22	[10.1-39.2]		27.8	27.8	19.4	2.8	2.8		19.4						
	Beef	14	[3.1-36.3]		42.9	42.9			9.5		4.8						
	Pork	0	[0.0-26.5]		33.3	41.7	25.0										
Bacitracin	Turkey meat	30	[6.7-65.3]					30.0	30.0	10.0			30.0				
	Broiler meat	67	[49.0-81.4]					19.4	2.8	2.8	8.3		66.7				
	Beef	24	[8.2-47.2]					23.8	4.8	9.5	38.1	14.3	9.5				
	Pork	17	[2.1-48.4]					16.7		16.7	50.0	8.3	8.3				
Nitrofurantoin	Turkey meat	20	[2.5-55.6]								80.0	20.0					
	Broiler meat	6	[0.1-18.7]								94.4	5.6					
	Beef	0	[0.0-16.1]								100						
	Pork	0	[0.0-26.5]								100						
Salinomycin	Turkey meat	0	[0.0-30.9]		90.0	10.0											
	Broiler meat	0	[0.0-9.7]		47.2	13.9	36.1	2.8									
	Beef	0	[0.0-16.1]		100												
	Pork	0	[0.0-26.5]		91.7	8.3											

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

Table A8. Distribution of MICs and occurrence of resistance among Enterococcus faecalis *from turkey meat (n=17), broiler meat (n=33), beef (n=18) and pork (n=29), Denmark, 2000*

DANMAP 2001

Compound	food type	% Resistant	[95% Confidence interval]	Distribution (%) of MICs												
				<=0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048
Tetracycline	Turkey meat	76	[50.1-93.2]		17.6	5.9					76.5 a)						
	Broiler meat	42	[25.5-60.8]		57.6					12.1	30.3						
	Beef	17	[3.6-41.4]		77.8		5.6				16.7						
	Pork	14	[3.9-31.7]		86.2						13.8						
Chloramphenicol	Turkey meat	0	[0.0-19.5]			11.8	29.4	58.8									
	Broiler meat	0	[0.0-10.6]			30.3	21.2	48.5									
	Beef	0	[0.0-18.5]				22.2	77.8									
	Pork	3	[0.1-17.8]			20.7	24.1	51.7		3.4							
Florfenicol	Turkey meat	0	[0.0-19.5]			58.8	41.2										
	Broiler meat	0	[0.0-10.6]			66.7	33.3										
	Beef	0	[0.0-18.5]			77.8	22.2										
	Pork	0	[0.0-11.9]			69.0	31.0										
Penicillin	Turkey meat	0	[0.0-19.5]			64.7	35.3										
	Broiler meat	0	[0.0-10.6]			87.9	12.1										
	Beef	6	[0.1-27.3]			77.8	16.7		5.6								
	Pork	0	[0.0-11.9]			79.3	20.7										
Erythromycin	Turkey meat	29	[10.3-56.0]		41.2	23.5	5.9				29.4						
	Broiler meat	21	[9.0-38.9]		57.6	18.2	3.0		6.1	6.1	9.1						
	Beef	22	[6.4-47.6]		61.1	16.7					22.2						
	Pork	3	[0.1-17.8]		62.1	34.5					3.4						
Gentamicin	Turkey meat	0	[0.0-19.5]									100					
	Broiler meat	0	[0.0-10.6]									100					
	Beef	0	[0.0-18.5]									100					
	Pork	3	[0.1-17.8]									96.6			3.4		
Kanamycin	Turkey meat	6	[0.1-28.7]									94.1					5.9
	Broiler meat	3	[0.1-15.8]									93.9	3.0				3.0
	Beef	6	[0.1-27.3]									94.4					5.6
	Pork	3	[0.1-17.8]									96.6					3.4
Streptomycin	Turkey meat	18	[3.8-43.4]									82.4					17.6
	Broiler meat	12	[3.4-28.2]									87.9			3.0		9.1
	Beef	17	[3.6-41.4]									83.3					16.7
	Pork	0	[0.0-11.9]									100					
Vancomycin	Turkey meat	0	[0.0-19.5]		52.9	47.1											
	Broiler meat	0	[0.0-10.6]		72.7	27.3											
	Beef	0	[0.0-18.5]		61.1	38.9											
	Pork	0	[0.0-11.9]		58.6	41.4											
Avilamycin	Turkey meat	6	[0.1-28.7]		17.6	64.7	11.8				5.9						
	Broiler meat	0	[0.0-10.6]		36.4	63.6											
	Beef	0	[0.0-18.5]		27.8	61.1	5.6	5.6									
	Pork	0	[0.0-11.9]		31.0	62.1	6.9										
Bacitracin	Turkey meat	41	[18.4-67.1]					17.6	29.4	5.9	5.9	5.9		35.3			
	Broiler meat	24	[11.1-42.3]					42.4	12.1	21.2		3.0		21.2			
	Beef	6	[0.1-27.3]					50.0	11.1	22.2	11.1	5.6					
	Pork	0	[0.0-11.9]					58.6	24.1	17.2							
Flavomycin	Turkey meat	0	[0.0-19.5]	17.6	17.6	52.9	5.9	5.9									
	Broiler meat	0	[0.0-10.6]	24.2	12.1	54.5	6.1	3.0									
	Beef	0	[0.0-18.5]	27.8	22.2	44.4	5.6										
	Pork	0	[0.0-11.9]	6.9	10.3	75.9	6.9										
Nitrofurantoin	Turkey meat	0	[0.0-19.5]								100						
	Broiler meat	0	[0.0-10.6]								100						
	Beef	0	[0.0-18.5]								100						
	Pork	0	[0.0-11.9]								100						
Salinomycin	Turkey meat	0	[0.0-19.5]		88.2		5.9	5.9									
	Broiler meat	0	[0.0-10.6]		90.9		9.1										
	Beef	0	[0.0-18.5]		100												
	Pork	0	[0.0-11.9]		100												

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration

Table A9. Susceptibility and occurrence of resistance among Escherichia coli *from turkey meat (n=51) broiler meat (n=79), beef (n=81) and pork (n=62), Denmark, 2000*

DANMAP 2001

Compound	Food type	% Resistant	[95% Confidence interval]	Distribution (%) of MICs															
				<=0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Tetracycline	Turkey meat	55	[40.3-68.9]							45.1			2.0	3.9	49.0 a)				
	Broiler meat	37	[26.1-48.3]							60.8	1.3	1.3	6.3	7.6	22.8				
	Beef	7	[2.8-15.4]							92.6				2.5	4.9				
	Pork	18	[9.2-29.5]							80.6	1.6			8.1	9.7				
Chloramphenicol	Turkey meat	6	[1.2-16.2]							37.3	41.2	13.7	2.0			5.9			
	Broiler meat	5	[1.4-12.5]							39.2	41.8	13.9		2.5		2.5			
	Beef	1	[0.0-6.7]							11.1	33.3	54.3				1.2			
	Pork	0	[0.0-5.8]							30.6	29.0	40.3							
Florfenicol	Turkey meat	0	[0.0-7.0]							49.0	41.2	9.8							
	Broiler meat	0	[0.0-4.6]							51.9	38.0	10.1							
	Beef	0	[0.0-4.5]							13.6	45.7	40.7							
	Pork	0	[0.0-5.8]							35.5	35.5	29.0							
Ampicillin	Turkey meat	27	[15.9-41.7]						41.2	29.4	2.0				27.5				
	Broiler meat	20	[12.0-30.8]						39.2	32.9	7.6				20.3				
	Beef	4	[0.8-10.4]						13.6	59.3	23.5				3.7				
	Pork	8	[2.7-17.8]						30.6	43.5	17.7				8.1				
Ceftiofur	Turkey meat	0	[0.0-7.0]					100											
	Broiler meat	0	[0.0-4.6]					98.7	1.3										
	Beef	0	[0.0-4.5]					100											
	Pork	0	[0.0-5.8]					98.4	1.6										
Sulfonamide	Turkey meat	35	[22.4-49.9]											64.7					35.3
	Broiler meat	30	[20.5-41.8]											68.4	1.3				30.4
	Beef	9	[3.5-17.0]											88.9	2.5				8.6
	Pork	15	[6.9-25.8]											82.3	1.6	1.6			14.5
Trimethoprim	Turkey meat	24	[12.8-37.5]								76.5				23.5				
	Broiler meat	18	[10.0-27.9]								82.3				17.7				
	Beef	6	[2.0-13.8]								93.8				6.2				
	Pork	8	[2.7-17.8]								90.3	1.6			8.1				
Apramycin	Turkey meat	0	[0.0-7.0]								98.0	2.0							
	Broiler meat	0	[0.0-4.6]								97.5	2.5							
	Beef	0	[0.0-4.5]								95.1	4.9							
	Pork	0	[0.0-5.8]								90.3	9.7							
Gentamicin	Turkey meat	0	[0.0-7.0]						98.0	2.0									
	Broiler meat	3	[0.3-8.8]						96.2	1.3				2.5					
	Beef	0	[0.0-4.5]						98.8	1.2									
	Pork	0	[0.0-5.8]						98.4	1.6									
Neomycin	Turkey meat	2	[0.0-10.4]							98.0			2.0						
	Broiler meat	6	[2.1-14.2]							92.4		1.3	2.5	2.5	1.3				
	Beef	4	[0.8-10.4]							96.3				1.2	2.5				
	Pork	0	[0.0-5.8]							98.4	1.6								
Spectinomycin	Turkey meat	2	[0.0-10.4]								3.9	43.1	33.3	9.8	7.8		2.0		
	Broiler meat	11	[5.3-20.5]								2.5	51.9	29.1	3.8	1.3	7.6	3.8		
	Beef	4	[0.8-10.4]								1.2	19.8	66.7	7.4	1.2	2.5	1.2		
	Pork	5	[1.0-13.5]									30.6	51.6	9.7	3.2		4.8		
Streptomycin	Turkey meat	27	[15.9-41.7]								43.1	21.6	7.8	2.0	5.9	19.6			
	Broiler meat	27	[17.3-37.7]								55.7	16.5	1.3	2.5	6.3	17.7			
	Beef	6	[2.0-13.8]								33.3	55.6	4.9	1.2		4.9			
	Pork	13	[5.7-23.9]								38.7	41.9	6.5		4.8	8.1			
Ciprofloxacin	Turkey meat	0	[0.0-7.0]	92.2	2.0	3.9		2.0											
	Broiler meat	4	[0.8-10.7]	83.5	2.5	7.6	1.3	1.3			1.3	2.5							
	Beef	0	[0.0-4.5]	98.8			1.2												
	Pork	0	[0.0-5.8]	100															
Nalidixic acid	Turkey meat	6	[1.2-16.2]								94.1				3.9		2.0		
	Broiler meat	14	[7.2-23.6]								83.5		2.5	3.8	5.1		5.1		
	Beef	1	[0.0-6.7]								96.3	2.5				1.2			
	Pork	0	[0.0-5.8]								100								
Colistin	Turkey meat	0	[0.0-7.0]								100								
	Broiler meat	0	[0.0-4.6]								100								
	Beef	0	[0.0-4.5]								100								
	Pork	0	[0.0-5.8]								100								

Lines indicate breakpoints for resistance

a) The white fields denote range of dilutions tested for each antimicrobial. Values above the range denote MIC values greater than the highest concentration in the range. MICs equal to or lower than the lowest concentration tested are given as the lowest concentration