

Chapter 5

ANTIMICROBIAL SENSITIVITY IN *SALMONELLA*

Salmonellas received for serological identification at VLA Weybridge and Lasswade are tested for their *in vitro* sensitivity to 16 antimicrobials. All these isolates come from animals and their environment in England and Wales. The choice of antimicrobials, which is reviewed periodically, is designed to comprise a core set which has been used in veterinary practice for many years, some of the more recently licensed antimicrobials and some of limited usage in Great Britain which are used in other European countries. In 2001, the 30 µg cefuroxime disc that had been used in previous years was replaced with a 30 µg ceftazidime disc.

All tests are performed using a disc diffusion technique on Oxoid "isosensitest" agar using antibiotic discs as follows:

	Antimicrobial	Concentration (µg per ml)	Code
1	Nalidixic acid	30	NA
2	Tetracycline	10	T
3	Neomycin	10	N
4	Ampicillin	10	AM
5	Furazolidone	15	FR
6	Ceftazidime (from 1/1/01)	30	CAZ
6	Cefuroxime (used until 31/12/00)	30	CX
7	Sulphamethoxazole/trimethoprim	25	TM
8	Chloramphenicol	10	C
9	Amikacin	30	AK
10	Amoxicillin/clavulanic acid	30	AMC
11	Gentamicin	10	CN
12	Streptomycin	25	S
13	Sulphonamide compounds	300	SU
14	Cefoperazone	30	CF
15	Apramycin	15	APR
16	Colistin	25	CT

Prior to 1996, all *Salmonella* isolates received were tested for antimicrobial susceptibility, but since then only the first isolate from each incident has been tested. The number of cultures received from a farm varies enormously, especially in the case of those from poultry. Some poultry companies have a continuous monitoring programme and large numbers of salmonellas may be received from a particular company. Thus the numbers of a particular serotype and its antimicrobial

susceptibility may not reflect its prevalence in the animal population as a whole but reflect the monitoring programme on a farm or group of farms. Therefore, to better indicate the prevalence of resistance, only the first isolate from each incident has been tested since the start of 1996.

SALMONELLA DUBLIN

Of the 687 *Salmonella* Dublin cultures tested during 2002, 97.5% were susceptible to all 16 antimicrobial drugs (Table 82). This has been the situation since surveillance began in 1971 and is of interest because most isolates come from cattle. Resistance to ampicillin, which had been observed for the first time for several years in a very low number of bovine isolates in 2000, was not recorded in 2001 or 2002. Conversely, resistance to furazolidone and neomycin, which had not been detected for several years in *S. Dublin*, was observed for the first time in recent years in 2002. 0.9% of *S. Dublin* isolates were resistant to trimethoprim/sulphonamides in 2002, higher than the figure for 2001, when only 0.2% of isolates were resistant. This figure is of interest, since trimethoprim/sulphonamide resistance also increased in *Salmonella* Typhimurium, though by a much greater degree.

SALMONELLA TYPHIMURIUM

The number of cultures examined was 533 of which 44.8% were DT104, DT104b or U302 (Table 83).

14.5% of the cultures were sensitive to all the antimicrobials tested, an increase from 1996 when only 10.8% of cultures were sensitive to all the antimicrobials tested, but a decline from the figure for 2001, when 20.6% of *S. Typhimurium* cultures were fully sensitive (Table 83). The generally high level of resistance of *Salmonella* Typhimurium isolates is partly a reflection of the numbers of DT104 and its variants DT104b and U302, only 0.8% of which were sensitive to all the antimicrobials tested in 2002. However, the proportion of *Salmonella* Typhimurium isolates comprising DT104 and its variants has declined significantly in recent years and this has been reflected in a decrease in resistance to several antimicrobials. In 2002, despite a continuing decline in the proportion of *S. Typhimurium* that was DT104 or its variants, the levels of resistance to a number of antimicrobials in fact increased. This occurred because the definitive types that are replacing DT104 are themselves commonly resistant to one or more antimicrobials. Figure 46 illustrates this fact graphically, showing the percentage of each of the eight most common definitive types of

S. Typhimurium that are fully susceptible to all of the antimicrobials tested.

Most *S. Typhimurium* DT104 isolates recovered from cattle had the typical pentavalent resistance pattern AM,C,S,SU,T; this was also the most common pattern observed in isolates of DT104 from pigs. The most common pattern for isolates from poultry was AM,C,S,SU,T,CF and this was the second most common pattern in isolates from cattle and pigs.

There were no *Salmonella Typhimurium* isolates resistant to ceftazidime recovered in 2002 or 2001 and no *Salmonella Typhimurium* isolates resistant to cefuroxime were recorded in 1998, 1999 or 2000. This is an important finding, since third generation cephalosporins are one of the important groups of antimicrobials for the treatment of invasive salmonellosis in man.

Overall, 6.3% of DT104 and 104b isolates were resistant to nalidixic acid and 20.5% resistant to sulphamethoxazole/trimethoprim in 2002; this can be compared to 19.8% of DT104 and 104b isolates that were resistant to nalidixic acid and 12.5% resistant to sulphamethoxazole/trimethoprim in 2001. Therefore over this two-year period there has been a decline in nalidixic acid resistance, although trimethoprim/sulphonamide resistance has increased. Taking a longer-term view, the figure of 20.5% resistance to sulphamethoxazole/trimethoprim in DT104 and 104b isolates in 2002 can be compared to 17.6% resistance in 1999 and 15.9% in 1998.

Considering all definitive types of *S. Typhimurium*, there has been a marked increase in resistance to sulphamethoxazole/trimethoprim from levels of around 16 - 24% in 1996 - 2001 to 44.1% in 2002. It is mainly isolates of *S. Typhimurium* from pigs that account for this rise; a high percentage of many definitive types of *S. Typhimurium* isolated from pigs are resistant to sulphamethoxazole/trimethoprim. These definitive types of *S. Typhimurium* recovered from pigs include DT193 (47 isolates, 85% resistant to TM), DT208 (14 isolates, all resistant to TM), U288 (51 isolates, 94% resistant to TM), U308a (59 isolates, 95% resistant to TM) and U310 (25 isolates, 88% resistant to TM). Three factors have influenced the sulphamethoxazole/trimethoprim resistance figures for *S. Typhimurium* isolates from pigs: (1) The numbers of incidents involving definitive types such as DT308a, which have been highly resistant to TM in previous years, have increased. (2) The proportion of TM-resistant isolates from some definitive types that have previously shown TM resistance has increased (for example in 2000, 53% and 38% of isolates of DT193 and 208 respectively, were resistant to sulphamethoxazole/trimethoprim). (3) There has also been a minor

contribution from some definitive types of *S. Typhimurium* from pigs that have not previously shown sulphamethoxazole/trimethoprim resistance in recent years (eg DT12, a strain related to DT104), but which are now showing resistance.

Nalidixic acid resistance in *S. Typhimurium* DT104 by species of origin is listed in Table 84.

Table 82: *Salmonella* Dublin: antimicrobial sensitivity monitoring 1998 - 2002

Year	No of cultures	Percentage sensitive to all 16 anti-microbials	Percentage of cultures resistant to:							
			S	SU	T	N	AM	FR	TM	C
1998	281	99.3	0.4	0.4	-	-	-	-	-	0.4
1999	357	98.3	1.1	-	-	-	-	-	-	-
2000	863	98.7	0.7	0.7	0.5	-	0.1	-	0.2	0.6
2001	467	98.3	0.2	1.3	-	-	-	-	0.2	0.6
2002	687	97.5	0.3	0.7	0.6	0.4	-	0.6	0.9	0.4

Table 83: *Salmonella* Typhimurium: antimicrobial sensitivity monitoring 1998 – 2002

Year	No of cultures	Percentage sensitive to all 16 anti-microbials	Percentage of cultures resistant to:									
			S	SU	T	N	AM	FR	TM	C	AP R	NA
1998	1112*	14.7	77.8	82.3	81.7	1.4	77.8	0.2	18.0	73.1	0.8	14.7
1999	1177†	18.4	61.2	72.0	78.8	2.0	63.0	0.3	23.1	53.2	1.6	11.3
2000	864**	15.3	63.2	70.8	80.4	2.5	63.8	0.1	23.4	56.5	3.2	7.5
2001	519††	20.6	57.8	71.7	75.5	2.9	66.7	0.4	24.3	55.9	2.3	11.9
2002	533***	14.5	61.0	77.9	80.1	3.4	70.5	2.6	44.1	62.1	2.4	7.1

- * 814 (73.2%) of these strains were DT104 and its variants.
- † 620 (52.7%) of these strains were DT104 and its variants.
- ** 460 (53.2%) of these strains were DT104 and its variants.
- †† 247 (52.8%) of these strains were DT104 and its variants.
- *** 239 (44.8%) of these strains were DT104 and its variants.

In 2002, 44.9% of all *Salmonella* Typhimurium isolates from poultry were resistant to cefoperazone; similar to the figure of 43.9% for 2001. In *Salmonella* Typhimurium isolates from cattle, sheep and pigs in 2001 (of all definitive types) resistance to cefoperazone was 46.4%, 42.9% and 18.2% respectively; levels in 2002 were 28%, 45.5% and 8.4% respectively.

Multiple antibiotic resistance (i.e. resistance to four or more antimicrobial agents in the panel of 16) was detected in DTs 104, 104b, 120, 193, 193a, 208 and U302 from cattle; in DTs 104, 104b, 120, 208, U302 and U308a from poultry; in DTs 104, 104b and U302 from sheep and in DTs 7 variant, 12, 104, 104b, 120, 193, 193A, 208, U288, U302, U308, U308a and U310 from pigs. Of the 31 different definitive types detected, 12 (namely 1, 2a, 2a variant, 8, 30, 40, 41, 49, 56, 56 variant, 85 and 204b) were fully susceptible to all of the antimicrobials in the test panel.

SEROTYPES OTHER THAN *SALMONELLA* DUBLIN AND *SALMONELLA* TYPHIMURIUM

Of the 2167 cultures tested 60.3% were sensitive to all the antimicrobials tested (Table 85), a decline from 2001 when 69.8% were sensitive. 53 (2.5%) of the cultures were *S. Enteritidis*, of which 19 were *S. Enteritidis* PT4, and of these *S. Enteritidis* PT4 isolates, 90% were sensitive to all of the antimicrobials used in the test panel. Levels of resistance to furazolidone and neomycin were higher than those observed in recent years. Neomycin resistant isolates originated mainly from poultry (6.7% of isolates from poultry were resistant, with 1,498 isolates tested), with a contribution from pigs (11.3% of isolates from pigs were resistant, with 80 isolates tested) and a very much lower contribution from other sources. Furazolidone resistant isolates again originated mainly from poultry (5.1% of isolates from poultry were resistant, with 1,498 isolates tested), with a minor contribution from pigs (2.5% of isolates from pigs were resistant, with 80 isolates tested) and a minor contribution from other sources.

INDIVIDUAL ANTIMICROBIALS

Of the 3425 salmonellas tested in 2002, 61.1% were sensitive to all of the antimicrobials tested – similar to the figure of 65.5% recorded in 2001. This can be compared with figures of 59.5% in 1999 and 58.0% in 1998. Levels of resistance to tetracyclines in isolates from all sources decreased from 33.3% in 1999 to 21.1% in 2000 and further declined to

20.5% in 2001; levels of resistance to tetracyclines were 21.2% in 2002. This probably reflects both the proportionate decrease in *Salmonella* isolates of all serotypes from pigs and the relative decline in frequency of isolation of *S. Typhimurium* DT104. The level of resistance to neomycin in all *Salmonella* serotypes was 3.9% in 2002, an increase on the figure of 1.2% recorded in 2001. Levels of resistance to furazolidone remained at 0.3% in 1999 and 2000, though increased slightly to 0.5% in 2001 and increased further in 2002 when levels of 2.9% were recorded. Resistance of *S. Virchow* isolates to furazolidone declined from 53% in 1998 to 28.5% in 1999, although the numbers of *S. Virchow* isolates tested each year were relatively low at 15 in 1998 and 7 in 1999. 39 isolates of *S. Virchow* were examined in 2001 and 12.8% were resistant to furazolidone; 59 isolates of *S. Virchow* were examined in 2002 and only 1.7% were resistant to furazolidone. Resistance to apramycin in all *Salmonella* serotypes was 0.5% in 2001 and increased marginally to 0.6% in 2002. The overall trend of decreasing resistance to nalidixic acid continued with 2.4% of all *Salmonella* isolates resistant in 2002, compared to 3.2% in 2001, 4.9% in 2000, 5.3% in 1999, 7.0% in 1998 and 6.5% in 1997.

No resistance was detected to amikacin or ceftazidime.

Table 84: Nalidixic acid resistance in *Salmonella* Typhimurium DT104 from domestic livestock. Number of cultures tested (percentage resistant to nalidixic acid) 1998 - 2002

Year	Livestock species					
	Cattle	Sheep	Pigs	Chickens	Turkeys	Ducks
1998	369 (10.3)	53 (5.7)	56 (10.7)	63 (4.8)	80 (71.3)	7 (14.3)
1999	231 (5.2)	35 (2.9)	114 (9.6)	5 (20.0)	24 (66.7)	1 (0)
2000	223 (10.8)	21 (0)	51 (2.0)	7 (14.3)	7 (0)	1 (0)
2001	115 (15.7)	8 (12.5)	19 (21.1)	22 (0)	25 (60.0)	0 (0)
2002	17 (11.8)	32 (0)	0 (0)	67 (7.5)	36 (5.6)	5 (40)

Table 85: Salmonellas, other than *Salmonella* Dublin and *Salmonella* Typhimurium: antimicrobial sensitivity monitoring 1998 - 2002

Year	No of cultures	Percentage sensitive to all 16 antimicrobials	Percentage of cultures resistant to:									
			S	SU	T	N	AM	FR	TM	C	APR	NA
1998	2227	74.4	6.2	16.3	11.0	0.4	3.3	0.8	11.6	1.8	0.2	4.0
1999	2417	73.7	6.8	12.6	16.1	1.0	2.8	0.4	6.6	2.2	0.3	3.1
2000	2877	70.7	5.0	18.0	9.5	0.9	4.8	0.5	13.7	3.5	0.1	5.5
2001	1814	69.8	8.1	20.0	10.0	1.0	5.7	0.6	12.1	6.4	0.2	1.4
2002	2167	60.3	11.2	24.0	13.7	5.2	6.5	3.7	19.5	8.0	0.3	1.9

Table 86: All salmonellas: antimicrobial sensitivity 2002

Origin	No of cultures	Percentage sensitive to all 16 antimicrobials	Percentage of cultures resistant to:									
			S	SU	T	N	AM	FR	TM	C	APR	NA
Cattle	862	84.7	8.9	11.6	12.8	0.3	10.8	1.3	4.2	9.9	-	1.4
Sheep	192	92.7	4.7	5.7	6.3	-	4.7	0.5	1.6	4.7	-	1.6
Pigs	309	8.7	54.7	79.0	83.8	7.1	60.5	2.3	62.5	49.8	4.9	5.5
Poultry	1580	51.5	16.1	30.6	16.0	6.5	10.3	4.9	23.9	13.4	0.1	2.0
Horses	33	57.6	27.3	36.4	36.4	-	30.3	-	15.2	21.2	-	6.1
Other spp	233	58.4	19.3	27.9	27.5	2.1	20.2	0.9	11.6	14.2	0.9	7.3
Feed	206	89.8	1.5	7.3	4.9	0.5	1.5	-	7.8	1.9	0.5	-
Environment	10	20.0	20.0	80.0	70.0	-	50.0	-	60.0	40.0	-	-
Total	3425	61.1	16.6	27.4	21.2	3.9	15.1	2.9	19.4	14.8	0.6	2.4

Fig 45: Proportion of isolates of *Salmonella* Typhimurium of the ten most frequent types presented to VLA in 2002

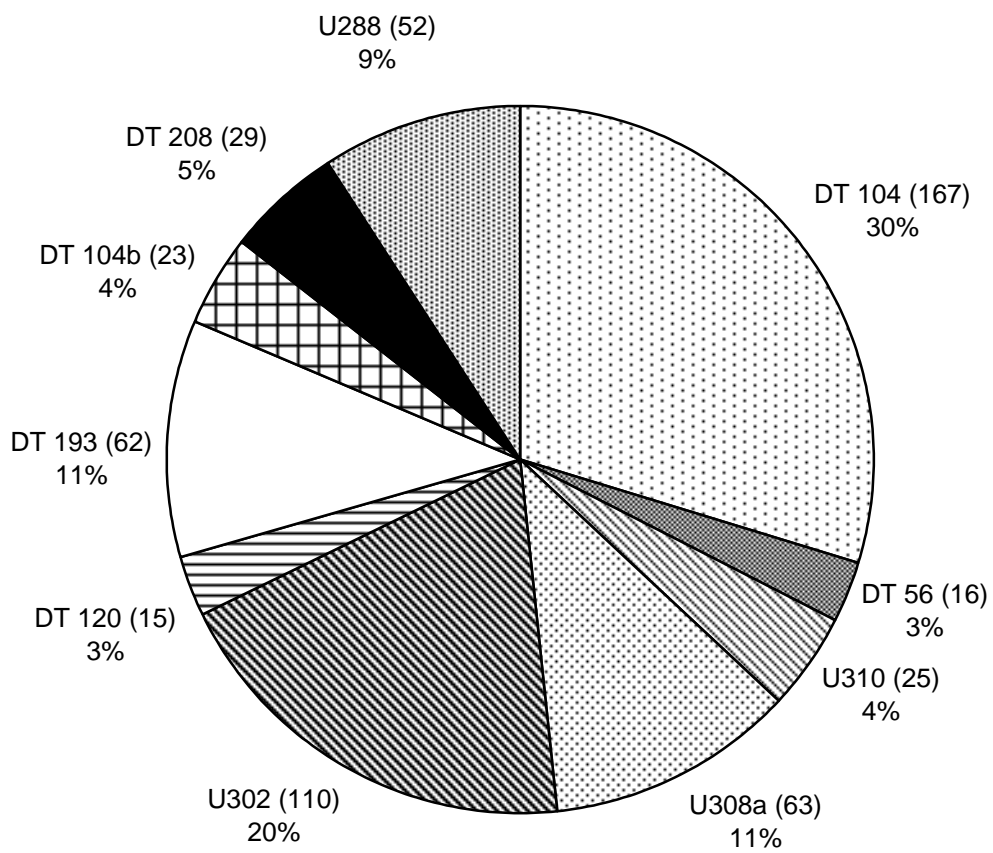


Fig 46: Percentage of the eight most common definitive types of *Salmonella* Typhimurium sensitive to 16 antimicrobial agents in 2002

