RISK ASSESSMENT – CAMPYLOBACTER INFECTION TRANSMISSION FROM PIGS TO MAN USING ERYTHROMYCIN RESISTANCE AS A MARKER

D.G.S. BURCH Octagon Services Ltd,
Old Windsor, Berks. SL4 2NR

The Pig Journal (2002) 50, 53-58.

Summary

The transmission of campylobacter infections from meat to man is considered one of the major routes of spread, along with water contamination, of this increasingly common form of infectious intestinal disease. To make a risk assessment of the likely transmission from pigs to man, a database was established from a variety of references, as there was much variation in the data and few were sufficiently complete to allow for a quantitative assessment to be made. It was noted that erythromycin resistance was very high in pigs for both C. jejuni and C. coli in comparison with man and chicken, thought to be one of the major sources of infection and that this would act as a possible marker to determine the transmission rate of campylobacter spp. from pigs to man. There was no evidence of transmission of C. jejuni from pigs to man, as the organism was rarely isolated in pigs (4%) in comparison with chicken (90%) and man (92%) and erythromycin resistance rates were very low at 2% in man, in chicken (4%) and 35% in pigs. With regard to C. coli, isolation in pigs is very high (96%) but low in chicken (10%) and man (8%) and erythromycin resistance in man (15%) is similar to chickens (15%) but much lower than in pigs (57%). This confirms that pig meat and environmental contamination by slurry/waste from pigs can be considered either a no risk or very low potential risk in the transmission of campylobacter infections to man and therefore also a no risk or very low risk in the transmission of antimicrobially resistant strains to man.

Introduction

Campylobacter *spp*. have become the most frequently reported cause of gastrointestinal infections in man, even more than salmonella *spp*. (House of Lords, 1998). In 1999, 61713 reports were recorded in the UK and it was estimated from earlier studies that only 50% of cases went to the doctor, about one eighth of cases were reported and that the best estimate of cases of campylobacter infections in the country was 870/100,000 population (0.87%). In Denmark it was estimated to be only 82 cases/100,000 population (Danmap, 2001) but in the United States an estimated 2.4 million persons were affected each year (0.84%),

reported by the Centre for Disease Control and Prevention (2001). An estimated 124 cases were fatal each year (0.00004%) and life-threatening sepsis could occur in immuno-compromised patients. The condition is thought to be primarily transmitted by contact with contaminated food, particularly raw or undercooked poultry meat and possibly unpasteurised milk. Water also has a role and the incidence increases 3-4 times in the summer months, possibly associated with swimming. *Campylobacter jejuni* is the main cause of disease in man but *C. coli* is also found. It was the purpose of this work to review the current literature, to determine the incidence of the different campylobacter *spp*. in each animal species, examine their antimicrobial resistance patterns and to assess the risk of transmission from pigs to man.

Campylobacter *spp*. incidence - determination for each animal species

Papers, which had a comparative isolation data of *C. jejuni* and *C. coli* from different animal species, were used to obtain comparative isolation percentages for each species.

Table 1 - Campylobacter *spp*. determination for each animal species

Reference	**Man**		**Chicken**		**Pig**		**Cattle**	
	CJ	CC	CJ	CC	CJ	CC	CJ	CC
Aarestrup *et al*, 1997	75	7	95	17	3	99	29	0
House of Lords, 1998	1113	150	-	-	-	-	-	-
Marano *et al*, 1999	535	28	-	-	-	-	-	-
Saenz *et al*, 2000	537	10	59	10	0	37	-	-
Kramer *et al,* 2000	133	16	-	-	-	-	-	-
Danmap 2000, 2001	49	0	438	40	11	154	50	1
SVARM 2001, 2002	-	-	42	7	7	91	67	0
Teale, 2002	-	-	-	-	27	712	-	-
Total	2442	211	634	74	48	1093	144	1
Isolation incidence (%)	**92**	**8**	**90**	**10**	**4**	**96**	**99**	**1**

Legend: CJ = *C. jejuni*; CC = *C. coli.*

C. jejuni predominates in man (92%), chicken (90%) and cattle (99%), but *C. coli* is the most frequently isolated species in the pig (96%).

Antimicrobial resistance patterns in Campylobacter *spp*. from several species

The antimicrobial resistance patterns of *C. jejuni* and *C. coli* from a variety of animal species were compared in a Danish national surveillance study

(Aarestrup *et al*, 1997) using an minimum inhibitory concentration (MIC) method with established breakpoints and it was highly noticeable that erythromycin (macrolide) resistance was higher in pigs in comparison with other animal species isolates.

Table 2 - Antimicrobial resistance (%) by Campylobacter *spp*. and by animal species (Denmark)

	Man		**Chicken**		**Pig**		**Cattle**	
Antimicrobial/Breakpoint	CJ	CC	CJ	CC	CJ	CC	CJ	CC
Erythromycin 8µg	**0**	**14**	**6**	**18**	**33**	**74**	**3**	**-**
Tylosin 64µg	0	14	6	18	33	73	3	-
Enrofloxacin 2µg	3	29	4	0	33	13	3	-
Tetracycline 16µg	11	0	2	0	0	1	0	-
Ampicillin 32µg	16	0	6	0	0	17	3	-
Gentamicin 16µg	0	0	0	0	0	0	0	-

(Source: Aarestrup *et al*, 1997)

A similar but regional Spanish study was also of interest for comparison purposes.

Table 3 - Antimicrobial resistance (%) by Campylobacter *spp*. and by animal species (Spain)

	Man		**Chicken**		**Pig**	
Antimicrobial/disc strength	CJ	CC	CJ	CC	CJ	CC
Erythromycin 15µg	**3**	**35**	**0**	**0**	**-**	**81**
Ciprofloxacin 5µg	75	71	99	100	-	100
Tetracycline 30µg	-	-	32	0	-	94
Ampicillin 10µg	38	29	47	90	-	66
Gentamicin 10µg	0	9	12	80	-	22

(Source: Saenz *et al*, 2000)

Resistance assessments were different between the two studies with the Spanish study using sensitivity discs but both were according to NCCLS guidelines. Fluoroquinolone resistance can be judged as high across all species tested in Spain and that erythromycin resistance is high for *C. coli* from pigs but not in poultry confirming it as a differentiating marker.

Establishing an international database to compare erythromycin resistance in Campylobacter *spp*. and animal species

There would appear to be a substantial variation in resistance between countries and not all countries have the full information required to be able to carry out a quantitative risk assessment of the likely transmission to man from animals of campylobacter *spp*. To give a more accurate overview of the situation and to better determine the relevance of the above observations, an international database was established to compare erythromycin resistance in campylobacter *spp*. isolated from the different animal species and compare them with man to see if it could be used to assess the risk of infection transference.

Table 4 - International database of Campylobacter *spp*. and erythromycin resistance (%)

Reference (Country)	**Man**		**Chicken**		**Pig**		**Cattle**	
	CJ	CC	CJ	CC	CJ	CC	CJ	CC
Weber *et al*, 1984 (G)	-	-	-	-	67	60	-	-
Bradbury & Monroe, 1985 (Can)	-	-	0	-	-	-	-	-
Aarestrup *et al,* 1997 (DK)	0	14	6	18	33	74	3	-
House of Lords, 1998 (UK)	2	10	-	-	-	-	-	-
Marano *et al*, 1999 (USA)	5	-	-	-	-	-	-	-
Mevius *et al*, 2000 (NL)	0	-	13	-	-	-	-	-
Saenz *et al*, 2000 (SP)	3	35	0	0	-	81	-	-
Kramer *et al*, 2000 (UK)	0	6	-	-	-	-	-	-
Danmap 2000, 2001 (DK)	2	-	5	40	-	38	0	-
Guevremont *et al*, 2001 (Can)	-	12	-	-	-	61	-	-
SVARM 2001, 2002 (SW)	-	-	0	0	0	1	0	-
Teale, 2002 (UK)	-	-	-	-	40	85	-	-
Average (%)	**2**	**15**	**4**	**15**	**35**	**57**	**1**	**-**

Legend: CJ = *C. jejuni*; CC = *C. coli.*

Assessing the risk of *C. jejuni* and *C. coli* transmission from pigs to man using erythromycin resistance as a marker

C. jejuni

Very few *C. jejuni* are isolated from the intestines of pigs, therefore the likely contamination of meat is likely to be low. Kramer *et al* (2000) reported on the presence of quite high levels of isolation from swine liver in a survey (34% *C. jejuni* and 42% *C. coli*) but these samples were taken from retail outlets, as both

pre-packaged and unwrapped items, where some cross contamination may have occurred. However as the erythromycin resistance of *C. jejuni* is very low in man (2%), similar to chicken and cattle, if pig isolates were responsible the resistance to erythromycin would be much higher. *Therefore the likely risk of transmission of C. jejuni from pigs to man either via meat or by environmental contamination is not evident.*

C. coli

The erythromycin resistance levels in *C. coli* isolated from man tend to be similar to those found in chicken, both 15% and in pigs at 57%. *Therefore pigs are considered unlikely to have a major role in the transmission of C. coli to man.*

Discussion

The routes of transmission of campylobacter *spp*. to man have not been fully determined. Besides food transmission, there is obviously a link to water and contamination of that water possibly by human waste, animal waste from farms or animal waste applied near or in water, e.g. cattle grazing meadows next to water, or wild birds excreting the organism. Fallacara *et al* (2001) showed that a variety of wildfowl in metropolitan parks in the US were excretors of *C. jejuni*; - Canada geese (52%), Mallard ducks (40%) and hybrids (60%). All of these would increase the risk of transmission either by swimming in contaminated water or picnicking next to water. Dingle *et al* (2002) demonstrated that *C. jejuni* found in beach sand was genetically identical to isolates found in man. Cooking by barbecue, particularly chicken products, may also be a major contributor of summer infections.

Transmission of campylobacter *spp* from pigs appears to be non-evident for *C. jejuni* and of very low risk for *C. coli* and this is confirmed by Kramer *et al* (2001) and also by Smerdon *et al* (2001), where only two out of 4604 incidents of infectious intestinal disease, investigated and reported to the Public Health Laboratory Service in the UK, over an eight year period, were linked to pig meat and one of these was due to cross contamination. The species of campylobacters involved were not recorded. If the transmission of campylobacter *spp*. from pigs to man either directly via pig meat or via environmental contamination is not evident, so also would be the risk of transmitting antimicrobial resistant strains to man.

References

Aarestrup, F.M., Nielsen, E.M., Madsen, M. and Engberg, J. (1997). Antimicrobial Agents and Chemotherapy, **41**, 2244-2250.

Bradbury, W.C. and Monroe, D.L.G. (1985). Journal of Clinical Microbiology, **22**, 339-346.

Centre for Disease Control and Prevention (2001). Campylobacter Infections. www.cdc.gov/ncidod/dbmd/diseaseinfo/campylobacter_t.htm

Danmap 2000 (2001) Chapter on Campylobacter. Eds. Bager, F. and Emborg, H-D. Danish Zoonosis Centre, Copenhagen, Denmark, pp. 26-28.

Dingle, K.E., Colles, F.M., Ure, R., Wagenaar, J.A., Duim, B., Bolton, F.J., Fox, A.J., Wareing, D.R.A. and Maiden, M.C.J. (2002) Emerging Infectious Diseases, 8, 9, on line www.cdc.gov/ncidod/EID/vol8no9/02-0122.htm

Fallacara, D.M., Monahan, C.M., Morishita, T.Y. and Wack, R.F. (2001). Avian Diseases, **45**, 128-135.

Guevremont, E., Sirois, M. and Quessy, S. (2001) Salinpork 2001, Proceedings of the 4th International Symposium on the Epidemiology and Control of Salmonella and other Food-Borne Pathogens in Pork, pp. 406-408.

House of Lords, Select Committee on Science and Technology (1998). Section on Campylobacter. In: Resistance to Antibiotics and other Antimicrobial Agents, p. 61.

Kramer, J.M., Frost, J.A., Bolton, F.J. and Wareing, D.R.A. (2000). Journal of Food Protection, **63**, 1654-1659.

Marano, N., Stamey, K., Barrett, T., Angulo, F. and NARMS (1999). Campylobacter, Helicobacter and Related Organisms Conference, Baltimore, Maryland, USA, September 1999, on line.

Mevius, D.J., Veldman, K.T., van der Giessen, A. and van Leeuwen, W.J. (2000). Tijdschrift voor Diergeneeskunde, **125**, 143-146.

Saenz, Y., Zarazaga, M., Lantero, M., Gastanares, M.J., Baquero, F. and Torres, C. (2000). Antimicrobial Agents and Chemotherapy, **44**, 267-271.

Smerdon, W.J., Adak, G.K., O'Brien, S.J., Gillespie, I.A. and Reacher, M. (2001). Communicable Disease and Public Health, **4**, 259-267.

SVARM 2001 (2002) Chapter on Resistance in zoonotic bacteria, National Veterinary Institute, Uppsala, Sweden, pp.14-19

Teale, C. J. (2002). The Pig Journal, **49**, 52-69.

Weber, A. Von, Lembke, C. and Schafer, R. (1984). Der Praktische Tierarzt, **11**, 995-998.