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The effect of banning avoparcin on VRE carriage in The Netherlands

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Sir,

Acquired resistance against antibiotics is closely related to the amount of drug used, a fact observed ever since these agents were introduced into human and veterinary medicine. However, the rate of development of resistance appears to have accelerated in the past decade. In animals, antibiotics are not only used for therapy and prevention of bacterial infections, but are also added to animal feed to act as growth promoters. In some countries, antibiotic use for growth promotion is greater than veterinary usage.[1]

In countries using avoparcin, a glycopeptide antibiotic, as a growth promoter, vancomycin-resistant enterococci (VRE) are commonly found in the commensal flora of food animals, on meat from these animals and in the commensal flora of healthy humans despite very limited use of vancomycin in hospitals.[1] In The Netherlands in 1996 and 1998, approximately 1500 and 1260 kg of vancomycin, respectively, was used for human therapy, whilst an estimated 80 000 kg of avoparcin was used yearly in farming until 1997. By contrast, in those countries not allowing the use of avoparcin, no VRE have been detected in food animals, food of animal origin or healthy humans in the general population.[1] Sweden banned the use of all antibiotics as growth promoters in 1986 and no VRE have been found in the faecal flora of animals, foods of animal origin or in healthy humans from the general population[1] or in hospitalized patients. The only VRE isolated from a hospital patient contained the *VanB* gene cluster and was acquired abroad.[2] The Swedish example strongly suggests that removal of the selective pressure in animals can remove VRE from the human population in time. Moreover, not only has clonal spread of VRE occurred from animals to humans, but it has also been shown that the *VanA* gene cluster can be disseminated from animal to human enterococcal strains.[3]

In April 1997, the European Commission suspended the use of avoparcin in animals. Denmark had already forbidden its use in 1995 and Germany in 1996. After the ban in Denmark the prevalence of VRE in poultry decreased from >80% in 1995 to <5% in 1998.[4] By contrast, the prevalence in pigs (*c.* 20%) did not change during this time. Similarly, in Germany a decrease in the prevalence of VRE in poultry meat decreased from 100% in 1995 to 25% of samples tested by 1997.[5] A decline in the prevalence of VRE was also seen in faecal samples of healthy persons, from 12% in 1994 to 3% in 1997. In Italy the prevalence of VRE in poultry meats decreased from 15% to 8%.[6]

In this report we have shown that, in The Netherlands, within 2 years of stopping the use of avoparcin, the prevalence and numbers of VRE have decreased significantly, not only in the faecal flora of food animals but also in the endogenous flora of healthy humans. Faecal samples of (sub)urban residents and of pigs and broilers from different farms were collected in 1996 and 1999. The prevalence and degree of resistance to vancomycin, erythromycin and quinupristin/dalfopristin was determined and calculated as previously described.[3]

The observed decreases in the prevalence of VRE and of samples with a high degree of VRE in broilers is in accordance with the results described by others[4–6] (Table). By contrast with the situation in Denmark,[4] the prevalence of VRE in Dutch pig faecal samples also declined. The unexpected finding was the significant decrease in prevalence of enterococci resistant against dalfopristin/quinupristin in all three populations studied. This decrease probably, however, resulted from the antimicrobial growth promoter virginiamycin (a mixture of pristinamycins like quinupristin/dalfopristin) being in short supply in The Netherlands during 1997 and 1998, because of production problems. No significant differences were noted for erythromycin resistance between 1997 and 1999.

The Swedish situation and the observed decrease in VRE in Germany, Italy, Denmark and The Netherlands after the ban on avoparcin makes it likely that discontinuation of the use of avoparcin in animals will eradicate VRE not only from animals exposed to this compound but also from the healthy human population. The observed decrease in faecal enterococci resistant to dalfopristin/quinupristin shows that the recent EU ban on the use of virginiamycin as a growth promoter may reduce the number of pristinamycin-resistant enterococci in the intestinal flora of healthy

Table. Prevalence of antibiotic-resistant enterococci and percentages of samples with a high degree (HD) of resistance in faecal samples collected in the South of The Netherlands

		1997						1999					
		humans ($n = 117$)[a]		pigs ($n = 282$)		broilers ($n = 50$)		humans ($n = 171$)		pigs ($n = 127$)		broilers ($n = 89$)	
Antibiotic	Antibiotic concentration in agar (mg/L)	prevalence	HD	prevalence	HD	prevalence	HD	prevalence	HD	prevalence	HD	prevalence	HD
Vancomycin	10	12	0	34	3	80	8	6*	0	17**	0	31**	0
Erythromycin	10	50	11	84	67	94	44	47	8	85	65	92	20
Dalfopristin/ quinupristin[b]	8	30	NT	75	NT	92*	NT	12**	NT	31**	NT	57**	NT

NT, not tested.
[a] Number of samples tested.
[b] Only *E. faecium*.
* Significantly different $P \leqslant 0.05$
** Significantly different $P \leqslant 0.001$.

humans. However, because of cross-resistance with macrolides and lincosamides, which are both commonly used in human and veterinary therapy, complete disappearance of resistance to this antibiotic is less likely to occur.

References

1. Van den Bogaard, A. E. & Stobberingh, E. E. (1999). Antibiotic usage in animals: impact on bacterial resistance and public health. *Drugs* **58**, 589–607.

2. Torell, E., Cars, O., Ollsson-Liljequist, B., Hoffman, B. M., Lindbäck, J. & Burman, L. G. (1999). Near absence of vancomycin resistant enterococci but high carriage rates of quinolone-resistant, ampicillin-resistant enterococci among hospitalized patients and non-hospitalized individuals in Sweden. *Journal of Clinical Microbiology* **37**, 3509–13.

3. Stobberingh, E., van den Bogaard, A., London, N., Driessen, C., Top, J. & Willems, R. (1999). Enterococci with glycopeptide resistance in turkeys, turkey farmers, turkey slaughterers and (sub)urban residents in the South of the Netherlands: evidence for transmission of vancomycin resistance from animals to humans? *Antimicrobial Agents and Chemotherapy* **43**, 2215–21.

4. Bager, F., Aarestrup, F. M., Madsen, M. & Wegener, H. C. (1999). Glycopeptide resistance in *Enterococcus faecium* from broilers and pigs following discontinued use of avoparcin. *Microbial Drug Resistance* **5**, 53–6.

5. Klare, I., Badstrübner, D., Konstabel, C., Böhme, G., Claus, H., Witte, W. *et al.* (1999). Decreased incidence of VanA-type vancomycin-resistant enterococci isolated from poultry meat and from faecal samples of humans in the community after discontinuation of avoparcin usage in animal husbandry. *Microbial Drug Resistance* **5**, 45–52.

6. Pantosti, A., Del Grosso, M., Tagliabue, S., Nacri, A. & Caprioli, A. (1999). Decreased of vancomycin-resistant enterococci in poultry meat after avoparcin ban. *Lancet* **354**, 741–2.