Figure 1. Detection of ESBLs using multiplex PCR. Lanes 1 and 7, 100 bp DNA ladder (Genel); lane 2, SHV (392 bp) positive control; lane 3, negative control; lanes 4 and 5, OXA (478 bp), CTX-M (550 bp) and TEM (867 bp) amplicons of Ec 461 and Ec 614, respectively; lane 6, OXA and CTX-M amplicons of Ec 782.

were equally discriminative; strains Ec 614 and Ec 782 had an identical pattern (pattern A), whereas Ec 461 was different (pattern B) by both of the typing methods.

The presence of the OXA-2 gene has been frequently detected in Pseudomonas and it was first reported in E. coli from Israel in 2005. To the best of our knowledge, the presence of this gene in E. coli is the first report from India and the second in the world. The implication/s of the recent detection of the OXA-2 group gene in E. coli needs further investigation and action.

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Plasmid-mediated quinolone resistance determinant qnrS1 detected in Salmonella enterica serovar Corvallis strains isolated in Denmark and Thailand

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Sir,

Until recently, chromosomal mutations in the topoisomerase genes involved in DNA transcription and replication were considered the main mechanisms of quinolone resistance in Enterobacteriaceae. A new and transferable mechanism was described in 1998 in a Klebsiella pneumoniae isolate obtained from a patient in 1994 in Alabama, USA. Other qnr genes (A, B and S) and several variants encoding plasmid-mediated quinolone resistance have recently been described.1 These encode Qnr proteins that are members of the pentapeptide family and are able to protect topoisomerases, and thus reduce their susceptibility to fluoroquinolones.1 Plasmid-mediated quinolone resistance, which was originally found very rarely, seems to have spread more rapidly than expected and is now found in the US, Africa, Asia and also in Europe.1 The genes are often located on transferable plasmids and co-transmitted with other important resistance genes, especially genes encoding resistance to cephalosporins.1

We have recently described the characterization of a collection of 59 S. Corvallis isolates from Denmark, Bulgaria and Thailand.2 A total of 23 isolates in this collection showed reduced susceptibility to ciprofloxacin (MIC >0.06 mg/L) but were found to be susceptible or intermediate to nalidixic acid (MIC 8–16 mg/L). All isolates showing this type of resistance profile were examined for the presence of qnrA, qnrB, qnrS and aac(6′)Ib by PCR amplification and sequencing of the gyrA and parC genes. Briefly, qnrA and qnrS were amplified using primers based on published sequences and qnrB using primers described before as FQ1 and FQ2.3 As positive control strains, we used E. coli J53 pMG252 positive for qnrA, E. coli J53 pMG298 positive for qnrB (both strains kindly provided by Dr George Jacoby) and for qnrS E. coli MT102 pBC-H2.6, obtained by electroporating the plasmid pBC-H2.6 (obtained from Dr M. Hata, through the Rikken DNA Bank) into E. coli MT102. For aac(6′)Ib, PCR was performed as described by Park et al.4 As positive control, we used the strain Salmonella enterica S74 (GenBank accession number: DQ278189).5

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Of the 23 isolates, 7 were obtained from humans in Denmark and the remaining 16 were isolated in Thailand from: humans ($n = 6$), chicken ($n = 5$), pork ($n = 3$) and beef ($n = 2$). All 23 isolates carried the $\text{qnrS}$ gene and sequencing revealed that it was the $\text{qnrS1}$ variant. None of the isolates tested was positive either for $\text{qnrA}$, $\text{qnrB}$ or $\text{aac(6')Ib}$ genes and none showed mutations in the quinolone resistance determining regions (QRDR) sequenced. PFGE revealed seven different types although all were related (Figure 1) and some of the types could be observed in both countries in humans and foodstuffs. Some of the isolates were susceptible to all antimicrobials tested except ciprofloxacin, others were in addition resistant to streptomycin, sulfamethoxazole and tetracycline ($n = 16$). In none of these isolates was resistance observed towards penicillins or cephalosporins and therefore we did not investigate the presence of ESBL genes in these isolates, although they are usually found in association with $\text{qnr}$ genes.

This is the first report of $\text{qnr}$ genes detected in 23 $\text{Salmonella}$ Corvallis isolates and also the first report of $\text{qnr}$ in $\text{Salmonella}$ isolates from Denmark and Thailand.

The epidemiology of $\text{Salmonella}$ infections in Denmark is complicated. It is interesting that isolates of the same serovar, with the same newly emerged resistance mechanisms and the same PFGE type were found in patients in Thailand, patients in Denmark and imported food products. Denmark has been importing an increasing amount of chicken meat, and much of the imported chicken originates from Thailand. These data support the possibility that some patients in Denmark acquired $\text{S. Corvallis}$ from imported chicken meat from Thailand. We have recently indicated a similar phenomenon of infections with multidrug-resistant $\text{S. Schwarzengrund}$.6

Regarding the detection of quinolone resistance, the presence of the $\text{qnr}$ genes alone does not necessarily mediate full resistance to nalidixic acid and thus makes the use of nalidixic acid for screening for fluoroquinolone resistance unreliable. This is in contrast to the mutation-mediated resistance, where one mutation encodes low-level resistance to fluoroquinolones and full resistance to nalidixic acid. Low-level fluoroquinolone resistance is difficult to detect in routine diagnostic laboratories and these isolates might easily be considered susceptible especially when using diffusion testing. Further studies are needed on optimization of detection in clinical laboratories of low-level resistance.

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Since antibiotic-lock therapy (ALT) was first proposed in 1988 to its relatively high failure rate.1 This report describes the use treating catheter-related fungal infections has been disputed due to its relatively high failure rate.2 Notably, ALT may be more successful for treating catheter-related infections, this is the first proof of its use in a patient.2

A 13-year-old female suffered short bowel syndrome after surgical treatment for Hirschsprung’s disease. After insertion of a Hickman catheter for home total parenteral nutrition, the patient suffered recurrent Hickman catheter infections with multiple pathogens. To control the infections, the Hickman catheter was replaced six times. No evidence of immunodeficiency was noted by immunological tests.

On 24 June 2006, the patient was hospitalized with fever. Due to her infection history, ampicillin/sulbactam, gentamicin and fluconazole were used empirically. Cultures of four blood specimens from the Hickman catheter on 25, 26, 27 and 30 June revealed growth of C. parapsilosis, indicating that systemic fluconazole could not eradicate the infection.

ALT was started on 1 July with 2.5 mg/mL amphotericin B in 5 mL of normal saline containing no heparin. The solution was retained for 24 h each day. Intravenous amphotericin B at a dose of 1 mg/kg/day was also given and total parenteral nutrition was infused through a peripheral venous line. Acute renal failure with a serum creatinine level of 2.5 mg/mL occurred on 7 July. Because systemic amphotericin B was the suspected cause of the renal dysfunction, the drug was replaced by intravenous fluconazole at a dose of 6 mg/kg/day. Culture for C. parapsilosis was negative throughout the 20 days of ALT. Fever and inflammatory changes at the catheter insertion site were noted 3 days after the completion of ALT. Blood drawn from the Hickman catheter and peripheral vein grew methicillin-susceptible S. aureus. Before the antibiotic susceptibility results were available, vancomycin was given at a dose of 28 mg/kg/day. Subsequent blood culture showed no growth of pathogen. However, the local lesion showed no improvement after 3 days. Antibiotic treatment was shifted to intravenous oxacillin and oral rifampicin, but no therapeutic effect was noted. After 5 days, 40 mg/kg/day of oral erythromycin was given. Surprisingly, local erythema and tenderness improved on the next day and local inflammatory changes completely subsided 2 days after adding erythromycin despite any drug susceptibility reference. Follow-up cultures 3 months later showed no growth of either S. aureus or C. parapsilosis.

In such a patient with repeated catheter reinsertions, any possible means of eradicating the pathogen and preserving the catheter should be considered. Although ALT is not a recognized option for treating catheter-related candidaemia in the 2001 Infectious Diseases Society of America (IDSA) guidelines for the management of catheter-related fungaemia,1,5 we chose to try ALT in this patient.

Previous reports have demonstrated that most failures to treat catheter-related infections are due to the biofilm formed by invading pathogens.1 As for the highly potentialized pathogen in patients receiving parenteral nutrition and with a catheter device, C. parapsilosis exhibits significantly less biofilm growth than the more pathogenic Candida albicans.3 This may explain why C. parapsilosis catheter-related infection has been reported to be associated with a better prognosis.4

Notably, ALT may be more successful for treating catheter-related fungaemia when duration of treatment is longer.5 Conversely, some failures have been observed in studies administering ALT over shorter periods.6 These experimental findings indicate that the total duration of treatment may be a key factor for successful ALT. In refractory cases such as

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Antibiotic-lock therapy and erythromycin for treatment of catheter-related Candida parapsilosis and Staphylococcus aureus infections

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Keywords: candidiasis, macrolides/azalides, catheter-related infections

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Sir,

Since antibiotic-lock therapy (ALT) was first proposed in 1988 as a solution to catheter-related biofilm infections, its value for treating catheter-related fungal infections has been disputed due to its relatively high failure rate.1 This report describes the use of ALT to treat catheter-related Candida parapsilosis candidaemia. Additionally, a catheter insertion site infection by Staphylococcus aureus was successfully treated with ALT by adding erythromycin after antistaphylococcal antibiotics had failed. Although in vitro studies have demonstrated that macrolides may be able to inhibit biofilms in catheter-related infections, this is the first proof of its use in a patient.2

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