plasmid by the integration of a partly truncated class 2 integron as well as the deletion of large parts of the mobA gene (including the mobB gene) and the tetracycline resistance gene tet(B).

To the best of our knowledge, this is the first description of class 2-associated resistance gene cassettes in members of the genus Pasteurella. In contrast to P. multocida, which is found in the respiratory tract of various animal species, P. aerogenes is commonly found in the intestinal tract of swine, and may be associated with diarrhoea and other infections. As such, it is in contrast with Enterobacteriaceae, which frequently carry class 1 and class 2 integrons on plasmids. Since plasmids from E. coli and other Enterobacteriaceae usually cannot replicate in Pasteurella hosts, recombination of a transferred entrobacterial plasmid with plasmids indigenous to Pasteurella ensures a stable maintenance of the newly acquired resistance genes in the Pasteurella host. The in-depth analysis of plasmid pCCK343 from P. aerogenes provides further support for such inter- and intra-plasmid recombination events. Moreover, the data presented in this study substantiate the assumption of a gene flux between Enterobacteriaceae and P. aerogenes, which has previously been suggested based on the finding that the tetracycline resistance gene tet(B)—the predominant tet gene among Enterobacteriaceae—is most frequently found in P. aerogenes.

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References

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OXA-72-producing Acinetobacter baumannii in Brazil: a case report

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Sir,
Acinetobacter baumannii is a threatening nosocomial pathogen that has been reported worldwide. Its ability to survive at different pHs, temperatures and under poor nutritional conditions makes this pathogen extremely successful. Besides its intrinsic resistance to different antimicrobial agents, A. baumannii is capable of accumulating additional mechanisms of resistance, such as β-lactamase production, altered antibiotic targets, efflux pump overexpression and porin loss. Carbapenem resistance among A. baumannii clinical isolates is frequently associated with the ISAba1-related overexpression of OXA-51, a carbapenem-hydrolysing class D β-lactamase (CHDL) that is intrinsic to this species. In addition, the acquisition of other CHDLs has been increasingly reported among carbapenem-resistant A. baumannii clinical isolates worldwide. These enzymes are capable of hydrolysing carbapenems, but not extended-spectrum cephalosporins.

The acquired CHDLs reported in Acinetobacter spp. are divided into four subgroups, according to their amino acid sequence identity: OXA-23-like; OXA-24/40-like; OXA-58-like; and OXA-143-like. To date, only two CHDL clusters were identified among A. baumannii clinical isolates in Brazil: OXA-23; and the recently described OXA-143. Here, we describe the occurrence
of OXA-72, an OXA-24-like enzyme, in an *A. baumannii* clinical isolate from Brazil, thus increasing the diversity of CHDL clusters reported in this country.

During winter 2007, an elderly patient underwent a total hip arthroplasty due to a fracture. Ten days after the surgery, he presented with fever and dyspnoea due to a wound infection. *A. baumannii* ATCC 19606 was empirically presented with fever and dyspnoea due to a wound infection. *A. baumannii* ATCC 19606 was empirically introduced. *A. baumannii* A30235 was isolated in a blood culture. According to disc diffusion following CLSI (M100-S19) recommendations, isolate A30235 was found to be susceptible to only ampicillin/sulbactam. The antimicrobial therapy was modified to 3 g of ampicillin/sulbactam iv every 6 h. The patient showed clinical resolution and was discharged from hospital after receiving 14 days of antimicrobial therapy. Unfortunately, the follow-up of this patient was lost.

Susceptibility testing was further performed using CLSI microdilution. Isolate A30235 showed susceptibility to polymyxin B and colistin, reduced susceptibility to ampicillin/sulbactam, and resistance to ceftazidime, cefepime, ceftriaxone, imipenem, meropenem, ciprofloxacin and amikacin (Table 1).

A multiplex PCR assay targeting CHDL-encoding genes was performed using previously published primers and cycling conditions. The presence of *bla*<sub>OXA-51-like</sub> and *bla*<sub>OXA-24/40</sub> was confirmed by PCR. DNA sequencing identified the *bla*<sub>OXA-24/40</sub> amplicon as *bla*<sub>OXA-72</sub>. A subsequent PCR targeting both *bla*<sub>OXA-72</sub> and the insertion sequence ISAb1 yielded a negative result, indicating that *bla*<sub>OXA-72</sub> expression was not driven by the promoter present in this insertion sequence element. Amplification of metallo-β-lactamase-encoding genes was not detected.

Plasmid extract obtained by the Kieser method was used to transform electrocompetent *A. baumannii* ATCC 19606, as previously described. Selection of transformants was performed in Luria–Bertani agar supplemented with 100 mg/L ticarcillin and the presence of *bla*<sub>OXA-72</sub> was confirmed by PCR. Electrophoresis of plasmids extracted from a transformant and subsequent Southern blot and hybridization with a *bla*<sub>OXA-72</sub>-specific probe showed that the *bla*<sub>OXA-72</sub> gene was located on a plasmid of ~86 kb. Susceptibility testing of transformants revealed increased meropenem and imipenem MICs, whereas cephalosporin MICs were identical to those for *A. baumannii* ATCC 19606, suggesting that other cephalosporin resistance determinants were not co-transferred (Table 1).

Studies with ampicillin/sulbactam have demonstrated the efficacy of this association as an alternative treatment of infections due to carbapenem-resistant *Acinetobacter* spp. According to the CLSI criteria, the strain A30235 was classified as susceptible and intermediate to ampicillin/sulbactam by disc diffusion and broth microdilution, respectively. Since minor errors have been observed for this combination by disc diffusion, determination of the ampicillin/sulbactam MIC is required when this compound is prescribed for the treatment of serious infections, such as sepsis. Despite being infected by an isolate that showed reduced susceptibility to ampicillin/sulbactam, the patient had a good clinical outcome after treatment.

The *OXA-72* enzyme was first identified in *A. baumannii* from Thailand, in 2004 (accession no. AY739646). Later on, this enzyme was reported in *Acinetobacter* spp. clinical isolates from China, South Korea, Taiwan, Italy, Spain and France. In this study, we identified a plasmid-encoded *OXA-72* in an *A. baumannii* clinical isolate from Brazil. The isolate (A30235) also showed increased resistance rates to extended-spectrum cephalosporins that are not hydrolysed by *OXA-72*, suggesting the presence of an additional mechanism of β-lactam resistance that was not transferable with *bla*<sub>OXA-72</sub>.

The occurrence of *bla*<sub>OXA-72</sub> located in a mobile genetic element points to the increasing diversity of CHDLs among *Acinetobacter* spp. clinical isolates in Brazil and its potential for spread. Consequently, it is essential that Brazilian Infection Control Committee members are aware of the emergence of *OXA-72*. This will allow appropriate control measures to be taken to avoid its dissemination among Brazilian hospitals.
which have experienced the spread of OXA-23-producing A. baumannii.\textsuperscript{12}

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\section*{References}


\section*{Tigecycline for severe infections: the gap between the warning and the necessity}

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Sir,

I have received the US FDA warning describing an increased mortality risk associated with the use of tigecycline when compared with other drugs in the treatment of a variety of serious infections. The increased risk of mortality was determined using a pooled analysis of randomized clinical trials (RCTs) and was seen most clearly in patients treated for hospital-acquired pneumonia (HAP), especially ventilator-associated pneumonia (VAP), but was also seen in patients with complicated skin and skin structure infections (cSSSIs), complicated intra-abdominal infections (cIAIs), infections due to resistant pathogens and diabetic foot infections.\textsuperscript{1} Although for each indication the mortality difference was not statistically significant, trends were present and, when pooled, a statistically significant difference was observed. Based on these data, the FDA recommends that alternatives to tigecycline should be considered in patients with severe infections.

The FDA recommendation is thus based upon a combination of RCTs that were the scientific support for the FDA licensing approvals for tigecycline in cSSSI,\textsuperscript{2} cIAI\textsuperscript{3} and community-acquired bacterial pneumonia (CABP),\textsuperscript{4} as well as other studies in which tigecycline did not achieve outcomes suitable for such approvals (e.g. VAP).\textsuperscript{5} Clinicians are now faced with the conundrum that at present the FDA licensed approvals for tigecycline remain unaltered but an alert has been issued against severe sepsis, although tigecycline does not have an explicit licence for this indication. Understanding the context of both the alert and its relevance to the clinical circumstances facing doctors as they make decisions about severe sepsis management is therefore critical.

The context of the FDA alert is that it is based on RCTs where only a small percentage of patients with severe infections were included. No severity score was used in the cSSSI RCT (only 25.8% of patients required surgery/drainage),\textsuperscript{2} only 19.8% from the CABP RCT showed high pneumonia severity index (IV-V) values\textsuperscript{4} and the mean APACHE II score in patients from the cIAI and HAP RCTs was ≤15 (6.2 and 12.3, respectively).\textsuperscript{3,5} This lack of patients with severe sepsis in licensing studies is commonplace and not unique to tigecycline. For example the Infectious Diseases Society of America guidelines recommend...