

## Nosocomial Infections Caused by *Acinetobacter baumannii*: A Major Threat Worldwide

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Currently, *Acinetobacter baumannii* is considered to be an important and emerging hospital-acquired pathogen worldwide.<sup>1</sup> It is responsible for 2%-10% of all gram-negative bacterial infections in intensive care units in Europe and the United States.<sup>2,3</sup> However, despite the importance of this organism as a public health problem, several shadow areas persist regarding its virulence, antimicrobial resistance, reservoirs, and epidemiology. Several articles published in this issue of ICHE shed some light on this fascinating bacterium.

Some of the uncertainties surrounding *A. baumannii* are related to the fact that bacteria classified as members of the genus *Acinetobacter* have a long history of taxonomic changes, moving from the family Neisseriaceae to the family Moraxellaceae. Within the genus *Acinetobacter*, studies based on DNA-DNA hybridization have described 25 "genomic species" that fulfilled the criteria to be considered as distinct species, and 17 of these have officially been validated to date.<sup>4</sup> This situation has led contributors to the *Manual of Clinical Microbiology* to state that the majority of the genomic species cannot be reliably distinguished by phenotypic tests.<sup>5</sup> Despite that, and because of the difficulties in differentiating the isolates according to their phenotypic characteristics, the term *Acinetobacter calcoaceticus*-*Acinetobacter baumannii* complex is often used. It is important to note, and this may be a limitation of the studies we comment on in this editorial, that in 3 of the 4 studies,<sup>6-9</sup> species identification was performed using phenotypic methods only, and the isolates were named either *A. baumannii* or *A. baumannii-calcoaceticus*. In the study in this issue of the journal by Griffith et al.,<sup>8</sup> ribotyping, which could have been used to identify the isolates, was used to compare the isolates but not to identify them, and the isolates were also classified as *A. baumannii-calcoaceticus*.

One of the main concerns about *A. baumannii* is a characteristic that makes it a major threat to public health, namely, its remarkable ability to rapidly develop antibiotic resistance, mostly by acquisition of gene clusters carried by plasmids,<sup>10</sup> transposons,<sup>11</sup> or integrons,<sup>12,13</sup> sometimes arranged in resistance islands within the genome.<sup>14</sup> This phenomenon led to

multidrug resistance in this species within a few decades.<sup>15</sup> With the emergence of increasingly resistant strains, the management of *A. baumannii* infection has become a public health problem in many countries. To date, some strains of *A. baumannii* have become resistant to almost all currently available antibacterial agents, including carbapenems, which were once considered the drug of choice for treatment of *A. baumannii* infection.<sup>16,17</sup> In this issue, Peleg et al.<sup>9</sup> describe the frightening emergence of carbapenem resistance in *A. baumannii* isolates over a 3-year period in an Australian hospital, significantly linked to an increased use of meropenem. They demonstrated, by pulsed-field gel electrophoresis, the clonal origin of these multidrug-resistant strains, but they failed to identify the mechanism associated with carbapenem resistance. The latter point is of particular interest, because Peleg et al.<sup>9</sup> screened strains for the presence of the genes for carbapenem-hydrolyzing  $\beta$ -lactamases most commonly found in other countries. However, although Peleg et al.<sup>9</sup> suggested that there may be a nonenzymatic mechanism of resistance or a new  $\beta$ -lactamase, they did not search all currently described genes coding for carbapenem-hydrolyzing  $\beta$ -lactamases.<sup>18,19</sup> The identification of the mechanism involved in carbapenem resistance in this clonal population of *A. baumannii* should warrant further investigation to determine whether the bacterium has acquired a resistance gene that is spreading around the world or a gene "made in Australia." Finally, this article by Peleg et al.<sup>9</sup> emphasizes the risk of misuse of antibiotics, because of the extremely rapid emergence of antibiotic resistance in *A. baumannii*, and the consequent need for strict rules for prescription of carbapenems.

In addition to its propensity to acquire antibiotic resistance, *A. baumannii* is feared for its ability to cause outbreaks of disease in healthcare facilities.<sup>20</sup> Such outbreaks may take particular forms, such as those that involve multiple facilities.<sup>13,21</sup> In France, the AYE strain, which produces an extended-spectrum  $\beta$ -lactamase, spread throughout 54 healthcare facilities in 8 administrative regions during an 11-month period.<sup>13</sup> In their study, Fillaux et al.<sup>6</sup> used pulsed-field gel electrophoresis to compare 1,277 *A. baumannii* strains, including 148 mul-

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tidrug-resistant strains, isolated from 2000 to 2003 in a French hospital. The study was conducted retrospectively to evaluate the epidemiology of *A. baumannii* in their hospital setting. However, although Fillaux et al.<sup>6</sup> identified an extended-spectrum  $\beta$ -lactamase-producing clone that was endemic during 2001-2003, they did not determine whether this strain was related to the AYE strain. In addition, although they described a decrease in antibiotic susceptibility over the study period, they did not correlate it with the level of antibiotic consumption in the hospital. Nonetheless, the study demonstrated the co-occurrence of several multidrug-resistant strains, with seasonal variations in the strains identified during the study years.

From January 1, 2002, to August 31, 2004, *A. baumannii* grew from the blood of 102 patients hospitalized at military medical facilities treating service members injured in Afghanistan and the Iraq/Kuwait region.<sup>22</sup> The sources of *A. baumannii* that led to the infections were not found, but, during the Vietnam War, *A. baumannii* was the most common gram-negative bacillus recovered from traumatic injuries to extremities.<sup>23</sup> In this issue, Griffith et al.<sup>8</sup> report on their search for the source and/or reservoir of these infections. They performed a prospective study in a population of healthy, nondeployed US Army soldiers. The results are interesting, even though the mystery of the source and/or reservoir of the strains infecting injured service members has not been found, because they confirm that skin colonization with *A. baumannii-calcoaceticus* in healthy individuals is common and may serve as a source for infection. In addition, the organisms were found on body sites, such as the forehead and the feet, usually not screened during epidemiologic studies.

In conclusion, *A. baumannii* remains a puzzling bacterium that requires additional studies to solve all its mysteries.

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