Acinetobacter baumannii is now considered a highly important pathogen implicated in hospital infections, especially in critically unwell patients in the intensive care unit. The presence of mechanical ventilator tubing, central venous lines, urinary catheters and exposure to broad-spectrum antibiotics are important risk factors. The combination of intrinsic and acquired antibiotic resistance mechanisms, virulence and survival factors, and the ability to cause wide-spread hospital outbreaks, make this a truly challenging pathogen in hospital-acquired infections.

Acinetobacter species are gram-negative, non-fermenting, often coccobacillary bacteria that belong in the family Moraxellaceae. The genus currently comprises 34 species, of which 25 have valid names and nine are named by their genomic group, with A. baumannii the most important in human infections. A. baumannii is part of the A. calcoaceticus–A. baumannii complex, which includes A. calcoaceticus (genomic species 1, an environmental species of limited clinical significance), A. baumannii (genomic species 2), A. pittii (genomic species 3) and A. nosocomialis (genomic species 13TU), which are all genetically related and difficult to distinguish phenotypically1,2. A. baumannii has been found to be associated with greater resistance to antibiotics compared with other genomic species3 and higher mortality among bacteraemic patients compared with A. nosocomialis4.

In clinical practice, A. baumannii may be difficult to decolorise on gram staining and may be falsely reported as gram-positive cocci from direct smears from blood culture bottles. A. baumannii will grow on standard, non-selective agar after 24–48 h incubation and colonies are non-hemolytic and smaller than Enterobacteriaceae on blood agar. Growth on MacConkey agar appears as a non-lactose fermenter. Most automated systems perform poorly in speciating Acinetobacter. Vitek2, API 20NE (bioMérieux, Marcy l’Etoile, France) and Phoenix (Becton Dickinson, Franklin Lakes, NJ, USA) systems will only identify down to A. calcoaceticus–A. baumannii complex. Matrix-assisted laser desorption ionisation-time of flight (MALDI-TOF) mass spectrometry systems appear to perform better at species differentiation than phenotypic systems5. For outbreak investigation, molecular typing has traditionally been performed using pulse-field gel electrophoresis (PFGE); however, newer technologies such as repetitive sequence-based PCR and broad-range PCR/electrospray ionisation mass spectrometry, both semi-automated systems, can generate rapid results with good concordance with PFGE6. Multilocus sequence typing (MLST) scheme, based on the nucleotide sequences of several housekeeping genes, also provides a high level of concordance with PFGE and is mainly used for global epidemiology studies7. Although inconsistencies have been reported with some of the selected genes (namely gyrB and gpi), typing isolates by their blaOXA-51-like gene has been shown to be another useful tool to quickly and easily identify isolates belonging to certain epidemic lineages8.

A. baumannii has been implicated in hospital outbreaks and in the endemic spread of resistant clones throughout the world9–11. It is a hardy organism that can survive in both moist and dry environments and has been found on a wide range of hospital surfaces. Outbreaks are classically clonal but horizontal-gene transfer has been an important mechanism for antibiotic resistance dissemination. Biofilm formation is a characteristic virulence attribute of A. baumannii (Figure 1) and this facilitates its ability to cause disease, particularly ventilator-associated pneumonia, bloodstream and urinary-tract infection, burn wound infections and less commonly hospital-acquired meningitis. Of most concern is the emergence of antibiotic resistance in A. baumannii. In an EU wide
point-prevalence study, 81.2% of A. baumannii isolates were resistant to carbapenem antibiotics (compared with 31.8% of P. aeruginosa isolates)\(^ {12}\). Large inter-country variation has been observed, with generally higher resistance reported from southern Europe than northern Europe. In 2013, only two countries (Iceland and Montenegro) reported no cases of carbapenem-resistant Acinetobacter spp. (CRAB) and six countries (Croatia, Greece, Israel, Italy, Latvia and Lithuania) reported an endemic situation, with CRAB regularly isolated from patients in most hospitals\(^ {13}\). US-wide surveillance data demonstrates that CRAB has grown nearly eight times, going from 5.2% in 1999 to 40.8% in 2010\(^ {14}\). Similar data were obtained from the Asia-Pacific region, where 42.3% of isolates were non-susceptible to carbapenems\(^ {15}\).

Acinetobacter species have a range of inherent enzymatic and membrane-based resistance mechanisms, which can be upregulated under selection pressure. The antimicrobial classes that remain active include some fluoroquinolones (e.g. ciprofloxacin), aminoglycosides (e.g. gentamicin, tobramycin and amikacin), carbapenems (imipenem, doripenem and meropenem), polymyxins (polymyxin B and colistin), tetracyclines (tigecycline and minocycline), trimethoprim-sulfamethoxazole and sulbactam (available in combination with ampicillin). Unfortunately, acquired resistance has now been reported to all of these agents through a range of plasmid-mediated enzymatic resistance mechanisms (OXA carbapenemases and metallo-beta-lactamas, aminoglycoside-modifying enzymes and 16S rRNA ribosomal methylases), modification of antimicrobial targets (topoisomerases, ribosomal proteins and lipopolysaccharide, which confer resistance to fluoroquinolones, aminoglycosides and colistin, respectively), loss of outer membrane proteins and upregulation of efflux pumps that can confer resistance to beta-lactams, fluoroquinolones, aminoglycosides and tigecycline.

Detection of carbapenemases remains a challenge for the clinical laboratory. Modern technology such as MALDI-TOF MS and the biochemical-based method CarbAcinetobacter test (adapted from the Carba NP test), as well as faster turnaround times for molecular techniques will continue to help in the timely identification of these resistant clones and allow for earlier directed therapy and prompt infection control procedures\(^ {16}\).

The preferred anti-infective agents for serious, invasive Acinetobacter infections are carbapenems (meropenem, doripenem or imipenem). Ertapenem is not effective against Acinetobacter. Last-line agents for carbapenem-resistant organisms include sulbactam (formulated as ampicillin-sulbactam in the United States), polymyxin class of antibiotics and tigecycline, which are often used in combination with other agents for synergy and to prevent the emergence of resistance that can occur with monotherapy. A range of combination therapies have been studied in vitro and in animal models, and combinations including a carbapenem plus a polymyxin, even when the organism is resistant to the carbapenem, appears most active. Combinations with non-traditional antimicrobials have also been studied, the most common of these being the addition of rifampicin to a carbapenem and a polymyxin\(^ {17}\).

Infection prevention for CRAB is also an important part of management and includes isolation, contact precautions, optimal hand hygiene and targeted environmental cleaning with hydrogen peroxide and peracetic acid\(^ {18}\). Antibiotic stewardship should also be performed in parallel. For outbreaks, an early case-control study and sampling of potential environmental reservoirs are often required.

References


---

**Biographies**

**Dr Iain Abbott** is an advanced trainee in Infectious Diseases and Microbiology in Melbourne. He has specific interests in multidrug resistant organisms and their impact on the critically ill patient.

**Associate Professor Anton Peleg** is a staff specialist in Infectious Diseases at the Alfred Hospital in Melbourne, and a Group Leader and NHMRC Research Fellow in the Department of Microbiology at Monash University. His research interests are in hospital-acquired infections, antibiotic resistance and mechanisms of pathogenesis of hospital-acquired organisms including *Acinetobacter baumannii*, *Staphylococcus aureus* and *Candida albicans*.

---

**Future issues of Microbiology Australia**

**May 2014:** AIDS

Guest Editors: Johnson Mak and Stephen Kent

**September 2014:** Microbial diseases and products that shaped world history

Guest Editor: Ipek Kurtböke (a joint issue with the Microbiology Society of Turkey)

**November 2014:** Environmental microbiology

Guest Editor: Andy Ball

**March 2015:** Gut symbioses

Guest Editor: Linda Blackall

**May 2015:** Medical mycology

Guest Editor: Wieland Meyer

---

**Under the Microscope**

---

**DOIs**

- 10.1128/JCM.43.9.4382-4390.2005
- 10.1111/j.1469-0691.12427