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Acinetobacter

Lul Raka, Gjyle Mulliqi-Osmani, Lumturije Begolli,
Arsim Kurti, Greta Lila, Rrezarta Bajrami and
Arbëresha Jaka-Loxha

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1. Introduction

Infections caused by bacteria of genus *Acinetobacter* pose a significant health care challenge worldwide (Munoz-Price & Weinstein, 2008; Visca et al., 2011). *Acinetobacter* infections in the past were sporadically identified in hospitalized patients and hospital infection outbreaks in intensive care units. But, nowadays *Acinetobacter* has emerged as an important healthcare-associated and multidrug-resistant microorganism (Peleg et al., 2008).

Acinetobacter was first described in 1911 by Beijerinck as *Micrococcus calco-aceticus*. The name “*Acinetobacter*” originates from the Greek word “*akinetos*” meaning “unable to move”, as these bacteria are not motile. *A. baumannii*, *A. calcoaceticus*, *A. haemolyticus* and *A. lwoffii* are the most important species in clinical practice.

Acinetobacter species are ubiquitous in nature and have been found in soil, water, animals and humans. Some strains of *Acinetobacter* can survive for weeks in environment, promoting transmission within the hospital settings (Doughari et al., 2011). *Acinetobacter baumannii* was recovered from the skin, throat, rectum and respiratory tract of humans. The species *A. baumannii* accounts for nearly 80% of reported *Acinetobacter* infections (CDC, 2007). This feature along with antimicrobial resistance, colonization potential and contact transmission are main challenges for prevention and control activities (Maragakis et al., 2008). Some strains of *Acinetobacter* produce verotoxins and others have been identified to have an impact on removal of biological phosphorus from wastewater.

2. Taxonomy and main features

Genus *Acinetobacter* belongs to the family Moraxellaceae and order Pseudomonadales.

Based on molecular studies, 32 species of *Acinetobacter* have now been recognized; 22 of them have assigned valid names, whereas other species are described as a “genomic” group. The most important clinical species in medicine is *Acinetobacter baumannii*. This micro-organism has phenotypic similarities with a group of species known as *A. calcoaceticus*-*A. baumannii* complex (Vanechoutte et al., 2011). In healthcare settings, this group is implicated in major outbreaks and healthcare-associated infections.

The genus *Acinetobacter* consists of strictly aerobic Gram-negative coccobacilli rods, which are nonmotile, catalase-positive, indole-negative, oxidase-negative, non-fermentative. The bacilli are 0.9 to 1.6 μm in diameter and 1.5 to 2.5 μm in length, often in pairs or assembled into longer chains. *Acinetobacter* spp. are non-fastidious and can be grown on standard laboratory media.

Acinetobacter is relatively nonreactive in many biochemical tests used to differentiate among gram-negative bacilli. Most clinical microbiology laboratories identify members of the genus *Acinetobacter* at the level of the following three groups with corresponding metabolic attributes (Allen et al., 2006):

- *Acinetobacter calcoaceticus*-*baumannii* complex: glucose-oxidizing non-hemolytic (*A. baumannii* can be identified by OXA-51 serotyping)
- *Acinetobacter lwoffii*: non glucose-oxidizing, non-hemolytic
- *Acinetobacter haemolyticus*: hemolytic.



Figure 1. Colonies of *Acinetobacter* spp. on sheep's blood agar after 24 hours at 37°C. CDC/ Pete Seidel. Public Health Image Library

Acinetobacter species are widely distributed in nature and can be found in soil, sewage, water, consumables (including fruits and vegetables), and on healthy skin and other body sites. *A. baumannii* can be found also in some unusual reservoirs, such as food or arthropods. The majority of *A. baumannii* strains survive longer than *Escherichia coli* on dry surfaces, and some strains survive for more than 4 months.

About 25% of adults carry this organism on their skin, whereas about 7% carry it in their pharynx. Hospitalized patients may become easily colonized. Half of the patients with tracheostomy may be colonized with *Acinetobacter*. Isolation of this microorganism from feces, urine, vaginal secretions is often considered as colonization or contamination. But, their presence from immunocompromised persons may have significant clinical impact (Mahon et al., 2010).

Clinical infections with *Acinetobacter* in healthcare settings are related to the use of invasive procedures (mechanical ventilation, vascular catheters) and patient's underlying conditions (Fournier & Richet, 2006). The most important risk factors for acquiring *Acinetobacter* infections are: prior antibiotic use (third-generation cephalosporins, fluoroquinolones or carbapenems), prolonged hospitalization, high APACHE II (Acute Physiology and Chronic Health Evaluation) score, recent surgical intervention, central vascular catheterization, tracheostomy, mechanical ventilation and enteral feeding.

Acinetobacter can contaminate many surfaces and medical equipment, such are: suctioning equipment, washbasins, bedrails, bedside tables, ventilators, sinks, pillows, mattresses, hygroscopic bandages, resuscitation equipment, and trolleys (Bernards et al., 2004). The hands

of healthcare workers are in frequent contact with these objects in patient surroundings. Hands become an important vectors of transmission in case of non-compliance with hand hygiene recommendations (Pittet et al., 2006). The ability of *Acinetobacter* to participate in biofilm formation promotes durability in surfaces and may contribute to continuation of environmental presence during outbreaks (Fournier et al., 2006).

Acinetobacter species possess the following virulence factors which enable transmission within health care settings: cell surface hydrophobicity, enzymes, toxic slime polysaccharides, verotoxins, siderophores and outer membrane proteins.

3. Clinical importance — Infections and outbreaks

Acinetobacter spp. can cause infections in both hospital settings and in community. They are the second most commonly isolated non-fermenters in human specimens, after *Pseudomonas aeruginosa*. About 1-3% of health care-associated infections are caused by *Acinetobacter* spp.

Acinetobacter poses little risk to healthy people. However, people who have weakened immune systems, chronic lung disease, or diabetes may be more susceptible to infections with *Acinetobacter*. Most infections caused by this multiresistant bacteria involve organ systems, which have a high fluid content (the respiratory tract, peritoneal fluid, and the urinary tract) and are associated with usage of indwelling devices. The distribution of the different types of hospital acquired infections is variable between hospitals and it depends on the hospital population and the type of performed procedures and interventions. Rates of mortality from *Acinetobacter* infections have a wide range from 5% in general wards to 54% in intensive care units (Kempf & Rolain, 2012).

One important feature of *A. baumannii* is its ability to cause outbreaks, which is in relation to antimicrobial resistance and resistance to desiccation (D'Agata et al., 2000; Villegas et Hartstein, 2003). *Acinetobacter* spp. cause a wide range of health care-associated infections such as: ventilator-associated pneumonia, bloodstream infections, urinary tract infections, surgical site infections, meningitis, cholangitis, peritonitis, skin and wound infections, ventriculitis, and infective endocarditis. Suppuration is common feature in infections caused by *Acinetobacter* (abscesses of the brain, lung and the thyroid; secondary infections of wounds or surgical trauma, and purulent lesions of the eye).

Acinetobacter can also cause infections in the community (Falagas et al., 2007). The predominant community-acquired infections are: pneumonia, meningitis, cellulitis and bacteremia. High fatality rates in community were correlated to underlying conditions and risk factors, such as : alcoholism, diabetes and cancer.

Acinetobacter infections were also frequently reported during the natural disasters and wars (Iraq, Kuwait and Afghanistan wars). Pathogenic *Acinetobacter* infections were encountered in military personnel during the wars in Afghanistan and Iraq (O'Shea, 2012). Therefore it was named by media as *Iraqibacter*.

Recent disasters suggested that *Acinetobacter* infections should be taken in consideration in differential diagnosis of soft-tissue infections (Asia tsunami on 2004).

Many *Acinetobacter* infections have a seasonal variation with 50% infection rates higher from July to October than at other times of the year. This variation was explained by warmer, more humid ambient air, which favors growth of *Acinetobacter* and potentially preventable environmental contaminants, such as condensate from air-conditioners.

4. Antimicrobial resistance

The main challenge with *A. baumannii* is its ability to acquire antimicrobial-resistance genes extremely rapidly, leading to multidrug resistance. Widespread use of antimicrobials within hospitals resulted to the emergence and increase of antimicrobial resistance among *Acinetobacter* strains, in particular, the wide use of extended-spectrum cephalosporins and quinolones (Imperi et al, 2011).

Acinetobacter spp. are intrinsically less susceptible to antimicrobial agents than other representatives from the family Enterobacteriaceae. Various mechanisms played a role in the acquisition of a multiresistance phenotype amongst Gram-negative bacteria, including *Acinetobacter* strains such as: loss of porins, production of β -lactamases, increased expression of efflux pumps, presence of antibiotic-modifying enzymes, target site mutations, ribosomal mutations or modifications, metabolic bypass mechanisms and a mutation in the lipopolysaccharide (Poirel et al, 2011). The role of plasmids in the acquisition of antimicrobial resistance in *A. baumannii* is mostly related to their integron structures.

Acinetobacter spp have ability to acquire antimicrobial-resistance genes rapidly, leading to multidrug resistance. As a result, the clinical management of these infections has become a public health challenge in many countries. Nowadays, the most serious problem in the treatment of *Acinetobacter* infection is acquired multidrug-resistance, leaving only few antimicrobial agents as treatment options. This resistance is attributed to the presence of multiple resistant determinant among bacteria, which confers resistance to many groups of antimicrobial agents (Livermore, 2012). One of the main concerns about antimicrobial resistance in *A.baumannii* has been the resistance to the last line of antimicrobials through acquisition of carbapenem resistance - mainly through the acquisition of B and D class carbapenemases(Bou et al., 2012).

5. Detection and typing systems

Infection or colonization with *Acinetobacter* is usually diagnosed by the culture of clinical samples and samples from environment. The most frequent clinical samples include blood, cerebrospinal fluid, endotracheal aspirate, wounds, sputum, urine, catheter tips, stool or sterile body fluid, skin, cordon of newborns, nasal swabs, hand swabs of hospital workers. The most

common environmental samples include swabs on surfaces of machines, wash-hand basins, floors, tables, UV lamps, etc.

Microbiologic cultures can be processed by standard methods on routine media. For routine clinical and laboratory investigations, traditional culture media are used: agar, brain heart infusion agar, tryptic soy agar, Eosin-methylene blue, MacConkey agar, Violet red bile agar, Luria Bertani agar and Holton medium. For environmental screening the most commonly used media are broth media such as MacConkey's broth, trypton soy, Brain Heart Infusion and Luria broth. Antimicrobial susceptibility can be determined by various means, with the agar-dilution method being the gold-standard (CLSI, 2011).

Biochemical typing methods include the use of colorimetric based GN card ID 32 GN, API 20NE, RapID NF Plus and Vitek 2 systems.

For detection of *Acinetobacter* strains a new molecular identification and typing methods have been developed, leading to successful identification and outbreak management (Ecker et al., 2006). The most important of them are : polymerase chain reaction (PCR), PFGE, RAPD-PCR DNA fingerprinting, fluorescent in situ hybridization (FISH), 16S rRNA gene restriction analysis (ARDRA) (amplified rDNA restriction analysis) and 16S rRNA gene PCR-DGGE (Denaturing Gradient Gel Electrophoresis) fingerprinting (Versalovic et al., 2011). A recent diagnostic method which was reported to have high specificity and can discriminate between *Acinetobacter* species is the microsphere-based array technique that combines an allele specific primer extension assay and microsphere hybridization. The use of DNA-DNA hybridization and sequence analysis is considered the gold standard, but the method is time consuming and impractical in most clinical laboratories.

Other methods that have been introduced in the epidemiological investigation of outbreaks caused by *Acinetobacter* spp. include biotyping, phage typing, cell envelope protein typing, plasmid typing, ribotyping, restriction fragment length polymorphisms and arbitrarily primed PCR (AP-PCR).

6. Treatment, prevention and control

Treatment of *Acinetobacter* infections should be individualized according to results of susceptibility testings. For effective treatment of *Acinetobacter* infections the combination therapy is usually required. Infections caused by antibiotic-susceptible *Acinetobacter* isolates have usually been treated with broad-spectrum cephalosporins, combinations of β -lactam: β -lactamase inhibitor or carbapenems, used alone or in combination with an aminoglycoside (Evans et al., 2012). The duration of treatment is similar to that for infections caused by other gram-negative bacilli.

Antibiotic choices may be limited in cases of infections caused by multidrug-resistant isolates. The emergence of multidrug-resistant *Acinetobacter* strains has brought the old antibiotic polymyxins back into clinical use. These antibiotics disrupt bacterial cytoplasmic membranes, causing leakage of cytoplasmic contents. Clinicians stopped using this antibiotic in 1970s due to several side effects in kidneys and neurons.

Another treatment option remain tigecycline, a new glycylcycline antibiotic. However, development of resistance to these last option antibiotics has been reported recently (Gimarellou & Poulakou, 2012).

Prevention and control of infections caused by *Acinetobacter* requires a coordinated effort involving all stakeholders including healthcare facilities and providers, public health, and industry (Siegel et al., 2007). CDC and APIC has recommend the cornerstones for prevention and control of multidrug resistant organisms, including *Acinetobacter* infections (CDC,2012; APIC,2010). Key measures to control spread of multi-drug resistant organisms are:

- Administrative Measures/Adherence Monitoring
- Education
- Judicious Antimicrobial Use
- Surveillance
- Infection Control Precautions to Prevent Transmission
- Environmental Measures Decolonization

Infection control measures should start with strict isolation and cohorting of infected or colonized patients accompanied by administrative measures, education, prudent antimicrobial use, surveillance, standard precautions to prevent transmission and environmental measures.

Control of hospital outbreaks caused by *Acinetobacter* species is an important challenge for all health care settings. If a source and/or reservoir are identified, than the outbreak is successfully controlled by the eradication of that source/reservoir. In other circumstances, various measures may be used, including unit closure, cohorting of patients and staff, strict hand hygiene, contact or strict isolation, environmental disinfection and discharge of colonized patients.

A review of 51 hospital outbreaks showed that 25 had a common source: 13 outbreaks with predominantly respiratory tract infections and 12 with predominantly bloodstream or other infections were controlled by removal or disinfection and sterilization of contaminated ventilator (or related) equipment or contaminated moist fomites (Villegas & Hartstein, 2003).

When neither common sources nor environmental reservoirs are identified, control has depended on active surveillance and contact isolation for colonized and infected patients, improvements in the hand hygiene of health care workers and aseptic care of vascular catheters and endotracheal tubes.

7. Conclusions

In conclusion, *Acinetobacter* strains are important pathogens due to the diversity of their reservoirs, capacity to accumulate mechanisms of antimicrobial resistance and outbreak potential. *Acinetobacter* infections prolong the length of hospital stay, increase mortality and have economic impact. The greatest challenge remain prevention, control and treatment of infections caused by multidrug-resistant strains of *Acinetobacter*.

Although our understanding of *Acinetobacter* made an significant step forward, there are still many unanswered questions for health care workers. Future directions should be directed toward research development of new antibiotics, well-controlled clinical trials of antimicrobial regimens and combinations, and prevention of health care-associated transmission of multi-drug-resistant *Acinetobacter* infections.

Author details

Lul Raka, Gjyle Mulliqi-Osmani, Lumturije Begolli, Arsim Kurti, Greta Lila, Rrezarta Bajrami and Arbëresha Jaka-Loxha

*Address all correspondence to: lul.raka@uni-pr.edu lulraka@hotmail.com

Faculty of Medicine, University of Prishtina & National Institute of Public Health of Kosova, Prishtina, Kosova

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