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### Review Article



## Acinetobacter baumannii in the Healthcare Facility Setting

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#### Abstract

Acinetobacter baumannii is a significant cause of healthcare-associated infections, particularly in intensive care units, where its ability to develop multidrug resistance complicates treatment and control efforts. This review highlights the bacteriology, ecology, virulence mechanisms, and antibiotic resistance strategies of A. baumannii, with an emphasis on its clinical impact in healthcare settings. The pathogen's resistance is fueled by genetic mutations, enzyme production, and efflux pumps, leading to resistance against carbapenems and other key antibiotics. It can cause infections in various body sites, including the lungs, bloodstream, and urinary tract, and has a high mortality rate, especially in vulnerable patients. A. baumannii's ability to survive on dry surfaces for extended periods contributes to its spread within healthcare facilities, exacerbating outbreak risks. Effective prevention strategies, such as strict infection control protocols, environmental cleaning, and antibiotic stewardship, are essential for minimizing the pathogen's impact. Continued research into new antibiotics and treatment approaches is critical to managing this formidable public health threat.

Keywords: Acinetobacter infections, Drug resistance, Infection control, Antimicrobial stewardship

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#### Introduction

Acinetobacter baumannii is a bacterial pathogen capable of instigating infections at multiple anatomical sites, encompassing the bloodstream, pulmonary tissues, urinary tract, and cutaneous wounds (1). A. baumannii is a prevalent causative agent of healthcare-associated infections, especially in intensive care units (ICUs), affecting critically ill patients and those with medical devices such as ventilators, catheters, or surgical wounds. Its transmission can occur via person-to-person contact or contact with contaminated surfaces and equipment (2). Managing these infections poses a significant challenge due to A. baumannii's often encountered resistance to a wide range of antibiotics, including carbapenems, typically reserved for severe cases. This limited arsenal of effective treatments results in elevated mortality rates, prolonged hospitalizations, and increased healthcare expenditures (3). To curtail the spread of A. baumannii in healthcare settings, it is imperative to adhere to robust infection prevention and control (IPC) measures, such as practicing thorough hand hygiene, implementing meticulous environmental cleaning, utilizing isolation precautions, and ensuring judicious antibiotic use. Patients and caregivers should be diligent in handwashing before and after contact with wounds or medical devices, and they should prompt healthcare providers to do the same. Moreover, healthcare facilities should diligently monitor A. baumannii occurrences and resistance patterns while employing preventive strategies to forestall outbreaks (4).

#### Morphology, Characteristics, and **Ecology** of Acinetobacter baumannii

Acinetobacter baumannii is a rod-shaped bacterium classified within the gram-negative coccobacilli group. During the stationary growth phase, its morphology transitions toward a more spherical shape, with dimensions ranging from 0.9 to 1.6  $\mu$ m in length and 1.5 to 2.5 µm in width. This bacterium frequently forms pairs or chains and exhibits specific characteristics, including nonmotility, encapsulation, absence of spore formation, strict aerobic metabolism, positive catalase activity, negative indole production, and negative oxidase reactions (5,6).

Acinetobacter baumannii possesses a singular circular chromosome composed of approximately 4 million base pairs, featuring around 3500 protein-coding genes. Notably, its genome exhibits high adaptability, incorporating various mechanisms variation, such as transposons, genomic islands, and point mutations. Comparative analysis of over 60 A. baumannii genome sequences has disclosed a modest core genome conservation of merely 16.5%, with each strain harboring 25% of its genome as unique (7-10).



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Furthermore, *A. baumannii* has the capacity to acquire resistance genes from other bacteria via horizontal gene transfer mechanisms, including plasmids, integrons, and transposons (11,12).

Moreover, A. baumannii has various virulence factors that help it to colonize and infect human hosts, such as polysaccharide biosynthesis, capsular polysaccharide synthesis, motility, biofilm formation, iron (Fe) acquisition, and quorum sensing. Biofilm formation is a complex process that involves the interaction of various factors, such as the genetic makeup, environmental conditions, and virulence factors of A. baumannii. One of the key components of biofilm is the extracellular polymeric substances (EPSs), which are composed of polysaccharides, proteins, and DNA. EPSs provide structural and functional support to the biofilm, as well as protection from external stressors. A. baumannii has several genes that are involved in EPS synthesis, such as bap, *csuE*, *ptk/pbpK*, and *acuA*. Biofilm formation confers several advantages to A. baumannii, such as increased antibiotic resistance and reduced susceptibility to disinfectants. Biofilm also helps the bacteria to evade the host immune system and persist in various environments (3,11,13,14). A. baumannii has developed several mechanisms to acquire Fe from various sources. One such mechanism involves lysing erythrocytes (red blood cells) to harvest heme molecules, which are Fe-containing compounds that bind to oxygen. Another mechanism involves the use of Fe-chelating siderophores, small molecules that bind to Fe with high affinity and transport it into the bacterial cell. A. baumannii can produce up to ten different siderophores, including acinetobactin, baumannoferrins, and fimsbactins. Additionally, A. baumannii can use outer membrane vesicles, spherical structures that bud from the bacterial surface and contain various proteins and lipids. Outer membrane vesicles can acquire Fe from host proteins, such as transferrin and lactoferrin, and deliver it to the bacterial cell (15-18). The quorum-sensing system of A. baumannii consists of a single divergent luxR/luxI-type locus named abaR/ abaI, which produces and detects a signal molecule called N-(3-hydroxydodecanoyl)-L-homoserine lactone (3-OH-C12-HSL). This system regulates various aspects of A. baumannii physiology and virulence, such as biofilm formation, motility, Fe acquisition, antibiotic resistance, and the type VI secretion system (T6SS) (19-21).

Acinetobacter baumannii is a highly adaptable opportunistic pathogen, owing in part to its exceptional desiccation tolerance, enabling it to persist on surfaces and equipment. This resilience increases the risk of transmission to new patients via contact. While the precise molecular mechanisms behind A. baumannii's desiccation survival remain incompletely understood, several potential factors have been identified, including alterations to the lipopolysaccharide component of the gram-negative bacterial outer membrane, influencing membrane permeability and stability, as well as

interactions with the host immune system. Another contributing factor is biofilm formation, enhancing resistance to desiccation and various environmental stressors, antibiotics, and host defenses. Additionally, the production of hydrophilic stress proteins, such as heat shock proteins and chaperones, plays a role in safeguarding cellular components from desiccationinduced damage. Furthermore, the accumulation of nonreducing sugars, particularly trehalose, a disaccharide acting as a compatible solute, offers protection against dehydration, a trait crucial for desiccation tolerance in a wide range of organisms, including bacteria, fungi, plants, and animals (22,23). A. baumannii, as an opportunistic pathogen, typically does not colonize human skin or the gastrointestinal tract. This bacterium exhibits remarkable adaptability, allowing it to thrive in various environmental conditions characterized by extreme temperatures, low pH, aridness, and exposure to disinfectants. Moreover, A. baumannii demonstrates the capacity to utilize diverse nutrient sources, including plant-derived compounds, aliphatic terpenes, and heme molecules (24,25). Notably, A. baumannii can enter a viable but nonculturable (VBNC) state, a condition in which the bacterium remains viable but eludes detection through conventional methods. Multiple stressors, such as temperature, pH, oxygen levels, nutrient availability, and antimicrobial agents, can trigger this VBNC state. Formic acid, an organic acid commonly used as a food preservative, is one such agent capable of inducing the VBNC state in A. baumannii. The effect of formic acid on A. baumannii depends on factors such as temperature and exposure duration, and it can enhance the expression of specific virulence and resistance-related genes in the bacterium (26,27).

Acinetobacter baumannii is a versatile and resilient bacterium capable of thriving in diverse natural and clinical environments. Its resilience presents a significant challenge, as it can lead to severe infections and antibiotic resistance (28,29). Addressing this threat necessitates a comprehensive exploration of the microorganism's morphology, characteristics, and ecology, alongside the development of effective strategies for infection prevention and treatment.

#### Antibiotic Resistance in Acinetobacter baumannii

Acinetobacter baumannii can develop antibiotic resistance through various mechanisms. One approach involves altering the shape or structure of the target molecule to which antibiotics bind, rendering the drug ineffective. For instance, specific A. baumannii strains may exhibit mutations or modifications in their ribosomes, the sites where protein synthesis occurs, and some antibiotics exert their action. Another strategy is the production of enzymes that can degrade or modify antibiotics, neutralizing their efficacy. For instance, certain A. baumannii strains can produce beta-lactamases, enzymes capable of hydrolyzing or inactivating beta-lactam antibiotics such as penicillins, cephalosporins, and carbapenems. A third mechanism

involves reducing antibiotic uptake into bacterial cells or increasing the efflux of the drug out of the cell, preventing it from reaching its target. This may occur through alterations in outer membrane proteins, which function as channels for substances to traverse the cell wall, or by the presence of efflux pump systems that expel toxins and drugs from the cell (30-35).

When *A. baumannii* becomes resistant to multiple classes of antibiotics, it is categorized as multidrugresistant. Extensive resistance to nearly all available antibiotics designates it as extensively drug-resistant. In exceptionally rare instances where it develops resistance to all known antibiotics, it is termed pandrug-resistant (30). *A. baumannii* can acquire resistance genes from other bacteria through horizontal gene transfer, a process involving the exchange of genetic material between different organisms. This transfer can transpire via plasmids, circular DNA fragments that can move between cells; transposons, DNA segments capable of jumping from one genomic location to another; or integrons, structures capable of capturing and integrating resistance genes (30,36).

#### Infections Caused by Acinetobacter baumannii

Acinetobacter baumannii is capable of causing severe and occasionally life-threatening infections in various regions of the body, including the lungs, bloodstream, brain, urinary tract, and skin (37).

Among the infections attributed to A. baumannii, pneumonia is noteworthy. Pneumonia involves lung inflammation, often resulting in breathing difficulties, fever, cough, and chest pain. There are two primary categories of pneumonia, including hospital-acquired pneumonia (HAP) and community-acquired pneumonia (CAP). HAP occurs when an individual develops pneumonia after being hospitalized for at least 48 hours,  $while \, CAP \, arises \, when \, pneumonia \, occurs \, outside \, a \, hospital \,$ environment or within 48 hours of hospital admission. A. baumannii is responsible for 5%-10% of HAP cases and is less common in CAP instances. Individuals with pre-existing lung conditions, such as chronic obstructive pulmonary disease or bronchiectasis, are at a higher risk of developing CAP caused by A. baumannii. Both HAP and CAP resulting from A. baumannii can be severe and life-threatening and may necessitate intensive care and extended hospitalization (38,39).

A rare but serious condition related to *A. baumannii* is *A. baumannii* meningitis, which may occur following neurosurgical procedures, head trauma, cerebrospinal fluid leakage, wound infections, or implantation of foreign bodies. This form of meningitis is associated with a high mortality rate, ranging from 15% to 71% (40).

Acinetobacter baumannii can also induce urinary tract infections in humans, often gaining access to the urinary tract through medical devices such as catheters, surgical wounds, or other invasive procedures. Untreated urinary tract infections caused by *A. baumannii* can lead to severe

consequences, including kidney damage, sepsis, or even death, underscoring the importance of timely diagnosis and treatment with appropriate antibiotics (38,41).

While *A. baumannii* skin and soft tissue infections are rare, they can occur in specific scenarios, such as after trauma, surgery, burn injuries, or via hematogenous spread from other infection sites. These infections are associated with a high rate of morbidity and mortality and may lead to complications such as delayed wound healing, skin graft failure, or sepsis (41-43). *A. baumannii* endocarditis, although extremely rare, can manifest in certain situations, such as post-cardiac surgery, intravenous drug use, or hematogenous spread from other infection foci. This form of endocarditis is linked to a substantial mortality rate, which can reach up to 50% (41,43).

#### Outbreaks of Acinetobacter baumannii

Acinetobacter baumannii outbreaks present a significant public health threat, particularly within healthcare facilities where susceptible or immunocompromised patients are at heightened risk of infection. Numerous factors contribute to the likelihood of an outbreak, including prolonged hospitalizations, exposure in ICUs, the use of mechanical ventilation, high colonization pressure, antimicrobial exposure, recent surgeries, invasive medical procedures, and the severity of underlying illnesses (2,41).

Outbreaks have been documented in diverse settings and regions, encompassing tropical environments, war zones, natural disaster areas, and healthcare facilities in temperate climates. For example, the coronavirus disease 19 pandemic triggered a substantial outbreak of carbapenem-resistant A. baumannii in a Chinese tertiary hospital, resulting in the infection or colonization of 102 patients from January to June 2020. This outbreak was associated with elevated mortality rates and prolonged hospital stays (44). Similarly, a year-long outbreak of multidrug-resistant A. baumannii impacted 35 patients in a 24-bed ICU at an English tertiary hospital. The outbreak's source was traced to environmental contamination, involving items such as curtains, laryngoscope blades, patient lifting equipment, door handles, mops, and keyboards. The implementation of enhanced IPC measures effectively brought the outbreak under control (2). These instances underscore formidable challenges and consequences associated with managing A. baumannii infections in healthcare settings.

# The Reservoirs of *Acinetobacter baumannii* in a Healthcare Setting

Acinetobacter baumannii exhibits prolonged survival on dry surfaces commonly found in healthcare settings, including bed rails, ventilators, sinks, faucets, keyboards, and monitors. Within healthcare facilities, the principal sources of *A. baumannii* include patients who are either infected or colonized by the bacterium and contaminated environmental surfaces and equipment. Transmission

can occur via direct contact with the hands of healthcare personnel or visitors who have touched either an infected or colonized patient or a contaminated object (45).

Environmental reservoirs of *A. baumannii* within healthcare settings encompass surfaces such as contaminated floors, walls, curtains, furniture, and medical devices. The bacterium can also be present in body fluids and secretions of infected or colonized patients. Inadequate hand hygiene practices among healthcare workers and visitors can further contribute to its dissemination. Moreover, the bacterium can find refuge within the water supply and air conditioning systems, thus facilitating transmission via tap water, ice machines, humidifiers, nebulizers, air vents, and filters. Food and beverages can also be susceptible to contamination at various stages, including preparation, storage, and delivery (45-47).

# Prevention and Control of *Acinetobacter baumannii* in Healthcare Facilities

The prevention and control of *A. baumannii* within healthcare facilities are paramount to safeguarding both patients and healthcare personnel from this menace. The World Health Organization advocates several measures to prevent and manage *A. baumannii* within healthcare settings. These include the establishment of comprehensive IPC programs, the screening of patients for *A. baumannii* colonization or infection, the implementation of contact precautions, the utilization of active surveillance cultures, and the optimization of antibiotic use (4,48).

In addition to these measures, several other strategies can be employed to prevent and manage *A. baumannii* in medical institutions. Contact isolation precautions, involving the use of gloves and gowns, dedicated equipment, and the restriction of patient mobility within the facility, are crucial for patients colonized or infected with *A. baumannii*. Adequate environmental disinfection is of utmost importance, given *A. baumannii*'s capacity to persist on inanimate surfaces and personal protective equipment for extended durations. Regular and thorough cleaning and disinfection of the environment and equipment are essential in preventing cross-transmission (49).

Educating/training healthcare providers, patients, and visitors about the risks and preventive measures for *A. baumannii* infection is also vital to enhance awareness and compliance. The provision of clear, consistent messages, feedback, and reminders can facilitate improvements in hand hygiene and infection control practices (38).

#### Treatment of Acinetobacter baumannii

Treatment of *A. baumannii* infections hinges on antibiotic selection based on bacterial susceptibility, as determined through laboratory testing. Carbapenems such as meropenem, imipenem, or doripenem are typically the first-line treatment. However, some *A. baumannii* strains have developed resistance to these antibiotics (50).

In such instances, alternative treatments may involve ampicillin-sulbactam, a combination of penicillin and a beta-lactamase inhibitor, or colistin, a polymyxin type known to damage bacterial cell membranes. Colistin is considered a last-resort option due to potential side effects, including kidney and nerve damage. Tigecycline and eravacycline, both tetracycline types, may prove effective against resistant strains. Additionally, cefiderocol, a novel cephalosporin type, may be effective against carbapenemresistant strains. Ultimately, the choice of therapy for *A. baumannii* infections depends on various factors, such as infection severity, location, the patient's condition, and antibiotic availability (38,51).

#### Conclusion

Acinetobacter baumannii is a bacterium with the potential to cause severe infections within healthcare environments, particularly in patients with compromised immune systems or those reliant on medical devices such as ventilators and catheters. Moreover, it poses a significant public health concern owing to its propensity to develop resistance against a spectrum of antibiotics, including carbapenems, which are crucial as last-resort treatments for Gramnegative infections. This paper offers a comprehensive review encompassing bacteriology, ecological aspects, antimicrobial resistance, clinical manifestations, outbreak scenarios, reservoirs, and treatment approaches for A. baumannii infections in healthcare settings. Furthermore, it explores the preventative and control measures that can be deployed to curtail the dissemination and impact of this formidable pathogen. The conclusion drawn is that *A*. baumannii stands as a formidable adversary, necessitating collaborative and multifaceted efforts from healthcare practitioners, microbiologists, infection control specialists, policymakers, and researchers to address its global ramifications on human health.

#### **Competing Interests**

The authors declare that they have no conflict of interests.

#### **Ethical Approval**

Not applicable.

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