Acinetobacter spp. – A Serious Enemy Threatening Hospitals Worldwide

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Abstract

Acinetobacter is gram-negative, strictly aerobic bacteria. It is a heterogeneous group of organisms that is ubiquitous, widely distributed in nature. Surviving in hospital environment (they are able to survive on dry particles and dust up to ten days, more then four months on both moist and dry surfaces such as PVC, rubber, ceramics and various types of medical equipment) they are an important cause of infection in immunocompromised patients. A. baumannii, the major cause of intrahospital infections, exhibits a remarkable ability to rapidly develop antibiotic resistance to several classes of antimicrobial agents that led to MDRA, or to almost all currently available antibacterial agents, except to polymixins. There is an increasing incidence of these infections in hospital intensive care units. The prevalence currently ranges from 2% to 10% of all gram-negative bacterial infections in Europe and about 2.5% of them in the United States. Good treatment choice, combined with infection control measures should help in preventing intrahospital spread of multiresistant strains of Acinetobacter spp. Nevertheless, their adaptation mechanisms to antibiotic selection pressure suggest that this problem will continue into the future.

Introduction

Acinetobacter is gram-negative (sometimes difficult to decolourise) genus of bacteria belonging to the phylum Proteobacteria. Growing under strictly aerobic conditions, this species is non-motile, non-fermentative, oxidase-negative, catalase-positive and citrate positive. When cultivated on non-selective agar, microscopy shows coccobacillary morphology under magnification. Rods predominate in fluid media, especially during early growth. Most strains can grow in a simple mineral medium containing single carbon and energy source. When growing on blood agar, colonies show typical morphology: non-pigmented, white or cream-coloured, smooth or mucoid (when capsule is present), opaque, 1-2mm in diameter (Fig. 1) (1). For direct isolation in order to suppress the growth of other microorganisms, use of selective media is recommended (2). New medium with selective and differential characteristics, Leeds Acinetobacter Medium, has been often used to recover most of Acinetobacter spp. from clinical or environment sources (3).
Currently, the genus *Acinetobacter* comprises at least 33 genomic species (DNA-DNA hybridization groups/DNA groups). Only 18 of them have given species names. Other DNA groups are designated by numbers (Table 1).

### Table 1: Taxonomy of *Acinetobacter*.

<table>
<thead>
<tr>
<th>Scientific classification</th>
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</tr>
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<tbody>
<tr>
<td>Kingdom</td>
<td>Bacteria</td>
</tr>
<tr>
<td>Phylum</td>
<td>Proteobacteria</td>
</tr>
<tr>
<td>Class</td>
<td>Gamma Proteobacteria</td>
</tr>
<tr>
<td>Order</td>
<td>Pseudomonadales</td>
</tr>
<tr>
<td>Family</td>
<td>Moraxellaceae</td>
</tr>
<tr>
<td>Genus</td>
<td><em>Acinetobacter</em> (DNA G+C content 39-47 mol%)</td>
</tr>
<tr>
<td>Species of Clinical Importance</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>A. baumannii</em></td>
</tr>
<tr>
<td></td>
<td><em>A. haemolyticus</em></td>
</tr>
<tr>
<td></td>
<td><em>A. calcoaceticus</em></td>
</tr>
<tr>
<td></td>
<td><em>A. lwofii</em></td>
</tr>
</tbody>
</table>

### Pathogenesis

Although *Acinetobacter* cause hospital-acquired infections, it is considered to be an organism of low virulence. There are characteristics that are possible virulence factors: 1) hydrophobicity of the bacteria which is related to adherence, hydrophobicity is higher in strains isolated from infected catheters and tracheal devices (10); 2) a polysaccharide capsule formed of L-rhamnose, D-glycose, D-glucuronic acid, and D-mannose, protects bacteria from phagocytosis (11); 3) two types of fimbriae: thin, about 3nm, responsible for the ability to adhere to human epithelial cells, and thick, about 5nm, responsible for twitching motility (12); 4) enzymes such as: butyrate esterase, caprylate esterase and leucine arylamidase that are involved in the hydrolysis of short chain fatty acids and damage of tissue lipids (13); 5) iron acquisition: ability to produce siderophores (aerobactin) and iron-respressible outer membrane receptor proteins, which enable transport of necessary iron for growth in the host organism (14, 15); 6) the potentially toxic role of the lipopolisaccharide component of the cell wall (16).

Lipopolysaccharide produced by *Acinetobacter* cause lethal toxicity in mice and pyrogenicity in rabbits. Experiments with *A. baumannii* have shown that virulence is limited (50% lethal dose, $10^6$ to $10^8$ CFU per mouse). It seems that production of slime is closely related with the enhancement of virulence, as slime is associated with cytotoxicity against neutrophils and inhibition of the migration of neutrophils into peritoneal exudate of mice (17).

### Mechanisms of resistance

*A. baumannii* exhibits a remarkable ability to rapidly develop antibiotic resistance to several classes of antimicrobial agents that led to multidrug resistance *Acinetobacter* (MDRA) within a few decades (18), or to almost all currently available antibacterial agents (19), except to polymixins (20). MDRA is defined as resis-
ance to: fluoroquinolones, aminoglycosides, cephalosporins, beta-lactams and beta-lactamase in-
hibitor combinations; carbapenemems are not included in this list.

Although all three of the chromosomal gene transfer modes are demonstrated, it seems that con-
jugation plays the most significant role in the resistant gene transfer (21). Acinetobacter develops resistance through acquisition of plasmids (22), transposons (23) or integrons (24). These elements carry clusters of genes encoding resistance to several antibiotic fami-
lies at once (25).

Numerous mechanisms of resistance to β-
lactams are described, associated with the production of β-lactamases that have penicillinase, cephalosporinase and carbapenemase activity. At least 15 aminoglycoside modifying enzymes (belong-
ing to all three types: acetylating, adenylylating and phosphorylating) are found. Mutations in DNA gyrase cause resistance to quinolones, but there can also be resistance due to outer membrane changes and de-
creased uptake.

Resistance to alcohol-based disinfectants is evident with increased antibiotic resistance (26).

With the emergence of increasingly resistant strains, the management of A. baumannii infections has become a public health problem in many countries (27).

Hospital-acquired infections

During recent years, A. baumannii has become a worldwide concern as the cause of many serious nosocomial infections (28), and the majority of clinical isolates involved in hospital outbreaks belong to this species (29). There is an increasing incidence of these infections in hospital intensive care units (30). It is often acquired by cross infection, but can be introduced initially by patients admitted from other hospitals (31). The prevalence of these infections currently ranges from 2% to 10% of all gram-negative bacterial infec-
tions in Europe (32) and about 2.5% of them in the United States (33), causing both sporadic as well as epidemic infections. Globally, this species is a major cause of hospital-acquired infection causing bacteremia, urinary tract infection, secondary meningitis, skin and soft tissue infections and in particular nosocomial pneumonia, with high mortality rate (18). Introduction into normally sterile sites is by medical instrumenta-
tion: intravenous or urinary catheters, endotracheal tubes or tracheostomies, or respiratory care
equipments. Outbreaks are linked to contaminated respiratory tract equipment (34), intravascular access devices (35), bedding materials (36), also transmission on medical personnel hands (37) or airborne transmission via aerosols (38).

Acinetobacter cause nosocomial pneumonia in ICU with a frequency of 3 to 5% (even higher in patients with mechanical ventilation) with crude mortality rates of 30 to 75% (39). Bacteremia is very common in elderly immunocompromised patients. The main source of bacteremia in these patients is bacterial pneumonia, and the most important predisposing factors are malignant diseases, trauma and burns. Another risk group of patients for bacteremia is neonates where low birth weight, previous antibiotic therapy, mechanical ventila-
tion, parenteral nutrition and long hospitalization are risk factors. Only sporadic cases of primary meningitis were described, always following neurosurgical proce-
dures or head trauma. Secondary meningitis is the predominant form with mortality rates from 20 to 27% (40). Hospital-acquired urinary tract infections caused by Acinetobacter are mostly in elderly men (80%) with persistent indwelling urinary catheters admitted to ICU (41).

Several studies have been investigated the epi-
demiology of A. baumannii infections in Europe (42), the United States (43), South America (44) and Asia (45). European investigators have recently suggested that very similar to methicillin resistant Staphylococ-
cus aureus few epidemic strains may be involved in outbreaks locally as well as globally (46, 47). Further investigations on the clinical significance of Acinetobacter spp. other then A. baumannii are re-
quired.

Therapy

Not many of classes of antimicrobial agents are now reliable and effective for the treatment of A. baumannii infections.

Carbapenems can be used as first line therapy if tested to be susceptible. Tigecycline can be used, but outbreaks involving resistant strains have been reported. Single agent treatment using amikacin, tobramycin, ceftazidim or ciprofloxacin has been rec-
nommended too.

Polymixin B and colistin are a second line therapy option, but their significant nephrotoxicity and neurotoxicity should be kept in mind (48). Combination therapy has been recommended by several authors eg: extended-spectrum penicillins, broad-spectrum
cephalosporins, or carbapenem, combined with an aminoglycoside (49-52).

Conclusion

Good treatment choice, combined with infection control measures should help in preventing intrahospital spread of multiresistant strains of Acinetobacter spp. Nevertheless, their adaptation mechanisms to antibiotic selection pressure suggest that this problem will continue into the future.

There is evidence that increased use of antibiotics favours the selection of multiresistant Acinetobacter strains in the hospital environment. Antibiotic prescribing policies in hospitals, especially in ICU, are therefore very important.

One of the most difficult challenges is to control the spread of these strains in the hospital environment, because of the variety of potential sources of contamination and infection.

References


