Antimicrobial Resistance Gallery

Aciba (*Acinetobacter baumannii*): an ESKAPE[1] pathogen

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Why is Aciba a problem and why is it also known as Iraqibacter?

Acinetobacter baumannii (Aciba) is a short, non-motile (does not move by swimming), rod-shaped pathogenic bacterium that is increasingly prevalent in hospitals and causes severe hospital-acquired (nosocomial) infections. It is also known as Iraqibacter, because it gained importance as the cause of severe infections in US soldiers injured during the conflicts in Iraq and Afghanistan. Infections with this supergerm increased worldwide at a rapid pace ever since. Aciba is a master in adaptation to different niches in the human body and is able to colonize wounds, the surface of the skin, the bladder and the lungs, thereby causing bloodstream and urinary tract infections, meningitis and ventilator-associated inflammation.

Who is Aciba and where does it live?

Aciba is a member of the *Acinetobacter calcoaceticus-baumannii* (ACB) complex which is a group of Acinetobacters whose members are naturally resistant to penicillins. Although Aciba is prevalent in hospitals, it also feels at home in many different environmental niches, such as birds nests, household pets, soils, rivers and treatment plants. However, the preferred natural habitat is still unknown. Moreover, knowledge of its virulence is also limited.

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[1] *Multidrug resistant Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa* and *Enterobacter* species comprise the ***ESKAPE*** bacteria (https://academic.oup.com/jid/article/197/8/1079/901561?login=false). These bacteria top the World Health Organization list of priority pathogens that pose the greatest threat to human health (https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed).

Why is Aciba so dangerous?

Today, Aciba is one of the most troublesome pathogens in healthcare facilities due to a significant increase in multidrug resistance, which arise from intrinsic and acquired mechanisms. Aciba has different ways to withstand the effects of an antibiotic, such as by modification of antibiotic target sites, exporting antibiotics by pumping them out through channel-like efflux pumps which act as "vacuum cleaners", or inactivating them by modifying their structure. The latter is a baseline defense of Aciba and stems from its ability to acquire new genetic information from other microbes. This information is translated into potent enzymes, which act like scissors cutting a conserved core structure present in many antibiotics. Such a core structure is the so-called ß-lactam ring, present in penicillin, the antibiotic first discovered by Alexander Fleming in 1928, and characteristic of a large class of antibiotics used to fight Aciba infections, the so-called ß-lactam antibiotics.

Because of its multiple antibiotic resistances, and frequency and seriousness of the infections it causes, the World Health Organization (WHO) ranked Aciba in 2017 as one of the most critical multidrug-resistant bacteria on a list of 56 bacteria for which new therapeutic approaches are urgently needed.

The deep slumber of *Acinetobacter baumannii*: Why infections can flare up again

The dangerous spread of Aciba is not only due to increasing antibiotic resistances but also to its enormous adaptability: it flourishes even under extremely harsh conditions, such as high salinity and desiccation. Aciba can survive for many months on dry surfaces in hospital environments, such as furniture, medical equipment, the possessions of medical professionals, and even computers. Aciba can survive under such inhospitable conditions because it can enter a dormancy state characterized by nearly no metabolic activity, a so-called "viable but not culturable state" (VBNC). This is a kind of deep sleep where the cells are no longer culturable on culture media but still show signs of life such as breathing. The dormancy state is induced in Aciba by stress conditions such as high salt content, refrigeration (4 °C), fever temperatures (42 °C), desiccation or absence of oxygen. In all cases, it is possible to "wake the bacteria up again" after two days of "rehab" in a culture with an optimum supply of nutrients and oxygen.

Cultivation of bacteria on culture media is still the gold standard in medicine but also in food safety. Therefore, the VBNC state could lead to big problems in conventional diagnostics since "sleeping" Aciba could escape detection. So it could be that after antibiotic treatment of an Aciba infection no bacteria are detected but they are just asleep in the nooks and crannies of the human body. Under improving living conditions, such as absence of antibiotics, they might wake up again and multiply so that the infection flares up again. This is a dangerous scenario particularly due to the multidrug resistance of Aciba.

Aciba is a fiendish bug we definitely should try to avoid!

How to combat Aciba infections? Search for the Achilles heel of a multi-drug resistant bug!

The increasing antibiotic resistances of Aciba underscore the urgent need for new antibiotics. Alternative strategies to combat Aciba are effective antibiotic drug combinations or even new paradigms. The increasing effort to find new drugs to fight Aciba was recently crowned with success. A combination of two new agents became recently available for treating Aciba infections:

cefiderocol, which competes with Aciba for iron, which is essential for growth of Aciba, and sulbactam-durlobactam (SD) which blocks drug cutting scissors of Aciba. Nevertheless, gaining more insights into Aciba´s mechanism of host adaptation and persistence in hospital environments together with new and innovative treatment paradigms are crucial for devising effective strategies to combat this pathogen and minimize its impact on public health in the future. And, especially, a better understanding of the "deep sleep" is very important for developing drugs that also kill deep slumbering multidrug-resistant Aciba.