ACINETOBACTER INFECTIONS IN MILITARY PERSONNEL

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The gram negative rod *Acinetobacter baumannii* is a soil and water saprophyte characterized by a high degree of innate and acquired antibiotic resistance. While it can colonize healthy hosts, it is also a well-established hospital-acquired pathogen, especially in intensive care and surgical units. The pathogen does not have many of the traditional virulence factors for producing disease in healthy hosts; most patients infected with *Acinetobacter baumannii* are elderly or otherwise immunocompromised.

Infections in Military Personnel

Acinetobacter baumannii has long been known to sporadically produce infections in war wounds, but a recent outbreak occurring in previously healthy, young military personnel returning from Iraq, Kuwait, and Afghanistan highlighted an important source and mechanism of infection (1). *Acinetobacter* infections have been historically documented in war wounds from military personnel injured in the Vietnam and Iran-Iraq Wars (2, 3), and many theories were generated to explain the sources of these infections, including prior skin colonization, acquisition from soil contamination, and nosocomial transmission. However, no formal outbreak studies were organized due to the relatively low incidence of such infections. In 2003, one of the first multidrug-resistant *Acinetobacter* wound infections was reported in soldiers stationed on a Navy ship in the Middle East. Subsequently, the outbreak grew and warnings were issued by the United Kingdom and the United States in attempts to limit its spread and effectively treat the infected (4). One hundred two cases of bacteremia/sepsis due to organisms pertaining to the *Acinetobacter baumannii-calcoaceticus* complex were reported between 2002 and 2004 (1). These were detected in medical facilities caring for injured military personnel returning from Operation Iraqi Freedom (OIF) or Operation Enduring Freedom (OEF) who were stationed in Iraq and Kuwait or Afghanistan, respectively. In the year prior, these same medical facilities had reported a total of 3 cases of *Acinetobacter* bacteremia/sepsis, suggesting that this was indeed a notable outbreak.

Antimicrobial Resistance

One of the striking features of the outbreak was the highly drug-resistant nature of the organisms. Four percent of all *Acinetobacter* isolates were resistant to all drugs tested, with this number rising to 15% in a follow-up study (1, 5). In addition to local outbreaks within intensive care units of military treatment facilities like the National Naval Medical Facility, *Acinetobacter* has spread across the globe to different hospitals caring for infected military personnel (6).

The *Acinetobacter* implicated in these military personnel has a multifarious genetic background. Pulsed-field gel electrophoresis (PFGE) identified at least 16 unique genes and 4 mobile genetic elements contributing to the multidrug-resistant profile of the *Acinetobacter* isolates. These resistance genes included beta-lactamases, like OXA-23, as well as the "IS" promoter, that when jointly expressed confers carbapenem resistance (5). Most traditional antibiotics, including broad-spectrum cephalosporins and penicillin-beta-lactamase-inhibtor combinations are not active *in vitro*. As such, clinicians have resorted to using carbapenems, colistin, polymixin-B, and amikacin for the treatment of the more serious outbreak infections despite concerns over toxicities and other adverse effects (7). *Acinetobacter* susceptibilities for these less traditional antibacterial agents are not always active *in vitro*, ranging from 63-90% for imipenem, 47-48% for amikacin, 99% for colistin, 99% for polymixin-B, and 97% for minocycline, the latter seemingly more active than even tigecycline (5, 7-9). It remains unclear how the prior use of imipenem as the prophylactic agent of choice for battle wound infections contributed to the rise of multidrug-resistant *Acinetobacter* isolates in field hospitals, and how ongoing broad-spectrum antibiotic use will contribute to drug-resistance evolution. Equally unclear are whether the mobile genetic elements will allow spread of drug-resistance from *Acinetobacter* to other nosocomial flora. Undoubtedly, this outbreak has significantly impacted antibiotic therapy policies in field hospitals, as well as in other hospitals caring for those infected with this drug-resistant pathogen.

Epidemiology

In the UK, PFGE-genotyping has linked outbreaks in local hospitals to patients originally treated in Iraqi field hospitals (10). As one example, an OXA-23 beta-lactamase–expressing *Acinetobacter* isolate, not previously represented in the UK hospital microbiology, was directly linked to a patient from Iraq. This isolate subsequently was newly detected in 30 other UK hospitals caring for Iraqi service members (11). Contributing to the persistence of this organism in hospital work areas is the ability of *Acinetobacter* to survive on dry, plastic surfaces for long periods of time (9, 12).

In an attempt to identify the source of the multidrug-resistant *Acinetobacter* outbreak, skin of hospitalized personnel, Iraqi soil, and field-hospital health-care environments were screened for colonization, and those isolates were then compared to strains obtained from infected patients. All of the field hospitals tested were positive for multidrug-resistant *Acinetobacter* colonization. This was in comparison to 0.6% of skin swabs and 2% of soil samples tested. The *Acinetobacter* isolates detected within the critical care treatment areas of field hospitals in Iraq and Kuwait matched the isolates from infected military personnel based both on PFGE genotyping as well as drug-resistance profiles. In contrast, the *Acinetobacter* isolates detected in the soil were much more susceptible to antibiotics, suggesting that the soil is not the source. This study strongly suggested that the health-care environment is the most likely outbreak source of *Acinetobacter* infections in military personnel serving in the Middle East (9).

These, as well as countless other investigations of the *Acinetobacter* outbreak, have led to the institution of heightened infection control measures and have changed the strategies used in determining empiric antibiotic therapy within affected health care settings.

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