REVIEW ARTICLE

CURRENT CONCEPTS

Acinetobacter Infection

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Acinetobacter is a gram-negative coccobacillus (Fig. 1)[1,2] that during the past three decades has emerged from an organism of questionable pathogenicity to an infectious agent of importance to hospitals worldwide.[3,4] Approximately one quarter of the PubMed citations for "nosocomial acinetobacter" in the past 20 years appeared in 2005 and 2006. Acinetobacter infections have long been clinically prominent in tropical countries, have been a recurrent problem during wars and natural disasters, and have recently caused multihospital outbreaks in temperate climates. Most alarming are the organism's ability to accumulate diverse mechanisms of resistance, the emergence of strains that are resistant to all commercially available antibiotics,[5] and the lack of new antimicrobial agents in development.[6] At more than 300 U.S. hospitals surveyed by the Centers for Disease Control and Prevention (CDC), rates of carbapenem resistance in 3601 isolates of *Acinetobacter baumannii*, clinically the most important of 25 acinetobacter genospecies,[1] increased from 9% in 1995 to 40% in 2004.[7]

Acinetobacter was first described in 1911 as *Micrococcus calco-aceticus*.[8] Since then, it has had several names, becoming known as acinetobacter in the 1950s.[1,2] Its natural habitats are water and soil, and it has been isolated from foods, arthropods, and the environment.[3] In humans, acinetobacter can colonize skin, wounds, and the respiratory and gastrointestinal tracts. Some strains of acinetobacter can survive environmental desiccation for weeks, a characteristic that promotes transmission through fomite contamination in hospitals.[1,9]

Acinetobacter is easily isolated in standard cultures but is relatively nonreactive in many biochemical tests commonly used to differentiate among gram-negative bacilli. This can delay isolate identification by a day. *A. baumannii*, *A. calcoaceticus*, and *A. lwoffii* are the acinetobacter species most frequently reported in the clinical literature. Because it is difficult to differentiate among acinetobacter species on the basis of phenotypic characteristics, the term *A. calcoaceticus–A. baumannii* complex is sometimes used.[1]

MECHANISMS OF RESISTANCE

Resistance mechanisms that are expressed frequently in nosocomial strains of acinetobacter include β-lactamases, alterations in cell-wall channels (porins), and efflux pumps (Fig. 2). *A. baumannii* can become resistant to quinolones through mutations in the genes *gyrA* and *parC* and can become resistant to aminoglycosides by expressing aminoglycoside-modifying enzymes.[10]

AmpC β-lactamases are chromosomally encoded cephalosporinases intrinsic to all *A. baumannii*. Usually, such β-lactamases have a low level of expression that does not cause clinically appreciable resistance; however, the addition of a promoter

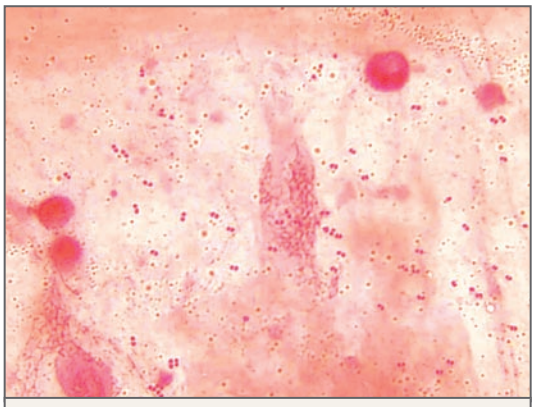

Figure 1. Gram's Staining of Sputum Specimen from a Patient with Suspected Ventilator-Associated Pneumonia.

Acinetobacter baumannii was recovered from this specimen, which shows gram-negative coccobacilli[1]; the diplococcal features help explain one of the early designations of acinetobacter as neisseria.[2] Bacilli may predominate, depending on the culture medium.[1] Photomicrograph courtesy of Kathleen G. Beavis, M.D.

insertion sequence, IS*Aba*1, next to the *ampC* gene increases β-lactamase production, causing treatment-limiting resistance to cephalosporins.[11] Although porin channels in *A. baumannii* are poorly characterized, it is known that reduced expression or mutations of bacterial porin proteins can hinder passage of β-lactam antibiotics into the periplasmic space, leading to antibiotic resistance.

Overexpression of bacterial efflux pumps can decrease the concentration of β-lactam antibiotics in the periplasmic space. To cause clinical resistance in acinetobacter, efflux pumps usually act in association with overexpression of AmpC β-lactamases or carbapenemases. In addition to removing β-lactam antibiotics, efflux pumps can actively expel quinolones, tetracyclines, chloramphenicol, disinfectants, and tigecycline.[12]

Clinically most troubling have been acinetobacter's acquired β-lactamases, including serine and metallo-β-lactamases, which confer resistance to carbapenems.[10] Acquired extended-spectrum β-lactamase carriage occurs in acinetobacter but is not as widespread as in *Klebsiella pneumoniae* or *Escherichia coli*.[13]

A recent report described a "resistance island" containing 45 resistance genes within the acinetobacter genome.[14] Resistance islands comprise one or more virulence genes located in a mosaic distribution within a large genomic region.[15]

Currently, the term "multidrug resistance" in reference to acinetobacter does not have a standard definition. It is sometimes used to denote resistance to three or more classes of drugs that would otherwise serve as treatments for acinetobacter infections (e.g., quinolones, cephalosporins, and carbapenems). The term "panresistance" has been used to describe strains of acinetobacter that are resistant to all standard antimicrobial agents tested (except colistin).[16]

EPIDEMIOLOGY

Historically, acinetobacter has been a pathogen of hot and humid climates, where it has been a major cause of infections, particularly in intensive care units (ICUs), and sometimes a cause of community-acquired pneumonia.[17-21] Acinetobacter was cited as the cause of 17% of cases of ventilator-associated pneumonias in a Guatemalan ICU — second only to pseudomonas, which caused 19% of cases — years before becoming a concern in ICUs in the United States.[21] Over the past two decades, acinetobacter infections have become an increasingly common nosocomial problem in temperate climates.

HEALTH CARE–ASSOCIATED INFECTIONS

Most information about health care–associated acinetobacter infections is based on outbreak investigations.[22] Infections with *A. baumannii* tend to occur in debilitated patients, mostly in ICUs. Residents of long-term care facilities, particularly facilities caring for ventilator-dependent patients, are at increased risk. In addition to a stay in the ICU, risk factors for colonization and infection are recent surgery, central vascular catheterization, tracheostomy, mechanical ventilation, enteral feedings, and treatment with third-generation cephalosporin, fluoroquinolone, or carbapenem antibiotics.[23,24]

Acinetobacter outbreaks have been traced to common-source contamination, particularly contaminated respiratory-therapy and ventilator equipment, to cross-infection by the hands of health care workers who have cared for colonized or infected patients or touched contaminated fomites, and to the occasional health care worker who carries an epidemic strain.[22,25,26] Once introduced into a hospital, acinetobacter often has an epidemiologic pattern of serial or overlapping outbreaks caused by various multidrug-resistant

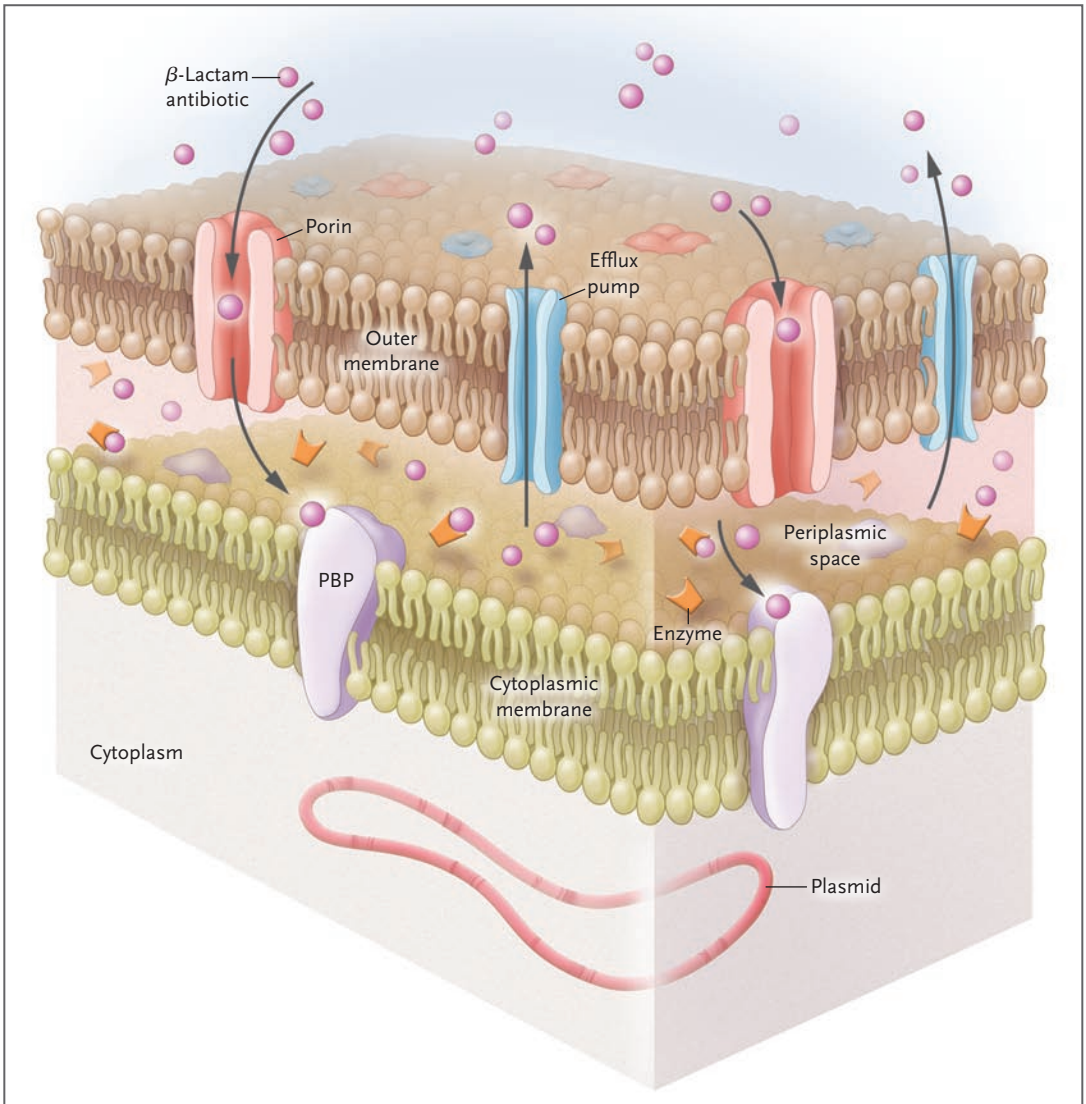

Figure 2. Potential Mechanisms of Antimicrobial Resistance in Acinetobacter.

Acinetobacter, like other gram-negative bacteria, has an outer membrane and a cytoplasmic membrane, between which (the periplasmic space) β-lactamases (carbapenemases, AmpC β-lactamases, and extended-spectrum β-lactamases) reside. Penicillin-binding proteins (PBPs), located at the level of the cytoplasmic membrane, constitute the final targets of β-lactam antibiotics. To bind to these targets, antibiotics must traverse the outer membrane through porin channels (outer-membrane proteins) into the periplasmic space. Once in the periplasmic space, β-lactam antibiotics bind to PBPs or are actively expelled from the bacterial structure through efflux pumps. Acinetobacter can harbor integrons and transposons, genetic elements on the bacterial chromosome or on plasmids, that can carry multiple cassettes with resistant genes (e.g., extended-spectrum β-lactamases and metallo-β-lactamases).

strains, with subsequent endemicity of multiple strains and a single endemic strain predominating at any one time.[22] Prolonged colonization — for up to 42 months and affecting 17% of patients in one study — may contribute to the endemicity of *A. baumannii* after an outbreak.[27]

Dramatic multihospital outbreaks have been described in Brooklyn, Chicago, northwestern Indiana, Detroit, and cities in Europe, South America, Africa, Asia, and the Middle East.[5,23,28,29] A single-strain outbreak — monoclonal, as identified by molecular typing — of carbapenemase-producing (OXA-40) acinetobacter was described recently in Chicago and neighboring northwest-

ern Indiana.[5] Since 2005, at least five hospitals, three long-term care facilities, and more than 200 patients have been affected by this outbreak. In a French multicity, monoclonal outbreak of multidrug-resistant *A. baumannii*, 290 isolates were collected in 53 hospitals from April 2003 to June 2004. The epidemic strain harbored an extended-spectrum β-lactamase known as VEB-1. Most infected patients were in ICUs, medical wards, or long-term care facilities.[28]

The occurrence of monoclonal outbreaks in multiple hospitals suggests interinstitutional spread, presumably by movement of patients or personnel, or exposure to common-source contamination of food or equipment. Such outbreaks highlight the importance of ongoing surveillance, interfacility communication, and measures to prevent the introduction of acinetobacter into, and the spread from, nursing homes.

SEASONAL VARIATION

Since 1974, the CDC has noted higher rates of nosocomial acinetobacter infections in the summer than in other seasons.[30,31] McDonald and colleagues evaluated 3447 acinetobacter infections in adults and children in ICUs that were reported to the CDC between 1987 and 1996; infection rates were approximately 50% higher from July to October than at other times of the year.[31] Possible explanations include warmer, more humid ambient air, which favors growth of acinetobacter in its natural habitats, and potentially preventable environmental contaminants, such as condensate from air-conditioning units, which has been implicated as a cause of epidemic acinetobacter infections.[31]

COMMUNITY-ACQUIRED INFECTIONS

Community-acquired infections with acinetobacter have been reported in Australia and Asia. These infections were characterized by pharyngeal carriage of the organism, aggressive pneumonia, and high case fatality rates and were linked to alcoholism and cancer.[17-19] The reason for the higher prevalence of acinetobacter infections in certain geographic areas is not known, but it may be due in part to differences in temperature and humidity that influence colonizing bacteria.

In the United States, community-acquired infections are rare. In 1979, *A. baumannii* pneumonias occurred in three foundry employees who worked within meters of each other. Postmortem evaluations in two of the patients showed severe underlying pneumoconiosis. *A. baumannii* was isolated from foundry air, but the source was not identified.[32]

MILITARY PERSONNEL

Descriptions of the role played by acinetobacter infections during war date to the 1955 report of bloodstream infection with a presumed strain of acinetobacter (then called achromobacter) in a Korean War military recruit.[33] During the Vietnam War, Tong and colleagues reported on 63 soldiers with soft-tissue acinetobacter infections.[34,35] Most recently, *A. baumannii* infections have been reported among U.S. military personnel injured in the Middle East.[36-40]

From January 2002 to August 2004, 85 bloodstream infections with *A. baumannii* were identified in soldiers in two military referral hospitals; the soldiers had been injured during Operation Enduring Freedom in Afghanistan and Operation Iraqi Freedom in the Iraq–Kuwait region. A total of 35% of the isolates were susceptible only to imipenem, and 4% showed resistance to all standard drugs.[36] According to another report, among 142 acinetobacter isolates recovered from October 2003 to November 2005, strains from deployed personnel showed a lower rate of susceptibility to imipenem than isolates from nondeployed personnel (63% vs. 87%, $P<0.01$).[37]

Several studies have assessed possible sources of wartime acinetobacter infections. Griffith and colleagues reported the results of skin cultures from 102 active-duty army personnel in Iraq; none of 303 samples yielded *A. baumannii*,[38] arguing against preinjury colonization. However, in an investigation of an outbreak, acinetobacter was recovered from environmental cultures of critical care treatment areas in seven field hospitals in the Iraq–Kuwait region.[39] Finally, 16 unique resistance genes were described recently among eight major clones of acinetobacter recovered from infected soldiers.[40] This heteroclonality and reappearance of acinetobacter in personnel participating in several military actions over the past 50 years suggest multiple sources, including local foods (also a potential source of global spread), contamination of wounds in the battlefield, and environmental spread and cross-infection in field and referral hospitals.

DISASTERS

Several recent disasters further suggest that acinetobacter should be included in the microbiologic differential diagnosis of soft-tissue infections after exposure to a tropical environment and that imported strains can cause widespread contamination and cross-infection in the hospital environment. After the Southeast Asia tsunami on December 24, 2004, a total of 17 people in critical condition were evacuated to Germany; all had severe trauma from floating debris, including large soft-tissue injuries and fractures. Multidrug-resistant acinetobacter was isolated from 20% of wounds and from blood and respiratory secretions.[41] *A. baumannii* was the most prevalent nosocomial pathogen reported in a Turkish ICU in which casualties of the 1999 Marmara earthquake were treated[42]; *A. baumannii* had previously been isolated only rarely in this ICU. After the 2002 terrorist bombing in Bali, a patient infected with *A. baumannii* was transferred to a Swiss ICU for patients with burn injuries and became the presumed source of extensive environmental contamination and an ICU outbreak.[43]

CLINICAL MANIFESTATIONS

The most frequent clinical manifestations of acinetobacter infection are ventilator-associated pneumonia and bloodstream infections.[7] Vascular catheters and the respiratory tract have been the most frequent sources of acinetobacter bacteremias,[44,45] for which crude mortality rates parallel those attributed to other gram-negative bacilli (28 to 32%).[46]

In a study of specimens from 10,852 patients with bloodstream infections, collected at 49 U.S. hospitals from 1995 to 1998, the proportion of infections due to acinetobacter was 1.5%, and 36% of the acinetobacter infections were polymicrobial. The most common coisolates were skin flora — coagulase-negative staphylococci or enterococci[46] — suggesting that some blood isolates represented specimen contamination from skin or environmental strains.[47,48] Nonetheless, a study of 48 patients with multidrug-resistant *A. baumannii* bacteremias, who were matched for severity of illness to a control group with infections from strains susceptible to treatment with drugs, showed that the group with resistant strains had a 21.8% attributable mortality, higher hospitalization costs, and longer ICU and hospital stays.[49] It is unclear whether such outcomes are due to strain virulence or whether they could be avoided by the prompt use of appropriate therapy.[50]

Acinetobacter pneumonia occurs predominantly in ICU patients who require mechanical ventilation and tends to be characterized by a late onset. Affected patients spend more days in the ICU and on a ventilator before having positive cultures than do patients with pneumonias caused by other gram-negative bacilli or uninfected patients.[24,51] The clinical effect of ventilator-associated acinetobacter pneumonias has been variable. A recent study showed higher mortality among patients with multidrug-resistant acinetobacter infections than among patients infected with susceptible acinetobacter strains or uninfected patients; however, when the severity of illness and underlying diseases were considered, the main difference was that patients with multidrug-resistant acinetobacter infections had longer hospital and ICU stays.[52]

In other studies, mortality among patients with pneumonia due to multidrug-resistant acinetobacter was similar to that among patients with infection caused by other pathogens[24] or among controls (with or without pneumonia) matched for severity of illness and length of ICU stay,[53] suggesting that coexisting conditions were the major predictors of the outcome or that in some cases acinetobacter may have been a colonizer rather than a pathogen.

TREATMENT

Infections caused by antibiotic-susceptible acinetobacter isolates have usually been treated with broad-spectrum cephalosporins, β-lactam–β-lactamase inhibitor combinations (e.g., a combination that includes sulbactam, a drug marketed only in combination intravenous products in the United States), or carbapenems (e.g., imipenem or meropenem, although there are reports of discordant susceptibility to carbapenems[54]), used alone or in combination with an aminoglycoside.[55] The duration of treatment is generally similar to that for infections caused by other gram-negative bacilli, is largely empirical, and depends mostly on the site of infection.

For infections caused by multidrug-resistant isolates, antibiotic choices may be quite limited;

the most active agents in vitro are the polymyxins — polymyxin B and polymyxin E (colistin).[23,56,57] Polymyxins are cationic detergents that disrupt bacterial cytoplasmic membranes, causing leakage of cytoplasmic contents.[58] Clinicians abandoned polymyxins in the 1960s and 1970s, prompted by problems of nephrotoxicity and neurotoxicity (mostly paresthesias).[59]

The emergence of multidrug-resistant gram-negative bacilli has brought polymyxins back into use during the past few years; recent studies show less toxicity, possibly because of lower doses, different drug formulations, and careful ICU monitoring.[59] Current nephrotoxicity rates range up to 36%, and neurotoxicity is now uncommon.[59] The main side effect of inhaled colistin — used in the past for prevention and more recently for treatment of ventilator-associated pneumonia — is bronchoconstriction.[56,59] Recently, in vitro studies have suggested colistin heteroresistance in some phenotypically susceptible acinetobacter strains,[60,61] but the clinical importance of this phenomenon is unknown.

Tigecycline, a new glycylcycline antibiotic, is another drug that has been active in vitro and clinically against some multidrug-resistant strains of *A. baumannii*[47,62]; however, development of resistance to tigecycline has been reported recently.[63] In addition, in some outbreaks of acinetobacter infections, most isolates were not susceptible to tigecycline.[5]

Only limited conclusions can be drawn from studies of resistant acinetobacter infections[64-76] (Table 1). These studies have been mostly retrospective, small case series that often included a mix of patients with infections at different sites, and in some of the studies, combined outcomes were reported for grouped cases of multidrug-resistant bacteria. In many series, intravenous colistin has shown success rates of 50% or more for the treatment of pneumonia, but a success rate of only 25% was reported in one series of 20 cases.[72] Kwa and colleagues used inhaled colistin as monotherapy in 17 patients with acinetobacter pneumonia and reported clinical improvement in 57.1%.[77]

Data on the treatment of bloodstream infections are even more limited. During the acinetobacter outbreak in Chicago and northwestern Indiana, 81 bloodstream infections were treated. In two thirds of the cases, only a single blood culture was positive; in 25% of patients, vascular catheters were changed before the first negative

Table 1. Examples of Treatment Regimens and Outcomes of Infections Due to Multidrug-Resistant *Acinetobacter baumannii*.*

Site of Infection	No. of Patients	Antimicrobial Dose†	Mean Duration of Therapy	Clinical Improvement	Mortality‡	Side Effects
			days	*percent of patients*		
Lung[64]	27	Ampicillin–sulbactam (18 g of ampicillin and 9 g of sulbactam or 24 g and 12 g, respectively per day, IV)	8	67	48	Rash, 7; renal failure, 4; diarrhea, 4
Lung[65]	12	Ampicillin–sulbactam (up to 12 g of ampicillin and 6 g of sulbactam per day, IV)	14	75	17	None
Lung[66]	16	Colistin (1×10^6 IU 3 times/day, inhaled) and rifampin (10 mg/kg of body weight every 12 hr, IV)	15	100	0	Elevated liver-function values, 12
Lung[67]	7	Colistin ($1.5–6\times10^6$ IU divided into 3 or 4 doses/day, inhaled; 5 patients also received $1–3\times10^6$ IU every 8 hr, IV)§	10 (inhaled colistin); 17 (IV colistin)	86	14	None
Lung[68]	21	Colistin (2.5–5 mg/day, divided in 3 doses, IV)	15	57	38 (Attributable)	Renal failure, 24
	14	Imipenem (2–3 g/day, IV)	13	57	36 (Attributable)	Renal failure, 43
Lung[69]	8	Polymyxin B (2.5–3.0 mg/kg, IV, then adjusted for renal function, with or without about 2.5 mg/kg/day, divided into 4 doses, inhaled)	19	NA	35 (Attributable)	Renal failure, 6; neurotoxicity, 7¶
Lung[70]	7	Doxycycline (100 mg every 12 hr, IV) or minocycline (100 mg every 12 hr, IV)	14	86	14 (Attributable)	NA
Lung[71]	4	Imipenem (500 mg 4 times/day, IV) and rifampin (600 mg every 12 hr, IV)	12	50	50	NA

Bloodstream[65]	13	Ampicillin–sulbactam (up to 12 g of ampicillin and 6 g of sulbactam/day, IV)	14	46	38	None
Bloodstream[66]	9	Colistin (2×10^6 IU 3 times/day, IV) and rifampin (10 mg/kg every 12 hr, IV)	15	100	0	Elevated liver-function values, 11
Central nervous system[72]	5	Colistin (2.5–5.0 mg/kg/day, divided into 2 or 3 doses, IV)	13	80	NA	Renal failure, 27¶
Lung, bloodstream, intraabdominal site, urinary tract, bone, or central nervous system[73]	48	Polymyxin B (1.5–2.5 mg/kg/day, divided into 2 doses, IV)	14	NA‖	20‖	14¶
Lung, bloodstream, or surgical site[74]	33 4	Polymyxin B (1.5–2.5 mg/kg/day, divided into 2 doses, IV) Doxycycline (100 mg every 12 hr, IV)	NA NA	76 50	9 (Attributable) 0 (Attributable)	Renal failure, 21; neurotoxicity, 6 None
Lung, bloodstream, intraabdominal site, urinary tract, skin, or sinus[75]	71	Colistin (5 mg/kg/day, divided into 2 doses, IV)	12	81	46	Renal failure, 31

* IV denotes intravenous, and NA not available.
† Doses shown are for patients with normal renal function. No patients had *A. baumannii* isolates that were carbapenem-susceptible, except for those treated with imipenem by Garnacho-Montero et al.[68] One milligram of colistin base is contained in 2.4 mg of colistimethate sodium and equals 30,000 IU. Because of differences in products manufactured in different countries, package inserts and the original articles cited here should be checked to verify dosages.[76]
‡ The value given is for crude mortality (or was not specified as crude or adjusted), unless otherwise noted.
§ Two patients with aminoglycoside-susceptible *A. baumannii* also received aminoglycoside intravenously.
¶ Microbiologic improvement was reported in 88% of 41 patients.
‖ The value given is based on larger treatment cohorts with other infection sites or on pathogens treated empirically.

culture result was obtained, suggesting aborted catheter-related infections. Active antibiotic therapy was never given in 49% of the cases or was started only after blood cultures became negative in 22% of the cases.[47] These data support the notion that in some cases acinetobacter bacteremia may represent specimen contamination.

Intravenous or intrathecal colistin has been used successfully for the treatment of central nervous system infections caused by acinetobacter. Intravenous administration of the drug results in moderate penetration of inflamed meninges, with cerebrospinal fluid levels that are approximately 25% of serum levels.[78]

When faced with infections due to multidrug-resistant bacteria, clinicians frequently use combinations of antibiotics. In vitro studies have demonstrated either synergy or additive effects when polymyxins were used with imipenem, rifampin, or azithromycin against multidrug-resistant acinetobacter.[23] Motaouakkil and colleagues successfully treated 16 ventilator-associated pneumonias or bloodstream infections with the combination of colistin and rifampin.[66] Clinical use of rifampin with imipenem for carbapenem-resistant acinetobacter infections has been less successful[71] (Table 1).

INFECTION CONTROL

The primary goals for the control of multidrug-resistant acinetobacter infection are recognizing its presence in a hospital or long-term care facility at an early stage, controlling spread aggressively, and preventing the establishment of endemic strains. Control measures are based almost entirely on experiences from outbreaks of acinetobacter infection and generally address the organism's major epidemic modes of transmission (Fig. 3) and the excessive use of broad-spectrum antibiotics.[22]

Control is most successful when a common source is identified and eliminated.[3,22,48,51,55] 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.[22]

In a single-hospital, multi-ICU outbreak of ventilator-associated pneumonia, *A. calcoaceticus*

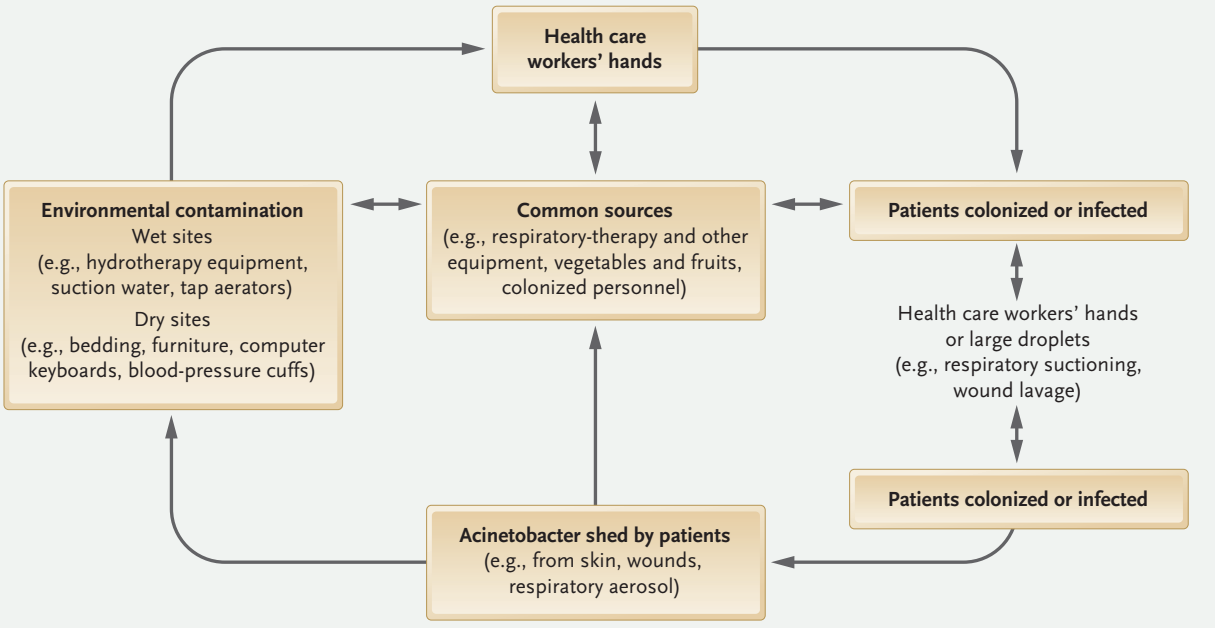

Figure 3. Reservoirs, Sources, and Transmission Patterns for Acinetobacter in Health Care Facilities.

Infection-control measures are directed against the major epidemiologic modes of transmission of acinetobacter, as determined mostly from outbreaks: common-source contamination, environmental contamination, and cross-infection due to lapses in hand hygiene.[22] Although environmental contamination is well documented as a cause of epidemic infections, there are fewer examples of environmental contribution to endemic acinetobacter.

was cultured from 18% of reusable ventilator circuits after pasteurization and from the hands of the four health care workers — one of whom was persistently colonized — who assembled circuits; both disinfection failure and recontamination of circuits by colonized workers during handling probably caused the outbreak.[25] Nevertheless, multidrug-resistant acinetobacter has remained largely susceptible to disinfectants and antiseptics; occasional reports of disinfectant failure are more likely to represent the failure of personnel to follow cleaning procedures than disinfectant resistance.

Aggressive cleaning of the general environment has been the next most frequent outbreak intervention,[22] reflecting the concern that acinetobacter's ability to survive for weeks on wet or dry surfaces facilitates nosocomial transmission.[9] A review of 1561 hospital epidemics reported over the past 40 years noted that closure, typically for cleaning, was considered necessary for outbreak control in 22.9% of 105 units affected by acinetobacter, as compared with 11.7% affected by other pathogens.[79] An outbreak attributed to dissemination of acinetobacter by high-pressure lavage of wounds demonstrated the effect of extensive environmental contamination on the risk of cross-infection.[26] Because multiple measures are usually introduced simultaneously, it has been difficult to assess the independent effect of cleaning. However, in one ICU outbreak, failure to maintain a low level of environmental contamination by *A. baumannii* correlated with an increased risk of patient colonization.[22]

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 (generally the hardest measure to implement), and aseptic care of vascular catheters and endotracheal tubes.[22,51,57,80] A few reports credit out-

break control to reduced prescribing of broad-spectrum antibiotics, such as fluoroquinolones or carbapenems.[22] Because antibiotic exposure is often a risk factor for an outbreak, these findings are plausible; however, use of multiple interventions and historical controls complicates interpretation of these studies. Finally, patient decolonization — by skin cleansing with chlorhexidine or the use of polymyxin topically, orally, or by aerosol — has been an occasional adjunctive control measure that warrants evaluation.[57]

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