Open Access

DOI 10.2376/0005-9366-127-435

© 2014 Schlütersche Verlagsgesellschaft mbH & Co. KG
ISSN 0005-9366

Korrespondenzadresse:
s.mueller@fu-berlin.de

Eingegangen: 04.03.2014
Angenommen: 10.06.2014

http://vetline.de/open-access/158/3216/

Summary

The proportion of multidrug resistant bacteria causing infections in animals has continuously been increasing. While the relevance of ESBL (extended spectrum beta-lactamase)-producing Enterobacteriaceae spp. and MRSA (methicillin resistant Staphylococcus aureus) is unquestionable, knowledge about multidrug resistant Acinetobacter baumannii in veterinary medicine is scarce. This is a worrisome situation, as A. baumannii are isolated from veterinary clinical specimens with rising frequency. The remarkable ability of A. baumannii to develop multidrug resistance and the high risk of transmission are known in human medicine for years. Despite this, data regarding A. baumannii isolates of animal origin are missing. Due to the changing role of companion animals with closer contact between animal and owner, veterinary intensive care medicine is steadily developing. It can be assumed that the number of "high risk" patients with an enhanced risk for hospital acquired infections will be rising simultaneously. Thus, development and spread of multidrug resistant pathogens is envisioned to rise. It is possible, that A. baumannii will evolve into a veterinary nosocomial pathogen similar to ESBL-producing Enterobacteriaceae and MRSA. The lack of attention paid to A. baumannii in veterinary medicine is even more worrying, as first reports indicate a transmission between humans and animals. Essential questions regarding the role of livestock, especially as a potential source of multidrug resistant isolates, remain unanswered. This review summarizes the current knowledge on A. baumannii in veterinary medicine for the first time. It underlines the utmost significance of further investigations of A. baumannii animal isolates, particularly concerning epidemiology and resistance mechanisms.

Keywords: multidrug resistance, companion animal, epidemiology, clinical impact

Zusammenfassung

Introduction

The Genus Acinetobacter, which belongs to the family Moraxella, contains Gram-negative, aerobic bacteria, currently classified into 32 named and unnamed species (Dijkshoorn et al., 2007; Giamarelloiu et al., 2008). Because A. baumannii, A. pittii, A. nosocomialis and A. calcoaceticus are phenotypically and genotypically closely related, unambiguous species identification is challenging and so far only achievable by molecular techniques (Gerner-Smidt et al., 1991; Dijkshoorn et al., 2007; Peleg et al., 2008; Visca et al., 2011). These species are therefore grouped into the Acinetobacter calcoaceticus-Acinetobacter baumannii (Acb-)complex (Gerner-Smidt et al., 1991; Dijkshoorn et al., 2007; Vila and Pachon, 2008; Visca et al., 2011). While A. calcoaceticus is primarily environment- associated, the other three species are pathogenic displaying a varying tendency for multidrug resistance. Therefore, reliable species identification is of utmost importance for adequate infection treatment as well as outbreak management. Being an opportunistic pathogen, A. baumannii usually infects immunocompromised patients suffering from various underlying diseases (Dijkshoorn et al., 2007; Perez et al., 2007; Peleg et al., 2008). Several predisposing factors have been identified in human medicine, including prolonged hospitalization, previous antimicrobial therapy, surgery and indwelling medical devices as there are intubation, venous and urinary catheters (Garcia-Garmendia et al., 2001; Fournier and Richet, 2006; Dijkshoorn et al., 2007; Maragakis and Perl, 2008; Wisplinghoff and Seifert, 2014). Main clinical manifestations are pneumonia (commonly ventilator associated), urinary tract and bloodstream infections as well as meningitis and wound infections (Bergogne-Berezin and Townner, 1996; Dijkshoorn et al., 2007; Perez et al., 2008). Less frequently, infections of other tissues, for example soft tissue infection, endocarditis and keratitis, have been reported (Bergogne-Berezin and Townner, 1996; Peleg et al., 2008).

Community-acquired infections, which usually show a clearly pronounced clinical course, are rarely occurring in humans living in the tropical climate zone (Chen et al., 2001; Falagas et al., 2007; Peleg et al., 2008; Eveillard et al., 2013). The clinical impact of A. baumannii infections, especially on mortality, is under ongoing discussion as the existing data are varying significantly. Mortality ranges from an attributable in-hospital mortality of 7.8% up to 70% in ventilator associated pneumonia and 72.7% in patients suffering from meningitis (Seifert et al., 1995; Falagas et al., 2006a; Perez et al., 2007; Maragakis and Perl, 2008; Vila and Pachon, 2008; Tuon et al., 2010; Chaari et al., 2013; Lemos et al., 2013; Yang et al., 2013). The contradictory results seem to be based on a difficult assessment of the contribution of the usually severe underlying disease, differentiation between infections and colonization and the methodological heterogeneity of the studies (Falagas et al., 2006a; Dijkshoorn et al., 2007; Perez et al., 2007; Giamarelloiu et al., 2008; Peleg et al., 2008). A. baumannii infections display a notable seasonality with a higher incidence during the summer months (McDonald et al., 1999; Giamarelloiu et al., 2008).

While in the 1970s A. baumannii infections could be treated with common antibiotics (Gootz and Marra, 2008; Peleg et al., 2008), reports of infections with multidrug or even pandrug resistant isolates (resistance against all classes of antibiotics) are alarmingly increasing (Hsueh et al., 2002; Landman et al., 2002; Mahgoub et al., 2002; Maragakis and Perl, 2008; Peleg et al., 2008; Vila and Pachon, 2008; Wadl et al., 2010; Visca et al., 2011). The ability of A. baumannii to survive under diverse environmental conditions leads to a prolonged hospital persistence up to five months and facilitates the development of resistance mechanisms (Jawad et al., 1998; Hanlon, 2005; Fournier and Richet, 2006; Dijkshoorn et al., 2007; Gootz and Marra, 2008). It additionally favors intra- and inter-hospital transmission via hospital equipment, staff and colonized patients (Cefai et al., 1990; Fournier and Richet, 2006; Dijkshoorn et al., 2007; Peleg et al., 2008; Wisplinghoff and Seifert, 2012; Wisplinghoff and Seifert, 2014). In human medicine clonal lineages are spreading between hospitals, countries and even continents (Vila et al., 1999; Turton et al., 2004; Schulte et al., 2005; Peleg et al., 2006; Da Silva et al., 2007; Naas et al., 2007; Peleg et al., 2008). As the information about A. baumannii in veterinary medicine is still limited, the current knowledge is primarily based on studies performed with focus on human medicine. This emphasizes the urgent need for further investigations regarding A. baumannii isolates of animal origin.

Epidemiology

Unlike the widespread misconception of A. baumannii being ubiquitous in the environment, the natural habitat still remains unknown (Dijkshoorn et al., 2007; Peleg et al., 2008; Visca et al., 2011) and therefore essential questions for the understanding of resistance development are still unanswered. Some authors suggest the hospital setting itself as a potential reservoir for multidrug resist-
A. baumannii and the increased percentage of multidrug resistant isolates in hospitals, accompanied with a higher clonality of these isolates (Zeana et al., 2003; Wisplinghoff and Seifert, 2012). As mentioned above, medical staff and hospital equipment serve as important vectors for pathogen transmission. Hence, a imaginable scenario could be the introduction of A. baumannii into the hospital setting, for example due to contaminated vegetables (Berlau et al., 1999) or colonized patients (Fournier and Richet, 2006), followed by the adaptation to the present antibiotic pressure. Given selective advantages, in particular multidrug resistance, several clonal lineages could persist and disseminate throughout the hospital. As this is still a hypothesis, it urgently needs to be determined whether animals play a role as infection source for multidrug resistant A. baumannii isolates. Some studies have already shown, that A. baumannii isolates from companion animals (dogs, cats, horses) belong to the human clonal lineages, which cause outbreaks in human medicine for several years (Endimiani et al., 2011; Zordan et al., 2011; Pomba et al., 2014). Because the number of infections in animals is rather low compared to the number of infections in human hospitals and isolates belonging to the main outbreak clones appeared first in humans, a transmission from humans to animals seems currently more likely. If A. baumannii would spill over from humans into livestock as MRSA have previously successfully done, a further enrichment of the resistome could be a worrisome scenario. Furthermore, systematic investigations concerning the role of A. baumannii as a potential part of the physiological microbiota of animals are lacking, although this possibility has already been proposed (Zordan, 2011; Evellard et al., 2013). Indeed, Acinetobacter spp. have been isolated from the canine oral microbiota (Saphir and Carter, 1976), but it remains unclear if A. baumannii or other Acinetobacter species of minor significance were present. Even wild birds have been considered a potential infection source (Muller et al., 2010). Coinfections with A. baumannii in falcons, suffering from cutaneous M. avium paratuberculosis lesions, have been assumed to be due to hunted wild birds (Muller et al., 2010), referring to the identification of A. baumannii in wild bird feces in a zoo (Ahmed et al., 2007). This should be evaluated with caution, as the bird was kept in a zoo. This situation does not reflect actual wild bird populations. Nevertheless, the hypothesis that wild birds can be carriers for multidrug resistant A. baumannii isolates, as it has been shown to be the case for ESBL-producing Enterobacteriaceae (Guenther et al., 2010, 2012), seems conceivable. A possible contribution of living vectors should also be kept in mind, as A. baumannii have already been identified in human body lice and head lice (La Scola and Raoult, 2004; Bouvresse et al., 2011; Kempf et al., 2012). The possible transmission pathways of multidrug resistant A. baumannii isolates are illustrated in Figure 1. Among human isolates an emergence of regional and trans-regional outbreaks due to only few clonal A. baumannii lineages is taking place. The so called European (= International) clones I–III have been described, associated with epidemic spread and multidrug resistance worldwide (Nemec et al., 2004a; van Dessel et al., 2004; Dijkshoorn et al., 2007; Peleg et al., 2008; Diancourt et al., 2010; Higgins et al., 2010; Visca et al., 2011). Yet, only a limited number of clonal lineages account for the worldwide epidemic situation, highlighting the high risk of clonal spread and transmission. The spread of A. baumannii within a small animal clinic and even to a close equine hospital (Boerlin et al., 2001) suggests a risk of transmission among animal clinics comparable to human hospitals.

**Resistance mechanisms**

There are several general mechanisms, known to mediate resistance in bacteria, namely modification of target sites, enzymatic inactivation, active efflux, and decreased influx of drugs (Dijkshoorn et al., 2007), and all have been shown in A. baumannii isolates. Because A. baumannii possesses different intrinsic resistance mechanisms e.g. against 1st and 2nd generation cephaplosporins, aminopenicillins and chloramphenicol (Vila et al., 1993; Bergogne-Berezin and Towner, 1996; Dijkshoorn et al., 2007; Damier-Piolle et al., 2008; Roca et al., 2009), the acquisition of further resistances seems to be even more threatening. While carbapenems were considered to be the antimicrobial of choice for several years, resistance against these antibiotic class or even last line antibiotics as colistin or tigecyclines, occur with increasing
frequency (Dijkshoorn et al., 2007; Peleg et al., 2008; Diancourt et al., 2010; Muguier et al., 2010). Particularly because beta-lactams still represent one of the most important antimicrobial substances in veterinary medicine (Ewers et al., 2011; Murphy et al., 2012), resistance to this class of antibiotics, caused by hydrolyzing enzymes called beta-lactamas, limits the therapeutic options significantly. A. baumannii both exhibits intrinsic beta-lactamas like the AmpC-cephalosporinase as well as acquired ones (Corvec et al., 2003; Hujer et al., 2005; Perez et al., 2007; Gootz and Marra, 2008; Peleg et al., 2008). Resistant phenotypes are especially in case of intrinsic genes often linked to the presence of additional promotor sequences like IS elements (Segal et al., 2005; Heritter et al., 2006; Poirel and Nordmann, 2006b; Turton et al., 2006). However, in A. baumannii, resistance to carbapenems derives from the widely distributed oxacillinases and the more seldom identified metallo-beta-lactamas (MBL) (Poirel and Nordmann, 2006a). Different variants of intrinsic and acquired oxacillinases in A. baumannii have been identified and grouped to date (Brown and Amyes, 2005, 2006; Poirel and Nordmann, 2006a; Perez et al., 2007; Peleg et al., 2008). Interestingly, Hamouda et al. (2011) detected differing oxacillinases in animal isolates, raising the question of a distinct origin of animal and human isolates. Since metallo-beta-lactamas show an up to 1.000-fold higher hydrolyzing activity and are therefore responsible for a high-level resistance against all carbapenems except aztreonam (Poirel and Nordmann, 2006a; Perez et al., 2007; Zarrilli et al., 2013), the presence of MBL genes in the genome is of great concern. Furthermore, Ambler Class A ESBLs can be found among A. baumannii isolates (Sechi et al., 2004; Bonomo and Szabo, 2006; Naas et al., 2006; Endimiani et al., 2007; Peleg et al., 2008).

Mechanisms mediating resistance against other classes of antibiotics than beta-lactams are mentioned only briefly. Decreased susceptibilities against tetracyclines and glycyglycines result from specific effluxpumps as there are tet(A), tet(B), tet(M) (Ribera et al., 2003; Huys et al., 2005). Aminoglycosides lose their effect by means of modifying enzymes like phospho-transferases or 16S rRNA methylisation (Lambert et al., 1994; Seward et al., 1998; Nemec et al., 2004b; Bonomo and Szabo, 2006), whereas mutations in the gyrase encoding genes 

Due to the fact, that no consistent definition of multidrug resistance for A. baumannii exists (Falagas et al., 2006b), the term “multidrug resistance” will be used in the following according to Schwarz et al., (2010) for isolates resistant to three or more classes of antibiotics.

**Acinetobacter baumannii in veterinary medicine**

Because various factors contribute to the infectious situation in different animal species, the following summary is structured in parts for a better understanding. Thus, a distinction between livestock and companion animals, which are furthermore grouped into “horses” and “cats and dogs”, has been made. Table 1 summarizes publications regarding A. baumannii in animals.

**Livestock**

Since there are only few studies concerning the occurrence of A. baumannii in livestock, it is difficult to provide unambiguous information. A first study examined isolates from food-producing animals, which i) exhibited no multidrug resistance and ii) belonged to a different genetic pool than human isolates (Hamouda et al., 2008). Correspondingly, Hamouda et al. (2011) compared A. baumannii isolates from animals slaughtered for human consumption to human isolates belonging to the European clones I–III. Again, animal isolates lacked important features typical for multidrug resistance. Molecular typing methods distinguished the animal isolates from the above mentioned European clones, suggesting there is no epidemiological link. As already mentioned by the author, genetic information of the investigated isolates indicate that these isolates had only been exposed to little antibiotic pressure. Within the investigation of the occurrence of carbapenemase producing Gram-negative bacteria in dairy cattle, analysis of isolates from rectal swabs of dairy cows revealed only oxacillinase-23 producing *Acinetobacter* genomic species 15TU (Poirel et al., 2012). Since the number of investigated samples is rather low, it remains to be elucidated to which results a larger study would lead, especially as the determined OXA-23 is widely distributed among A. baumannii isolates and has just been identified in a cat (Pomba et al., 2014). Recently, an A. baumannii strain isolated from a pig suffering from pneumonia and sepsis harbored the NDM-1 metallo-beta-lactamase, which is usually associated with carbapenem resistance (Zhang et al., 2013). This is the first report of high potential carbapenemase producing *A. baumannii* in livestock, indicating, that MBL producing isolates are at least to a low extend present in farm animal populations. To be mentioned, in Korea bulk tank milk samples and mastitis milk samples were shown to contain Acb-complex and A. baumannii isolates (Nam et al., 2009, 2010; Gurung et al., 2013). However, in case of A. baumannii isolates, species-identification was performed by unreliable phenotypical methods, questioning the obtained results. Moreover, Korea belongs to a climate zone in which A. baumannii is more often isolated from the environment and human skin (Houang et al., 2001; Huys et al., 2007; Peleg et al., 2008; O’Shea, 2012), mak-
### TABLE 1: Publications concerning Acinetobacter spp. in animals with emphasis on Acinetobacter baumannii

<table>
<thead>
<tr>
<th>Acinetobacter species</th>
<th>Animal species</th>
<th>Clinical symptoms/ specimen</th>
<th>Country</th>
<th>Antibiotic resistance</th>
<th>Additional information</th>
<th>Study information</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. baumannii</td>
<td>livestock</td>
<td></td>
<td>UK</td>
<td>not multidrug resistant</td>
<td>isolates distinct from European clones I–III</td>
<td>A, B, C</td>
<td>Hamouda et al. (2008)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>refrigerated meat</td>
<td></td>
<td>Italy</td>
<td>unspecified</td>
<td>possible transmission of A. baumannii due to contaminated meat?</td>
<td>D</td>
<td>Ercolini et al. (2009)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>mastitis milk</td>
<td></td>
<td>Korea</td>
<td>variable</td>
<td>possible contamination of milk due to colonized udders?</td>
<td>A, C</td>
<td>Nam et al. (2010)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>feces, skin, nostril and ear swabs</td>
<td></td>
<td>UK (Scotland)</td>
<td>not multidrug resistant</td>
<td>isolates distinct from European clones I–III, new animal specific oxacillinas (OXA-148, OXA-149, OXA-150), absence of typical resistance features</td>
<td>A, B, C</td>
<td>Hamouda et al. (2011)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>pneumonia, sepsis</td>
<td></td>
<td>China</td>
<td>multidrug resistant ³</td>
<td>strain carried NDM1 metallo-β-lactamase (high potential carbapenemase)</td>
<td>A, B</td>
<td>Zhang et al. (2013)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>bulk tank milk</td>
<td></td>
<td>Korea</td>
<td>variable</td>
<td>possible contamination of milk due to colonized udders?</td>
<td>A, C, G</td>
<td>Gurung et al. (2013)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>soil sample after pig manure fertilization</td>
<td></td>
<td>UK (England)</td>
<td>sulfonamides, tetracycline, nalidixic acid, chloramphenicol</td>
<td>presence of sulfonamide resistant A. baumannii strains in soil for up to one year after pig manure fertilization</td>
<td>D</td>
<td>Byrne-Bailey et al. (2009)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>horse</td>
<td>jugular catheter tips</td>
<td>Belgium</td>
<td>variable, two strains multidrug resistant ³</td>
<td>no information about contribution to disease, pus formation in one case of A. baumannii pure culture</td>
<td>A, B, C</td>
<td>Vanechoute et al. (2000)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>horse</td>
<td>sepsis, neonatal encephalopathy</td>
<td>United States</td>
<td>unspecified</td>
<td></td>
<td>A</td>
<td>Bentz et al. (2002)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>horse</td>
<td>wound swab</td>
<td>Ireland</td>
<td>multidrug resistant ³</td>
<td>strain carried class 1 integron largely identical to a human isolate</td>
<td>B</td>
<td>Abbott et al. (2005)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>horse</td>
<td>uterus, eye, thoracic cavity, blood culture, catheter, tissue</td>
<td>United States</td>
<td>variable, 5 of 8 isolates multidrug resistant ³</td>
<td>infections possibly hospital acquired</td>
<td>A, C</td>
<td>Brosnahan (2008)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>horse</td>
<td>bronchopneumonia</td>
<td>Ireland</td>
<td>multidrug resistant ³</td>
<td>previous intensive treatment with antimicrobials</td>
<td>A, C</td>
<td>Jokisalo et al. (2010)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>dog, cat</td>
<td>urinary, respiratory, wound and bloodstream infections</td>
<td>Switzerland</td>
<td>variable, most isolates resistant against common antibiotics ³</td>
<td>evidence for intra-hospital spread</td>
<td>A, B, C</td>
<td>Francey et al. (2006)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>dog, cat, horse</td>
<td>various</td>
<td>Switzerland</td>
<td>most isolates multidrug resistant ³, still carbapenem sensitive</td>
<td>evidence for intra- and inter-hospital spread</td>
<td>A, B, C</td>
<td>Boerlin et al. (2001)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>cat</td>
<td>necrotizing fasciitis, septic shock</td>
<td>Switzerland</td>
<td>multidrug resistant ³</td>
<td>probably hospital-acquired infection with intravascular catheter as port of entry</td>
<td>A</td>
<td>Brachelente et al. (2007)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>dog, cat</td>
<td>various</td>
<td>United States</td>
<td>variable, 21% of isolates multidrug resistant ³</td>
<td>A. baumannii accounted for the majority of multidrug resistant isolates, no information about species identification method</td>
<td>A</td>
<td>Black et al. (2009)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>dog, cat</td>
<td>various</td>
<td>Germany</td>
<td>multidrug resistant ³</td>
<td>isolates belonged to European clones I–III</td>
<td>A, B, C</td>
<td>Zordan et al. (2011)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>dog, cat, horse</td>
<td>various</td>
<td>Switzerland</td>
<td>variable, some isolates multidrug resistant ³</td>
<td>majority of infections hospital-acquired, isolates belonged to European clones I–II, isolates showed molecular background of resistance common in human isolates</td>
<td>A, B, C</td>
<td>Endimiani et al. (2011)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>cat</td>
<td>urinary tract infection</td>
<td>Portugal</td>
<td>multidrug resistant ³</td>
<td>isolate belonged to European clone II, showed OXA-23 mediated carbapenem resistance in an isolate from a cat</td>
<td>A, B</td>
<td>Pompa et al. (2014)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>wild bird</td>
<td>feces</td>
<td>Japan</td>
<td>not multidrug resistant ³</td>
<td>isolate belonged to European clone II, showed OXA-23 mediated carbapenem resistance in an isolate from a wild bird kept in a zoo, no evidence to actual wild bird populations</td>
<td>A, B, C</td>
<td>Ahmed et al. (2007)</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>falcon</td>
<td>cutaneous lesions</td>
<td>United Arab Emirates</td>
<td>unspecified</td>
<td>M. avium paratuberculosis coinfection, wild bird as potential A. baumannii source</td>
<td>A, B</td>
<td>Muller et al. (2010)</td>
</tr>
<tr>
<td>A. calcoaceticus-A. baumannii complex</td>
<td>livestock</td>
<td>raw milk</td>
<td>Korea</td>
<td>variable</td>
<td>possible contamination of milk due to colonized udders?</td>
<td>A, C</td>
<td>Nam et al. (2009)</td>
</tr>
</tbody>
</table>
TABLE 1 (CONTINUED): Publications concerning Acinetobacter spp. in animals with emphasis on Acinetobacter baumannii

<table>
<thead>
<tr>
<th>Acinetobacter species</th>
<th>Animal species</th>
<th>Clinical symptoms/ specimen</th>
<th>Country</th>
<th>Antibiotic resistance</th>
<th>Additional information</th>
<th>Study information</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. genomic species 15TU</td>
<td>livestock</td>
<td>rectal swabs</td>
<td>France</td>
<td>multidrug resistant¹</td>
<td>presence of carbapenemase-producing Acinetobacter spp. in cattle, most animals carrying OXA-23 producing isolates received antimicrobials previously</td>
<td>A, B, C Poirel et al. (2012)</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp.</td>
<td>horse</td>
<td>keratitis</td>
<td>United States</td>
<td></td>
<td>previous treatment with immunosuppressive drugs</td>
<td>A Moore et al. (1995)</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp.</td>
<td>horse</td>
<td>upper respiratory tract infection</td>
<td>Poland</td>
<td>unspecified</td>
<td></td>
<td>A Boguta et al. (2002)</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp.</td>
<td>dog</td>
<td>purulent pericarditis, pericardial fluid</td>
<td>Japan</td>
<td>multidrug resistant¹</td>
<td>Candida albicans coinfection, previous treatment with immunosuppressive drugs</td>
<td>A Mohri et al. (2009)</td>
<td></td>
</tr>
<tr>
<td>A. calcoaceticus var. lwoffii¹</td>
<td>dog</td>
<td>gingival scrapings</td>
<td>United States</td>
<td></td>
<td></td>
<td>A, C Saphir and Carter (1976)</td>
<td></td>
</tr>
<tr>
<td>A. calcoaceticus¹</td>
<td>horse</td>
<td>myositis, septicaemia</td>
<td>United States</td>
<td></td>
<td></td>
<td>A Dickie and Regnier (1978)</td>
<td></td>
</tr>
<tr>
<td>A. calcoaceticus¹</td>
<td>horse</td>
<td>chronic haematuria</td>
<td>India</td>
<td></td>
<td></td>
<td>A Rajasekhar et al. (1978)</td>
<td></td>
</tr>
<tr>
<td>A. calcoaceticus var. lwoffii</td>
<td>orangutan</td>
<td>respiratory tract infection</td>
<td>United States</td>
<td>ampicillin</td>
<td></td>
<td>A Iverson and Connelly (1981)</td>
<td></td>
</tr>
<tr>
<td>A. calcoaceticus</td>
<td>dog, cat, horse, cow, others</td>
<td>various</td>
<td>United States</td>
<td></td>
<td></td>
<td>A Mathewson and Simpson (1982)</td>
<td></td>
</tr>
<tr>
<td>A. calcoaceticus¹</td>
<td>cow</td>
<td>mastitis</td>
<td></td>
<td></td>
<td></td>
<td>A Rahman and Baxi (1985)</td>
<td></td>
</tr>
<tr>
<td>A. calcoaceticus¹</td>
<td>cow</td>
<td>metritis</td>
<td>Turkey</td>
<td></td>
<td></td>
<td>A Diker et al. (1986)</td>
<td></td>
</tr>
<tr>
<td>A. calcoaceticus¹</td>
<td>water buffalo</td>
<td>late abortion</td>
<td>India</td>
<td></td>
<td></td>
<td>A Das and Paranjape (1986)</td>
<td></td>
</tr>
<tr>
<td>A. calcoaceticus¹</td>
<td>hens</td>
<td>septicemia</td>
<td>Turkey</td>
<td></td>
<td></td>
<td>A Erganis et al. (1988)</td>
<td></td>
</tr>
</tbody>
</table>

¹ no reliable species-identification
² varying resistances against several antibiotics
³ definition of multidrug resistance according to Schwarz et al. (2010)
⁴ no definition of multidrug resistance given

ing it more difficult to distinguish between infection, colonization and contamination. Yet, mastitis due to A. baumannii infections remains possible, especially in weakened cows. Livestock and/or food of animal origin are nowadays considered to be a possible infection source for extended-spectrum beta-lactamase producing Enterobacteriaceae spp. (Phillips et al., 2004; Grami et al., 2014). Accordingly, ESBL-producing E. coli have been isolated from agricultural soil samples (Hartmann et al., 2012), as it has already been shown for sulfonamide resistant A. baumannii isolates after pig manure fertilization (Byrne-Bailey et al., 2009).

Companion animals

Horses

While the occurrence of A. baumannii in livestock has only been of recent interest, first reports of Acinetobacter spp. in horses go back to the 1990s. Considering the fact that unambiguous species-identification was not possible in earlier days, some infections in different kinds of animals reported in the 1970s and 1980s as being caused by A. calcoaceticus might presumably be due to A. baumannii (Dickie and Regnier, 1978; Rajasekhar et al., 1978; Iverson and Connelly, 1981; Mathewson and Simpson, 1982; Rahman and Baxi, 1985; Das and Paranjape, 1986; Diker et al., 1986; Erganis et al., 1988). However, in 1993 and 1995, Acinetobacter spp. have been associated with keratitis and lower respiratory tract infections in horses, although there is no proof for a contribution to the infectious diseases (Kester et al., 1993; Moore et al., 1995; Boguta et al., 2002). These and later reports include 48-h old foals as well as adult horses suffering from various infectious conditions, like respiratory and ophthalmological diseases, catheter, uterine and bloodstream infections (Bentz et al., 2002; Brosnahan, 2008; Jokisalo et al., 2010). Some of the isolated A. baumannii strains were resistant against several classes of antibiotics (Brosnahan, 2008). Most of the affected patients had been critically ill, accompanied with a prolonged hospitalization and previous antibiotic treatment (Brosnahan, 2008; Jokisalo et al., 2010). Still, as most of the publications are case reports, there is no information regarding species-identification methods. Hence, infections could possibly be caused by the other pathogenic Acb-complex species A. pittii and A. nosocomialis. Future studies should implicitly apply reliable species-identification methods.

In this regard, the first reliable report about A. baumannii in horses was published in 2000 by Vanechoutte et al. While examining vascular catheter tips in hospitalized horses, A. baumannii isolates resistant against several classes of antibiotics had been isolated. Nevertheless, despite one isolate obtained in pure culture from a horse suffering from thrombophlebitis, isolation of A. baumannii has not been associated with disease (Vanechoutte et al., 2000).
While the majority of the previous reports are more or less based on accidental observations, Endimiani et al. (2011) systematically examined *A. baumannii* isolates from dogs, cats and horses, using methods established for the investigation of human isolates. The vast majority of the analyzed isolates belonged to the human European clones I and II and showed resistance determinants formerly known for human isolates. Furthermore, several infections had presumably been hospital acquired, affecting animals displaying typical predisposing factors. Based on their results, the authors judged animals as a potential infection source for multidrug resistant *A. baumannii* isolates. Consistent with these findings, it has also been verified that the class 1 integron of an equine multidrug resistant *A. baumannii* isolate is in large parts identical to an integron of a human isolate (Abbott et al., 2005). Such class 1 integrons play an important role in the acquisition of multidrug resistance.

**Dogs and cats**

Epidemiological similarities between human and animal isolates have also been observed in small animal clinics (Francey et al., 2000; Boerlin et al., 2001). A retrospective investigation of 19 cases of *A. baumannii* infections in dogs and cats gained evidence for nosocomial spread within a clinic, accompanied with an increase in morbidity and lethality (Francey et al., 2000). Just one year later, a second outbreak of epidemiologically unrelated *A. baumannii* strains in the same clinic in Switzerland has been reported (Boerlin et al., 2001). During this outbreak, not just patient-to-patient transfer between two cats, but also transmission to a hospitalized horse patient from a nearby horse clinic has been proven. The potential of *A. baumannii* isolates to cause life-threatening infections also in animals was demonstrated by a case of necrotizing fasciitis in a cat (Brachelente et al., 2007). During treatment of an underlying disease of minor significance, venous catheterization probably served as a port of entry for *A. baumannii*, thus leading to an impetuous clinical course with septic shock and death. Simultaneously, two dogs developed *A. baumannii* infections with isolates of the same resistance profile, including quinolone resistance. These three cases of *A. baumannii* infection occurred, again, in the same Swiss hospital. Unfortunately, no further molecular genetic analysis of the three isolates exists. Hence, the question of a possible persistence of strains of the second outbreak (Boerlin et al., 2001), which moreover acquired quinolone resistance due to antibiotic selective pressure, is left unanswered.

Also among companion animals, a considerable percentage of *A. baumannii* isolates exhibits multidrug resistance. Black et al. (2009) observed that *A. baumannii* accounted for only 7% of all Gram-negative infections, but at the same time for 21% of all multidrug resistant isolates. Thus, *A. baumannii* was the most common multidrug resistant Gram-negative species (Black et al., 2009). Moreover, length of hospitalization seemed to correlate with the risk of developing an infection with multidrug resistant bacteria. In accordance with the results of Endimiani et al. (2011), a current study demonstrated the belonging of *A. baumannii* animal isolates from Germany to the European clones I–III (Zordan et al., 2011). This is even more concerning, as these clones are usually associated with multidrug resistance and an enormous potential for epidemic spread. In fact, an OXA-23 producing *A. baumannii* isolate belonging to European clone II could be isolated from a cat (Pomba et al., 2014). This clearly indicates the presence of carbapenem resistant strains belonging to human epidemic clonal lineages in animal populations.

**Discussion**

There are only few studies providing valid data concerning *A. baumannii* in veterinary medicine. Restricted sample numbers, retrospective data analysis, unreliable species identification methods or unique reports of accidental observations are just some of the limitations noted in the conducted studies. This is why the current knowledge of *A. baumannii* of animal origin is in parts based on indications rather than evidence. However, the present studies mark the beginning of a new understanding of the importance of multidrug resistant *A. baumannii* as a veterinary pathogen and give important stimuli for future studies. Based on the limited existing information, *Acinetobacter baumannii* seems to be the predominant pathogenic *Acinetobacter* spp. in veterinary clinical specimens (Francey et al., 2000). Some of the reported cases of *A. baumannii* infection in animals have been described to be hospital-acquired (Boerlin et al., 2001; Brachelente et al., 2007; Endimiani et al., 2011). Moreover, there is evidence for intra- and inter-hospital spread, similar to the spread between human hospitals (Francey et al., 2000; Boerlin et al., 2001; Zordan et al., 2011). The risk for opportunistic infections with *A. baumannii* is enhanced in case of predisposing factors like prolonged hospitalization, antibiotic therapy or invasive procedures (Boerlin et al., 2001; Brachelente et al., 2007; Endimiani et al., 2011). Such infections can result in an increase in morbidity and lethality (Francey et al., 2000), as *A. baumannii* of animal origin also display multi drug resistance (Boerlin et al., 2001; Brachelente et al., 2007; Black et al., 2009; Zordan et al., 2011; Pomba et al., 2014). Interestingly, the current emergence of multidrug resistant *A. baumannii* infections in small animal clinics provides similarities to the rise of MRSA as a nosocomial pathogen for companion animals in veterinary medicine.

A higher prevalence of multidrug resistant isolates belonging to the European clones I–III can be observed in companion animals compared to livestock. This is possibly due to the closer contact between companion animal and owner, providing opportunity for pathogen transmission, and the growing field of small animal intensive care. Thus, companion animals currently seem to be exposed to a higher risk for infections with multidrug resistant *A. baumannii* isolates, facilitating the evolution of *A. baumannii* into a veterinary nosocomial pathogen. A spillover of multidrug resistant *A. baumannii* into livestock clearly is of concern as this would provide new transmission pathways and an enrichment of the resistome, owing to the present antibiotic pressure on farms. A NDM-1 carrying strain has in fact already been isolated from a pig (Zhang et al., 2013). Because animal *A. baumannii* isolates often belong to the known human outbreak clones and harbor resistance determinants formerly known for human isolates on the one hand (Abbott et al., 2005; Endimiani et al., 2011; Zhang et al., 2013; Pomba et al., 2014), and multidrug resistant strains previously occurred in humans on the other hand, an initial transmission from humans to animals appears more likely than the other way around. Once
introduced into the animal population, transmission back to humans seems quite possible. Hence, *A. baumannii* could be considered a zoonotic pathogen, but evidence is still pending.

As mentioned above, a class 1 integron from a horse has been almost identical to the one from a human isolate. Because class 1 integrons play an important role in acquisition of multidrug resistance, the presence of such genetic elements in animal isolates is of profound epidemiological interest as it suggests i) possibly the same origin of animal and human isolates and ii) provides the opportunity for horizontal gene transfer between human and animal isolates. As valid data is lacking, further studies regarding the origin of multidrug resistant strains and possible transmission mechanisms should implicitly be conducted. In this context more focus should be placed on the role of livestock in the epidemiology of *A. baumannii* of animal origin. Antibiotic treatment in farm animals enhances the antimicrobial selective pressure for present strains and seems to be one of the most important factors contributing to the development of resistance. It even is conceivable that colonized wild birds could have introduced *A. baumannii* into farms, agricultural land and horse stables. Since the species of the *Acb*-complex show varying virulence and incidence of multidrug resistance, unambiguous species identification is indispensable for adequate infection treatment and outbreak management. A rapid, easy and cost-efficient method for routine species identification is implicitly required. Veterinarians should become aware of the new and arising risk of infections with multidrug resistant *A. baumannii* isolates. Consequently, bacterial species identification, including determination of resistance profiles, is recommended as the basis of each antimicrobial therapy. Careful assessment of the necessity of antimicrobial treatments should routinely be performed in order to reduce the antibiotic selective pressure in the hospital setting and on farms. Furthermore, thorough hygiene practice including patients, staff and hospital equipment to prevent the spread of outbreak strains is of outstanding importance.

In conclusion, it becomes alarmingly obvious, that *A. baumannii* is an emerging pathogen in veterinary medicine with a high potential for multidrug resistance and epidemic spread. In addition, transmission between humans and animals seems to be likely, introducing unpredictable epidemiological risks.

**Acknowledgement**

Stefanie Müller was funded by the H. Wilhelm Schau- mann Stiftung, Hamburg. The funder had no role in the decision to publish or in the preparation of the manuscript.

Conflict of interest: The authors declare that no competing interests exist.

**Literature**


**Address for correspondence:**
Stefanie Müller
Institute of Microbiology and Epizootics
Centre for Infection Medicine
Robert-von-Ostertag Str. 7–13
14163 Berlin
Germany
s.mueller@fu-berlin.de