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Review

Acinetobacter in veterinary medicine, with an emphasis on *Acinetobacter baumannii*

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ABSTRACT

Acinetobacter spp. are aerobic, rod-shaped, Gram-negative bacteria belonging to the Moraxellaceae family of the class Gammaproteobacteria and are considered ubiquitous organisms. Among them, *Acinetobacter baumannii* is the most clinically significant species with an extraordinary ability to accumulate antimicrobial resistance and to survive in the hospital environment. Recent reports indicate that *A. baumannii* has also evolved into a veterinary nosocomial pathogen. Although *Acinetobacter* spp. can be identified to species level using matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF/MS) coupled with an updated database, molecular techniques are still necessary for genotyping and determination of clonal lineages. It appears that the majority of infections due to *A. baumannii* in veterinary medicine are nosocomial. Such isolates have been associated with several types of infection such as canine pyoderma, feline necrotizing fasciitis, urinary tract infection, equine thrombophlebitis and lower respiratory tract infection, foal sepsis, pneumonia in mink, and cutaneous lesions in hybrid falcons. Given the potential multidrug resistance of *A. baumannii*, treatment of diseased animals is often supportive and should preferably be based on in vitro antimicrobial susceptibility testing results. It should be noted that animal isolates show high genetic diversity and are in general distinct in their sequence types and resistance patterns from those found in humans. However, it cannot be excluded that animals may occasionally play a role as a reservoir of *A. baumannii*. Thus, it is of importance to implement infection control measures in veterinary hospitals to avoid nosocomial outbreaks with multidrug-resistant *A. baumannii*.

Contents

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1. Introduction

Acinetobacter spp. are aerobic, rod-shaped, Gram-negative bacteria belonging to the Moraxellaceae family of the class Gammaproteobacteria. *Acinetobacter* spp. occupy an important position in nature because of their ubiquitous presence in diverse environments such as soil, fresh water, oceans and sediments [1,2]. Versatile metabolic characteristics allow species of this genus to catabolise a wide range of natural compounds, implying active participation in the nutrient cycle in the ecosystem. On the other hand, multidrug-resistant (MDR) *Acinetobacter baumannii* causing nosocomial infections with high mortality have been raising serious concerns in human medicine. It is very likely that *A. baumannii* will also evolve into a serious veterinary nosocomial pathogen, similar to what has happened in human hospitals, as its association with infections in animals is increasingly reported. The lack of attention paid to *A. baumannii* in veterinary medicine is particularly worrying as there are now reports indicating the presence of similar or even identical successful clones both in humans and animals [3–5]. Despite this, data regarding *A. baumannii* of animal origin are still scarce [4]. Of importance, carbapenem-resistant *A. baumannii* rank as priority 1 of the considered pathogens by the World Health Organization (WHO) according to a recent publication [6].

This review aims to provide an overview of the epidemiology of *A. baumannii* in animal species relevant to veterinary medicine. As numerous harmless non-*baumannii Acinetobacter* spp. occur in the environment and possibly in animals, identification of *A. baumannii* should be based on well-validated methods such as *rpoB* sequence analysis and matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF/MS) coupled with an updated database [7,8]. In the present review, the term '*Acinetobacter* spp.' was used if species identification was not defined or was not obtained with sufficiently powerful methodologies (Table 1).

2. The bacterium

Nowadays, the genus *Acinetobacter* comprises more than 50 validly named species. Of note, many comprise only one strain and their ecology is not well known. They belong to the class Gammaproteobacteria and order Pseudomonadales and comprise a group of genetically-related, sugar-non-fermenting, oxidase-negative, Gram-negative and strictly aerobic coccobacilli [1,9,10]. The genus includes both non-pathogenic and pathogenic species [1,11]. Among them, *A. baumannii* is the most clinically significant *Acinetobacter* species implicated in human nosocomial infections. However, *Acinetobacter pittii* and *Acinetobacter nosocomialis* are also increasingly reported as causes of infections [10]. It should be noted that the development of molecular methods in the last 10 years also allowed a better identification of *Acinetobacter* spp., particularly species of the *Acinetobacter calcoaceticus–Acinetobacter baumannii* (ACB) complex. For up-to-date information regarding the current taxonomy of the *Acinetobacter* genus, please visit the website http://apps.szu.cz/anemec/Classification.pdf curated by Prof. Alexandr Nemec.

Clinically relevant species are mostly confined to the ACB complex, namely *A. baumannii*, *A. calcoaceticus*, *A. pittii*, *A. nosocomialis* and the recently added species *Acinetobacter seifertii* and *Acinetobacter dijkshoorniae*, of which *A. baumannii* is the most important [12,13]. Due to the association of MDR *A. baumannii* infections with high mortality, the bacterium has also been classified as an ESKAPE organism (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *A. baumannii*, *Pseudomonas aeruginosa* and *Enterobacter* spp.), a group of pathogens with a high rate of antimicrobial resistance that are responsible for an important share of human nosocomial infections [1,14]. Originally, three international *A. baumannii* clones [the so-called International or European clones I, II and III, with preference of the use of International clones (ICs)] have been reported from hospitals [15–18]. With the introduction of multilocus sequence typing (MLST) [19], these clones I, II and III have been shown to belong to specific sequence types (STs) that mainly cluster into three clonal complexes (CCs), i.e. CC1, CC2 and CC3. There are two MLST approaches, the Pasteur [20] and Oxford [21] schemes, and both of them can identify ICs.

Little is known about the natural occurrence of *Acinetobacter* spp. in animals or whether animals truly are a reservoir from which spread to humans occurs. It should be noted that some *Acinetobacter* spp. are commensal in animals like they may also represent the normal flora in humans, but these *Acinetobacter* spp. appear to be unrelated and are in general distinct in their sequence types and resistance patterns from those found in humans. It is therefore important to use appropriate identification and genotyping methods in order to obtain comparable data. In this regard, the types of methodologies used in projects studying *Acinetobacter* spp. from animals are listed in Table 1 to determine whether *A. baumannii* has been correctly identified and whether the results are reliable to evaluate the zoonotic aspect of *A. baumannii*.

3. Antimicrobial resistance and pathogenesis

Acinetobacter baumannii has become one of the most problematic hospital-acquired human pathogens in the last two decades owing to its ability to survive in the healthcare environment and to overexpress intrinsic β-lactamases and multidrug resistance efflux genes as well as to accumulate additional antimicrobial resistance traits [10,23]. Overexpression of chromosomally located β-lactamases such as the AmpC cephalosporinases [also known as ADCs (*Acinetobacter*-derived cephalosporinases)] and the OXA-51-like oxacillinases has been associated with insertion sequence (IS) elements (e.g. IS*Aba1* and IS*Aba3*) next to the genes [10,24,25]. Furthermore, efflux pumps belonging to the resistance–nodulation–cell division (RND) family are particularly effective in generating resistance as they form a tripartite complex together with the periplasmic proteins belonging to the membrane fusion protein (MFP) family and the outer membrane protein (OMP) channels so that drugs are pumped out directly to the external medium [26,27]. The RND efflux complex in *A. baumannii*,

Table 1
Overview of methodologies used for identification of *Acinetobacter* spp. isolated from animals.

Animal	Infection site	Identification method	Reference methodology	Species identification at time of publication	Reliable identification	Year of publication	Reference
Dog ($n = 2$)	UTI	NM	*rpoB* sequencing	*A. baumannii*	Yes	2016	[5]
Dog ($n = 168$)	Urine, CVCs, throat and trachea, skin and hairs, BAL, nose, abscesses and fistula	MALDI-TOF/MS (Bruker)	*gyrB* multiplex PCR	*A. baumannii*	Yes	2017	[89]
Dog ($n = 4$)	Mouth and rectal swabs	VITEK®2 system (bioMérieux)	PCR of *rpoB*	*A. baumannii*	Yes	2016	[91]
Dog ($n = 11$)	Pus/wound, eye, urine, blood and pericardial effusion	MALDI-TOF/MS (Bruker)	PCR of $bla_{\text{OXA-51-like}}$	*A. baumannii*	Yes	2011	[3]
Dog ($n = 17$)	Pus/wound, urinary tract, respiratory tract and blood	API ID32GN galleries (bioMérieux)	Sequencing of 16S ribosomal DNA of selected isolates	*A. baumannii*	Yes	2000	[83]
Dog ($n = 5$)	Samples routinely submitted for bacteriological culture and susceptibility testing	In-house aerobic bacteriological culture	None	*A. baumannii*	No	2009	[85]
Dog ($n = 5$)	Gingival scrapings from healthy dogs	Non-specified standard biochemical procedures	None	*A. calcoaceticus* var. *lwoffii* ($n = 4$) and *anitratus* ($n = 1$)	No	1976	[86]
Dog ($n = 1$)	Ulcerated pyoderma lesions	Non-specified API galleries	None	*A. baumannii–calcoaceticus*	No	2014	[87]
Dog ($n = 10$)	Chronic eczema	Gram-negative, penicillin-resistant, oxidase negative coccobacilli	None	*Acinetobacter* spp.	No	1978	[88]
Dog ($n = 1$)	UTI	MALDI-TOF/MS (Bruker)	WGS	*A. baumannii*	Yes	2018	[81]
Cat ($n = 5$)	UTI	NM	*rpoB* sequencing	*A. baumannii*	Yes	2016	[5]
Cat ($n = 42$)	Wounds, urine, throat and trachea, skin and hairs, nose, abscesses and fistula	MALDI-TOF/MS (Bruker)	*gyrB* multiplex PCR	*A. baumannii*	Yes	2017	[89]
Cat ($n = 1$)	Urine	NM	WGS	*A. baumannii*	Yes	2016	[90]
Cat ($n = 2$)	Pus/wound and liver	MALDI-TOF/MS (Bruker)	PCR of $bla_{\text{OXA-51}}$	*A. baumannii*	Yes	2011	[3]
Cat ($n = 2$)	NM	API ID32GN galleries (bioMérieux)	Sequencing of 16S ribosomal DNA	*A. baumannii*	Yes	2000	[83]
Cat ($n = 10$)	Chronic eczema	Gram-negative, penicillin-resistant, oxidase negative coccobacilli	None	*Acinetobacter* spp.	No	1978	[88]
Cat ($n = 1$)	Skin, liver, spleen and kidney	API ID32GN galleries (bioMérieux)	PCR of $bla_{\text{OXA-51-like}}$ gene	*A. baumannii*	Yes	2007	[92]
Cat ($n = 1$)	UTI	MALDI-TOF/MS (Bruker)	PCR of $bla_{\text{OXA-51-like}}$ gene	*A. baumannii*	Yes	2014	[80]
Horse ($n = 9$)	Faecal samples, nostril swabs	MALDI-TOF/MS (Bruker)	None	*A. baumannii*	Yes	2018	[146]
Horse ($n = 4$)	Pus/wound and catheter tip	MALDI-TOF/MS (Bruker)	PCR of $bla_{\text{OXA-51-like}}$ gene	*A. baumannii*	Yes	2011	[3]
Horse ($n = 2$)	Faeces of hospitalised horses	Selective *Acinetobacter* medium	Sequencing of 16S ribosomal DNA	Possibly novel *Acinetobacter* spp.	Yes	2012	[93]
Horse ($n = 7$)	Intravenous jugular catheter tips	API 20NE galleries and growth at 44 °C as complementary test	ARDRA	*A. baumannii*	Yes	2000	[94]
Horse ($n = 24$)	Tracheal washes from horses with respiratory diseases or 'poor performance'	Bacteriological culture and subsequent biochemical characterisation revealing *Acinetobacter* spp.	NM		No	1993	[96]
Foal ($n = 1$)	Blood	Blood culture with undefined identification method	None	*A. baumannii*	No	2002	[98]
Foal ($n = 1$)	Percutaneous transtracheal wash	Bacteriological culture	None	*A. baumannii*	No	2010	[145]
Cow ($n = 1$)	Faeces	API 20E galleries, (bioMérieux), Sensititre GNID (TREK Diagnostic Systems Inc.)	WGS	*A. baumannii*	Yes	2016	[99]
Cow ($n = 1$)	Faeces	MALDI-TOF/MS	None	*A. baumannii*	Yes	2015	[76]
Cow ($n = 8$)	Recovered from faecal specimens, skin, nostril and ear swabs	NM	ARDRA and PCR of $bla_{\text{OXA-51-like}}$ gene	*A. baumannii*	Yes	2011	[75]
Cattle ($n = 5$)	Mouth swabs	VITEK®2 system (bioMérieux)	PCR of *rpoB*	*A. baumannii*	Yes	2016	[142]
Cattle ($n = 8$)	Faecal and nostril samples	API 20E galleries (bioMérieux)	ARDRA	*A. baumannii*	Yes	2008	[22]
Pig ($n = 1$)	Faeces	MALDI-TOF/MS	None	*A. baumannii*	Yes	2015	[76]
Pig ($n = 8$)	Recovered from faecal specimens, skin, nostril and ear swabs	NM	ARDRA and PCR of $bla_{\text{OXA-51-like}}$ gene	*A. baumannii*	Yes	2011	[75]
Pig ($n = 1$)	Lung	NM	NM	*A. baumannii*	No	2013	[77]
Pig ($n = 8$)	Faecal samples	API 20E galleries, (bioMérieux)	ARDRA	*A. baumannii*	Yes	2008	[22]
Meat		MALDI-TOF/MS (Bruker)	None	*A. baumannii*	Yes	2014	[41]

Table 1 (*Continued*)

Animal	Infection site	Identification method	Reference methodology	Species identification at time of publication	Reliable identification	Year of publication	Reference
	Chicken (n = 43), turkey (n = 4), veal (n = 9), pork (n = 3) and beef (n = 3)						
American mink (*Neovison vison*) cadavers (n = 3)	Liver and lung	MALDI-TOF/MS (Bruker)	Sequencing of 16S ribosomal DNA	*A. baumannii*	Yes	2015	[102]
European mink (*Mustela lutreola*) (n = 1)	Lung and kidney	API20NE galleries and MALDI-TOF/MS	None	*A. baumannii*	Yes	2017	[103]
Falcon (n = 12)	Cutaneous lesions	Sequencing of 16S ribosomal DNA amplified by PCR directly from DNA extracted from fresh tissue	Sequence analysis of the 16S–23S rRNA gene spacer region	*A. baumannii*	Yes	2010	[104]
Fowl (n = 3)	Faeces	MALDI-TOF/MS	None	*A. baumannii*	Yes	2015	[76]
Parrot (n = 1)	Choanal swab	MALDI-TOF/MS (Bruker)	WGS	*A. baumannii*	Yes	2017	[144]
Others (n = 13), including rabbit, ferret, snake, rat and duck	NM specifically	MALDI-TOF/MS (Bruker)	*gyrB* multiplex PCR	*A. baumannii*	Yes	2017	[89]

UTI, urinary tract infection; NM, not mentioned; CVC, central venous catheter; BAL, bronchoalveolar lavage; MALDI-TOF/MS, matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry; WGS, whole-genome sequencing; ARDRA, amplified ribosomal DNA restriction analysis.

comprising AdeI (the MFP) and AdeJ (transporter) together with AdeK (OMP), was found to confer resistance to β-lactams, aminoglycosides, fluoroquinolones and structurally unrelated compounds [28]. The first member of the RND family of exporters discovered in *A. baumannii* was the AdeABC system, which is known to pump out mostly aminoglycosides, tetracyclines, macrolides and fluoroquinolones [10,29,30]. In addition to these resistance mechanisms, *A. baumannii* may acquire other resistance genes that specify for aminoglycoside-modifying enzymes, tetracycline efflux, sulfonamide resistance dihydropteroate synthase and carbapenemases [10,31–34]. Among the carbapenemases, which are specific β-lactamases able to hydrolyse almost all classes of β-lactam antimicrobials [10], the OXA-type carbapenemases (OXA-23, OXA-24/40, OXA-58 group, OXA-143 group and OXA-235 group) as well as the KPC and NDM carbapenemases have already been acquired by human *A. baumannii* isolates, seriously compromising treatment outcomes [2,3,10,35–37]. Of concern, carbapenem resistance is nowadays becoming common, accounting for the majority of *A. baumannii* strains in many hospitals over the world [10], with colistin (polymyxin E) remaining the last-resort antimicrobial option [23]. The emergence of colistin-resistant *A. baumannii* is a serious public-health concern as it limits therapeutic options for patients [38]. Colistin resistance has been attributed to the loss of lipopolysaccharide (LPS) and to mutations into the PmrAB operon that lead to the addition of phosphoethanolamine to the lipid A region of LPS through activation of the phosphoethanolamine transferase PmrC [39,40].

Carbapenem resistance has been identified in different *Acinetobacter* spp. from animals including *A. baumannii*, the majority of them being associated with clinical infection cases (Table 2).

Tracking antimicrobial resistance genes in *A. baumannii* as well as in other *Acinetobacter* spp. from animals revealed that they share common genes and genetic elements as those isolated from humans (Table 2). Among the isolates that acquired a carbapenemase gene, $bla_{\text{OXA-23}}$ appears to be the most promiscuous since it has been identified in different animal hosts associated with transposons and plasmids, whereas $bla_{\text{NDM-1}}$, $bla_{\text{IMP-1}}$, $bla_{\text{OXA-58}}$ and $bla_{\text{OXA-72}}$ are so far sporadically identified in different *Acinetobacter* spp. In addition to acquired carbapenemases, these isolates may also contain resistance genes conferring resistance to other classes of antimicrobials such as aminoglycosides, tetracyclines, sulphonamides, phenicols and macrolides (Table 2). Additionally, a few studies reported the presence of colistin resistance in *Acinetobacter* spp. from meat, but the resistance mechanisms have not been characterised [41,42]. It should be noted that the number of studies characterising the antimicrobial resistance mechanisms of *Acinetobacter* spp. of animal origin is still very low compared with the large number of studies reporting resistance genes in human isolates [32,34,37,43,44].

Bacterial factors known to play a role in the pathogenesis of *A. baumannii* are numerous and versatile, likely contributing to its ability to survive and adapt in different environments and also to cause a variety of infections both in humans and animals [32,45,46]. The virulence factors include porins, surface structures such as capsular polysaccharides and LPS, phospholipases, iron acquisition systems, outer membrane vesicles, protein secretion systems, regulatory proteins, biofilm-associated proteins, as well as several different types of binding proteins and metabolic and survival profiles such as utilising peptide nitrogen sources more efficiently and the thickness of biofilms formed, respectively [32,45,46]. Alterations in cell wall synthesis [the UDP-*N*-acetylmuramate–l-alanine ligase (MurC) protein] and upregulated virulence-associated proteins (OmpA and YjjK) are suggested to be fundamental for pathogenesis and virulence in the airways [47].

The demonstrated ability of nosocomial isolates to grow as a biofilm both on biotic and abiotic surfaces is believed to play a significant role in their persistence and antimicrobial resistance [30,48]. Consistently, although biofilm-infected wounds did not show marked differences in wound closure, the repaired skin demonstrated a disrupted epidermal barrier function [49]. This altered function was associated with two putative acyltransferases in *A. baumannii* designated LpxLAb and LpxMAb, which transfer one and two lauroyl (C12:0) acyl chains, respectively, during lipid A biosynthesis. LpxMAb-dependent acylation of lipid A is essential for *A. baumannii* desiccation survival, a key mechanism for survival in hospital settings [50]. Of note, iron starvation is not sensed as an overall biofilm-inducing stimulus by *A. baumannii*, illustrating the impressive iron-withholding capacity of this bacterium [51].

Table 2
Transmissible antimicrobial resistance genes identified in carbapenemase-producing *Acinetobacter* spp. from animals.

Antimicrobial class/resistance gene	*Acinetobacter* spp.	Animal host	Country	Genetic location (plasmid/transposon)	Reference
Carbapenems					
bla$_{OXA-23}$	*A. baumannii*	Dog	Germany	Plasmid:Tn*2008*	[89]
	A. baumannii	Cat	Germany	pOXA-23-IHIT7853	[90]
	A. baumannii	Dog	France	N/D	[91]
	A. baumannii	Cat, dog	France	Chromosome:Tn*2008B*	[5]
	A. baumannii	Cat	Portugal	Tn*2006*	[80]
	A. baumannii	Dog	Thailand	Tn*2006*	[81]
	A. baumannii	Cattle, pig, fowl	Lebanon	N/D	[76]
	A. variabilis (15TU)	Cattle	France	Unknown:Tn*2008*	[100]
	A. indicus-like	Cattle	Germany	Chromosome:ΔTn*2008*	[101]
	A. radioresistens	Cat, dog	Japan	N/D	[143]
	Acinetobacter sp.	Horse	Belgium	N/D	[93]
bla$_{OXA-24}$	*A. baumannii*	Cattle	France (Reunion Island)	N/D	[142]
bla$_{OXA-58}$	*A. pittii*	Dog, cat	Germany	pAP24944-OXA58	[143]
	A. baumannii	Fowl	Lebanon	N/D	[76]
bla$_{OXA-72}$	*A. baumannii*	Parrot	Luxemburg	pIHIT32296	[144]
bla$_{NDM-1}$	*A. baumannii*	Pig	China	pNDM-AB	[77]
	A. lwoffii	Chicken	China	pAL-01	[147]
	A. lwoffii	Cat	China	pNDM-Iz4b	[77]
bla$_{IMP-1}$	*A. radioresistens*	Cat, dog	Japan	N/D	[143]
Aminoglycosides					
aph(3′)-VI (*aph6*)	*A. baumannii*	Pig	China	pNDM-AB	[77]
	A. baumannii	Cat	Germany	N/D	[90]
	A. radioresistens	Cat	Japan	N/D	[143]
aph(3′)-Ic	*A. pittii*	Dog, cat	Germany	N/D	[89]
	A. indicus-like	Cattle	Germany	N/D	[101]
aac(3)-Ia (*aac1*)	*A. baumannii*	Dog	Germany	N/D	[89]
	A. baumannii	Cat	Germany	N/D	[90]
	A. baumannii	Dog	Thailand	N/D	[81]
aac(3)-IIc (*aacC2*)	*A. pittii*	Dog, cat	Germany	N/D	[89]
aac(3)-IIa	*A. indicus*-like	Cattle	Germany	N/D	[101]
aac(6′)-31	*A. radioresistens*	Cat, dog	Japan	N/D	[143]
aac(6′)-Im	*A. baumannii*	Dog	Thailand	N/D	[81]
aadA1	*A. baumannii*	Cat	Germany	N/D	[90]
aadB	*A. indicus*-like	Cattle	Germany	N/D	[101]
	A. radioresistens	Cat, dog	Japan	N/D	[143]
strA–strB	*A. baumannii*	Cat	Germany	pOXA-23-IHIT7853	[90]
	A. baumannii	Cat	Portugal	N/D	[80]
	A. baumannii	Dog	Thailand	N/D	[81]
	A. pittii	Dog, cat	Germany	pAP24944-OXA58	[89]
	A. radioresistens	Cat	Japan	N/D	[143]
	A. indicus-like	Cattle	Germany	N/D	[101]
Tetracyclines					
tet(A)	*A. baumannii*	Cat	Germany	N/D	[90]
	A. indicus-like	Cattle	Germany	N/D	[101]
tet(B)	*A. baumannii*	Cat	Portugal	N/D	[80]
	A. baumannii	Dog	Thailand	N/D	[81]
tet(X)	*A. indicus*-like	Cattle	Germany	N/D	[101]
tet(Y)	*A. indicus*-like	Cattle	Germany	N/D	[101]
tet(39)	*A. pittii*	Dog, cat	Germany	pAP24944-OXA58	[89]
Sulfonamides					
sul1	*A. baumannii*	Cat	Germany	N/D	[90]
	A. radioresistens	Cat, dog	Japan	N/D	[143]
	A. indicus-like	Cattle	Germany	N/D	[101]
sul2	*A. pittii*	Dog, cat	Germany	pAP24944-OXA58	[89]
	A. radioresistens	Cat	Japan	N/D	[143]
	A. indicus-like	Cattle	Germany	N/D	[101]
Macrolides					
msr(E)–*mph*(E)	*A. baumannii*	Pig	China	pNDM-AB	[77]
Phenicols					
floR	*A. indicus*-like	Cattle	Germany	N/D	[101]
catA1	*A. baumannii*	Cat	Germany	N/D	[90]

N/D, not determined.

4. Species identification and genotyping

Acinetobacter of the ACB complex can be identified to species level using MALDI-TOF/MS. Of note, MALDI-TOF/MS and other systems are as good as their database, i.e. they should include reference strains of all species, preferably multiple strains per species to cover the variation within species. As a consequence, MALDI-TOF/MS allows the identification of *A. baumannii*, *A. pittii*

and *A. nosocomialis* with acceptable accuracy. It does not yet identify *A. dijkshoorniae* and *A. seifertii*, but these species should also be identifiable by MALDI-TOF/MS once their mass spectra are introduced into the database [52–54]. However, molecular techniques are still necessary to ensure unambiguous species identification [55].

The use of $bla_{\text{OXA-51}}$ as a target gene has been advocated but is not recommended since it may lead to false identification owing to amplification of variants and the presence of plasmid-located $bla_{\text{OXA-51-like}}$ genes in *A. nosocomialis* and in some non-*baumannii Acinetobacter* spp. such as in one clone of *Acinetobacter* genomic species close to 13TU [56,57]. In addition, multiplex PCR showed atypical $bla_{\text{OXA-51-like}}$ amplification products in three clinical *A. baumannii* isolates (Ab-508, Ab-511 and Ab-653) recovered from South Africa, South Korea and Turkey, respectively [57]. Multiplex PCR targeting either *gyrB* alone or in combination with internal fragments of the 16S–23S rRNA intergenic region and the *recA* gene has been shown to be useful to differentiate *A. baumannii*, *A. pittii*, *A. calcoaceticus* and *A. nosocomialis* [58–60].

Molecular methods have also been developed for genotyping and distinction between genetically diverse strains. These methods include whole-genome sequencing (WGS), pulsed-field gel electrophoresis (PFGE), multilocus variable-number tandem repeat analysis (MLVA), amplified fragment length polymorphism (AFLP) analysis, RNA spacer fingerprinting, rapid amplification of polymorphic DNA (RAPD), repetitive extragenic palindromic PCR (rep-PCR), single-locus genotyping (e.g. *rpoB*, *adeB*, *gyrB*, *recA* and $bla_{\text{OXA-51-like}}$ genotyping), trilocus sequence typing (3LST) (*ompA*, *csuE* and $bla_{\text{OXA-51-like}}$ genes) and MLST [12,61–64]. Currently, both the Pasteur and Oxford MLST schemes remain the most widely used genotyping methods for characterisation of *Acinetobacter* spp., although WGS will soon become essential, especially in outbreak situations [12]. So far, PFGE and PCR fingerprinting methods still represent methods with high resolving capacity to identify clones [62,65]. Other rapid molecular diagnostic methods, such as the single-locus sequence-based typing of $bla_{\text{OXA-51-like}}$ genes, have been used for rapid assignment of *A. baumannii* clinical isolates to IC lineages, and multilocus broad PCR coupled with electrospray ionisation mass spectrometry (PCR/ESI-MS) has been developed as an alternative to MLST [2,66–70].

Furthermore, phenotypic features and antimicrobial spectra as well as plasmid typing and resistance island typing may be useful to some extent for epidemiological studies [64]. All these different epidemiological methods have been evaluated and discussed in a recent review according to the setting of application and the type of investigation, such as population structure studies, epidemiological studies as well as local and large-scale investigation of *A. baumannii* dissemination and outbreaks [69].

5. Zoonotic aspects

The last two decades witnessed a surge in the incidence of infections due to several highly antimicrobial-resistant bacteria in hospitals worldwide. *Acinetobacter baumannii* is one such organism that can develop from an occasional respiratory pathogen into a major nosocomial pathogen [1,10]. Besides methicillin-resistant *S. aureus* (MRSA), MDR *A. baumannii* belongs to the most frequently isolated bacteria during outbreaks in burn units, where they were also recovered from staff and environmental samples [71]. Outbreaks within a hospital may also be caused by several different *A. baumannii* strains, including those resistant to carbapenems, which may be introduced repeatedly or maintained in hospitals unnoticed. This emphasises the need for molecular typing to trace back potential sources of the isolates and to implement infection control interventions [72,73].

It has been stated that animals can be a potential reservoir of *A. baumannii* and contribute to the dissemination of new emerging carbapenemases [74]. However, clear evidence demonstrating the role of animals in the dissemination of *Acinetobacter* spp. to humans is lacking. Nevertheless, the situation may be different between food-producing animals and companion animals, which are in more direct contact and closer vicinity with humans and are more prone to transfer or acquire *A. baumannii*. In addition, studies reporting *Acinetobacter* spp. in food-producing animals were done on healthy animals, whilst those of *A. baumannii* in companion animals include both carriage as well as clinical infection.

In food-producing animals, it has been shown that *Acinetobacter* spp. isolates were not MDR and lacked significant antimicrobial resistance features such as resistance islands (RIs), class 1 integrons and IS*Aba1*, suggesting that MDR *A. baumannii* found in hospitals may not have directly evolved from such animals and from food products made thereof [75]. Another study using PFGE typing also showed that *A. baumannii* isolated from food-producing animals were not MDR and belonged to a different pool from those of humans [22]. However, raw meat has been found to contain *A. baumannii* and may still play a role as a vehicle for transmission of this bacterium from animals to humans [41,42]. In Switzerland, *A. baumannii* was present in 25% of retail meat samples, with those derived from poultry being the most contaminated (48%) [41]. Resistance to piperacillin/tazobactam, ciprofloxacin, colistin and tetracycline was only sporadically observed (ca. 2–5%). The absence of resistance to carbapenems also does not support the speculation of an animal reservoir of *A. baumannii* with mobile carbapenemase genes. In addition, the strains were genetically very diverse from each other and belonged to 29 different STs, forming 12 singletons and six CCs, of which three were new (CC277, CC360 and CC347). Of note, *A. baumannii* belonging to CCs already detected in humans (i.e. CC32, CC33 and CC79) were found in these meat samples, emphasising that food cannot be excluded as a potential source for dissemination. In Portugal, different *Acinetobacter* spp. were detected in all 50 meat products (chicken, turkey, pork and beef) analysed, with 166 isolates identified to belong to thirteen different *Acinetobacter* spp. [42]. The most common species was *Acinetobacter guillouiae* ($n = 35$), followed by *Acinetobacter johnsonii* ($n = 25$) and *Acinetobacter bereziniae* ($n = 20$). Of the 166 strains, 31 were identified as members of the *A. baumannii* group including *A. baumannii* ($n = 7$), *A. pittii* ($n = 12$), *A. seifertii* ($n = 8$) and *A. nosocomialis* ($n = 4$) [42]. Among the seven isolates identified as *A. baumannii*, one from turkey exhibited resistance to amikacin, tetracycline and colistin and one from chicken was resistant to meropenem [42]. In Lebanon, MLST analyses of *Acinetobacter* spp. from different environmental, food and animal origins revealed the presence of 36 STs, among which 24 were novel. $bla_{\text{OXA-51}}$ sequence-based gene typing showed the presence of 34 variants, among which 21 were novel and all were isolated from animals. Finally, 30 isolates had new partial *rpoB* sequences, indicating the high genetic diversity among *Acinetobacter* spp. and the importance of accurate identification methods. Overall, 161 *Acinetobacter* spp. isolates were recovered, among which 42 were identified as *A. baumannii* by *rpoB* gene sequencing. The other identified species were *A. pittii* ($n = 61$), *A. bereziniae* ($n = 10$), *A. calcoaceticus* ($n = 4$), *A. johnsonii* ($n = 1$), *Acinetobacter lwoffii* ($n = 1$), *Acinetobacter schindleri* ($n = 3$), *Acinetobacter radioresistens* ($n = 1$), *Acinetobacter beijerinckii* ($n = 1$), *Acinetobacter junii* ($n = 1$), *Acinetobacter soli* ($n = 1$), *Acinetobacter gerneri* ($n = 1$), *Acinetobacter variabilis* ($n = 4$) as well as 30 possible novel *Acinetobacter* spp. This wide variability and uniqueness of STs does not support the idea of animals as a reservoir of (nosocomial) *A. baumannii* either. Furthermore, *A. baumannii* was detected in 6.9% of the environmental water samples, 2.7% of the milk samples, 8.0% of the meat samples, 14.3% of the cheese samples and 7.7% of

the animal samples. All isolates showed a susceptible phenotype against most of the antimicrobials tested and lacked carbapenemase-encoding genes, except one carrying $bla_{OXA-143}$ [74]. Importantly, a few studies reported the presence of acquired carbapenemase genes in *A. baumannii* from food-producing animals, such as bla_{OXA-23} in a cow and a pig in Lebanon and bla_{NDM-1} in a pig in China [76,77], indicating that further attention must be paid to this potential reservoir.

The presence of *A. baumannii* in companion animals has been investigated in clinical settings and frequently in association with infections. The prevalence of *A. baumannii* carriage was 6.5% in dogs and cats [9 carriers (2 cats and 7 dogs) out of 138 animals] in a veterinary clinic on Réunion Island, which belongs to French Overseas Departments [78]. In this population, hospitalisation in a veterinary clinic (>1 day) and antimicrobial treatment administered within the 15 preceding days were significantly associated (odds ratio = 10.8 and 4.4, respectively) with *A. baumannii* carriage [78]. Of importance, an increase in the prevalence of MDR *Acinetobacter* spp. (52 *A. baumannii*, 3 *A. pittii* and 1 unidentified) was observed over 9 years (from 2000–2008) in hospitalised companion animals at Justus-Liebig-University in Giessen, Germany [79]. PFGE and AFLP typing revealed the presence of IC types I, II and III, suggesting possible exchange of *A. baumannii* between humans and animals [79]. Similarly, 19 clinical isolates of *A. baumannii* collected from dogs ($n = 12$), horses ($n = 4$) and cats ($n = 3$) in Switzerland were analysed and also belonged to IC types I, II and III [3]. Recent studies revealed the presence of acquired carbapenemases in clinical *A. baumannii* isolates from companion animals, suggesting that they may be related to those from humans (Table 2). In two cases of urinary tract infection (UTI) in a cat from Portugal and a dog from Thailand, OXA-23-producing ST2 *A. baumannii* was identified [80,81]. *Acinetobacter baumannii* ST2 producing OXA-23 were also reported in these countries in humans, indicating that such clones may be adapted both to humans and animals, representing a zoonotic lineage and possible community acquisition [80,81]. Another study revealed a possible endemicity of OXA-23-producing ST25 *A. baumannii* from UTIs in cats and dogs in France, but the epidemiology appeared to be independent to that of humans, since ST25 *A. baumannii* from humans in this country mostly harboured OXA-58 [5,82].

To date, the zoonotic role of food-producing animals as reservoir for MDR *Acinetobacter* spp. appears to be low, even if carbapenemase-producing *Acinetobacter* spp. including *A. baumannii* have been sporadically isolated from cattle and pigs. However, the presence of *A. baumannii* in meat indicates that food may contribute to the dissemination of this bacterium in the community. On the other hand, infections caused by *A. baumannii* in animals and humans are more likely to be associated with MDR isolates that belong to the same genetic lineage but whose epidemiological origin may differ [3,79]. The emergence of carbapenemase-producing *A. baumannii* in animals and the presence of possible zoonotic lineages emphasise the importance of avoiding the selection and spread of MDR *A. baumannii* in animals and humans.

6. Veterinary host spectrum

The most frequently hospitalised animals are companion animals, with dogs, cats and horses being most relevant globally. As a consequence, most data regarding *A. baumannii* infections concern these animal species (Table 1). In general, these infections were commonly hospital-acquired and involved various body sites, with a slight preponderance of wound infections and abscesses. Furthermore, the majority of animals had underlying diseases and risk factors that could favour nosocomial infection [3]. Clinical and epidemiological evidence indicated that these bacterial pathogens were responsible for an increase both in morbidity and mortality with ca. 15% [3] to 50% [83] of systemic infections resulting in death [3–5,79,83]. As horizontal transmission of *A. baumannii* may occur from human patients to personnel and to other patients in human hospital settings [1,10,84], we emphasise that *A. baumannii* behaves to some extent as such in veterinary hospitals, affecting severely ill patients or those with an underlying condition or with indwelling devices.

6.1. Dogs

A total of 7% of cultures sent for bacteriological culture and susceptibility testing from canine intensive care unit (ICU) patients in the USA were positive for *Acinetobacter* spp. [85]. These samples were routinely submitted at the discretion of the clinician attending the case with input from board-certified critical care specialists. However, it should be noted that dogs also carry *Acinetobacter* spp. in their oral flora as has been reported previously [86]. This finding underlines that *Acinetobacter* spp. are widely distributed in different natural niches and, apart from *A. baumannii* that developed into a clinically relevant species, the precise ecology and epidemiology of *Acinetobacter* is not well known. It is therefore not surprising that animals, which are in close contact with their environment, also carry different *Acinetobacter* spp. It is therefore important to use appropriate identification methods to clearly identify the *Acinetobacter* species in cases of surveillance studies. Among the Gram-negative bacteria from cases of canine pyoderma in Grenada (West Indies), the most common species isolated was *K. pneumoniae* (7.8%), followed by *Acinetobacter* spp. (6.9%) [87]. In addition, *Acinetobacter* spp. have also been reported in dogs with chronic eczema without clinical signs of secondary infection some time ago [88].

In a Swiss university veterinary hospital clinic, *A. baumannii* was isolated from 17 dogs over a 2.5-year period, representing a proportional morbidity of 7.3 per 1000 ICU admissions [83]. In seven dogs, *A. baumannii* induced systemic illness, whereas 10 dogs showed signs of local infection. In all animals with systemic infection and in two with localised infection, *A. baumannii* contributed to the death of the animal or led to its euthanasia. The low median animal trauma triage score at presentation showed that most animals from which *A. baumannii* was later isolated were not in a critical condition or a debilitated state. However, all of the animals had at least one device (e.g. indwelling urinary catheter, chest tube or central venous line) that could have served as a port of entry for *A. baumannii*. Following this report, cases of infections continued to be recorded in the same animal hospital, with 12 dogs developing an *A. baumannii* infection [3]. The isolates belonged to two main clonal lineages (as determined by rep-PCR and MLST) that were related to STs of IC I and II also of importance in human medicine. Of concern is the emergence of OXA-23 carbapenemase production in genetically diverse *A. baumannii* from dogs with UTI in France and Thailand as well as from vaginal and phlegmon samples from dogs in Germany (Table 2) [5,81,89–91]. The two isolates from Germany belonged to ST10 (IC8) with the bla_{OXA-23} gene located on Tn*2008* [89], whereas the two French isolates belonged to ST25 with bla_{OXA-23} also located on Tn*2008B*. The same isolates were also found in cats with UTI in both countries [5,90]. The isolate from Thailand belonged to ST2 and contained bla_{OXA-23} on Tn*2006*. This isolate was found to be related to an OXA-23-producing ST2 *A. baumannii* from a cat with UTI in Portugal as determined by rep-PCR [80]. These canine cases were predominantly characterised by UTI (Table 1).

6.2. Cats

In a Swiss university hospital clinic, *A. baumannii* with undefined resistance profile was isolated from two domestic shorthair cats associated with intravenous (i.v.) catheters inserted during pre-isolation over a 2.5-year period. Both cats recovered [83]. In addition, a case of necrotizing fasciitis with septic shock caused by *A. baumannii* exhibiting resistance to gentamicin, fluoroquinolones and tetracycline has been reported in a 4-year-old sterilised female domestic shorthair cat in the same hospital [92]. In Portugal, a MDR *A. baumannii* isolate caused a UTI in a 3-year-old outdoor cat presenting with dysuria and haematuria, illustrating that resistant isolates affecting felines do not exclusively circulate in hospital environments [80]. Aseptic urine culture revealed bacteriuria due to a ST2*A. baumannii*, which has been associated with IC II. The isolate produced the OXA-23 carbapenemase and also exhibited resistance to trimethoprim/sulfamethoxazole, tetracycline and fluoroquinolones. The $bla_{\text{OXA-23}}$ gene was located on transposon Tn*2006*. Another case of UTI caused by *A. baumannii* in a cat was also reported in Switzerland, but the isolate did not carry $bla_{\text{OXA-23}}$. In the same animal hospital, another cat developed an *A. baumannii* infection after liver biopsy. Both isolates were clonal as determined by rep-PCR and belonged to ST12 (IC II), suggesting a nosocomial source of infection. The two isolates exhibited resistance to trimethoprim/sulfamethoxazole, tetracycline and fluoroquinolones [3]. OXA-23-producing *A. baumannii* has also been reported in cats with UTI in Germany and France [5,90]. The isolate from Germany belonged to ST1 (IC I) and carried the $bla_{\text{OXA-23}}$ gene on a 54-kb plasmid [90]. The five isolates from France belonged to ST25 with $bla_{\text{OXA-23}}$ located on Tn*2008B*. They were obtained from different clinics and in one of them dogs were also affected with the same clone, indicating nosocomial and community dissemination of OXA-23-producing *A. baumannii* among companion animals [5]. The infected cats mainly were affected regarding UTI and skin/wounds (Table 2).

6.3. Horses

Faecal samples from 20 hospitalised horses at a teaching hospital in Belgium identified four not yet formally defined *Acinetobacter* spp. [93]. In another study from Belgium, seven *A. baumannii* were obtained from catheter tips originating from seven different horses. The organism was also isolated in pure culture from a case of thrombophlebitis [94]. Several reports indicated that the occurrence of *A. baumannii* in horses has not always been associated with disease [3,94–97]. On the other hand, *Acinetobacter* spp. sepsis and systemic inflammatory response syndrome (SIRS)-associated severe thrombocytopenia resulting in coagulopathy has been reported in a 48-h-old orphan Thoroughbred colt [98].

6.4. Cattle

Of note, only one *A. baumannii* isolate was recovered from 159 faecal samples of dairy cattle in the High Plains Region of the USA [99]. It contained a chromosomal $bla_{\text{OXA-51-like}}$ variant ($bla_{\text{OXA-497}}$), an intrinsic OXA-51 variant of *A. baumannii* that confirms species identification. In Lebanon, a clonal *A. baumannii* isolate from faecal samples from livestock (comprising pigs, fowl and cattle) was found to possess both $bla_{\text{OXA-23}}$ and $bla_{\text{OXA-58}}$ [76]. Samples from the same species also contained a VIM-2 carbapenemase-producing *P. aeruginosa*. In addition, three new $bla_{\text{OXA-51-like}}$ genes ($bla_{\text{OXA-148}}$, $bla_{\text{OXA-149}}$ and $bla_{\text{OXA-150}}$), which have not been found previously in human *A. baumannii*, were identified in strains from bovine faecal samples [75]. Of 50 faecal samples from a French dairy herd, 9 revealed *A. variabilis* (formerly 15 TU [98]) possessing the $bla_{\text{OXA-23}}$ gene on Tn*2008* [100], and 2 of 45 nasal and rectal samples from cattle in Germany revealed *Acinetobacter indicus*-like isolates harbouring $bla_{\text{OXA-23}}$ localised on an interrupted Tn*2008* transposon [101], suggesting that these *Acinetobacter* spp. may play a role in the dissemination of $bla_{\text{OXA-23}}$ to *A. baumannii*. One *A. baumannii* ST2 harbouring $bla_{\text{OXA-23}}$ was isolated from faeces of cattle in Lebanon [76].

6.5. Pigs

Like cattle, pigs may also harbour *A. baumannii*. Healthy pigs sampled at slaughterhouses in Scotland were found to contain genetically related strains as determined by PFGE and $bla_{\text{OXA-51-like}}$ gene sequencing [75]. Compared with *A. baumannii* clinical isolates ECI, ECII and ECIII, the pig isolates had different PFGE patterns and were grouped in three different clusters (A, B and C) with genetic similarity ranging between 82% and 90%. One *A. baumannii* strain isolated in China from a lung sample of a pig with pneumonia and sepsis was found to harbour the carbapenemase gene $bla_{\text{NDM-1}}$ on a plasmid [77]. In Lebanon, an OXA-23-producing *A. baumannii* ST491 was recovered from the faeces of a healthy pig [76].

6.6. Other animals

Acinetobacter baumannii has also been isolated from a variety of different animals with different clinical signs, including rabbit, ferret, snake, rat and duck in Germany [89]. An outbreak of fatal pneumonia and acute mortality associated with *A. baumannii* has been described in a group of farmed mink in the Netherlands. Gross post-mortem examination revealed extensive haemorrhagic pneumonia in examined animals. On histology, all of the lung samples showed a suppurative and haemorrhagic bronchopneumonia [102]. Another fatal case of severe fibrinous–haemorrhagic pneumonia in a mink was reported in Spain. The main lesions of an acute, severe fibrinous–haemorrhagic pneumonia were associated with proliferation of coccobacilli identified as *A. baumannii* and generalised acute–subacute congestion [103]. In ca. 60% of predominantly hybrid falcons admitted to Abu Dhabi Falcon Hospital (Abu Dhabi, UAE) with identically localised, yellowish discoloured cutaneous lesions in the thigh and lateral body wall region, *A. baumannii* was co-cultured with *Mycobacterium avium* complex [104]. Culture of a choanal swab from a captive grey parrot with progressive dyspnoea and nasal discharge in Luxemburg revealed the presence of carbapenem-resistant *A. baumannii* within a mixed bacterial culture. The *A. baumannii* isolate belonged to ST294 and contained a plasmid-mediated $bla_{\text{OXA-72}}$ gene [105]. Three *A. baumannii* ST20, ST492 and ST493 containing $bla_{\text{OXA-23}}$ were recovered from faeces of fowls in Lebanon; *A. baumannii* ST20 also contained the $bla_{\text{OXA-58}}$ gene [76].

7. Susceptibility of *Acinetobacter baumannii*

According to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) expert rules regarding human isolates, *A. baumannii* is naturally (or intrinsically) resistant to the following antimicrobials: ampicillin; amoxicillin/clavulanic acid (AMC); cefazolin; cefotaxime; ceftriaxone; ertapenem; trimethoprim; and fosfomycin [106]. Therefore, the list of antimicrobials that are usually active against wild-type *A. baumannii* infections is already short, consisting of carbapenems (doripenem, imipenem and meropenem), polymyxins [colistin (polymyxin E) and polymyxin B], tigecycline, fluoroquinolones and aminoglycosides [107]. However, most of the above available treatment options can also be reduced by further mechanisms of resistance due to the acquisition of mobile genetic elements (e.g. plasmids, IS elements, transposons) and/or chromosomal mutations (e.g. those in the *gyrA* and *parC* genes affecting fluoroquinolones) (Table 2). It should be

realised that available treatment options are mainly derived from human studies.

In a recent study [108], the best approach to treat MDR *A. baumannii* pneumonia in critically ill patients was assessed based on estimates of Bayesian network meta-analysis reported as rank probabilities to identify the relative rankings of antimicrobial treatments based on the surface under the cumulative ranking curve, ranging from 0% (statistically certain to be the worst treatment) to 100% (statistically certain to be the best treatment). The best approach to treat MDR *A. baumannii* pneumonia in critically ill patients with antimicrobials was shown to be in the following order: fosfomycin + i.v. colistin; inhaled colistin + i.v. colistin; high-dose tigecycline (defined as a total daily dose of 200 mg/day after a loading dose of 200 mg); and i.v. colistin therapy. However, resistance to these antimicrobials has also been reported and the advent of pandrug resistance might become a very plausible and concerning scenario [1,10,23,109–111]. Carbapenem-resistant *A. baumannii* (especially those producing the OXA-23 carbapenemase) has become common in many hospitals. Moreover, such isolates are frequently co-resistant to all other antimicrobial families (e.g. aminoglycosides and fluoroquinolones) routinely tested. Therefore, treatment of carbapenem- and/or pandrug-resistant *A. baumannii* infection involves the use of combinations of last-resort agents such as colistin and sometimes tigecycline, but the efficacy and safety of these approaches are yet to be well determined [10,112]. Of interest, a systematic review and meta-analysis favoured the clinical use of antimicrobial monotherapy in contrast to a tigecycline-based combination therapy regimen for the treatment of MDR *A. baumannii* infections [113]. However, the value of tigecycline combination therapy in managing pandrug-resistant or extensively drug-resistant *A. baumannii* ventilator-associated pneumonia requires further evaluation [114].

In veterinary medicine, there is no such standard approach and the treatment of diseased animals with MDR *A. baumannii* strains is mostly supportive, and specific therapies should be preferably based on in vitro antimicrobial susceptibility testing (AST) results. The emergence of carbapenem resistance in clinical *A. baumannii* isolates from animals should stress the use of AST. These isolates frequently exhibit a MDR profile associated with the acquisition of additional resistance genes conferring resistance to aminoglycosides, tetracyclines and sulfonamides (Table 2), leaving colistin one of the last active antimicrobials.

In veterinary farm animal medicine, colistin has been used for decades for the treatment and prevention of infectious diseases. Colistin has been administered frequently as a group treatment for animal gastrointestinal infections caused by Gram-negative bacteria within intensive husbandry systems. Despite its extensive use in veterinary medicine, there had been limited evidence for the development of resistance to the drug or for the transmission of resistance to colistin in bacteria that have spread from animals to humans [115]. However, resistance to colistin may occur by point mutations in *A. baumannii* [116], and a recent report showed the presence of a plasmid-mediated colistin resistance gene *mcr-1* in Enterobacteriaceae [117]. It is likely a question of time before we also see *mcr-1* in *Acinetobacter* spp.

As antimicrobial therapeutic options are also limited in veterinary medicine, in our opinion regarding the treatment of diseased animals with MDR *A. baumannii*, consulting in vitro AST should be mandatory as a standard approach before the use of last-resort antimicrobials.

8. Vaccination

The first steps towards a vaccine against *A. baumannii* include the identification of antigen candidates [118]. A limitation of this approach, however, is that the strain-to-strain variation in carbohydrate structures is so great that a multivalent vaccine to target all pathogenic *Acinetobacter* is unrealistic [119,120].

9. Prevention

As mentioned previously, members of the genus *Acinetobacter* are considered ubiquitous organisms [16] as *Acinetobacter* spp. prevail in natural environments, including soil, fresh water, oceans, trout intestinal contents, frozen shrimps, meat, sediments, the polar region and hydrocarbon-contaminated sites [1,41,119,121,122]. In addition, species of the genus *Acinetobacter* normally reside on the human skin, oropharynx and perineum [123] and have been recovered from human milk [124,125]. Early detection combined with AST and implementation of rigorous infection control measures is essential to prevent major outbreaks due to MDR *A. baumannii* that has a high potential to spread among patients [10,125] and staff [84]. The most likely explanation for the isolation of the same strain from consecutive patients in the same ward is patient-to-patient transmission of the isolate, usually through the hands of staff, contaminated equipment or the overall hospital environment [1,2,126]. It should be realised that available preventive measures are mainly derived from human studies.

Given the rapid spread of MDR *A. baumannii* in clinical institutions, two different approaches are essential to limit the spread of antimicrobial-resistant *A. baumannii*, namely infection control and antimicrobial control programmes. The first approach requires compliance with a series of methods, including strict environmental cleaning, effective sterilisation of reusable medical equipment, concentration on proper hand hygiene practices and use of contact precautions, together with appropriate administrative guidance. The second strategy is also of paramount importance. Both are essential for control of antimicrobial-resistant *A. baumannii* spread and infections [16,124,127]. In line, it is critical for the veterinary community to engage in discussions pertaining to prudent and effective use of antimicrobials and to consider ways to improve antimicrobial use practices, to optimise animal care, to reduce antimicrobial resistance selection pressure and to maintain access to important antimicrobial agents. However, there are no simple solutions to this complex problem, yet veterinarians must consider the influence of the decisions that they make on a daily basis and optimise antimicrobial use for the benefit of their patients and society as a whole [128].

Furthermore, innovations associated with potent antibacterial efficacy against MDR isolates of *A. baumannii* should be mentioned here too. For instance, light modulates the ability of *A. baumannii* to persist in the environment, its virulence against eukaryotic hosts and even its susceptibility to certain antimicrobials. The light signal is sensed through different mechanisms, in some cases involving specialised photoreceptors of the BLUF type, whereas in others directly by a photosensitiser molecule [129]. Ultraviolet light continuous (UVC) flow-through unit (45 J/cm^2) treatment of colostrum and sterile commercial whole milk inoculated with *A. baumannii* caused a significant reduction of bacterial counts [130]. In addition, both maleic anhydride-based novel cationic polymers appended with amide side chains [48] and an electrochemical scaffold that generates a local low concentration of hydrogen peroxide [129] were shown to disrupt surface-established MDR *A. baumannii* biofilms. As a consequence, these innovations were associated with potent antibacterial efficacy against MDR *A. baumannii* with minimal toxicity to mammalian cells. Furthermore, newly isolated bacteriophages can serve as potential candidates for phage cocktails to control *A. baumannii* infections [131]. Nevertheless, antimicrobials remain to date the therapeutic option and it is therefore of major importance to use them

appropriately after consultation of an antibiogram and in case of infections only.

There is an increase in awareness regarding antimicrobial stewardship in veterinary medicine [132]. Establishment of antimicrobial stewardship programmes requires: (i) co-ordination ideally by an infectious diseases specialist or at least by a clinician with a strong interest in and good knowledge of antimicrobial resistance and therapy; (ii) commitment by clinical staff; and (iii) collaboration with the microbiology laboratory.

Although the problems associated with healthcare-associated infections and the emergence of zoonotic and MDR pathogens in companion animal (dogs, cats and horses) medicine have been well known for decades, current progress with respect to practical implementation of infection control programmes in veterinary clinics has been limited [133]. Significantly reducing transmission of infections in small-animal veterinary clinics, as in human hospitals, will require 'clear goals, a committed leadership, access to resources, a best-practice mindset, effective people management, and ongoing vigilance' [134]. However, this field needs more awareness in veterinary medicine. For instance, only about one-half of the small-animal practitioners and less than one-third of the large-animal or equine practitioners reported always washing their hands before eating, drinking or smoking. The frequency of hand washing between contacts with patients was even lower [135,136]. Increasing concerns about zoonoses and antimicrobial resistance are bringing public health and private veterinary practice together. An emphasis on prevention will pay rich dividends for the safety of our patients and staff as well as the broader community [136].

10. Public-health significance

Most *A. baumannii* infections in humans involve the respiratory tract, although bacteraemia, meningitis, UTI, (prosthetic) valve endocarditis, endophthalmitis, keratitis and wound/soft tissue infection may also occur [10,16,137], especially in ICUs [1,138]. Community-acquired *A. baumannii* is a rare but serious cause of community-acquired pneumonia in tropical regions of the world. These infections predominantly affect individuals with risk factors, which include excess alcohol consumption, diabetes mellitus, smoking and chronic lung disease. Community-acquired *A. baumannii* pneumonia presents a surprisingly fulminant course and is characterised by a rapid onset of fever, severe respiratory symptoms, necrotizing fasciitis and multi-organ dysfunction, with a mortality rate reported as high as 64% [16,139–143].

The rapid spread of MDR *A. baumannii* in clinical institutions has made choosing a suitable antimicrobial to treat these infections and executing contact precautions to isolate these MDR *A. baumannii* difficult for clinicians [125,128].

Since animals may represent a reservoir for *A. baumannii*, it is of public-health importance to avoid selecting MDR strains through the uncontrolled application of clinically essential antimicrobials.

11. Conclusions

Nowadays *A. baumannii* represents an important veterinary nosocomial pathogen. However, it seems that the majority of *A. baumannii* infections in veterinary medicine are secondary and as a sequela might be fatal or lead to euthanasia in some cases. The recent report on *A. baumannii* infection in farmed mink might be regarded as an exception with reference to the associated fatal pneumonia. In other species relevant to veterinary medicine, fatal pneumonia as a sequela of *A. baumannii* infection appears rare. The emergence of cases of infections in companion animals associated with carbapenem-resistant isolates emphasises the need for accurate diagnostics. Treatment of diseased animals is often supportive and specific treatment should be based preferably on in vitro ASTs results. Although the role of animals is still not clear in the dissemination of specific clones into the human community and hospitals, studies have demonstrated that similar or even identical *A. baumannii* clones have been identified in both settings. However, this finding is limited to hospitalised animals with nosocomial infections. It is therefore of major importance to avoid the selection and spread of MDR *A. baumannii* in animals as it is in humans, to use targeted antimicrobial therapy as well as to implement infection control. Among effective control procedures of antimicrobial-resistant *A. baumannii* infections in veterinary hospitals, in our experience concentration on proper hand hygiene practices is the key.

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Competing interests

None declared.

Ethical approval

Not required.

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