Letters in Applied Microbiology

Letters in Applied Microbiology ISSN 0266-8254

Editor's Choice

REVIEW ARTICLE

Antibiotic resistance in *Escherichia coli* in husbandry animals: the African perspective

C.A. Alonso[1], M. Zarazaga[1], R. Ben Sallem[2], A. Jouini[3], K. Ben Slama[2] and C. Torres[1]

1 Área Bioquímica y Biología Molecular, Universidad de La Rioja, Logroño, Spain
2 Faculté des Sciences de Tunis, Laboratoire des Microorganismes et Biomolécules Actives, Université de Tunis El Manar, Tunis, Tunisia
3 Laboratoire d'Épidémiologie et Microbiologie Vétérinaire. Institut Pasteur de Tunis, Université de Tunis El Manar, Tunis, Tunisia

Keywords
Africa, antibiotic resistance, *Escherichia coli*, husbandry animals, β-lactamases.

Correspondence
Carmen Torres, Área Bioquímica y Biología Molecular, Universidad de La Rioja, Madre de Dios 51, 26006 Logroño, Spain.
E-mail: carmen.torres@unirioja.es

2016/2558: received 1 December 2016, revised 8 February 2017 and accepted 10 February 2017

doi:10.1111/lam.12724

Abstract

In the last few years, different surveillances have been published in Africa, especially in northern countries, regarding antimicrobial resistance among husbandry animals. Information is still scarce, but the available data show a worrying picture. Although the highest resistance rates have been described against tetracycline, penicillins and sulphonamides, prevalence of plasmid-mediated quinolone resistance genes and extended spectrum β-lactamase (ESBL) are being increasingly reported. Among ESBLs, the CTX-M-1 group was dominant in most African surveys. Within this group, CTX-M-15 was the main variant both in animals and humans, except in Tunisia where CTX-M-1 was more frequently detected among *Escherichia coli* from poultry. Certain $bla_{\text{CTX-M-15}}$-harbouring clones (ST131/B2 or ST405/D) are mainly identified in humans, but they have also been reported in livestock species from Tanzania, Nigeria or Tunisia. Moreover, several reports suggest an inter-host circulation of specific plasmids (e.g. $bla_{\text{CTX-M-1}}$-carrying IncI1/ST3 in Tunisia, IncY- and Inc-untypeable replicons co-harbouring *qnrS1* and $bla_{\text{CTX-M-15}}$ in Tanzania and the worldwide distributed $bla_{\text{CTX-M-15}}$-carrying IncF-type plasmids). International trade of poultry meat seems to have contributed to the spread of other ESBL variants, such as CTX-M-14, and clones. Furthermore, first descriptions of OXA-48- and OXA-181-producing *E. coli* have been recently documented in cattle from Egypt, and the emergent plasmid-mediated colistin resistance *mcr-1* gene has been also identified in chickens from Algeria, Tunisia and South Africa. These data reflect the urgent need of a larger regulation in the use of veterinary drugs and the implementation of surveillance programmes in order to decelerate the advance of antimicrobial resistance in this continent.

Introduction

The rapid increase in the rate of antimicrobial-resistant bacteria (AMR) reinforced by the opposite tendency in the development of new active drugs is currently one of the most serious public health threats, as recognized by the World Health Organization (http://www.who.int/dru gresistance/documents/surveillancereport/en). Resistance trends in Gram-negative bacilli are particularly alarming due to limited antibiotic options to treat infections caused by some organisms (especially Enterobacteriaceae, *Pseudomonas aeruginosa* and *Acinetobacter*) that are becoming resistant to nearly all available antimicrobials, including carbapenems.

This global emergence of multidrug-resistant bacteria has been attributed to the overuse and misuse of antibiotics, not only in human medicine but also in farming and veterinary sectors. In fact, the worldwide use of antibiotics for animal health and production purposes exceeds the use in humans, and most of the drugs designed exclusively for veterinary use are closely related or belong to the same antimicrobial classes of those indicated for humans (Aarestrup *et al.* 2008; Cantas *et al.* 2013). In Europe, according to the data

from 10 countries, the amount of veterinary antimicrobial agents sold in 2007 varied from 18 to 188 mg kg^{-1} biomass of food-producing animals (FPA), and were globally predominant the sales of sulphonamides and trimethoprim (alone or in combination), tetracyclines and β-lactams (Grave *et al.* 2010). In Japan, the amounts varied between 132 mg kg^{-1} and 153 mg kg^{-1} from 2005 to 2010 (Hosoi *et al.* 2013). In general, in developed countries, the use of antibiotics is strictly controlled and documented, but this is not the case in developing countries of the African continent where veterinary antimicrobials are often readily sold in shops and markets without prescriptions (Mainda *et al.* 2015).

Unfortunately, as expected, it has been demonstrated that the use of antimicrobial agents in husbandry is directly related to the incidence of resistant bacteria in FPA (Baron *et al.* 2014; Chantziaras *et al.* 2014). Selection of these antimicrobial-resistant (AMR) bacteria that asymptomatically colonize the gut of animals might play an epidemiological role in the spread of resistance between FPA and humans, either through direct contact or consumption of contaminated food. Inter-host transmission is more likely to happen in rural areas of developing countries with mainly subsistence-based agricultural economies, such as some regions in Africa, where people frequently live in close contact with livestock animals.

Because of the growing problem of antibiotic resistance worldwide, the number of studies focusing on the epidemiology of AMR bacteria, with special attention to extended spectrum β-lactamase (ESBL), plasmid-mediated AmpC β-lactamase (pAmpC) and carbapenemase production in Enterobacteriaceae, has increased over the last few years. The majority of these reports have been carried out in *Escherichia coli*, generally considered a useful indicator of antimicrobial resistance due to its medical importance and its presence in a wide range of hosts. This allows comparisons of prevalence between different populations and the evaluation of antimicrobial resistance transmission from animals to humans and vice versa (Van den Bogaard and Stobberingh 2000). Despite limited resources, the incidence of AMR Enterobacteriaceae in Africa, and more specifically, ESBL producers has also been studied at the local level in different countries. There are also some reviews about the general situation in the whole continent, but most of them are concentrated in human clinical and community settings (Storberg 2014; Sangare *et al.* 2015; Sekyere *et al.* 2016). In the present review, we aim to describe the situation of AMR *E. coli* in FPA and foods of animal origin in Africa, with particular focus on ESBL/pAmpC-producing isolates.

Literature search strategy and data extraction

A literature search was conducted in PubMed database for original articles reporting data on AMR *E. coli* from African countries. The review was limited to studies published in English between January 2007 and November 2016. We used combinations of relevant keywords, such as (i) '*E. coli*'; (ii) 'antimicrobial resistance', 'antibiotic resistance', 'antimicrobial usage', 'antibiotic usage', 'ESBL', 'extended spectrum β-lactamases', 'carbapenemases'; (iii) general ('livestock animals', 'farm animals', 'husbandry', 'food-producing animals') and specific animal descriptors (e.g. 'poultry', 'chickens', 'swine', 'pigs', 'cattle'); (iv) 'Africa' and the names of each African nation. References of articles were reviewed to identify any other relevant publication and, additionally, an online search was carried out to consult documents from international organizations (e.g. WHO, OIE).

The first author, country, year of sampling, sample type, sample size, animal health status, prevalence and distribution of antimicrobial resistance, resistance genes/mechanisms and molecular typing data were extracted from all the included studies.

Antimicrobial usage in livestock and resistance patterns in *E. coli*

Antimicrobial agents can be used in animal husbandry not only for the treatment and prevention of infectious diseases but also, at low and subtherapeutic doses, as growth promoters. Although their use allows to protect animal health and welfare with lower incidence of disease and also contributes to food safety, there is evidence to suggest that are leading to the spread of antimicrobial resistance (Chantziaras *et al.* 2014) with important public health implications. In this sense, on the basis of precautionary principles, European Union banned in 2006 the use of all growth-promoting antibiotics (Hao *et al.* 2014). Unfortunately, this preventive measure has not been taken all over the world, and antimicrobial agents are still used for this purpose in many developed and developing countries.

In general, the use and control of antimicrobials in the developing world, including countries of the African continent, remains largely unregulated (Maron *et al.* 2013). According to the World Organisation for Animal Health (http://www.oie.int/), many countries—mainly developing and emerging ones—do not yet have relevant legislation concerning appropriate conditions for the use of veterinary products, including antimicrobials. In some cases, legislation is totally nonexistent, and where it does exist it is very often not properly applied. Some African studies focused on the antimicrobial usage in livestock indicate

that there is an irrational use due to the unregulated access and even administration of veterinary drugs (Eager *et al.* 2012; Adesokan *et al.* 2015; Mainda *et al.* 2015). Even though in many African countries it is illegal for any person who is not a registered veterinarian to administer antibiotics, there are no strict control measures, and often farmers purchase and administer a drug without veterinary prescription and supervision (Adesokan *et al.* 2015; Mainda *et al.* 2015). Unfortunately, the use of antimicrobials in animals by untrained personnel is not confined to developing and emerging countries (http://www.oie.int/).

Furthermore, it is also important to note that the first study estimating the global trends in antimicrobial use in livestock production found that the global consumption of antimicrobials will increase in the future and this rise is likely to be driven by the growth in consumer demand for livestock products in middle-income countries and a shift to large-scale farms where antimicrobials are used routinely (Van Boeckel *et al.* 2015).

The data of different surveys conducted in Nigeria (Adesokan *et al.* 2012), Zambia (Mainda *et al.* 2015) and South Africa (Eager *et al.* 2012) about the sales of antimicrobials for farm animals indicate that, even considering variations between countries or animal species (mammals or poultry), tetracyclines and β-lactams (mainly penicillins) are among the first four leading antibiotics commonly employed in livestock animal production. Sulphonamides and macrolides are also frequently consumed antimicrobials, this last group (with reference specifically to tylosin) has been reported as the most extensively sold in South Africa for treatment and prevention of veterinary diseases and also, at subtherapeutic levels, as a registered growth promoter (Eager *et al.* 2012). Equally worrisome is the veterinary overuse of fluoroquinolones (critically important in human medicine) in some African regions, as it has been documented in a survey conducted in south-western Nigeria (Adesokan *et al.* 2015).

In a study carried out in Ghana, 395 commercial livestock keepers who practice intensive or extensive farming were interviewed about their antibiotic usage practice (Donkor *et al.* 2012). Most of the farmers used veterinary drugs mainly for disease prevention, followed by the dual purpose of prevention and treatment, only treatment and, less often, also for growth promotion. Of course, it is important to mention that the data collected from livestock keepers were self-reported, which may pose certain limitations. Another significant aspect to consider is the antibiotic administration bias commonly employed in livestock production, which is obviously different from those used in human medicine. A survey conducted in South Africa showed that in-feed dosage forms constituted almost 70% of the total of antimicrobial dosages sold in this country (Eager *et al.* 2012). This practice favours that an entire group of animals be medicated at the same time contrary to the individual treatment given to patients.

Moreover, recent data from Nigeria show a significant increasing trend in the veterinary antimicrobial consumption, which is not proportional to the annual livestock rate in the area (Adesokan *et al.* 2015). Regarding the type of livestock species, some studies suggest a relatively higher rate of antimicrobial usage among chickens, which is expressed in the more elevated percentage of resistant isolates detected among this particular animal population (Ben Sallem *et al.* 2012b; Donkor *et al.* 2012; Adenipekum *et al.* 2015). A European report based on data gathered from seven countries also showed higher resistance rates in poultry (Chantziaras *et al.* 2014). This may be explained, in part, by the fact that antibiotic usage is even higher in intensive farming, more common in poultry, where animals are reared in close proximity.

In general, although resistance percentages vary significantly among regions and studied animal populations, the highest rates have been reported for tetracycline (10·6–95%), ampicillin (6·02–95·7%) and trimethoprim/sulfamethoxazole (4·49–80%) (Wesonga *et al.* 2010; Donkor *et al.* 2012; Adelowo *et al.* 2014; Adenipekum *et al.* 2015; Mainda *et al.* 2015; Rugumisa *et al.* 2016). African studies on foods of animal origin (retail chicken or turkey meat, beef and pork carcasses) also report that resistance levels to these antimicrobials are among the most relevant ones (Soufi *et al.* 2009; Odwar *et al.* 2014; Luanda *et al.* 2016; Mrutu *et al.* 2016). This is not surprising because these drugs have been in use for the longest time both in human and veterinary medicine (Tadesse *et al.* 2012). Their combined resistance, often due to the co-location of different determinants in the same mobile genetic elements (plasmids, transposons and/or integrons), has contributed to the selection of multidrug-resistant (MDR) isolates worldwide (Wesonga *et al.* 2010; Tadesse *et al.* 2012; Adenipekum *et al.* 2015). The presence and diversity of integrons in *E. coli* from poultry, poultry meat and cattle have been studied in various reports from Africa (Soufi *et al.* 2009; Ben Slama *et al.* 2010; Inwezerua *et al.* 2014; Maamar *et al.* 2016) and showed high rates of prevalence of class 1 and class 2 integrons (60%) containing, as commonly occur, trimethoprim (*dfr*) and streptomycin (*aad*) resistance encoding genes.

Regarding other antimicrobial classes, such as quinolones and cephalosporins, the picture is even more worrying due to their vital importance in the treatment of a wide variety of infections in humans and the fact that resistance against them leaves few therapy options. Livestock as reservoirs of ESBL-producer bacteria will be

discussed in the following sections because of its relevance in terms of emerging resistance properties and the substantial literature available. Some studies performed in Tunisia and Nigeria reported unexpected high prevalence of resistance to quinolones among cattle (61·2%) (Grami *et al.* 2014) and poultry (42-55%) (Fortini *et al.* 2011; Adelowo *et al.* 2014), because this antimicrobial class was introduced later than others in livestock and is relatively expensive. Resistance to quinolones and fluoroquinolones is mainly driven by chromosomal mutations at the quinolone resistance determining region (QRDR) of DNA gyrase and topoisomerase IV. However, plasmid-mediated quinolones resistance mechanisms (PMQR) (such as, *qnr* proteins, *aac(6)-Ib-cr* aminoglycoside acetyltransferase and efflux pump proteins like QepA or OqxAB) have been progressively detected and contribute to an increase in the MIC of quinolones and fluoroquinolones. In Nigeria, a country where previous studies had reported a high prevalence of PMQR genes in clinical samples from humans (Ogbolu *et al.* 2011), an important study was carried out in poultry and pigs to characterize PMQR determinants and associated plasmids and clones (Fortini *et al.* 2011). The resulting data, which identified four PMQR gene variants (*qnrB*10, *qnrB*19, *qnrS*1 and *qepA*1) located on five different plasmid types (IncHI2, ColE, IncI1, IncN and IncX2), suggested that FPA can act as reservoirs of PMQR determinants. In particular, this work demonstrated the wide circulation in the area of *qnrS*1 gene harboured mainly in IncX2, IncN and IncI1 plasmids, *qnrB*19 in small ColE-like plasmids and *qepA*1 in plasmids of HI2 incompatibility group. Moreover, the same IncI1-ST12 plasmid harbouring *qnrS*1 was detected in commensal *E. coli* isolates from poultry in the mentioned study and in *Salmonella* strains in other independent work carried out previously in Nigeria (Fashae *et al.* 2010). Regarding other remarkable aspect of this study, all the strains carried the $bla_{\text{TEM-1}}$ gene and one was positive for CTX-M-15 β-lactamase. In fact, association between *qnr* or *aac(6)Ib-cr* and *bla* genes has been frequently reported worldwide, including some African countries (Mnif *et al.* 2012; Ben Sallem *et al.* 2014; Inwezerua *et al.* 2014; Kilani *et al.* 2015; Belmahdi *et al.* 2016; Ojo *et al.* 2016; Seni *et al.* 2016).

It is also important to highlight the detection of *E. coli* isolates carrying the emerging plasmid-mediated colistin resistance gene *mcr-1* in chickens from Algeria (Olaitan *et al.* 2016), South Africa (Perreten *et al.* 2016) and three poultry farms from Tunisia (Grami *et al.* 2016). Tunisian isolates, collected from chickens imported from France, were further characterized and demonstrated to carry $bla_{\text{CTX-M-1}}$ and *mcr-1* genes co-localized on the same IncHI2-type plasmid. This plasmid was also found in veal calves in France (Haenni *et al.* 2016) and food samples in Portugal (Tse and Yuen 2016), highlighting the impact of food animal trade on the dissemination of *mcr-1*-mediated colistin resistance. This polymyxin is currently considered a last-resort antibiotic for the treatment of highly resistant pathogenic bacteria in human medicine. However, it has been also extensively used in animal production worldwide (Rhouma *et al.* 2016) leading to a potential selection of resistant strains which reflects, once again, the urgent need of a better control in the global market of veterinary drugs.

Regarding surveillances performed on specific pathogenic strains, such as Shiga-toxin producing *E. coli* O157, a high prevalence of MDR isolates (>90%) were reported in two studies conducted in South Africa (Ateba and Bezuidenhout 2008; Iweriebor *et al.* 2015). In both cases, elevated rates of resistance against sulphametoxazol and tetracycline were reported, but even more alarming was the detection of $bla_{\text{CTX-M}}$ and bla_{CMY} genes encoding third-generation cephalosporin resistance (Iweriebor *et al.* 2015). Healthy domestic ruminants, particularly cattle and sheep, are considered natural reservoirs of these pathogens, associated to clinical diseases such as diarrhoea, haemorrhagic colitis or haemolytic uraemic syndrome in humans. Thus, indirect selection of MDR isolates can contribute to an emergence of pathogenic strains posing a risk to public health.

ESBL, plasmid-mediated AMPc and carbapenemase-producing *E. coli* in husbandry animals

The first description of ESBL-producing *E. coli* from livestock origin in the African continent dates back to 2011 (Fortini *et al.* 2011). Since then, many surveillance reports have been published, especially in northern Africa, reflecting an increased effort to understand the role of animals as reservoirs of ESBL and establish good control measures to avoid the spread of these bacteria.

Data from Table 1, which collects all the published studies on ESBL-producing *E. coli* among African livestock and derived food, show that the prevalence of these resistant bacteria among healthy animals was highly variable depending on the study (from 0% to 42·8%). This variability can be explained, in part, to differences in the methodology used. Of course, other factors like specific selective driving forces (antimicrobial usage), farming practices, geographical particularities, such as the predominance of specific clones, and even the studied animal breed (local/exotic) or age have demonstrated to affect the carriage percentages of ESBL among animals (Reist *et al.* 2013; Seni *et al.* 2016). It is also important to mention that most of the surveys were carried out among poultry in comparison with other FPA species such as

cattle or pigs. Although the vast majority of analysed samples were faeces, one study conducted in Algeria (not considered in the previously given prevalence estimation because of the small number of samples included) reported the presence of ESBL-producing *E. coli* in the reproductive and gastrointestinal tract of nine broiler breeding roosters (Mezhoud *et al.* 2015). Considering the few data available on diseased animal population (Table 2), the number of studies among cattle and poultry is more homogeneous and mainly focused on chickens suffering from colibacillosis and cattle with clinical or subclinical mastitis. The prevalence of ESBL-producing *E. coli* among sick poultry varied from 0 to 24·7% and for cattle was reported between 0 and 10% (although the number of studied *E. coli* strains was considerably lower in cattle).

Focusing on the diversity of ESBL enzymes among *E. coli* isolates from African livestock, those belonging to CTX-M-1 group have demonstrated to be more abundant than other ESBL groups or types (SHV or TEM ESBLs). In the majority of the surveys, $bla_{\text{CTX-M-15}}$ was the most common ESBL gene detected with the exception of Tunisia, where many works reported CTX-M-1 as the main enzyme among poultry (Ben Sallem *et al.* 2012b; Mnif *et al.* 2012; Maamar *et al.* 2016) (Fig. 1a). In Tunisia, CTX-M-1 has also been found as the most prevalent variant among ESBL-producing *E. coli* of healthy humans' intestinal microbiota (Ben Sallem *et al.* 2012a), whereas CTX-M-15 is the predominant enzyme among clinical ESBL-producer isolates (Dahmen *et al.* 2010; Ben Slama *et al.* 2011). In fact, $bla_{\text{CTX-M-15}}$ is in general the most frequently found ESBL gene among African hospital strains, regardless of the country (Storberg 2014). In Algeria, a study carried out in slaughtered broilers showed a high prevalence of $bla_{\text{SHV-12}}$ (Belmahdi *et al.* 2016). However, most of the isolates carrying this *bla* gene were taken from chickens belonging to the same farm and showed equal sequence type, suggesting a possible spread of a specific clone in this farm more than a picture of the situation in the country. It is also remarkable the high rate of plasmid AmpC (pAmpC) β-lactamase, belonging in all cases to CMY-2 variant, identified among commensal *E. coli* from healthy chickens in Tunisia (Ben Sallem *et al.* 2012b; Mnif *et al.* 2012; Maamar *et al.* 2016), Algeria (Belmahdi *et al.* 2016) and septicemic broilers in Egypt (Ahmed *et al.* 2013). CMY-2, together with DHA-1, is the most frequently detected pAmpC variant among human clinical isolates in Africa (Storberg 2014).

Considering carbapenemase production among *E. coli* isolates in the African continent, although many descriptions have been reported in humans (Robin *et al.* 2010; Moquet *et al.* 2011; Barguigua *et al.* 2013; Leski *et al.* 2013; Mushi *et al.* 2014) and the hospital environment (Chouchani *et al.* 2011) over the last 5 years, it has not been until very recently when the first carbapenemase-producing *E. coli* was detected in pets (Yousfi *et al.* 2016) and livestock animals (Braun *et al.* 2016). The previously described study, conducted in different dairy cattle farms from Egypt, reported four *E. coli* strains harbouring $bla_{\text{OXA-48}}$ and one carrying $bla_{\text{OXA-181}}$ carbapenemase genes, all of them phenotypically resistant to meropenem and imipenem. It is also important to mention the detection of an ertapenem-resistant ESBL-*E. coli* strain in a chicken from Nigeria. However, no carbapenemase was detected in this strain. The resistant phenotype was attributed to a synergistic effect between CTX-M-15 production and dysfunctionality of outer membrane protein (Ojo *et al.* 2016).

Although CTX-M-15 was the predominant ESBL enzyme detected among livestock in many African countries such as Nigeria, Tanzania or Egypt, only in two surveillances this *bla* gene was shown to be associated with the human epidemic clone ST131. These ST131-CTX-M-15-producing *E. coli* isolates were identified in a healthy swine from Tanzania (Seni *et al.* 2016) and the blood of three septicemic broilers from Egypt (Ahmed *et al.* 2013). ST405-D strains, which have also been considered vehicles driving CTX-M-15 worldwide and are frequently associated with clinical conditions in humans (Ben Slama *et al.* 2011; Alghoribi *et al.* 2015; Day *et al.* 2016), were also identified among healthy chickens and cattle in Tunisia and Nigeria respectively. Other clones, such as those belonging to ST10 complex (ST10 or ST617), are equally highly distributed among various livestock species and humans in many African countries like Nigeria (Aibinu *et al.* 2012; Ojo *et al.* 2016) or Tanzania (Mshana *et al.* 2016; Seni *et al.* 2016). Concerning the distribution of ESBL/pAmpC-producing *E. coli* strains according to the major phylogenetic groups (A, B1, B2, D), the majority of the studies showed a dominance of phylogroups A and B1 over isolates from healthy FPA and derived meat (Ben Slama *et al.* 2010; Schaumburg *et al.* 2014; Abdallah *et al.* 2015; Rasmussen *et al.* 2015; Maamar *et al.* 2016; Seni *et al.* 2016). Although phylogroup D has also been detected quite frequently among ESBL/AmpC producers from healthy poultry (Mnif *et al.* 2012), phylogroup B2 was present at lower rates in all the studies considered in this review. Regarding publications on diseased animals, few of them provide a phylogenetic analysis of the ESBL isolates, making it difficult to generalize.

However, epidemiology of ESBL involves not only a clonal spread of bacteria but also the horizontal transfer of *bla* genes via plasmids and/or other transferable genetic structures. In this sense, although molecular information on mobile elements is scarce in Africa, there are some works that prove the importance of specific plasmids in

Table 1 Summary of data extracted from prevalence studies on extended spectrum β-lactamase/plasmid-mediated AmpC β-lactamase (ESBL/pAMPc)-producing *Escherichia coli* in healthy husbandry animals and derived food products in Africa

Region	Country	Study period	Animal species	Type of sample	Detection test	Sample size (number of animals)	ESBL/pAmpC-producing *E. coli* prevalence (%, of total animals/samples tested)	ESBL/pAmpC enzymes (% in relation with total no. of ESBL/pAmpC)	MLST (number of ESBL/pAmpC-producing *E. coli* isolates)	Reference
Northern Africa	Tunisia	2010	Chickens	Faeces	Double disc test PCR Sequencing	136	42	CTX-M-1 (58·2), CTX-M-15 (6·0), CMY-2 (37·3)	NS[a] (025b-ST131 clone discarded by PCR)	Mnif *et al.* (2012)
	Tunisia	2011	Sheep, chickens, cattle, horse, rabbit, dromedaries	Faeces	Double disc test PCR Sequencing	80	13·8	CTX-M-1 (81·8), CMY-2 (18·2)	NS[a]	Ben Sallem *et al.* (2012b)
	Tunisia	2013	Chickens	Faeces	Double disc test PCR Sequencing	65	26·1	CTX-M-15 (88·2), CTX-M-1 (5·8), unknown (5·8)	NS[a]	Kilani *et al.* (2015)
	Tunisia	2013	Chickens	Faeces	Double disc test PCR Sequencing	137	35	CTX-M-1 (60·4), CTX-M-15 (10·4), CTX-M-14 (2·1), CMY-2 (27·1)	ST2197 (9), ST58 (7), ST405 (6), ST155 (3), ST93 (3), ST349 (3), ST542 (2), ST1196 (2), ST212 (2), ST117 (2), ST4968 (1), ST1431 (1), ST350 (1), ST1056 (1)	Maamar *et al.* (2016)
	Algeria	NS[a]	Chickens	Gastrointestinal and Reproductive tracts	Double disc test PCR	9	55·5	CTX-M-type (100)	NS[a]	Mezhoud *et al.* (2015)

(continued)

Table 1 (continued)

Region	Country	Study period	Animal species	Type of sample	Detection test	Sample size (number of animals)	ESBL/pAmpC-producing *E. coli* prevalence (%, of total animals/samples tested)	ESBL/pAmpC enzymes (% in relation with total no. of ESBL/pAmpC)	MLST (number of ESBL/pAmpC-producing *E. coli* isolates)	Reference
	Algeria	2014	Chickens	Intestinal swabs	Double disc test PCR Sequencing	61	32·8	SHV-12 (70), CTX-M-1 (10), CMY-2 (20)	ST744 (4), ST38 (1), ST1011 (12), ST2179 (1), ST5086 (2)	Belmahdi *et al.* (2016)
	Egypt	2014	Cattle	Rectal swabs	VITEK® 2 Multiplex microarray assays	266 (210 from cattle, 56 environmental samples from the stalls)	42·8 2·25 (carbapenemase producing *E. coli*)	CTX-M-15 (46·4), CTX-M-9 (2·7), TEM-type (40·5), SHV-type (0·4), CMY-type (9·9) Carbapenemase encoding genes: OXA-48 (83·3, *n* = 5), OXA-181 (16·7, *n* = 1)	NS[a]	Braun *et al.* (2016)
	Tunisia	2007	Chickens, cattle, horses, turkeys, sheep, fishes	Faeces/Meat	Double disc test PCR Sequencing	78	12·8 (ESBLs were only detected in food samples, representing 26% of them)	CTX-M-1 (60), CTX-M-14 (20), CTX-M-8 (10), SHV-5 (10)	NS[a]	Jouini *et al.* (2007)
	Tunisia	2007	Chickens, turkeys, sheep, cattle, fishes, horse	Meat	Double disc test PCR Sequencing	79	16·4	CTX-M-1 (92·8), CMY-2 (7·2)	NS[a]	Ben Slama *et al.* (2010)
	Tunisia	2009	Chickens, Turkeys	Meat	Double disc test PCR	55	0	–	NS[a]	Soufi *et al.* (2009)
	Egypt	2013	Chickens	Meat	Double disc test PCR Sequencing	112 Enterobacteriaceae (38 *E. coli*)	61·6% of the meat samples (10/38 *E. coli* isolates; 26·3%)	Among all Enterobacteria isolates: CTX-M-15 (63·8), other types belonging to CTX-M-1-group (4·3), CTX-M-9 group (2·9), SHV-type (36·2)	NS[a]	Abdallah *et al.* (2015)

(continued)

Table 1 (continued)

Region	Country	Study period	Animal species	Type of sample	Detection test	Sample size (number of animals)	ESBL/pAmpC-producing *E. coli* prevalence (%, of total animals/samples tested)	ESBL/pAmpC enzymes (% in relation with total no. of ESBL/pAmpC)	MLST (number of ESBL/pAmpC-producing *E. coli* isolates)	Reference
Eastern Africa	Tanzania	2014	Sheep, goats, chickens, pigs, cattle, dogs	Rectal/Cloacal swabs	VITEK® 2 Whole-genome sequencing (25 ESBL-producing *E. coli* isolates)	600	20·8	Among the 25 sequenced ESBL-*E. coli* isolate: CTX-M-15 (100)	Among the 25 sequenced ESBL-*E. coli* isolate: ST617 (7; cattle, chicken, dog, pig), ST1303 (3; cattle, pig), ST2852 (3; pig, dog), ST131 (2; pig, dog)	Seni *et al.* (2016)
	Zambia	2013-2014	Cattle	Faeces	–	376	0	–	–	Mainda *et al.* (2015)
	Zambia	NS[a]	Chickens	Poultry swabs samples collected at the slaughterhouse	Double disc test PCR	384	20·1	CTX-M-type (92·2), SHV-type (9·1), TEM-type (29·9)	NS[a]	Chishimba *et al.* (2016)
Western Africa	Ghana	2007	Humans, chickens, sheep, goats, pigs	Faeces	–	268	0	–	NS[a]	Donkor *et al.* (2012)
	Nigeria	2006	Chickens, pigs	Faeces	PCR Sequencing	200	0·5	CTX-M-15 (100)	NS[a]	Fortini *et al.* (2011)
	Nigeria	NS[a]	Cattle, pigs	Faeces	Double disc test PCR	350	20·57	CTX-M-type (70·8)	NS[a]	Olowe *et al.* (2015)
	Nigeria	2009-2014	Chickens	Faeces/Meat	Double disc test PCR Sequencing	405	1 (ESBLs were only detected in chicken faeces, representing 1·4% of them)	CTX-M-15 (100)	ST10 (3), ST405 (1)	Ojo *et al.* (2016)

(continued)

Table 1 (continued)

Region	Country	Study period	Animal species	Type of sample	Detection test	Sample size (number of animals)	ESBL/pAmpC-producing *E. coli* prevalence (%, of total animals/samples tested)	ESBL/pAmpC enzymes (% in relation with total no. of ESBL/pAmpC)	MLST (number of ESBL/pAmpC-producing *E. coli* isolates)	Reference
	Gabon	2011-2012	Chickens	Meat (imported)	VITEK® 2 Double disc test PCR Sequencing (only CTX-M genes)	60	23·3	CTX-M-14 (35·3), CTX-M-1 (23·5), CTX-M-32 (5·9), SHV-type (41·2), TEM-type (35·3)	NS[a]	Schaumburg *et al.* (2014)
	Ghana	NS[a]	Chickens	Meat (local/imported)	Double disc test PCR Sequencing	188	15·4	CTX-M-15 (34·5), CTX-M-1 (3·4), CTX-M-61 (3·4), CTX-M-1 group unknown subtype (10·3), CTX-M-2 group unknown subtype (6·9), blaCIT gene positive (not sequenced) (27·6), unknown ESBL/pAmpC enzyme (13·8)	ST38 (4), ST10 (2), ST354 (2), ST1158 (1), ST2167 (1), ST117 (1), ST4121 (1), ST542 (1), ST2461 (1), ST4120 (1), ST4028 (1), ST642 (1), ST162 (1), ST1304 (1), ST212 (1), ST124 (1), ST1431 (1), ST4122 (1), ST156 (1), ST155 (1), ST205 (1)	Rasmussen *et al.* (2015)

[a]NS: Not specified.

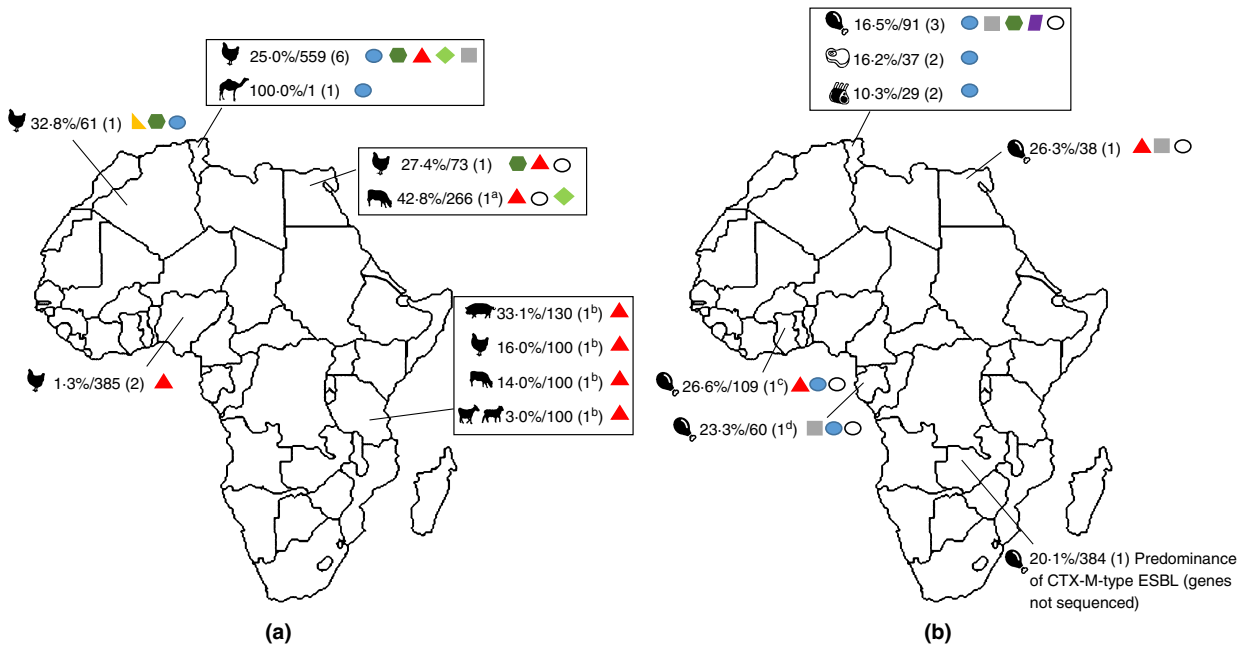

Figure 1 Husbandry animal species (a) and food products (b), prevalence of extended spectrum β-lactamase/plasmidic AmpC β-lactamase (ESBL/pAMPc)-producing *Escherichia coli* (%) and distribution of ESBL/pAmpC enzymes detected in the African continent. Prevalence at each location was calculated considering the global data of published studies [prevalence (%)/number of samples (number of studies considered at each location)]. ESBL/pAmpC enzymes are ordered, from left to right, with respect to its detection frequency. [a]Rectal samples from cattle (n = 210) and environmental samples from the stalls (n = 56) were considered. [b]Only a few samples were sequenced (n = 25). [c]Imported and locally produced chicken meat. [d]Imported chicken meat. (●) CTX-M-1; (▲) CTX-M-15; (■) CTX-M-14; (◆) CTX-M-9; (◣) SHV-12; (▮) SHV-5; (⬬) CMY-2 and (○) Other; (🐔) Poultry; (🐄) Beef; (🐑) Sheep. [Colour figure can be viewed at wileyonlinelibrary.com]

the geographical and even interspecies dissemination of ESBL determinants (Grami *et al.* 2013, Ojo *et al.* 2016; Seni *et al.* 2016). In this regard, as it has been previously shown in other continents, the dominance of IncF-type plasmids carrying the $bla_{\text{CTX-M-15}}$ gene among *E. coli* from human and animal origin has been also reported in Africa (Grami *et al.* 2014; Ojo *et al.* 2016; Seni *et al.* 2016). But this emergent CTX-M-15 encoding gene has been also associated with other less common replicon plasmids such as IncY-type, which have shown to be very prevalent in animal isolates from Tanzania. Interestingly, in the same surveillance, the presence of an Inc-untypeable plasmid, co-harbouring $bla_{\text{CTX-M-15}}$ and *qnrS1* genes and genetically homologous to a previously described one from human origin in Nigeria, was detected in various animals. In Tunisia, where CTX-M-1 enzyme is broadly disseminated among poultry, two molecular studies confirmed its frequent association with IncI1/ST3 plasmids (Ben Sallem *et al.* 2014; Grami *et al.* 2013). One of these surveys showed a comparison of clonal lineages and plasmids from healthy humans, animals and pets in Tunisia and demonstrated that $bla_{\text{CTX-M-1}}$-carrying IncI1/ST3 plasmids and $bla_{\text{CMY-2}}$-carrying IncI1/ST12 plasmids play a crucial role in the spread of these β-lactamases among different host and ecosystems (Ben Sallem *et al.* 2014). Likewise, the other work concluded that examined $bla_{\text{CTX-M-1}}$-harbouring IncI1/ST3 plasmids of *E. coli* from Tunisian poultry and pets were identical or highly similar to those reported in various animal species in Europe (Dahmen *et al.* 2012) and in some humans infected with *Salmonella enterica* (Cloeckaert *et al.* 2010), highlighting the international role of these mobile elements in CTX-M-1 epidemiology. In addition to plasmid promiscuity, the spread of CTX-M determinants is also favoured by flanking transposable elements, which can co-mobilize *bla* genes. This is the case of the IS*Ecp1* element, usually located immediately upstream $bla_{\text{CTX-M}}$ and $bla_{\text{CMY-2}}$ genes. Occasionally, it appears truncated by other insertion sequences such as IS*26* (Jouini *et al.* 2007), IS*10* (Ben Sallem *et al.* 2012b) or IS*5* (Maamar *et al.* 2016), which could affect the mobilization and/or the expression of the β-lactamase gene (Lahlaoui *et al.* 2014; Maamar *et al.* 2016).

ESBL, plasmid-mediated AMPc and carbapenemase-producing *E. coli* in animal-derived food

There are a wide number of studies concerning the microbiological quality of different types of food derived

Table 2 Distribution and clonal lineages of extended spectrum β-lactamase/plasmid-medicated AmpC β-lactamase (ESBL/pAMPc)-producing *Escherichia coli* in sick husbandry animals in Africa

Country	Study period	Animal species	Disease	Type of sample	Sample size (number of animals)	ESBL/pAmpC -producing *E. coli* prevalence (%, of total animals/samples/ isolates tested)	ESBL/pAmpC enzymes (% in relation with total no. of ESBL/pAmpC)	MLST (number of ESBL/pAmpC -producing *E. coli* isolates)	Reference
Tunisia	2011–2012	Chickens	Colibacillosis	Faeces	193	4·1	CTX-M-1 (87·5), CTX-M-9 (12·5)	NS[a]	Grami *et al.* (2013)
Tunisia	2010–2011	Chickens	Colibacillosis	Liver	60	0	–	–	Grami *et al.* (2014)
		Cattle	Clinical mastitis	Milk	10	10	CTX-M-15 (100)	ST10 (1)	
Algeria	2006–2011	Chickens	Colibacillosis	Internal organs (spleen, liver, pericardium, ovary)	NS[a] (220 *E. coli* isolates)	5	CTX-M-15 (100)	NS[a]	Meguenni *et al.* (2015)
Egypt	2008	Cattle	Clinical and subclinical mastitis	Milk	86 (99 samples, 42 *E. coli* isolates)	0 (ESBL were detected among other Gram-negative bacteria species)	–	–	Ahmed and Shimamoto (2011)
Egypt	2011	Chickens	Septicemia	Heart blood	NS[a] (100 samples, 73 APEC isolates)	27·4	CMY-2 (55), CTX-M-15 (30), SHV-2 (15)	O25b-ST131 (3) (PCR assay)	Ahmed *et al.* (2013)
Uganda	2010–2011	Cattle	Clinical mastitis	Milk	97 (97 samples, 12 *E. coli* isolates)	0	–	–	Kateete *et al.* (2013)

[a]NS: Not specified.

from FPA (milk, cheese, meat, eggs, etc.) conducted in Africa. Most of them are focused on the detection of pathogenic bacteria (especially *E. coli* 0157) in order to determine the rate of contamination of the studied product (Bankole *et al.* 2014; Ombarak *et al.* 2016) or even to analyse the resistance and/or virulence patterns of bacteria present in milk collected from cattle suffering mastitis (Ahmed and Shimamoto 2011; Kateete *et al.* 2013). However, there are just a few articles regarding the prevalence and characterization of ESBL/pAmpC *E. coli* among food products derived from healthy animals in different countries of the African continent. Remarkable data extracted from these reports is summarized in Table 1.

All the studies, but two which included different animal species (Jouini *et al.* 2007; Ben Slama *et al.* 2010), were carried out on meat samples or swabs collected from poultry carcasses. This fact may be a reflection of the religious and cultural factors which influence the diet of people in many African countries. General prevalence of ESBL/pAmpC *E. coli* among meat products was an average of 16·3%, although the risk of cross-contamination at the slaughterhouses should be considered. This percentage is significantly lower than those reported in many European countries such as Spain (84%-93·3%) (Egea *et al.* 2012; Ojer-Usoz *et al.* 2013) or the Netherlands (76·8%) (Overdevest *et al.* 2011), which may indicate that resistance rates are higher in industrial large-scale meat production.

Figure 1b shows the diversity of ESBL/pAmpC types detected among poultry (chicken and turkey), beef and sheep meat in different countries from Africa. Comparing with the distribution of enzymes detected among *E. coli* isolates from faecal poultry microbiota, a higher percentage of CTX-M-14 was identified among derived meat products. It is important to consider different factors that can help to understand these differences. First, it is difficult to elucidate the animal, human or environmental origin of the isolates due to the fact that contamination could take place at all the stages of the food-processing chain including processing, packing and distribution. Moreover, there are studies that demonstrate the contribution of imported meat from industrialized countries to the emergence of ESBL and multidrug-resistant isolates in developing countries (Schaumburg *et al.* 2014; Rasmussen *et al.* 2015). One of these works, carried out in Ghana, showed significantly higher rates of ESBL/pAmpC *E. coli* in imported chicken meat (32·9%) compared to locally reared chickens (13·9%). CTX-M-15 was the most frequently detected ESBL variant. However, $bla_{\text{CTX-M-2}}$ was also identified in two samples, one of them from an imported chicken thigh from Brazil, where this CTX-M enzyme is well known to be the most prevalent, together with CTX-M-15, among clinical isolates (Rocha *et al.* 2016). In the other study, conducted in Gabon, only imported frozen chicken meat samples were screened and a predominance of CTX-M-14, followed by CTX-M-1, was detected. Interestingly, all ESBL-producing *E. coli* isolates were identified in meat imported from Spain and, consequently, the distribution of ESBL types was shown to be in accordance to the proportion of CTX-M subtypes described in this country (Egea *et al.* 2012; Ojer-Usoz *et al.* 2013).

Regarding studies on food from healthy animals, only two performed a molecular study of the clonal lineages associated with the spread of ESBLs (Jouini *et al.* 2013; Rasmussen *et al.* 2015). Considering data from both reports, a high clonal diversity was observed, being slightly prevalent *E. coli* isolates belonging to ST155, ST10 and ST38. These sequence types have been previously identified in humans and livestock animals (Ben Sallem *et al.* 2012a; Day *et al.* 2016), also associated to CTX-M-1 group ESBLs, suggesting a potential implication of the food chain in the spread of these resistant clones among different settings.

Although none of the studies performed in Africa have reported carbapenemase-producing *E. coli* isolates among food derived from livestock animals, it is important to highlight the detection of 12 NDM-producing *Klebsiella* isolates in retail chicken meat samples from Egypt (Abdallah *et al.* 2015). Moreover, a recent study conducted in the same country has demonstrated a high rate of carbapenemase-producing *Klebsiella pneumoniae* strains, harbouring bla_{NDM}, $bla_{\text{OXA-48}}$ and/or bla_{KPC} genes in broiler chickens (35%), drinking water (25%) and humans living in contact with chickens (56%) (Hamza *et al.* 2016). Further studies based on multilocus sequence typing (MLST) or whole-genome sequencing should be performed to determine the potential inter-host transmission of these strains through direct contact and/or ingestion of derived contaminated meat.

Conclusions

The increasing rate of antimicrobial resistance bacteria is a global problem that affects both human and animal ecosystems. In the African region, the real magnitude of this issue is difficult to estimate due to the fact that antimicrobial resistance surveillance programmes are limited to a few countries (Ndihokubwayo *et al.* 2013). The potential inter-host spread of resistant clones or even their encoding determinants through direct contact or ingestion of contaminated food pose a worrisome public health risk. Although in the last decade the number of surveys in Africa has increased, available information is still scarce in many countries, especially in Southern and Eastern Africa. Moreover, further

molecular studies are required to characterize the prevailing clonal lineages and plasmids harbouring resistance encoding genes in this continent. The combination of factors such as the uncontrolled use of antimicrobials in livestock production, certain farming practices and manure management systems as well as close contact with animal may favour the selection of AMR bacteria and transmission from animals to humans and vice versa. Additionally, international livestock and derived meat trade is leading to an emergence in the dissemination of resistant strains and genetic determinants. Resistance to 'old' antimicrobials, such as tetracycline, penicillins or sulphonamides, which have been in use for a long time both in human and veterinary medicine is not surprising. However, in the last few years a significant increase in the prevalence of resistance to other clinically critical drugs (i.e. quinolones and third/fourth generation cephalosporins) has been reported among commensal *E. coli* from healthy livestock species. In most cases, resistance to both antimicrobial families is co-selected and disseminated not only by clonal spread but also horizontally via plasmids carrying *qnr* or *aac(6)Ib-cr* and *bla* genes (especially, of the CTX-M group). Furthermore, carbapenem- and colistin-resistant *E. coli* strains are also emerging among husbandry animals in Africa, which demonstrates the urgent need of a better control of the usage of veterinary drugs and the implementation of effective surveillance programmes to stop the dissemination of MDR *E. coli* strains.

Conflict of Interest

No conflict of interest declared.

References

Aarestrup, F.M., Wegener, H.C. and Collignon, P. (2008) Resistance in bacteria of the food chain: epidemiology and control strategies. *Expert Rev Anti Infect Ther* **6**, 733–750.

Abdallah, H.M., Reuland, E.A., Wintermans, B.B., Al Naiemi, N., Koek, A., Abdelwahab, A.M., Ammar, A.M., Mohamed, A.A. *et al.* (2015) Extended-spectrum β-lactamases and/or carbapenemases-producing Enterobacteriaceae isolated from retail chicken meat in Zagazig, Egypt. *PLoS ONE* **10**, e0136052.

Adelowo, O.O., Fagade, O.E. and Agersø, Y. (2014) Antibiotic resistance and resistance genes in *Escherichia coli* from poultry farms, southwest Nigeria. *J Infect Dev Ctries* **8**, 1103–1112.

Adenipekum, E.O., Jackson, C.R., Oluwadun, A., Iwalokun, B.A., Frye, J.G., Barrett, J.B., Hiott, L.M. and Woodley, T.A. (2015) Prevalence and antimicrobial resistance in *Escherichia coli* from food animals in Lagos, Nigeria. *Microb Drug Resist* **21**, 358–365.

Adesokan, H.K., Akanbi, I.O., Akanbi, I.M. and Obaweda, R.A. (2015) Pattern of antimicrobial usage in livestock animals in south-western Nigeria: the need for alternative plans. *Onderstepoort J Vet Res* **82**, 816.

Ahmed, A.M. and Shimamoto, T. (2011) Molecular characterization of antimicrobial resistance in Gram-negative bacteria isolated from bovine mastitis in Egypt. *Microbial Immunol* **55**, 318–327.

Ahmed, A.M., Shimamoto, T. and Shimamoto, T. (2013) Molecular characterization of multidrug-resistant avian pathogenic *Escherichia coli* isolated from septicemic broilers. *Int J Med Microbiol* **303**, 475–483.

Aibinu, I., Odugbemi, T., Koenig, W. and Ghebremedhin, B. (2012) Sequence type ST131 and ST10 complex (ST617) predominant among CTX-M-15-producing *Escherichia coli* isolates from Nigeria. *Clin Microbiol Infect* **18**, E49–E51.

Alghoribi, M.F., Gibreel, T.M., Famham, G., Al Johani, S.M., Balkhy, H.H. and Upton, M. (2015) Antibiotic-resistant ST38, ST131 and ST405 strains are the leading uropathogenic *Escherichia coli* clones in Riyadh, Saudi Arabia. *J Antimicrob Chermother* **70**, 2757–2762.

Ateba, C.N. and Bezuidenhout, C.C. (2008) Characterisation of *Escherichia coli* O157 strains from humans, cattle and pigs in the North-West Province, South Africa. *Int J Food Microbiol* **128**, 181–188.

Bankole, H.S., Dougnon, V.T., Johnson, R.C., Dougnon, T.J., Yehouenou, B., Kougblenou, S., Agonsa, M., Dadie, T. *et al.* (2014) Assessment of the contamination of some foodstuffs by *Escherichia coli* O157 in Benin, West Africa. *Int J Microbiol* **2014**, 417848.

Barguigua, A., El Otmani, F., Talmi, M., Zerouali, K. and Timiniouni, M. (2013) Prevalence and types of extended spectrum β-lactamases among urinary *Escherichia coli* isolates in Moroccan community. *Microb Pathog* **61–62**, 16–22.

Baron, S., Jouy, E., Larvor, E., Eono, F., Bougeard, S. and Kempf, I. (2014) Impact of third-generation-cephalosporin administration in hatcheries on fecal *Escherichia coli* antimicrobial resistance in broilers and layers. *Antimicrob Agents Chemother* **58**, 5428–5434.

Belmahdi, M., Bakour, S., Al Bayssari, C., Touati, A. and Rolain, J.M. (2016) Molecular characterisation of extended-spectrum β-lactamase- and plasmid AmpC-producing *Escherichia coli* strains isolated from broilers in Béjaïa, Algeria. *J Glob Antimicrob Resist* **6**, 108–112.

Ben Sallem, R., Ben Slama, K., Estepa, V., Jouini, A., Gharsa, H., Klibi, N., Sáenz, Y., Ruiz-Larrea, F. *et al.* (2012a) Prevalence and characterisation of extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* isolates in healthy volunteers in Tunisia. *Eur J Clin Microbiol Infect Dis* **31**, 1511–1516.

Ben Sallem, R., Ben Slama, K., Sáenz, Y., Rojo-Bezares, B., Estepa, V., Jouini, A., Gharsa, H., Klibi, N. *et al.* (2012b) Prevalence and characterization of extended spectrum beta-lactamase (ESBL)- and CMY-2-producing *Escherichia coli* isolates from heatlhy food-producing animals in Tunisia. *Foodborne Pathogen Dis* **9**, 1137–1142.

Ben Sallem, R., Ben Slama, K., Rojo-Bezares, B., Porres-Osante, N., Jouini, A., Klibi, N., Boudabous, A., Sáenz, Y. *et al.* (2014) IncI1 plasmids carrying *bla*(CTX-M-1) or *bla* (CMY-2) genes in *Escherichia coli* from healthy humans and animals in Tunisia. *Microb Drug Resist* **20**, 495–500.

Ben Slama, K., Jouini, A., Ben Sallem, R., Somalo, S., Sáenz, Y., Estepa, C., Boudabous, A. and Torres, C. (2010) Prevalence of broad-spectrum cephalosporin-resistant *Escherichia coli* isolates in food samples in Tunisia, and characterization of integrons and antimicrobial resistance mechanisms implicated. *Int J Microbiol Food* **137**, 281–286.

Ben Slama, K., Ben Sallen, R., Jouini, A., Rachid, S., Moussa, L., Sáenz, Y., Estepa, V., Somalo, S. *et al.* (2011) Diversity of genetic lineages among CTX-M-15 and CTX-M-14-producing *Escherichia col*i strains in a Tunisian hospital. *Curr Microbiol* **62**, 1794–1801.

Braun, S.D., Ahmed, M.F.E., El-Adawi, H., Hotzel, H., Engelmann, I., Weiβ, D., Monecke, S. and Ehricht, R. (2016) Surveillance of extended-spectrum beta-lactamase-producing *Escherichia coli* in dairy cattle farms in the Nile Delta, Egypt. *Front Microbiol* **7**, 1020.

Cantas, L., Shah, S.Q.A., Cavaco, L.M., Manaia, C.M., Walsh, F., Popowska, M., Garelick, H., Bürgmann, H. *et al.* (2013) A brief multi-disciplinary review on antimicrobial resistance in medicine and its linkage to the global environmental microbiota. *Front Microbiol* **4**, 96.

Chantziaras, I., Boyen, F., Callens, B. and Dewulf, J. (2014) Correlation between veterinary antimicrobial use and antimicrobial resistance in food-producing animals: a report on seven countries. *J Antimicrob Chemother* **69**, 827–834.

Chishimba, K., Hang'ombe, B.M., Muzandu, K., Mshana, S.E., Matee, M.I., Nakajima, C. and Suzuki, Y. (2016) Detection of extended-spectrum beta-lactamase-producing *Escherichia coli* in market-ready chickens in Zambia. *Int J Microbiol* **2016**, 5275724.

Chouchani, C., Marrakchi, R., Ferchichi, L., El Salabi, A. and Walsh, T.R. (2011) VIM and IMP metallo-β-lactamases in *Escherichia coli* and *Klebsiella pneumoniae* from environmental samples in a Tunisian hospital. *APMIS* **119**, 725–732.

Cloeckaert, A., Praud, K., Lefevre, M., Doublet, B., Pardos, M., Granier, S.A., Brisabois, A. and Weill, F.X. (2010) IncI1 plasmid carrying extended-spectrum β-lactamase gene $bla_{\text{CTX-M-1}}$ in *Salmonella enterica* isolates from poultry and humans in France, 2003 to 2008. *Antimicrob Agents Chemother* **54**, 4484–4486.

Dahmen, S., Bettaieb, D., Mansour, W., Boujaafar, N., Bouallèque, O. and Arlet, G. (2010) Characterization and molecular epidemiology of extended-spectrum beta-lactamases in clinical isolates of Enterobacteriaceae in a Tunisian University Hospital. *Microb Drug Resist* **16**, 163–170.

Dahmen, S., Haenni, M. and Madec, J.Y. (2012) IncI1/ST3 plasmids contribute to the dissemination of the $bla_{\text{CTX-M-1}}$ gene in *Escherichia coli* from several animal species in France. *J Antimicrob Chemother* **67**, 3011–3012.

Day, M.J., Rodríguez, I., van Essen-Zandbergen, A., Dierikx, C., Kadlec, K., Schink, A.K., Wu, G., Chattway, M.A. *et al.* (2016) Diversity of STs, plasmids and ESBL genes among *Escherichia coli* from humans, animals and food in Germany, the Netherlands and the UK. *J Antimicrob Chemother* **71**, 1178–1182.

Donkor, E.S., Newman, M.J. and Yeboah-Manu, D. (2012) Epidemiological aspects of non-human antibiotic usage and resistance: implications for the control of antibiotic resistance in Ghana. *Trop Med Int Health* **17**, 462–468.

Eager, H., Swan, G. and van Vuuren, M. (2012) A survey of antimicrobial usage in animals in South Africa with specific reference to food animals. *J S Afr Vet Assoc* **83**, 16.

Egea, P., López-Cerero, L., Torres, E., Gómez-Sánchez Mdel, C., Serrano, L., Navarro Sánchez-Ortiz, M.D., Rodríguez-Baño, J. and Pascual, A. (2012) Increased raw poultry meat colonization by extended spectrum beta-lactamase-producing *Escherichia coli* in the south of Spain. *Int J Food Microbiol* **159**, 69–73.

Fashae, K., Ogunsola, F., Aarestrup, F.M. and Hendriksen, R.S. (2010) Antimicrobial susceptibility and serovars of *Salmonella* from chickens and humans in Ibadan, Nigeria. *J Infect Dev Ctries* **4**, 484–494.

Fortini, D., Fashae, K., García-Fernández, A., Villa, L. and Carattoli, A. (2011) Plasmid-mediated quinolone resistance and β-lactamases in *Escherichia coli* from healthy animals from Nigeria. *JAC* **66**, 1269–1272.

Grami, R., Mansour, W., Dahmen, S., Mehri, W., Haenni, M., Aouni, M. and Madec, J.Y. (2013) The *bla*CTX-M-1 IncI1/ST3 plasmid is dominant in chickens and pets in Tunisia. *J Antimicrob Chemother* **68**, 2950–2952.

Grami, R., Dahmen, S., Mansour, W., Mehri, W., Haenni, M., Aouni, M. and Madec, J.Y. (2014) *bla*CTX-M-15-carrying F2:A-:B- plasmid in *Escherichia coli* from cattle milk in Tunisia. *Microb Drug Resis* **20**, 344–349.

Grami, R., Mansour, W., Mehri, W., Bouallègue, O., Boujaâfar, N., Madec, J.Y. and Haenni, M. (2016) Impact of food animal trade on the spread of *mcr*-1-mediated colistin resistance. *Euro Surveill* **21**, doi:10.2807/1560-7917.

Grave, K., Torren-Edo, J. and Mackay, D. (2010) Comparison of the sales of veterinary antibacterial agents between 10

European Countries. *J Antimicrob Chemother* **65**, 2037–2040.

Haenni, M., Poirel, L., Kieffer, N., Châtre, P., Saras, E., Métayer, V., Dumoulin, R., Nordmann, P. *et al.* (2016) Co-occurrence of extended spectrum β lactamase and MCR-1 encoding genes on plasmids. *Lancet Infect Dis* **16**, 281–282.

Hamza, E., Dorgham, S.M. and Hamza, D.A. (2016) Carbapenemase-producing *Klebsiella pneumoniae* in broiler farming in Egypt. *J Glob Antimicrob Resist* **7**, 8–10.

Hao, H., Cheng, G., Igbal, Z., Ai, X., Hussain, H.I., Huang, L., Dai, M., Wang, Y. *et al.* (2014) Benefits and risks of antimicrobial use in food-producing animals. *Front Microbiol* **5**, 288.

Hosoi, Y., Asai, T., Koike, R., Tsuyuki, M. and Suqiura, K. (2013) Use of veterinary antimicrobial agents from 2005 to 2010 in Japan. *Int J Antimicrob Agents* **41**, 489–490.

Inwezerua, C., Mendoça, N., Calhau, V., Dominques, S., Adeleke, O.E. and Da Silva, G.J. (2014) Occurrence of extended-spectrum beta-lactamases in human and bovine isolates of *Escherichia coli* from Oyo state, Nigeria. *J Infect Dev Ctries* **8**, 774–779.

Iweriebor, B.C., Iwu, C.J., Obim, L.B., Nwodo, U.U. and Okoh, A.I. (2015) Multiple antibiotic resistances among Shiga toxin producing *Escherichia coli* O157 in feces of dairy cattle farms in Eastern Cape of South Africa. *BMC Microbiol* **15**, 213.

Jouini, A., Vinué, L., Slama, K.B., Sáenz, Y., Klibi, N., Hammami, S., Boudabous, A. and Torres, C. (2007) Characterization of CTX-M and SHV extended-spectrum beta-lactamases and associated resistance genes in *Escherichia coli* strains of food samples in Tunisia. *J Antimicrob Chemother* **60**, 1137–1141.

Jouini, A., Slama, K.B., Klibi, N., Sallem, R.B., Estepa, V., Vinué, L., Ruiz-Larrea, F., Boudabous, A. *et al.* (2013) Lineages and virulence gene content among extended-spectrum β-lactamase producing *Escherichia coli* strains of food origin in Tunisia. *J Food Prot* **76**, 323–327.

Kateete, D.P., Kabugo, U., Baluku, H., Nyakarahuka, L., Kyobe, S., Okee, M., Najjuka, C.F. and Joloba, M.L. (2013) Prevalence and antimicrobial susceptibility patterns of bacteria from milkmen and cows with clinical mastitis in and around Kampala, Uganda. *PLoS ONE* **8**, e63413.

Kilani, H., Abbassi, M.S., Ferjani, S., Mansouri, R., Sghaier, S., Ben Salem, R., Jaouani, I., Douja, G. *et al.* (2015) Occurrence of bla CTX-M-1, *qnr*B1 and virulence genes in avian ESBL-producing *Escherichia coli* isolates from Tunisia. *Front Cell Infect Microbiol* **5**, 38.

Lahlaoui, H., Ben Haj Khalifa, A. and Ben Moussa, M. (2014) Epidemiology of Enterobacteriaceae producing CTX-M type extended spectrum β-lactamase (ESBL). *Med Mal Infect* **44**, 400–404.

Leski, T.A., Bangura, U., Jimmy, D.H., Ansumana, R., Lizewski, S.E., Li, R.W., Stenger, D.A., Taitt, C.R. *et al.* (2013) Identification of *bla*OXA-51, *bla*OXA-58, *bla*DIM-1 and *bla*VIM carbapenemase genes in hospital Enterobacteriaceae isolates from Sierra Leone. *J Clin Microbiol* **51**, 2435–2438.

Luanda, C.M., Buza, J., Mwanyika, G., Lyimo, B., Mrutu, R., Call, D.R. and Subbiah, M. (2016) Bacterial contamination of pork carcasses from Arusha, Tanzania. *GJAR* **3**, 806–817.

Maamar, E., Hammami, S., Alonso, C.A., Dakhli, N., Abbassi, M.S., Ferjani, S., Hamzaoui, Z., Saidani, M. *et al.* (2016) High prevalence of extended-spectrum and plasmidic AmpC beta-lactamase-producing *Escherichia coli* from poultry in Tunisia. *Int J Food Microbiol* **231**, 69–75.

Mainda, G., Bessell, P.R., Muma, J.B., McAteer, S.P., Chase-Topping, M.E., Gibbons, J., Stevens, M.P., Gally, D.L. *et al.* (2015) Prevalence and patterns of antimicrobial resistance among *Escherichia coli* isolated from Zambian dairy cattle across different production systems. *Sci Rep* **5**, 12439.

Maron, D.F., Smith, T.J. and Nachman, K.E. (2013) Restrictions on antimicrobial use in food animal production: an international regulatory and economic survey. *Global Health* **9**, 48.

Meguenni, N., Le Devendec, L., Jouy, E., Le Corvec, M., Bounar-Kechih, S., Rabah Bakour, D. and Kempf, I. (2015) First description of an extended-spectrum cephalosporin- and fluoroquinolone-resistant avian pathogenic *Escherichia coli* clone in Algeria. *Avian Dis* **59**, 20–23.

Mezhoud, H., Boyen, F., Touazi, L.H., Garmyn, A., Moula, M., Smet, A., Haesbrouck, F., Martel, A. *et al.* (2015) Extended-spectrum β-lactamase producing *Escherichia coli* in broiler breeding roosters: presence in the reproductive tract and effect on sperm motility. *Anim Reprod Sci* **159**, 205–211.

Mnif, B., Ktari, S., Rhimi, F.M. and Hammami, A. (2012) Extensive dissemination of CTX-M-1 and CMY-2-producing *Escherichia coli* in poultry farms in Tunisia. *Lett Appl Microbiol* **55**, 407–413.

Moquet, O., Bouchiat, C., Kinana, A., Seck, A., Arouna, O., Bercion, R., Breurec, S. and Garin, B. (2011) Class D OXA-48 carbapenemase in multidrug-resistant enterobacteria, Senegal. *Emerg Infect Dis* **17**, 143–144.

Mrutu, R., Luanda, C., Rugumisa, B., Mwanyika, G., Subbiah, M., Call, D.R. and Buza, J. (2016) Detection of microbial surface contamination and antibiotic resistant *Escherichia coli* on beef carcasses in Arusha, Tanzania. *Afr J Microbiol Res* **10**, 1148–1155.

Mshana, S.E., Falgenhauer, L., Mirambo, M.M., Mushi, M.F., Moremi, N., Julius, R., Seni, J., Imirzalioglu, C. *et al.* (2016) Predictors of *bla*CTX-M-15 in varieties of *Escherichia coli* genotypes from humans in community settings in Mwanza, Tanzania. *BMC Infect Dis* **16**, 187.

Mushi, M.F., Mshana, S.E., Imirzalioglu, C. and Bwanga, F. (2014) Carbapenemase genes among multidrug resistant Gram negative clinical isolates from a tertiary hospital in Mwanza, Tanzania. *Biomed Res Int* **2014**, 303104.

Ndihokubwayo, J.B., Yahaya, A.A., Desta, A.T., Ki-Zerbo, G., Asamoah-Odei, E., Keita, B., Pana, A.P. and Nkhoma, W. (2013) Antimicrobial resistance in the African Region: issues, challenges and actions proposed. *Afr Heal Monit* **16**, 27–30.

Odwar, J.A., Kikuvi, G., Kariuki, J.N. and Kariuki, S. (2014) A cross-sectional study on the microbiological quality and safety of raw chicken meats sold in Nairobi, Kenya. *BMC Res Notes* **7**, 627.

Ogbolu, D.O., Daini, O.A., Ogunledun, A., Alli, A.O. and Webber, M.A. (2011) High levels of multidrug resistance in clinical isolates of gram-negative pathogens from Nigeria. *Int J Antimicrob Agents* **37**, 62–66.

Ojer-Usoz, E., González, D., Vitas, A.I., Leiva, J., García-Jalón, I., Febles-Casquero, A. and Escolano, M de L. (2013) Prevalence of extended-spectrum β-lactamase-producing Enterobacteriaceae in meat products sold in Navarra, Spain. *Meat Sci* **93**, 316–321.

Ojo, O.E., Schwarz, S. and Michael, G.B. (2016) Detection and characterization of extended-spectrum β-lactamase-producing *Escherichia coli* from chicken production chains in Nigeria. *Vet Microbiol* **194**, 62–68.

Olaitan, A.O., Chabou, S., Okdah, L., Morand, S. and Rolain, J.J. (2016) Dissemination of the *mcr*-1 colistin resistance gene. *Lancet Infect Dis* **16**, 147.

Olowe, O.A., Adewuni, O., Odewale, G., Ojurongbe, O. and Adefionye, O.J. (2015) Phenotypic and molecular characterisation of extended-spectrum beta-lactamase producing *Escherichia coli* obtained from animal fecal samples in Ado Ekiti, Nigeria. *J Environ Public Health* **2015**, 497980.

Ombarak, R.A., Hinenoya, A., Awasthi, S.P., Iguchi, A., Shima, A., Elbagory, A.R. and Yamasaki, S. (2016) Prevalence and pathogenic potential of *Escherichia coli* isolates from raw milk and raw cheese in Egypt. *Int J Food Microbiol* **221**, 69–76.

Overdevest, I., Willemsen, I., Rijnsburger, M., Eustace, A., Xu, L., Hawkey, P., Heck, M., Savelkoul, P. *et al.* (2011) Extended-spectrum β-lactamase genes of *Escherichia coli* in chicken meat and humans, The Netherlands. *Emerg Infect Dis* **17**, 1216–1222.

Perreten, V., Strauss, C., Collaud, A. and Gerber, D. (2016) Colistin resistance gene *mcr*-1 in avian pathogenic *Escherichia coli* in South Africa. *Antimicrob Agents Chemother* **60**, 4414–4415.

Rasmussen, M.M., Opintan, J.A., Frimodt-Møller, N. and Styrishave, B. (2015) Beta-lactamase-producing *Escherichia coli* isolates in imported and locally produced chicken meat from Ghana. *PLoS ONE* **10**, e0139706.

Reist, M., Geser, N., Hächler, H., Schärrer, S. and Stephan, R. (2013) ESBL-producing Enterobacteriaceae: occurrence, risk factors for fecal carriage and strain traits in the Swiss slaughter cattle population younger than 2 years sampled at abattoir level. *PLoS ONE* **8**, e71725.

Rhouma, M., Beaundry, F., Thériault, W. and Letellier, A. (2016) Colistin in pig production: chemistry, mechanism of antibacterial action, microbial resistance emergence, and one health perspectives. *Front Microbiol* **7**, 1789.

Robin, F., Aggoune-Khinache, N., Delmas, J., Naim, M. and Bonnet, R. (2010) Novel VIM metallo-β-lactamse variant from clinical isolates of Enterobacteriaceae from Algeria. *Antimicrob Agents Chemother* **54**, 466–470.

Rocha, F.R., Pinto, V.P. and Barbosa, F.C. (2016) The spread of CTX-M-type extended-spectrum β-lactamases in Brazil: a systematic review. *Microb Drug Resist* **22**, 301–311.

Rugumisa, B.T., Call, D.R., Mwanyika, G.O., Mrutu, R.I., Luanda, C.M., Lyimo, B.M., Subbiah, M. and Buza, J.J. (2016) Prevalence of antibiotic-resistant fecal *Escherichia coli* isolates from penned broiler and scavenging local chickens in Arusha, Tanzania. *J Food Prot* **79**, 1424–1429.

Sangare, S.A., Maiga, A.I., Guindo, I., Maiga, A., Camara, N., Savadogo, S., Diallo, S., Bougoudogo, F. *et al.* (2015) Prevalence of extended-spectrum beta-lactamase-producing Enterobacteriaceae isolated from blood cultures in Africa. *Med Mal Infect* **45**, 374–382.

Schaumburg, F., Alabi, A.S., Frielinghaus, L., Grobusch, M.P., Köck, R., Becker, K., Issifou, S., Kremsner, P.G. *et al.* (2014) The risk to import ESBL-producing Enterobacteriaceae and *Staphylococcus aureus* through chicken meat trade in Gabon. *BMC Microbiol* **14**, 286.

Sekyere, J.O., Govinden, U. and Essack, S. (2016) The molecular epidemiology and genetic environment of carbapenemases detected in Africa. *Microb Drug Resist* **22**, 59–68.

Seni, J., Falgenhauer, L., Simeo, N., Mirambo, M.M., Imirzalioglu, C., Matee, M., Rweyemamu, M., Chakraborty, T. *et al.* (2016) Multiple ESBL-producing *Escherichia coli* sequence types carrying quinolone and aminoglycoside resistance genes circulating in companion and domestic farm animals in Mwanza, Tanzania, harbor commonly occurring plasmids. *Front Microbiol* **7**, 142.

Soufi, L., Abbassi, M.S., Sáenz, Y., Vinué, L., Somalo, S., Zarazaga, M., Abbas, A., Dbaya, R. *et al.* (2009) Prevalence and diversity of integrons and associated resistance genes in *Escherichia coli* isolates from poultry meat in Tunisia. *Foodborne Pathog Dis* **6**, 1067–1073.

Storberg, V. (2014) ESBL-producing Enterobacteriaceae in Africa-a non-systematic literature review of research published 2008-2012. *Infect Ecol Epidemiol* **4**, 50–55.

Tadesse, D.A., Zhao, S., Tong, E., Ayers, S., Singh, A., Bartholomew, M.J. and McDermott, P.F. (2012)

Antimicrobial drug resistance in *Escherichia coli* from humans and food animals, United States, 1950–2002. *Emerg Infect Dis* **18**, 741–749.

Tse, H. and Yuen, K.Y. (2016) Dissemination of the *mcr*-1 colistin resistance gen. *Lancet Infect Dis* **16**, 145–146.

Van Boeckel, T.P., Brower, C., Gilbert, M., Grenfell, B.T., Levin, S.A., Robinson, T.P., Teillant, A. and Laxminarayan, R. (2015) Global trends in antimicrobial use in food animals. *Proc Natl Acad Sci USA* **112**, 5649–5654.

Van den Bogaard, A.E. and Stobberingh, E.E. (2000) Epidemiology of resistance to antibiotics. Links between animals and humans. *Int J Antimicrob Agents* **14**, 327–335.

Wesonga, S.M., Muluyi, G.M., Okemo, P.O. and Kariuki, S. (2010) Antibiotic resistant salmonella and *Escherichia coli* isolated from indigenous *Gallus domesticus* in Nairobi, Kenya. *East Afr Med J* **87**, 205–210.

Yousfi, M., Touati, A., Mairi, A., Brasme, L., Gharout-Sait, A., Guillard, T. and De Champs, C. (2016) Emergence of carbapenemase-producing *Escherichia coli* isolated from companion animals in Algeria. *Microb Drug Resist* **22**, 342–346.