Revista de Ciência Veterinária e Saúde Pública

Rev. Ciên. Vet. Saúde Públ., v.6, n. 2, p. 251-261, 2019

ESCHERICHIA COLI: ANTIMICROBIAL SUSCEPTIBILITY MONITORING 2015 – 2018 IN THE NORTH REGION OF THE STATE OF RIO GRANDE DO SUL, SOUTHERN BRAZIL

(Escherichia coli: monitoramento da susceptibilidade antimicrobiana entre 2015 – 2018 no norte do Rio Grande do Sul)

LEVANDOWSKI, Rafael[1*]; DAROIT, Luciane[2]; SANTOS, Luciana Ruschel dos[2]

1. Faculdade de Agronomia e Medicina Veterinária. Curso de Medicina Veterinária, Universidade de Passo Fundo – UPF.
2. Programa de Pós Graduação em Bioexperimentação. Universidade de Passo Fundo – UPF.
*Autor para correspondência: rafaelldk28@gmail.com
Artigo enviado em: 25/04/2019, aceito para publicação em 29/06/2019
DOI: **http://dx.doi.org/10.4025/revcivet.v6i2.47685**

ABSTRACT

Commensal bacteria, such as *Escherichia coli*, are involved in the transmission of resistance genes because it is widely distributed and constantly exposed to antibiotics. In this study, we examined multidrug resistance (MDR) in 282 collections of *Escherichia coli* isolates recovered from hospitalized animals in Brazil. A total of 2186 disc diffusion susceptibility tests were performed for 22 antibiotics. We verified 100% resistance for Lincomycin, metronidazole and penicillin and for other drugs we observed: sulfonamide (77%), amoxicillin (75%), cephalothin (70%), ampicillin (57%), tetracycline (52%), doxycycline (48%), amoxicillin plus clavulanic acid (47%), cephalexin (45%), sulfamethoxazole plus trimethoprim (41%), ciprofloxacin (40%), cefazolin (40%), trimethoprim (39%), norfloxacin (34%), enrofloxacin (34%), neomycin (33%), florfenicol (27%), ceftiofur (24%), chloramphenicol (20%) and gentamicin (17%). In addition, multidrug resistance was observed in 39% (151/282) of the samples tested. The study demonstrated that E. coli isolates showed resistance to antibiotics used in human medicine and, due to the ability to transfer resistance genes, is a public health issue. Multidrug resistance limits the drug choice for the treatment of *E. coli* infections, suggesting that veterinarians seek antimicrobial alternatives.

Keywords: *Escherichia coli*, multidrug resistance, veterinary hospital.

RESUMO

Bactérias comensais, como a *Escherichia coli*, estão envolvidas na transmissão de genes de resistência por estarem amplamente distribuídas e constantemente expostas aos antibióticos. Neste estudo, analisamos a multirresistência de 282 isolados de *Escherichia coli* de animais hospitalizados no Brasil. Um total de 2186 testes de suscetibilidade por disco-difusão foi realizado para 22 antibióticos. Verificou-se 100% de resistência para Lincomicina, metronidazol e penicilina e para os demais fármacos observou-se: sulfonamida (77%), amoxicilina (75%), cefalotina (70%), ampicilina (57%), tetraciclina (52%), doxiciclina (48%), amoxicilina e ácido clavulânico (47%), cefalexina (45%), sulfametoxazol e trimetoprima (41%), ciprofloxacina (40%), cefazolina (40%), trimetoprim (39%), norfloxacina (34%), enrofloxacina (34%), neomicina (33%), florfenicol (27%), ceftiofur (24%), cloranfenicol (20%) e gentamicina (17%). Além disso, o padrão de multirresistência foi

observado em 39% (151/282) das amostras. O estudo demonstrou que os isolados de *E. coli* apresentaram resistência para antibióticos utilizados em humanos e, pela capacidade de transferência de genes de resistência, é um problema de saúde pública. O padrão de multirresistência implica na escolha do fármaco para o tratamento de infecções causadas pela bactéria, sugerindo o médico veterinário buscar antimicrobianos alternativos.

Palavras-chave: *Escherichia coli*, multirresistência, hospital veterinário.

INTRODUCTION

The indiscriminate use of antibiotics, to treat of infections or as growth promoters, is the main factor for selection and dissemination of multidrug resistant bacteria in veterinary and human medicine (LAXMINARAYAN et al., 2016). Bacteria, even when not exposed to antibiotics, are subject to horizontal transmission of virulence genes through plasmid conjugation (MATAMOROS et al., 2017). In addition, resistant strains can be transferred between animals and humans. Van Den et al. (2001) reported resistant bacterial clones isolated in different bird species as homologous agents in infections of workers with daily contact with these animals (VAN DUIJKEREN E et al., 2004; VAN DEN BOGAARD et al., 2001).

Commensal bacteria, such as *Escherichia coli*, are involved in the transmission of resistance genes because it is widely distributed and constantly exposed to antibiotics (PORSE et al., 2017). *E. coli* is the main facultative anaerobic bacterium of animal flora, including humans, and has a wide genetic variability through the horizontal transmission of genetic elements such as plasmids and phages (PORSE et al., 2017; LEIMBACH et al., 2013). When in equilibrium, it brings benefits to the host and is confined in the intestine. However, when immunosuppressed, or when gastrointestinal barriers are compromised, even non-pathogenic strains may cause infections (NATARO et al., 1998). The bacterium has been reported as resistant in strains isolated from swine, poultry, and humans, and in the latter, they were resistant even when there was no exposure to such antimicrobials (BARROS et al., 2012; BACCARO et al., 2002; PIDDOCK, 1996).

Pathogenic strains of *E. coli* are serologically classified by their somatic antigen (O) and cell surface (K). In veterinary medicine it causes diseases such as colibacillosis and mastitis, and in humans the enterohemorrhagic strain, serotype O157:H7, has emerged as a cause of severe clinical manifestations of hemorrhagic colitis, thrombocytopenia,

and renal disorders, often fatal in children (RIBEIRO et al., 2006; RIBEIRO et al., 1999; MAGALHÃES et al., 1991).

Thus, in order to understand the dynamics of antimicrobial resistance, this study aimed to verify the antimicrobial resistance profile of *E. coli* isolated in a Veterinary Hospital of northern Rio Grande do Sul, Brazil, between 2015 and 2018.

MATERIALS AND METHODS

A retrospective study was carried out on the results of *E. coli* antibiograms isolated from animals hospitalized at the Veterinary Hospital of the University of Passo Fundo (HV/UPF, Brazil) and from external samples between 2015 and 2018. The Veterinary Hospital of the University of Passo Fundo is a reference veterinary hospital and receives both internal and external samples from all the northern region of the state of Rio Grande do Sul, Brazil. Samples were isolated from different sources and from different animals, domestic and wild.

The isolated samples were confirmed by biochemical tests (Edwards and Ewing, 1972) and the antibiograms were performed by the disc diffusion method based on the recommendations of the National Committee for Clinical Laboratory Standards (NATIONAL COMMITTEE FOR CLINICAL LABORATORY STANDARDS, 2003).

The results of the antibiograms were evaluated by the standards of the Clinical and Laboratory Standards Institute (CLSI, 2013) and classified as sensitive, intermediate or resistant. The data were evaluated by Microsoft Excel Software and the multiresistance standard defined by Magiorakos (2012), as follows: multidrug resistance (MRD), non-susceptible to ≥1 agent in ≥3 classes of antibiotics. The p-value < 0.05 was considered statistically significant for linear regression analysis.

RESULTS

We verified 282 positive cultures for *Escherichia coli* between 2015 and 2018. Each sample, tested in the antibiogram for eight or fewer antibiotics, presented different resistance rates. Overall, 22 different antibiotics were evaluated in a total of 2186 trials (Table 1). Table 1 shows the prevalence of bacterial resistance to antibiotics tested in the antibiogram. The antibiotics lincomycin and metronidazole showed resistance *in vitro* in 100% of times tested, and penicillin 99% of the time. The average resistance among all antibiotics was 51%. Also according to Table 1, the most chosen antibiotic by veterinarians for the antibiogram test was enrofloxacin (11%),

Table 1 - Bacterial resistance to antibiotics in veterinary infections between the years 2015 and 2018. Passo Fundo, Brazil.

Antibiotic	2015			2016			2017			2018			Total			p-value
	nº	N	%	nº	N	%	nº	N	%	nº	N	%	nº	N	%	
AMO	53	42	79	22	17	77	49	35	71	33	23	70	157	117	75	0.0142
AMP	34	21	62	8	5	62	34	15	44	30	19	63	106	60	57	0.0841
CFE	23	14	61	22	9	41	50	18	36	27	14	52	122	55	45	0.1739
CF	18	11	61	11	9	82	17	11	65	17	13	76	63	44	70	0.2357
CZ	3	2	67	0	0	0	15	6	40	2	0	0	20	8	40	0.0233
PEN	28	27	96	10	10	100	26	26	100	16	16	100	80	79	99	0.0009
CIP	25	8	32	15	6	40	23	8	35	17	10	59	80	32	40	0.8285
EM	68	27	40	36	12	33	82	21	26	52	20	38	238	80	34	0.266
NOR	22	8	36	13	5	38	20	6	30	9	3	33	64	22	34	0.0451
LIN	6	6	100	5	5	100	8	8	100	3	3	100	22	22	100	0.0001
GEN	69	11	16	29	9	31	43	7	16	27	2	7	168	29	17	0.3006
NEO	25	12	48	18	4	22	36	12	33	7	0	0	86	28	33	0.0773
DOX	22	14	64	9	1	11	26	10	38	10	7	70	67	32	48	0.2088
TET	62	36	58	25	11	44	36	15	42	28	16	57	151	78	52	0.0268
SUL	33	25	76	2	1	50	8	7	88	0	0	0	43	33	77	0.0011
TRI	23	6	26	1	0	0	5	3	60	9	6	67	38	15	39	0.2191
CLO	16	2	13	2	0	0	9	1	11	8	4	50	35	7	20	0.5997
FIF	22	8	36	16	5	31	23	5	22	12	2	17	73	20	27	0.214
AMC	43	19	44	39	23	59	55	18	33	37	21	57	174	81	47	0.2075
SUT	37	21	57	34	10	29	64	21	33	45	21	47	180	73	41	0.5423
CTF	62	16	26	23	8	35	35	6	17	24	4	17	144	34	24	0.0996
MTZ	15	15	100	15	15	100	20	20	100	25	25	100	75	75	100	0.0001
Total	709	351	50	355	165	46	684	279	41	438	229	52	2186	1024	47	

N: total number of resistance; AMO: amoxicillin; AMP: ampicillin; CFE: cephalexin; CF: cephalothin; CZ: cefazolin; PEN: penicillin; CIP: ciprofloxacin; EM: enrofloxacin; NOR: norfloxacin; LIN: lincomycin; GEN: gentamicin; NEO: neomycin; DOX: doxycycline; TET: tetracycline; SUL: sulfonamide; TRI: trimethoprim; CLO: chloramphenicol; FIF: florfenicol; AMC: amoxicillin plus clavulanic acid; SUT: sulfamethoxazole plus trimethoprim; CTF: ceftiofur; MTZ: metronidazole.

followed by amoxicillin associated with clavulanic acid and sulfamethoxazole associated with trimethoprim, both 8% of the time.

Table 2 shows that the MRD (multidrug resistance) was noted in 60% of all antibiograms analyzed in 2015, 49% in 2016, 47% in 2017, and 58% in 2018. In general, during the four years, 39% of the multidrug resistance pattern was observed in the 282 antibiograms analyzed.

Table 2 - Time evolution of multidrug resistance *Escherichia coli* isolates between the years 2015 and 2018. Passo Fundo, Brazil.

	2015 (n = 94)		2016 (n = 47)		2017 (n = 86)		2018 (n = 55)		p-valor
Resistance	N	%	N	%	N	%	N	%	
MRD	56	60	23	49	40	47	32	58	0.0671

MRD: multidrug resistance; N: total number.

DISCUSSION

In this study, it is demonstrated that *Escherichia coli* presents a bacterial resistance rate different from other studies carried out in Brazil and worldwide (BACCARO et al., 2002; BARROS et al., 2012; REINTHALER et al., 2003). Older antibiotics, such as penicillin and sulfonamide, have shown high rates, other antibiotics may have resistance explained to their use as growth promoters, the presence of the β-lactamase enzyme or reckless use.

The presence of β-lactamase enzymes has been reported as the main mechanism of resistance to β-lactam antibiotics (WILLIAMS, 1999). Within the group of these enzymes is penicillinase, an enzyme responsible for resistance to penicillins through the hydrolysis of the beta-lactam ring (MEHTA et al., 2016). In this study, penicillin (99%), amoxicillin (75%) and ampicillin (57%) presented high rates when compared to other authors. Henquell et al. (1995), for example, reports the presence of the enzyme in 40-50% of *E. coli* strains isolated from urinary tract infections in the 1990s. The increased rate may be due to increased use of antibiotics and horizontal transmission of virulence genes among pathogens (MATAMOROS et al., 2017). The association of amoxicillin with clavulanic acid (47%) presented the

lowest rate among penicillins due to the presence of the β-lactamase inhibitor (WILLIAMS, 1999).

Other types of β-lactamases (class A and C) are responsible for hydrolyzing cephalosporins (WILLIAMS, 1999). In this study, first-generation cephalosporins: cephalexin (45%), cephalothin (70%) and cefazolin (40%) presented a moderate resistance rate and may indicate the presence of *E. coli* strains positive for the enzyme. Second-generation cephalosporin, ceftiofur (24%), had the lowest rate of resistance among all cephalosporins. There are also extended spectrum β-lactamases (ESBLs) capable of hydrolyzing third-generation cephalosporins, such as cefotaxime (JACOBY & MEDEIROS, 1991).

According to Albuquerque (2005), lincomycin is one of the antibiotics used in poultry feed as growth promoters. Several authors demonstrate complete resistance to this antibiotic. Barros et al. (2012) report that 100% of the isolates are resistant to lincomycin in poultry samples, and Ikuno et al. (2008) reported the same rate in wild bird samples. In this study 100%, of the samples were resistant to lincomycin in different animal species and types of infections, noting that other species are also exposed to resistance to the lincosamide class.

For Reese and Beets (1995) metronidazole is commonly used in amebiasis and giardiasis and is not active against staphylococci, streptococci, and *Enterobacteriaceae*. In this study, it presented resistance in 100% of the analyzed times and agrees to the author. However, for Onderdonk et al. (1979) has an *in vivo* effect even when it has high resistance *in vitro*, but only when a susceptible bacteria is present.

Gentamicin (17%) was the antibiotic that presented lower frequency of resistance and this rate appears to vary among the authors. Baccaro et al. (2002) show 86% resistance rate in piglets with diarrhea in the southwestern region of the state of São Paulo and Brito and Tagliari (2000) in 4% in the state of Paraná, both in Brazil. In cows, Malinowski et al. (2011) report 88% of antibiotic sensitivity in 99 samples from metritis and endometritis.

Florfenicol, a veterinary analog of thiamphenicol, is commonly used for bovine respiratory tract diseases and has been shown to be resistant in 92% of 48 *E. coli* strains in the United States,

differing from this study that found 27% of resistance in 282 samples (WHITE et al., 2018). White et al. (2018) also found a different rate for chloramphenicol (90% compared to 20% of this study).

Cooke et al. (1971) have already shown that animals are reservoirs of *E. coli* strains found in humans and can transfer resistance genes. This fact associated with the present study suggests that the high rate of multidrug resistance bacteria (39%) can be transferred to humans and, consequently, will make treatment difficult when antibiotics equivalent to those used in veterinary medicine are necessary. It is not always possible to compare this result with other studies since some authors define MRD without considering the classes of antibiotics.

The multidrug resistance pattern is not statistically significant (p-value > 0.05) due to the unequal number of samples tested over the four years. However, when analyzed individually, they still represent concern due to the expressive rate, evidencing that it is necessary to search for alternative antimicrobials to treat infections caused by *E. coli*.

CONCLUSION

The *Escherichia coli*, isolated from different animals, presented resistance to multiple antibiotics. Lincomycin (100%), metronidazole (100%) and penicillin (99%) had the highest resistance rates, and only two antibiotics had a 20% or less rate: gentamicin (17%) and chloramphenicol (20%). *E. coli* strains were also resistant to sulfonamide (77%), amoxicillin (75%), cephalothin (70%), ampicillin (57%), tetracycline (52%), doxycycline (48%), amoxicillin plus clavulanic acid (47%), cephalexin (45%), sulfamethoxazole plus trimethoprim (41%), ciprofloxacin (40%), cefazolin (40%), trimethoprim (39%), norfloxacin (34%), enrofloxacin (34%), neomycin (33%), florfenicol (27%) and ceftiofur (24%). In addition, multidrug resistance was observed in 39% of the 282 samples tested.

Thus, the study demonstrated that *E. coli* isolates showed resistance to antibiotics used in human medicine and, due to the ability to transfer resistance genes, is a public health issue. Multidrug resistance limits the drug choice for the treatment of *E. coli* infections, suggesting that veterinarians seek antimicrobial alternatives.

REFERENCES

ALBUQUERQUE, R.D. Antimicrobianos como promotores do crescimento. Farmacologia aplicada à avicultura: boas práticas no manejo de medicamentos. 2005.

BACCARO, M.R.; MORENO, A.M.; CORRÊA, A.; FERREIRA, A.J.P.; CALDERARO, F.F. Resistência antimicrobiana de amostras de Escherichia coli isoladas de fezes de leitões com diarréia. Arquivos do Instituto Biológico. v. 69, n. 2, p. 15-18, 2002.

BARROS, M.R.; SILVEIRA, W.D.; ARAÚJO, J.M.D.; COSTA, E.P.; OLIVEIRA, A.A.D.F.; SANTOS, A.P.D.S.; MOTA, R.A. Resistência antimicrobiana e perfil plasmidial de Escherichia coli isolada de frangos de corte e poedeiras comerciais no Estado de Pernambuco. Pesquisa Veterinária Brasileira, 2012.

BAUER, A.W.; KIRBY, W.M.M.; SCHERRIS, J.C.; TURCK, M. Antibiotic susceptibility testing by a standardized single disk method. **Am J Clin Pathol**. v45, p.493-496, 1976.

BRITO, B.G and TAGLIARI, K.C. Sensibilidade antimicrobiana de amostras de Escherichia coli isoladas de leitões lactentes com diarréia. **Rev. Bras. Cienc. Vet.**, v.7, n.2, p.117-119, 2000.

CLSI. 2013. Performance standards for antimicrobial disk and dilution susceptibility tests for bacteria isolated from animals VET01-S2. Second information supplement. Clinical and Laboratory Standards Institute, Wayne, PA.

COOKE, E.M.; BREADEN, A.; SHOOTER, R.A.; O'FARRELL, S. Antibiotic sensitivity of Escherichia coli isolated from animals, food, hospital patients, and normal people. **The Lancet**, v. 298, n. 7714, p. 8-10, 1971. <DOI: 10.1016/S0140-6736(71)90004-3Get>.

EDWARDS, P.R. and EWING, W.H. Identification of Enterobacteriaceae, Burgess Publ. **Co., Minneapolis, Minn**, 1972.

HENQUELL, C.; CHANAL, C.; SIROT, D.; LABIA, R.; SIROT, J. Molecular characterization of 9 different types of mutants among 107 inhibitor-resistant TEM (IRT) from clinical isolates of Escherichia coli. **Antimicrob. Agents Chemother**, v. 39, n. 2, p. 427-430, 1995. <DOI: 10.1128/AAC.39.2.427>.

IKUNO, A.A.; GAMA, N.M.S.Q.; GUASTALLI, E.A.L.; GUIMARÃES,

M.B.; FERREIRA, V.C.A. Características de isolados de Escherichia coli provenientes de aves silvestres quanto a genes de virulência e resistência a antibióticos. In: Anais 38º Congresso Brasileiro de Medicina Veterinária (Conbravet.), Gramado, RS.

JACOBY, G.A. and MEDEIROS, A.A. More extended spectrum β-lactamases. **Antimicrob. Agents Chemother**, v. 35, n. 9, p. 1697, 1991.

LAXMINARAYAN, R.; SRIDHAR, D.; BLASER, M.; WANG, M.; WOOLHOUSE, M. Achieving global targets for antimicrobial resistance. Science, v. 353, n. 6302, p. 874-875, 2016. < DOI: 10.1126/science.aaf9286>.

LEIMBACH, A.; HACKER, J.; DOBRINDT, U. *E. coli* as an all-rounder: the thin line between commensalism and pathogenicity. In: Between pathogenicity and commensalism. Springer, Berlin, Heidelberg, 2013. p. 3-32. <DOI: 10.1007/82_2012_303>.

LEIMBACH, A.; HACKER, J.; DOBRINDT, U. Ocorrência, aspectos bacteriológicos e histopatológicos na colibacilose de bezerros. **Pesquisa Agropecuária Brasileira**, v. 26, n. 4, p. 555-564, 1991.

MAGIORAKOS, A.P.; SRINIVASAN, A.; CAREY, R.B.; CARMELI, Y.; FALAGAS, M. E.; GISKE, C.G.; PATERSON, D.L. Multidrug□resistant, extensively drug□resistant and pandrug□resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. **Clinical microbiology and infection**, v. 18, n. 3, p. 268-281, 2012. <DOI: 10.1111/j.1469-0691.2011.03570.x>.

MALINOWSKI, E.; LASSA, H.; MARKIEWICZ, H.; KAPTUR, M.; NADOLNY, M.; NIEWITECKI, W.; ZIĘTARA, J. Sensitivity to antibiotics of Arcanobacterium pyogenes and Escherichia coli from the uteri of cows with metritis/endometritis. The Veterinary Journal, v. 187, n. 2, p. 234-238, 2011. <DOI: 10.1016/j.tvjl.2009.12.010>.

MATAMOROS, S.; VAN HATTEM, J.M.; ARCILLA, M.S.; WILLEMSE, N.; MELLES, D.C.; PENDERS, J.; SCHULTSZ, C. Global phylogenetic analysis of Escherichia coli and plasmids carrying the mcr-1 gene indicates bacterial diversity but plasmid restriction. **Scientific Reports**, v. 7, n. 1, p. 15364, 2017. <DOI: 10.1038/s41598-017-15539-7>.

MEHTA, S.C.; SAMANTA, M.; CHOW, D.C.; PALZKILL, T. Avoiding the carbapenem trap: KPC-2 β-lactamase sequence requirements for carbapenem hydrolysis. **The FASEB Journal**, v. 30, n. 1_supplement, p. 1083.20-1083.20, 2016.

NATARO, J.P. and KAPER, J.B. Diarrheagenic escherichia coli. **Clinical microbiology reviews**, v. 11, n. 1, p. 142-201, 1998. < DOI: 10.1128/CMR.11.1.142>.

National Committee for Clinical Laboratory Standards. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. NCCLS Documents M2-A8 and M100-S13. Wayne, PA, USA, 2003.

ONDERDONK, A.B.; LOUIE, T.J.; TALLY, F.P.; BARTLETT, J.G. Activity of metronidazole against Escherichia coli in experimental infra-abdominal sepsis. **Journal of Antimicrobial Chemotherapy**, v. 5, n. 2, p. 201-210, 1979. <DOI: 10.1093/jac/5.2.201>.

PIDDOCK, L.J.V. Does the use of antimicrobial agents in veterinary medicine and animal husbandry select antibiotic-resistant bacteria that infect man and compromise antimicrobial chemotherapy?. **Journal of Antimicrobial Chemotherapy**, v. 38, n. 1, p. 1-3, 1996. (DOI: 10.1093/jac/38.1.1>.

PORSE, A.; GUMPERT, H.; KUBICEK-SUTHERLAND, J.Z.; KARAMI, N.; ADLERBERTH, I.; WOLD, A.E.; SOMMER, M.O. Genome dynamics of Escherichia coli during antibiotic treatment: transfer, loss, and persistence of genetic elements in situ of the infant gut. **Frontiers in cellular and infection microbiology**, v. 7, p. 126, 2017. <DOI: 10.3389/fcimb.2017.00126>.

REESE, R. and BETTS, R.F. Manual de antibióticos. In: **Manual de antibióticos**. 1995.

REINTHALER, F.F.; POSCH, J.; FEIERL, G.; WÜST, G.; HAAS, D.; RUCKENBAUER, G.; MARTH, E. Antibiotic resistance of E. coli in sewage and sludge. **Water research**, v. 37, n. 8, p. 1685-1690, 2003. <DOI: 10.1016/S0043-1354(02)00569-9>.

RIBEIRO, M.G.; COSTA, E.O.; LEITE, D.S.; LANGONI, H.; GARINO, J.F.; VICTÓRIA, C.; LISTONI, F.J.P. Fatores de virulência em linhagens de Escherichia coli isoladas de mastite bovina. **Arquivo Brasileiro de Medicina Veterinária e**

Zootecnia, p. 724-731, 2006. <DOI: 10.1590/S0102-09352006000500004>.

RIBEIRO, M.G.;PINTO, J.P.D.A.N. Escherichia coli 0157: H7, de hambúrger, leite e outros gêneros alimentícios à colite hemorrágica e síndrome urêmico-hemolítica. **Higiene Alimentar**, v. 13, n. 66/67, p. 88-99, 1999.

VAN DEN BOGAARD, A.E.; LONDON, N.; DRIESSEN, C.A.G.G.; STOBBERINGH, E.E. Antibiotic resistance of faecal Escherichia coli in poultry, poultry farmers and poultry slaughterers. **Journal of Antimicrobial Chemotherapy**, v. 47, n. 6, p. 763-771, 2001. <DOI: 10.1093/jac/47.6.763>.

VAN DUIJKEREN, E.; WOLFHAGEN, M.J.; BOX, A.T.; 85-0>.

HECK, M.E.; WANNET, W.J.; FLUIT, A.C. Human-to-dog transmission of methicillin-resistant Staphylococcus aureus. Emerging infectious diseases. v. 10, n. 12, p. 2235, 2004. <DOI: 10.3201/eid1012.040387>.

WHITE, D.G.; HUDSON, C.; MAURER, J.J.; AYERS, S.; ZHAO, S.; LEE, M.D.; SHERWOOD, J. Chloramphenicol and Florfenicol Resistance in Escherichia Coli of Characterization. **Sci J of Ani and Vet Sci**, v. 1, n. 1, p. 001-006, 2018.

WILLIAMS, J.D. β-lactamases and β-lactamase inhibitors. Inter. J. Antimicrob. Agents, 12: 3-7, 1999. <DOI: 10.1016/S0924-8579(99)000