Journal of Veterinary Science and Public Health

J. Vet. Sc. Public Health, v. 8, n. 2, p. 026-039, 2021

ANTIMICROBIAL RESISTANT BACTERIA ISOLATED FROM DOGS

RESISTÊNCIA A ANTIBIÓTICOS POR BACTÉRIAS ISOLADAS DA SALIVA DE CÃES

Lígia Abboud Gerke[1]; Carlos Eduardo Santi[2]; Rosinei Kafka[2]; Renata Defante Lopes[2]; Júlia Ronzella Ottoni[1]; Michel Rodrigo Zambrano Passarini[1]*

1. Laboratório de Biotecnologia Ambiental. Curso de Biotecnologia, Universidade Federal da Integração Latino-Americana – UNILA. Foz do Iguaçu, Paraná.
2. Centro de Controle de Zoonoses - CCZ. Foz do Iguaçu, Paraná.
*Autor para correspondência: michel.passarini@unila.edu.br
DOI: 10.4025/revcivet.v8i2.51752

ABSTRACT

Domestic dogs are present in thousands of homes around the world. Because they are in contact with their owners, they can transmit microorganisms that are eventually tolerant to certain antimicrobial drugs. Knowing the existence of bacterial strains of clinical interest in the saliva of these domestic dogs can be considered a way of verifying potential sources of infections to humans. The present study aimed to analyze the resistance to antibiotic drugs in clinical bacterial strains or of clinical importance, associated with the saliva of dogs from Foz do Iguaçu. Seven saliva samples were collected from dogs. Using selective culture media, 12 clinical genera including *Enterococcus*, *Escherichia*, *Haemophilus*, *Pseudomonas*, *Staphylococcus*, *Salmonella*, and *Streptococcus* were found. The paper disc diffusion technique was used to verify the resistance of bacteria to drugs for human use including azithromycin, amoxicillin + potassium clavulanate and chloramphenicol. Amoxicillin + potassium clavulanate was inefficient for *E. coli*, *Haemophilus*, *Pseudomonas*, *Salmonella* and *Streptococcus*. Chloramphenicol was not efficient for a *Pseudomonas* strain. However, azithromycin showed a slight efficiency against strains of *Pseudomonas* and *E. coli*. Strains of *Pseudomonas* and *E. coli* showed the most worrying results of resistance. The results suggest that domestic dogs can represent a risk of bacterial spread, possibly pathogenic to humans with resistance to commercial antimicrobials, demonstrating the importance of maintaining hygiene habits in living with dogs.

Keywords: Microbial resistance, antimicrobial drugs, clinical importance, domestic dogs.

INTRODUCTION

Currently, domestic dogs usually live very close to their owners, which can lead to an eventual transmission of bacteria responsible for diseases, and that occasionally overcome the effects of some antibiotics, mainly through licks and bites caused by dogs on their owners (ARIAS and CARRILHO, 2012; ISHII et al., 2011). Works show that the bacterial diversity present in human skin can be affected due to this daily approximation between dogs and owners (DA SILVA and DA SILVA, 2014). Bacterial genera found in humans such as *Staphylococcus*, *Streptococcus* and *Actinomyces* have already been observed in oral samples from dogs (DA SILVA and DA SILVA, 2014; ELLIOTT et al., 2005).

The uncontrolled use of antibiotics in human and veterinary clinical practices has favored the appearance of many bacteria that no longer respond to the same drugs, which has hampered the fight against different infections and may increase the probability of death of patients affected by these resistant strains (MINISTÉRIO DA SAÚDE and SECRETARIA DE CIÊNCIA, TEC. E INSUMOS ESTRATÉGICOS, 2012).

Antimicrobial drugs can become ineffective for bacteria due to their respective cellular mechanisms: i) horizontal transfer of R-resistance plasmids; ii) modification of molecules that bind to drugs, such as restructuring of penicillin binding proteins (PBPs); iii) the ribosome can be bonded to a protein, blocking the interaction with the active principle; iv) alterations in the sequences of genes responsible for topoisomerase IV and DNA gyrase enzymes, reducing specificity with the active principle; v) reduced permeability of membranes by porins, resulting in decreased affinity of the active ingredient; vi) increased extracellular transport of the drug due to increased efflux, mediated by membrane pumps (LIN et al., 2015; LOPES, 2009; DA SILVA and AQUINO, 2018).

Thus, the indiscriminate use of these drugs and the contact between humans and their dogs led to the existence of clinically important bacteria resistant to antimicrobials in the saliva of these animals, which can stimulate actions such as population awareness campaigns on periodic veterinary monitoring of the health of their dogs, detecting and early treating diseases that can affect the animal, such as canine periodontitis (BRAGA et al., 2005). Other important actions would be the population control of abandoned dogs accompanied by campaigns to inhibit the abandonment of these animals on the streets and, also, education of the population about the consequences of the uncontrolled use of antibiotics, minimizing the emergence of resistant pathogens. With these measures, the coexistence of healthy dogs and

their owners will not pose risks to the health of guardians and the general population (DA SILVA and DA SILVA, 2014).

In this sense, with the participation of the Zoonoses Control Center (CCZ), the study aimed to isolate clinical bacteria from salivary samples of domestic dogs, for detection of strains resistant to commercial antimicrobials. The results obtained will support the CCZ to raise awareness of the importance of preventive measures for society regarding the risks that this interaction can represent to citizens in the west of Paraná State.

METHODS

Animal saliva collection

The collection was executed at the CCZ of the city. Small, medium, and large domestic animals (dogs), all healthy, were used. Swabs (sterilized) were used. The swabs were rubbed into the gums of each dog, properly prepared at the Zoonoses Center, and placed in Stuart medium (Olen) on ice, to be taken to the UNILA Laboratories, at Jardim Universitário campus.

Isolation of clinically important bacterial strains

Petri dishes with Chocolate Agar, Blood Agar, CLED Agar and MacConkey Agar media were used. The swabs were placed in a solution with 0.5% peptone and shaken for 1 minute (vortex). The streaking technique was performed to seed the plates, using the swab with the peptone sample. After sowing, plates were incubated for 48 to 72 hours at 37 °C. Blood Agar, Chocolate Agar and MacConkey media were kept in microaerophilia (by using a candle inside a can, where, when closing the can, the candle consumes almost all the oxygen present), favoring the appearance of facultative aerobic cells.

Identification of isolated strains

After microbial growth, the bacteria were identified based on information reported in the literature and in the manuals of the differential media used (LEVY, 2004). The methods of Gram (staining that distinguish between Gram positive and negative bacteria) and catalase (addition of hydrogen peroxide to a microbial smear and, with the formation of bubbles, the test indicates positive catalase) were used. Only strains of clinical importance were identified and stored at 4 °C.

Antibiogram test (resistance to antimicrobial compounds)

The identified bacteria were evaluated for their resistance to antimicrobials, following the Kirby-Bauer diffusion method (LABORCLIN, 2011). The isolates were transferred to test tubes containing 3 mL of sterile distilled water, being homogenized for 10 seconds by vortexing. Sterile swabs were embedded in the cell suspensions and used to seed plates containing Mueller-Hinton Agar (MH) medium. An MH plate was used for each bacteria tested (LEVY, 2004).

Solutions of the commercial broad-spectrum antimicrobials, azithromycin (500 $mg.L^{-1}$), amoxicillin + potassium clavulanate (500/125 $mg.L^{-1}$) and chloramphenicol (500 $mg.L^{-1}$), were prepared. Sterile filter paper discs (5 mm diameter) soaked for 1 minute in each antibiotic solution were added to the plates (MH) with the bacteria previously striated and, as a control, discs soaked with Lysoform® (Johnson) were used. Each assay was performed in triplicate, and the plates were incubated under microaerophilic conditions for 24 - 48 hours at 37 °C. The formation of microbial growth inhibition halos around the discs was considered a result of antibiotic susceptibility. The halos were measured with the aid of a ruler and the inhibition was defined by the average of the three repetitions.

RESULTS

Isolation of clinically important bacterial strains

Twelve clinically-important bacterial strains were isolated, *i.e.*: sample 1: *Staphylococcus* sp. (n=1) and *E. coli* (n=1); sample 2: *Streptococcus* sp. (n=1); sample 4: *E. coli* (n=1) and *Salmonella* sp. (n=1); sample 5: *Pseudomonas* sp. (n=1) and *Staphylococcus* spp. (n=2); sample 6: *Haemophilus* sp. (n=1) and *E. coli* (n=2) and sample 7: *Enterococcus* sp. (n=1) (Table 1). No bacteria were isolated from sample 3. During the isolation, the growth of several bacteria in addition to those identified in the study was observed. However, as they did not show color, hemolysis, and morphology characteristics of colonies of clinical strains, it was decided to disregard them, which is why a small number of bacteria was isolated (n=12).

Table 1. Bacterial strains of clinical importance found in the samples and their physiological and morphological characteristics.

Sample	Dog Size	Blood Agar	Chocolate Agar	MacConkey	CLED Agar	Catalase	Ferm. Lactose	Morphology	Gram
1	Small	n.f.	n.f.	*Staphylococcus*	n.f.	+	+	Coccus	+
		n.f.	n.f.	n.f.	*E. coli*	+	-	Bacillus	-
2	Medium	*Streptococcus*	n.f.	n.f.	n.f.	-	n.f.	Coccus	+
4	Big	n.f.	n.f.	*E. coli*	n.f.	n.f.	+	Bacillus	+
		n.f.	n.f.	*Salmonella*	n.f.	+	-	Bacillus	-
5	Medium	n.f.	n.f.	*Pseudomonas*	n.f.	+	-	Bacillus	-
		n.f.	n.f.	*Staphylococcus*	n.f.	+	+	Coccus	+
		n.f.	n.f.	n.f.	*Staphylococcus*	+	-	Coccus	+
6	Medium	n.f.	*Haemophilus*	n.f.	n.f.	n.f.	n.f.	Coccobacillus	-
		n.f.	n.f.	n.f.	*E. coli*	n.f.	+	Bacillus	-
		n.f.	n.f.	*E. coli*	n.f.	n.f.	+	Bacillus	-
7	Big	n.f.	n.f.	n.f.	*Enterococcus*	-	+	Coccus	+

n.f.: not found

Antibiogram assay

The plate antibiogram assays (Table 2 and Figure 1) showed that the antimicrobial amoxicillin + potassium clavulanate was the least efficient drug in inhibiting microbial growth. Among the 12 bacteria identified, 7 (58.3%) were resistant to this drug, being them *E. coli* (n=4), *Streptococcus* sp. (n=1), *Pseudomonas* sp. (n=1) and *Salmonella* sp. (n=1). The test also showed a partial sensitivity (formation of 01 halo in only 01 disc) of *Haemophilus* sp. (n=1). Thus, it was possible to verify that all *E. coli* strains found presented resistance to this drug.

Chloramphenicol was the second least efficient antibiotic, being unable to inhibit the development of a strain of *Pseudomonas* sp. However, the drug azithromycin showed partial sensitivity against 3 bacterial isolates, which were *E. coli* (n=2) and *Pseudomonas* sp. (n=1) isolates (Table 2).

The bacterial genus with the greatest resistance to the antimicrobial drugs tested was *Pseudomonas* sp. strain, isolated from sample 5, a healthy medium-size dog. This strain was resistant in its entirety (microbial growth in the 3 discs) to amoxicillin + potassium clavulanate and chloramphenicol drugs, as well as showing partial resistance to the drug azithromycin.

Table 2: Antibiogram results of bacterial isolates recovered from saliva samples.

Isolates Genera	**Sample/ number isolates**	**Chloramphenicol**		**Amoxicillin + clav. of potassium**		**Azithromycin**	
		Resistance/ sensibility	Test Average (cm)	Resistance/ sensitivity	Test Average (cm)	Resistance/ sensitivity	Test Average (cm)
Staphylococcus	1/1	S	Total[a]	S	Total[a]	S	Total[a]
E. coli	1/1	S	0.33	**R**	0	S	0.1
Streptococcus	2/1	S	0.16	**R**	0	S	0.43
E. coli	4/1	S	0.23	**R**	0	S	0.15
Salmonella	4/1	S	0.56	**R**	0	S	0.16
Pseudomonas	5/1	**R**	0	**R**	0	S	0.4
Staphylococcus	5/2	S	0.25 1.03	S	0.4 0.76	S	0.76 Total[a]
Haemophilus	6/1	S	0.5	S	0.2	S	0.2
E. coli	6/2	S	0.76 0.66	**R** (2)	0 0	S	0.23 0.29

S = Sensibility (inhibition halo in 03 discs)
S = Partial sensibility (inhibition halo in 01 disc)
R = Resistance
Total[a] = Wide halo

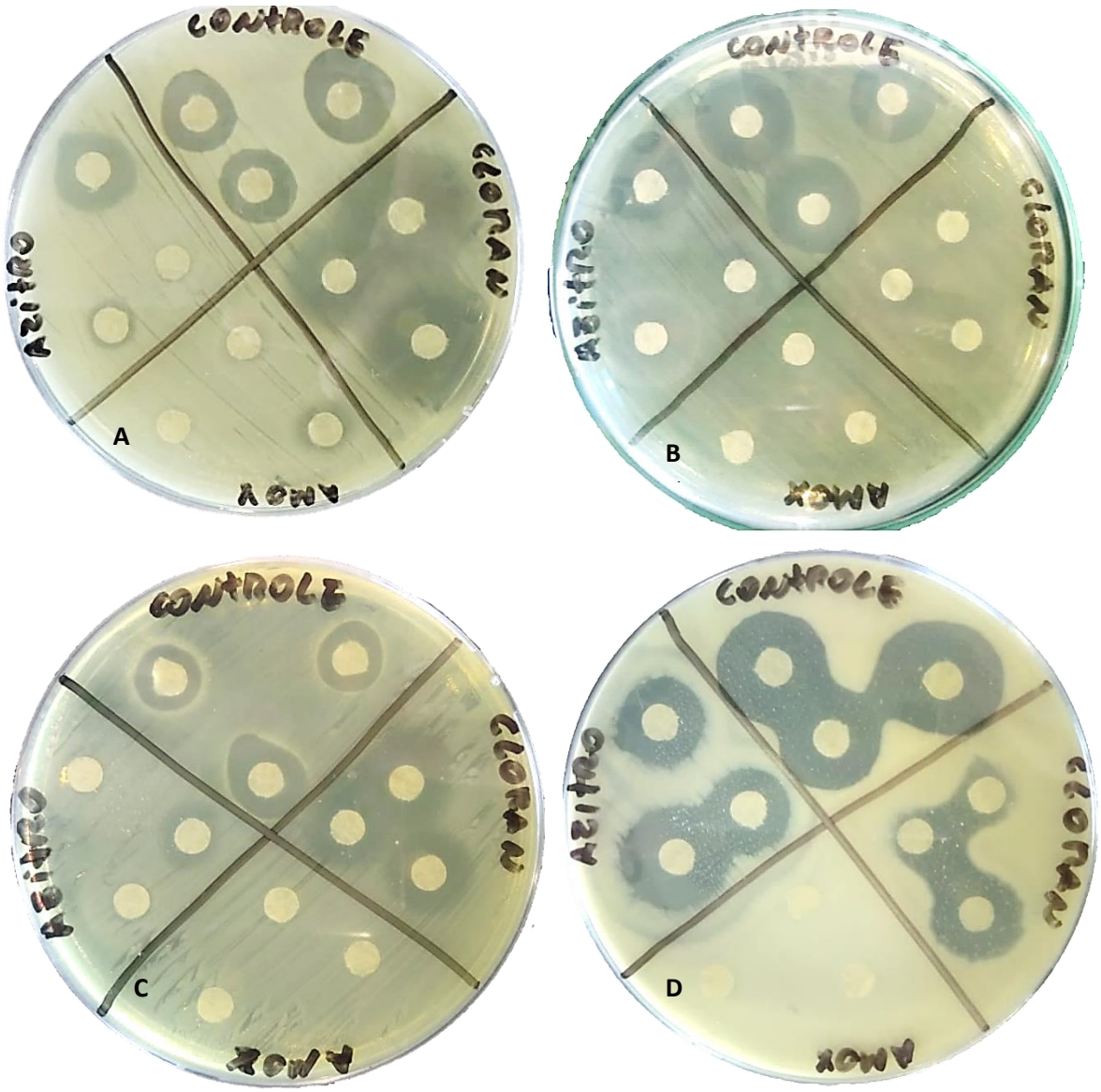

Figure 1: Plates with antibiogram tests with resistant bacteria. a) *Haemophilus* sp. (sample 6); b) *Pseudomonas* sp. (sample 5); c) *Escherichia coli* (sample 1); d) *Streptococcus* sp. (sample 2). Control: Lyzoform®. Azithr = azithromycin; Chloran = chloramphenicol; Amox = amoxicillin + potassium clavulanate.

DISCUSSION

The isolation of clinically important bacteria from canine saliva samples using Blood Agar and Chocolate Agar media recovered a low number of strains (*Streptococcus* sp. n=1 and *Haemophilus* sp. n=1), respectively, and this is due to the specificities of these media and the good health conditions of the animals. Chocolate agar is used for the cultivation of demanding microorganisms, *i.e.*, *Haemophilus* spp., *Neisseria* spp., *Branhamella catarrhalis* and *Moxarella* spp., while blood agar, despite being rich in nutrients and enabling the growth

of various microorganisms, especially favors growth and differentiation of *Streptococcus* spp. and *Staphylococcus* spp. (ANVISA, 2010). The low incidence of these microorganisms in the samples shows that dogs are healthy and live in places with good hygienic-sanitary conditions.

On the other hand, the use of less selective media favored the growth of a greater number of clinically important genera. In MacConkey medium, bacteria of the genera *Escherichia*, *Salmonella*, *Staphylococcus* and *Pseudomonas* were found, while in assays with CLED medium, colonies of *Enterococcus*, *Escherichia* and *Staphylococcus* were found. These culture media are considered differentials for disease-causing bacteria, including those that ferment lactose (CLED) and enterobacteria and other Gram-negative bacteria with rod morphology (MacConkey) (BECTON DISCKINSON, 2012). Thus, the growth and identification of a greater number of microbial genera of clinical importance recovered in these media was expected.

The genera found in this study have already been retrieved from other samples of animal origin. Genera such as *Escherichi*a, *Haemophilus*, *Staphylococcus*, *Pseudomonas* and *Streptococcus* have already been isolated from dog saliva and nostrils, as described in the works by Bailie et al. (1978) and Elliott et al. (2005).

Isolates of the *E. coli* species are commonly found in the human and animal intestines and can cause enteric diseases in their hosts. However, in the study carried out by Beutin (1999) it was shown that canine enterotoxigenic *E. coli* (ETEC) strains are different from ETEC found in other animals and in humans, due to their serotypes and adhesion factors. Like canine enteropathogenic strains (EPEC), they are also different from EPECs isolated from humans compared to those isolated from different animals, due to their serotypes and the presence of adhesion proteins of EPECs to cells of the intestinal mucosa.

Oehler et al. (2009) showed transmissions of strains of *Streptococcus* spp. to men by the bite of dogs. Schriber et al. (2014) also reported that *Streptococcus* sp. found in the human host have virulence for both humans and dogs. *Haemophilus* spp. have already been isolated from the nostrils of dogs (VARGHESE et al., 1977), while *Staphylococcus* spp., such as the species *S. pseudintermedius* and *S. aureus*, were transmitted to dogs through contact with people (LOZANO et. al., 2017; VAN DUIJKEREN et al., 2004). Likewise, *Pseudomonas aeruginosa*, *Enterococcus faecalis* and *Salmonella* spp. have been reported to be transmitted between humans and dogs, and vice versa, as well as being found in canine feces (FERNANDES et al., 2018; JOHNSON et al., 2006; JAY-RUSSELL et al., 2014).

Works described in the literature have already shown resistance by clinical bacteria affiliated to the same genera described in this work, for the same antibiotics tested. According to Fernandes et al. (2018), *Pseudomonas aeruginosa* strains recovered from social environment shared between dogs and their owners were resistant to tests with chloramphenicol. Other works showed that amoxicillin, chloramphenicol, and azithromycin were ineffective against strains of *E. coli*, *Staphylococcus* spp. and *Salmonella* spp., isolated from canine samples (ZOGG et al., 2018; PEREIRA 2009; TORKAN et al., 2015).

The literature points out that the events for resistance to conventional drugs can be: a) Chloramphenicol: *i)* inactivation of acetylation, by acetyl transferase (enzyme) (MURRAY and SHAW, 1997); *ii)* DNA sequence encoding information for the drug to be expelled from the cell (MOSHER et al., 1995); *b)* amoxicillin: *i)* synthesis of β-lactamase, which can be overcome by the use of clavulanic acid (MURRAY and SHAW, 1997), and that in our study did not show satisfactory results; *c)* azithromycin: *i)* ribosome structure alteration, making drug binding impossible (CHISHOLM et al., 2010). For veterinary use, the drugs of choice to treat infections, are: cephalosporins, amoxicillin + potassium clavulanate, macrolides (azithromycin), lincosamides and fluoroquinolones (GUARDABASSI et al., 2010).

Isolates of major relevance recovered from samples were the four strains of *Escherichia coli*, due to their resistances to amoxicillin + potassium clavulanate, as well as *Pseudomonas* sp., due to its resistance to two of three antimicrobials tested. This result of multiple resistance showed by *Pseudomonas* sp. strain is of great relevance, as reported by Mohammadi et al. (2014), in the Intensive Care Units, infections caused by strains resistant to multiple drugs such as *Acinetobacter* spp. or *Pseudomonas* spp., can increase the mortality of patients with pneumonia associated to mechanical ventilation in around 80% (TURKOVIĆ et al., 2015). Rodrigues et al. (2018) reported that bacteria commonly resistant to hospital infections are *Acinetobacter baumannii, Enterobacter* spp*., Enterococcus faecium, Klebsiella pneumonia, Pseudomonas aeruginosas* and *Staphylococcus aureus.*

Domestic dogs can be reservoir of bacteria potentially pathogenic and resistant to commercial antimicrobials. Antimicrobial resistance is originated by the incorrect use of these drugs by the population, requiring actions to raise awareness about the risks associated with health, especially for patients hospitalized in ICUs (Intensive Care Unit). The results show that bacteria of clinical interest with resistance to commercially available antimicrobials are close and in constant contact with humans, which can cause infections that are difficult to treat.

CONCLUSIONS

The high number of isolates resistant to amoxicillin administered with potassium clavulanate and the identification of a bacterium resistant to multiple drugs raises concern. With the possibility of transmission of diseases and their agents between dogs and their guardians, the existence of bacterial strains that have shown resistance to commercial drugs brings a warning.

Antimicrobial resistance is an obstacle to curing infectious diseases, putting the health of people and animals at risk. Population awareness actions, through educational campaigns about the importance of the correct use of antimicrobials, as well as the relevance of monitoring the health of their pets, should be carried out periodically. The results found in this work will be used by the Zoonoses Center to take actions, which should also address the consequences for the community of abandoning animals and contact with dogs indoors. Thus, new studies need to be developed to expand the sampling of dogs, enabling a better approach to the problem of the indiscriminated use of antibiotics for animal and humans.

Ethical approval: the authors declare no ethical issues**.**

Funding Information: the authors would like to thank the Federal University of Latin American integration and the Zoonoses Control Center for providing the necessary inputs and samples for the study.

Author's Contributions: LAG: manuscript preparation and study development; CES: availability of ZCC materials; RK: availability of ZCC materials; RDL: provision of saliva samples; JRO: manuscript preparation; MRZP: manuscript preparation and LAG student advisor.

Acknowledgement: The authors thank the Federal University of Latin American Integration, the Zoonoses Control Center, and the Municipality of Foz do Iguaçu.

REFERÊNCIAS

AGÊNCIA NACIONAL DE VIGILÂNCIA SANITÁRIA – ANVISA. **Módulo, I. V. Descrição dos Meios de Cultura Empregados nos Exames Microbiológicos**. 1. ed. Brasília: [s.n.], 2010. Disponível em: <https://www.gov.br/anvisa/pt-br/centraisdeconteudo/publicacoes/servicosdesaude/publicacoes/modulo-5-tecnologias-em-servicos-de-saude-descricao-dos-meios-de-cultura-empregados-nos-exames-microbiologicos>. Acessed in: 06 mai. 2021.

ARIAS, M.V.B.; CARRILHO C.M.D.M. Resistência antimicrobiana nos animais e no ser humano. Há motivo para preocupação? **Semina: Ciências Agrárias, Londrina**, v.33, p.775-790, 2012.

BAILIE, W.E.; STOWE E.C.; SCHMITT A.M. Aerobic bacterial flora of oral and nasal fluids of canines with reference to bacteria associated with bites. **Journal of Clinical Microbiology**, v.7, p.223–231, 1978.

BECTON DICKINSON GmbH. BD CLED **Agar. Instruções de utilização – Meios em placas prontos a usar.** Becton Dickinson GmbH. 2012. 4p.

BEUTIN, L. *Escherichia coli* as a pathogen in dogs and cats. **Veterinary Research**, BioMed Central, v.30, p.285-298, 1999.

BRAGA, C.A.D.S.B.; RESENDE, C.M.F.; PESTANA, A.C.N.R.; CARMO, L.S.; COSTA, J.E.; SILVA, L.A.F.; ... & CARVALHO, M.A.R. Isolamento e identificação da microbiota periodontal de cães da raça Pastor Alemão. Ciência Rural, v.35, p.385-390, 2005.

CHISHOLM, S.A.; DAVE J.; ISON C.A. High-Level Azithromycin Resistance Occurs in *Neisseria gonorrhoeae* as a Result of a Single Point Mutation in the 23S rRNA Genes. **Antimicrobial Agents and Chemotherapy**, v.54, p.3812–3816, 2010. <DOI: 10.1128/AAC.00309-10>.

DA SILVA, E.A.; DA SILVA P.R.S. Investigação microbiológica da saliva de animais de estimação. **Revista Saúde em Foco**, v.1 p.109–122, 2014.

DA SILVA, M.O.; AQUINO S. Resistência aos antimicrobianos: uma revisão dos desafios na busca por novas alternativas de tratamento. **Revista de Epidemiologia e Controle de Infecção**. Santa Cruz do Sul, v.8, p.472-482, 2018. <DOI: 10.17058/reci.v8i4.11580>.

ELLIOTT, D.R.; WILSON M.; BUCKLEY C.M.F.; SPRATT D.A. Cultivable oral Microbiota of domestic dogs. **Journal of Clinical Microbiology**, v.43 p.5470–5476, 2005. <DOI: 10.1128/JCM.43.11.5470-5476.2005>.

FERNANDES, M.R.; SEKKERA F.P.; MOURA Q.; CARVALHO M.P.N.; ROSATO P.N.; CERDEIRA L.; LINCOPAN N. Zooanthroponotic transmission of drug-resistant *Pseudomonas aeruginosa*, Brazil**. Emerging Infectious Diseases**, v.24, p.1160-1162, 2018. <DOI: 10.3201/eid2406.180335>.

GUARDABASSI, L.; JENSEN L.B.; KRUSE H. **Guia de antimicrobianos em veterinária**. Porto Alegre: Artmed; 2010.

ISHII, J.B.; FREITAS J.C.; ARIAS M.V.B. Resistência de bactérias isoladas de cães e gatos no Hospital Veterinário da Universidade Estadual de Londrina (2008-2009). **Pesquisa Veterinária Brasileira**, v.31, p.533-537, 2011.

JAY-RUSSELL, M.; HAKE A.F.; BENGSON Y.; THIPTARA A.; NGUYEN T. Prevalence and Characterization of *Escherichia coli* and *Salmonella* Strains Isolated from Stray Dog and Coyote Feces in a Major Leafy Greens Production Region at the United States-Mexico Border. **PLOS ONE**, v.20, p.1-14, 2014. < DOI: 10.1371/journal.pone.0113433>.

JOHNSON, J.K.; PERENCEVICH E.N.; LINCALIS D.P.; VENEZIA R.A. Dog Bite Transmission of Antibiotic-Resistant Bacteria to a Human. **Infection Control & Hospital Epidemiology**, v.7, p.762–763, 2006. <DOI: 10.1086/505101>.

LABORCLIN P**rodutos para Laboratórios Ltda. Manual para antibiograma Difusão em Disco Kirby & Bauer**. Laborclin Produtos para Laboratórios Ltda. 2011. 29p.

LEVY, C.E. **Manual de Microbiologia Clínica para o Controle de Infecção em Serviços de Saúde**. 1. ed. Brasília: Agência Nacional de Vigilância Sanitária, 2004.

LIN, J.; NISHINO K.; ROBERTS M.C.; TOLMASKY M.; AMINOV R.I.; ZHANG L. Mechanisms of antibiotic resistance. **Frontiers in Microbiology**, v.6, p.1-3, 2015. <DOI: 10.3389/fmicb.2015.00034>.

LOPES, H.V. Antibióticos, resistência e novos mecanismos de ação. **Revista Panamericana de Infectología**, v.11, p.67-68, 2009.

LOZANO, C.; REZUSTA A.; FERRER I.; PÉREZ-LAGUNA M.; RUIZ-RIPA L.; REVILLO M.J.; TORRES C. *Staphylococcus pseudintermedius* Human Infection Cases in Spain: Dog-to-Human Transmission. **Vector-Borne and Zoonotic Diseases**, v.17, p.268–270, 2017. <DOI: 10.1089/vbz.2016.2048>.

MINISTÉRIO DA SAÚDE; SECRETARIA DE CIÊNCIA, TECNOLOGIA E INSUMOS ESTRATÉGICOS**. Uso racional de medicamentos: Temas Selecionados**. 1 ed. Brasília: Athalaia, 2012.

MOHAMMADI, P.; KALANTAR E.; BAHMANI N.; FATEMI A.; NASERI N.; GHOTBI N.; NASERI M.H. Neonatal bacteriemia isolates and their antibiotic resistance pattern in neonatal insensitive care unit (NICU) at Beasat Hospital, Sanandaj, Iran. **Acta Medica Iranica**, v.52, p.337-340, 2014.

MOSHER, R.H.; CAMP D.J.; YANG K.; BROWN M.P.; SHAW W.V.; VINING L.C. Inactivation of Chloramphenicol by O-Phosphorylation. **The Journal of Biological chemistry**, v.270, p.27000 – 27006, 1995. <DOI: 10.1074/jbc.270.45.27000>.

MURRAY, I.; SHAW W. O-acetyltransferases for Chloramphenicol and Other Natural Products. **Antimicrobial Agents and Chemotherapy**, v.41, p.1-6, 1997.

OEHLER, R.L.; VELEZ A.P.; MIZRACHI M.; LAMARCHE J.; GOMPF S. Bite-related and septic syndromes caused by cats and dogs**. The Lancet Infectious Diseases**, v.9, p.439-447, 2009. <DOI: 10.1016/S1473-3099(09)70110-0>.

PEREIRA, I.A.; SOARES L.C.; COELHO S.M.O.; BALBINO F.A.; PRIBUK B.R.; SOUZA M.M.S. Suscetibilidade à azitromicina de agentes bacterianos isolados de processos infecciosos em diferentes sítios de animais de companhia. **Arquivo Brasileiro de Medicina Veterinária e Zootecnia**, v.61, p.577-584, 2009. <DOI: 10.1590/S0102-09352009000300009>.

RODRIGUES, T.S.; DOS SANTOS A.M.R.; LIMA P.C.; MOURA M.E.B.; GOIANO P.D.O.L.; FONTINELE D.R.S. Resistência bacteriana á antibióticos na unidade de terapia intensiva: Revisão Integrativa**. Revista Prevenção de Infecção e Saúde**, v.4, p.7350, 2018. <DOI: 10.26694/repis.v4i0.7350>.

SCHRIEBER, L.; TOWERS R.; MUSCATELLO G.; SPEARE R. Transmission of *Streptococcus dysgalactiae subsp. equisimilis* between Child and Dog in an Aboriginal Australian Community. **Zoonoses and Public Health**, v.61, p.145–148, 2014. <DOI: 10.1111/zph.12057>.

TORKAN, S.; KHAMESIPOUR F.; ANYANWU M.U. Detection of virulence and antibacterial resistance genes in *Salmonella* isolates from diarrheic dogs in Iran**. Revue de Médecine Vétérinaire,** v.166, p.221-228, 2015.

TURKOVIĆ, T.M.; GRGINIĆ A.G.; CUCUJIĆ B.Đ.; GAŠPAR B.; ŠIRANOVIĆ M.; PERIĆ M. Microbial profile and antibiotic susceptibility patterns of pathogens causing ventilator-associated pneumonia at intensive care unit, Sestre Milosrdnice University Hospital Center, Zagreb, Croatia. **Acta Clinica Croatica**, v.54, p.127-135, 2015.

VAN, DUIJKEREN E.; WOLFHAGEN M.J.H.M.; BOX A.T.A.; HECK M.E.O.C.; WANNET W.J.B.; FLUIT A.C. Human-to-Dog Transmission of Methicillin-Resistant *Staphylococcus aureus***. Emerging Infectious Diseases**, v.10, p.2235-2237, 2004.

VARGHESE, R.; MELO J.C.; BARNWELL P.B.; CHUN C.H.; RAFF M.J. Endocarditis due to *Hemophilus aphrophilus*: Report of a Case with Possible Transmission from Dog to Man. **Chest**, v.72, p.680-682, 1977. <DOI:

10.1378/chest.72.5.680>.

ZOGG, A.L.; ZURFLUH K.; SCHIMITT S.; NÜESCH-INDERBINEN M.; STEPHAN R. Antimicrobial resistance, multilocus sequence types and virulence profiles of ESBL producing and non-ESBL producing uropathogenic *Escherichia coli* isolated from cats and dogs in Switzerland. **Veterinary Microbiology**, v.216, p.79–84, 2018. <DOI: 10.1016/j.vetmic.2018.02.011>.