Article

6 years of Pasteurella spp. in the Pitiusas.

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Abstract: *Pasteurell*a spp. is a gram-negative bacterium that is part of the oral and upper respiratory tract microbiota of many animals such as canids and felines. In humans it can produce pathology primarily associated with animal bites or scratches. In addition, members of this genus, and especially *Pasteurella multocida*, may also be involved in systemic infections, mainly in immunocompromised patients in close contact with pets.

The aim of this study is to analyse the prevalence and clinical characteristics of infections caused by Pasteurella spp. as well as the sensitivity profile of these isolates obtained in the Microbiology laboratory of the Hospital Can Misses (Ibiza, Ibiza and Formentera Health Area, ASEF) in the period from January 2013 to December 2018.

Retrospective descriptive study in which all *Pasteurella* spp. isolates were analysed in the Microbiology Laboratory of Hospital Can Misses from 1 January 2013 to 31 December 2018. Bacterial identification was performed by Vitek 2 automated biochemical test panel (bioMérieux, Spain) and antimicrobial susceptibility also by Vitek2 automated microdilution panel, interpreted based on Clinical and Laboratory Standards Institute (CLSI) standards. Medical records were systematically reviewed by collecting demographic data of infected patients, comorbidities, epidemiological data and clinical features of the infection.

A total of 22 isolates of *Pasterurella* spp. were obtained from 22 different patients, 62.8% female, from three different species: 18 *P. multocida*, 2 *P. canis* and 2 *P. pneumotropica*. Most isolates came from soft tissue infection samples: 7 wound exudates and 5 abscess material. The antibiotics tested with the highest sensitivity profile were gentamicin and cefepime (100% sensitivity

Keywords: *Pasteurell*a spp; pets; *P. multocida*; beta-lactams; skin and soft tissue infection; urinary tract infection.

1. Introduction

Different species of *Pasteurella* spp. are among the major human pathogens originating from both wild and domestic animal wildlife, with a special focus on dogs and cats (1). The most common way of acquiring a *Pasteurella* spp. infection is through direct contact following a bite or scratch by a dog or cat, or also through licking open wounds. Many *Pasteurella* species can be pathogenic in humans, such as *P. dogmatis*, *P. canis*, *P. stomatis*, etc., but the most frequently isolated species is *P. multocida*, which has several subspecies: multocida, septica or gallicida. The most frequent of the subspecies in human pathology is *P. multocida* sbs *multocida* and is associated as an anthropozoonosis in many warm-blooded animals (2). *P. multocida septica* is associated with cat wounds and *P. multocida gallicida* is rarely found in human isolates.

There are multiple factors that cause this facultative anaerobic gram-negative coccobacillus, *Pasteurella* spp. to survive in the host: the polysaccharide membrane, the capsule and its resistance to phagocytosis, adhesive properties, various enzymes that act on the extracellular matrix facilitating dissemination and often the production of *P. multocida*

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toxin (PMT) (2). Some authors associate *Pasteurella* spp. bacteraemia with comorbidities such as cancer (3).

Pasteurella spp. causes in most cases localised infections such as cellulitis, abscesses or arthritis near the site of inoculation, but can also lead to bacteraemia (4), endocarditis or deep organ infections by haematogenous spread (2). Contact with cats seems to be more associated with bacteraemia and contact with dogs, especially if a bite occurs, with local and superficial infections (5).

Understanding the full spectrum of Pasteurella spp. infections allows for a balanced perspective on the severity of such infections, risk of complications and most appropriate treatment. This study reviews the demographic, clinical and microbiological characteristics of patients in whom *Pasteurella* spp. was isolated at least once in the Microbiology laboratory covering the entire area of Ibiza and Formentera over a period of 6 years.

2. Results

A total of 22 patients were included (mean age 65.9 years; only one minor, an 11-day-old neonate; 7 males (31.8%) and 15 females (68.2%). Isolations were 18 *P. multocida*, 2 *P. canis* and 2 *P. pneumotropica*. Cultures requested were as follows: 7 wound exudate cultures, 5 cultures of abscess material, 3 blood and 3 urine cultures, 2 joint fluid cultures and finally 1 sputum and 1 stool culture. 20 of the requests came from hospital EDs (90.9%) and 2 from primary care (9.1%). On 8 occasions the patient had contact with domestic animals that had caused an injury and in all 8 cases the micro-organism isolated was *P. multocida*; 7 were dog bites and 1 was a cat scratch. *P. pneumotropica* was isolated in a stool culture and in a urine culture with a significant count, and *P. canis* in an abscess and in a urine culture with a significant count as well. The 3 blood cultures with isolation of *Pasteurella* spp. were requested for urinary tract infection (UTI), cellulitis and fever of unknown origin. *Pasteurella* spp isolates over the years were 5 in 2013, 4 in 2014, 4 in 2015, 3 in 2016, 2 in 2017 and finally 2 in 2018. The sensitivity to the different antibiotics is reflected in table 1:

Table 1. Total susceptibility of *Pasteurella* spp. isolates.

	Resistant	Intermediate / Susceptible with increased exposure	Susceptible	Not tested
Ampicillin	1	2	18	1
Amoxicillin/Clavulanic acid	1	1	20	0
Cefuroxime	0	0	21	1
Cefotaxime	0	0	21	1
Ceftazidime	0	2	19	1
Cefepime	0	0	22	0
Imipenem	0	0	21	1
Amikacin	0	0	21	1
Gentamicin	0	0	22	0
Ciprofloxacin	0	0	21	1
Trimethoprim - Sulfomethoxazole	2	0	19	1
Piperacillin / Tazobactam	0	0	18	8
Fosfomycin	1	0	2	19

*Antibiotic susceptibility interpreted according to CLSI criteria.

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3. Discussion

The genus *Pasteurella* was named after Luois Pasteur, who was the first to isolate this bacterium in 1880 as the causative agent of fowl cholera. *Pasteurella* ssp. and especially *P. multocida*, is one of the most frequent commensal microorganisms found in domestic animals worldwide, being very common in the oropharynx of dogs and cats, and most infections in humans are related to exposure to these pets, as in our study with 8 cases of *P. multocida* isolation with direct inoculation by cat or dog wounds (6). Cats are the animals with the highest percentage of colonisation by *Pasteurella* spp. with 70-90%, followed by dogs with 20-50%. Other microorganisms frequently isolated from animal bite or scratch wounds are *Bartonella henselae* or *Staphylococcus aureus*.

This is a small, gram-negative, facultatively anaerobic, immobile, oxidase- and catalase-positive, gram-negative coccobacillus, which typically stains bipolar with methylene blue (7). Pasteurella spp. grows on blood agar and chocolate agar, but not on MacConkey agar. It grows well on TSI (Trypticase Soy Agar) or BHI (Brain-Heart Agar) enriched media. Transmission occurs even through small microtrauma caused mainly by cats and dogs. Once inoculated in humans, it can produce a wide spectrum of infection, both local and invasive, with particular attention to cellulitis and osteomyelitis at sites close to the point of inoculation (8)(9). Despite acting as an opportunistic organism, *P. multocida* has a high pathogenic potential due to various virulence factors such as capsular lipopolysaccharide, cytotoxin, haemagglutinin, adhesins and iron sequestering proteins (2). Therefore, complications of local infection such as necrotising fasciitis, bacterial arthritis, endocarditis, meningitis and sepsis are not uncommon after trauma.

In the existing literature, the most isolated species in human pathology are *P. multocida*, especially the subspecies multocida, P. canis and P. dogmatis, the latter being absent in our cases, where we did find *P. pneumotropica* (5). There are 5 serogroups of *P. multocida*, A, B, D, E and F, with A and D being the most isolated in human pathology, especially associated with animal oral microbiota (7). The most frequent of the subspecies in human pathology is *P. multocida multocida* (2). *P. multocida septica* is usually found in cat scratch wound infections and *P. multocida gallicida* rarely causes pathology in humans.

Both in the literature and in our experience, we found a wide spectrum of infections caused by *Pasteurella* spp. but skin and soft tissue infections after inculcation of the organism by violent contact with the animal always stand out. Among our isolates, 12 come directly from the collection of samples of this type of infections: 7 wound exudates and 5 abscesses. It is not uncommon for these infections to be complicated by bacteraemia due to haematogenous dissemination or arthritis or tenosynovitis due to contiguous dissemination. It is much less common for distant dissemination complication to result in meningitis or arthritis far from the point of inoculation.

There are cases in the literature of *Pasteurella* bacteraemia treated adequately with a 14-day course of ceftazidime and single-dose gentamicin, with no recurrence, even in patients with significant underlying pathology (4). In the case of bacteraemia, intravenous antibiotic treatment and catheter sealing are highly recommended (10).

If we take into account the wide range of possible infections of different locations that can occur, we can find that they occur more frequently in patients with comorbidities such as diabetes, alcoholism, cirrhosis, cancer, anesplenia or prolonged use of corticosteroids (3).

We found isolation of *P. multocida* in 2 joint fluids, one in 2013 and the other in 2015. Zoonotic intra-articular infections by various microorganisms, such as *Brucella* spp. *Salmonella* spp. *Campylobacter* spp. and *Streptococcus suis*, have been reported, especially in prosthetic joint infections (11)(12)(13)(14). Tenosynovitis and osteomyelitis caused by *Pasteurella* spp. usually originate in an episode of direct traumatic inoculation through the teeth and nails of the animal, and from there, like any other type of infection, it can pass into the bloodstream and cause disseminated infections such as septicaemia, meningitis or pneumonia (15). In our cases it is not known whether the joints had prostheses, whether there was a nearby bite or scratch or whether there was distant dissemination, which

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would have been interesting to address, and would have provided a more specific and adequate view of the local epidemiology to be taken into account in joint infections in our area. However, prosthetic infection by *P. multocida* is still an uncommon phenomenon, with fewer than 30 cases described in the literature, and is associated with the presence of comorbidities, notably diabetes and immunosuppressive treatment, among others, as well as pet ownership (16)(17)(18)(19)(20).

Pasteurella joint infections are generally mono-microbial and respond well to treatment with ampicillin and doxycycline, although most of the time treatment had to be accompanied by appropriate replacement of the prosthesis if present. Unfortunately, the antibiogram panel available in the laboratory did not include doxycycline, so we do not know the sensitivity percentage of our strains, whereas, to ampicillin, 18 (81.2%) were sensitive and only one resistant (4.5%). *P. multocida* is usually sensitive to beta-lactams, tetracyclines and co-trimoxazole, with variable resistance to erythromycin and 50% of the strains are resistant to clarithromycin. Beta-lactamase producing strains have been described (21). Few beta-lactam resistances were detected in our isolates, none of them due to beta-lactamases. Sensitivity to erythromycin and clarithromycin was not tested.

Infections of other, let's call them non-traumatic, types, even if there is contact with an animal, such as respiratory tract infections or urinary tract infections, are rare. In these cases, the individual has been colonised by close and continuous contact with the pet, through saliva, either by licking or by playing with and chewing on external devices carried by the patient, such as urinary catheters.

In our series, we only found one isolate from a respiratory sample, a sputum, because *Pasteurella* spp. infection of the upper respiratory tract is exceptional, usually found in carriers or contamination in patients in contact with farm or domestic animals, and it is rare for these patients to have underlying respiratory pathology or immunosuppression (22), unlike other infections already described, where the underlying pathology seems to have a certain determining power. Another pathology rarely caused by *Pasteurella* spp. is endocarditis (22).

The literature does not include a study of the possible clinical significance of the isolation of *Pasteurella* spp. in the faeces of a patient; however, in our area we found *P. pneumotropica* predominantly in a stool culture of a patient with diarrhoea of short duration and close contact with animals. It remains to be clarified whether this was really the micro-organism causing this pathology or whether it was only a reflection of colonisation by this micro-organism in this patient, since no antibiotherapy was given and the symptoms subsided in a few days without further complications, as is usually the case in most infectious gastroenteritis.

It was not possible to collect reliable information about antibiotic regimens as most of the patients completed antibiotic treatment at home, as these were not invasive infections, and therefore no information about these has been added to the study. However, all isolates appeared to be broadly sensitive to beta-lactams and aminoglycosides, so intravenous treatment would rarely be necessary, except in cases of invasive infections such as bacteraemia. The 3 occasions on which fosfomycin was tested correspond to the 3 isolates with significant counts from urine culture, so it seems necessary to continue testing this antibiotic in subsequent isolates to find out the true percentage of sensitivity of *Pasteurella* spp. to fosfomycin, since it seems that with 4 (18.2%) episodes of UTI out of the total number of isolates by this family of microorganisms (3 detected by urine culture and another by blood culture) it does not seem to be a particularly infrequent uropathogen, contrary to what is reported in the existing literature (2)(6)(23).

In this study, we found that despite the wide spectrum of infections caused by *Pasteurella* spp. there are only less than 20 cases of UTI in the literature, most of them in patients with urological pathology, especially anatomical alterations (6) and only by *P. multocida* (24), while in our area we also found other species of *Pasteurella* spp. There is a known case of a UTI due to *P. aerogenes* in an 11-year-old girl with a history of neurogenic bladder and in contact with a rabbit, although this species seems to be more frequently related to contact with pigs (25). However, the identification of the bacterial species was

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performed by biochemical panel tests, so a more reliable identification result would have required the use of other more sensitive techniques that were not available at that time, such as mass spectrometry or 16S sequencing. However, it appears that dulcitol and sorbitol fermentations are quite useful to differentiate subspecies of *P. multocida*, where *P. multocida multocida* is dulcitol positive and sorbitol negative, while *P. multocida septica* is negative for the fermentation of both sugars. The panels available in the laboratory did not have the dulcitol fermentation test available. It seems that not only exposure to pets accompanied by anatomical alterations of the urinary tract is predisposing for UTI by this micro-organism, but also the presence of urinary catheters, diabetes or vascular complications, although further studies are clearly needed. They could also be due to non-traumatic contact with pets in which the perineal area is colonised and from there penetrates the urinary tract through the urethral meatus (24) (26) (23) (6). It would be interesting to investigate the possible reasons why there seems to be a higher incidence of UTI due to *Pasteurella* spp. in ASEF than in other areas, whether due to the rurality of the area, the large number of individuals with pets or for any other reason.

As empirical treatment for bites, and especially if *Pasteurella* spp. is suspected, amoxicillin/clavulanic acid is usually recommended, amoxicillin/clavulanic acid is usually recommended, which in our series would have been effective in all but one isolate, with a sensitivity of 95.5% in our case, but, in addition, for *Pasteurella* spp. it is recommended to use as an alternative other antibiotics with good activity such as doxycycline (not tested in our case as already mentioned), trimethoprim/sulfamethoxazole (86. 4% sensitivity in our isolates), penicillin (extrapolated to the sensitivity obtained for ampicillin), cefuroxime (95.5% sensitivity), ciprofloxacin (95.5% sensitivity) or clindamycin (also not tested in our laboratory as it was not included in the panel). Among our isolates, the highest sensitivity of 100% was found for two antibiotics that are not generally recommended for the treatment of this type of infection, gentamicin and cefepime. In any case, gentamicin could be useful in cases of bacteraemia, endocarditis or meningitis in combination therapy with a beta-lactam. Cefepime is an antibiotic recommended as a treatment for AmpC-producing *Enterobacteriaceae* infections, the use of which in these cases makes no sense. Empirical use of erythromycin is not recommended. However, as in all infections, it is recommended that treatment be reconsidered for appropriateness after culture and antibiogram. In addition, often, when an abscess or other purulent collection has formed, the prognosis of the infection will depend on drainage, debridement or even reconstruction if necessary.

4. Materials and Methods

This is a retrospective observational study covering the period from 1 January 2013 to 31 December 2018 during which, through the computer system of the Microbiology laboratory (CSM) of the Hospital Can Misses (Ibiza, Balearic Islands), which covers the entire hospital and primary care area of Ibiza and Formentera (ASEF), all data were extracted from patients in whom *Pasteurella* spp. was isolated in at least one sample, as well as the possible focus or origin of the infection through consultation of the clinical history. Bacterial identification was performed by automated biochemical test panel Vitek 2 (bioMérieux, Spain) as well as antibiotic sensitivity, interpreted according to Clinical and Laboratory Standards Institute (CLSI) standards. Medical records were systematically reviewed by collecting demographic data of infected patients, comorbidities, epidemiological data and clinical characteristics of the infection.

5. Conclusions

Despite its low prevalence, infection by *Pasteurella* spp. is of great relevance due to the complications it entails, being necessary to apply invasive procedures such as cleaning or surgical drains in more than half of the cases due to its involvement in skin and soft tissue infection.

The species most commonly isolated in our environment is *P. multocida*, which is consistent with the existing literature on human infections. It was not known which subspecies of *P. multocida* was involved, which would be interesting to know in future studies.

Close contact with companion animals, especially cats and dogs, is the main risk factor for *Pasteurella* spp. infections, although in many cases such contact cannot be established. Underlying pathology such as diabetes, cirrhosis or treatment with immunomodulatory drugs may be a predisposing factor in some of these infections, and underlying urological pathology is a risk factor for UTIs due to *Pasteurella* spp.

Pasteurella spp. infection should be considered a zoonosis in possible emergency, especially considering the large proportion of the population with pets, even more so in a predominantly rural area such as Ibiza and Formentera.

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References

1. Wilkie IW, Harper M, Boyce JD, Adler B. Pasteurella multocida: diseases and pathogenesis. Curr Top Microbiol Immunol. 2012;361:1–22.
2. Wilson BA, Ho M. Pasteurella multocida: from zoonosis to cellular microbiology. Clin Microbiol Rev. 2013 Jul;26(3):631–55.
3. Giordano A, Dincman T, Clyburn BE, Steed LL, Rockey DC. Clinical Features and Outcomes of Pasteurella multocida Infection. Medicine (Baltimore). 2015 Sep;94(36):e1285.
4. Chatelier E, Mahieu R, Hamel J-F, Chenouard R, Lozac'h P, Sallé A, et al. Pasteurella bacteraemia: Impact of comorbidities on outcome, based on a case series and literature review. Int J Infect Dis IJID Off Publ Int Soc Infect Dis. 2020 Mar;92:89–96.
5. Mahony M, Menouhos D, Hennessy J, Baird RW. Spectrum of human Pasteurella species infections in tropical Australia. PLoS One. 2023;18(1):e0281164.
6. Liu W, Chemaly RF, Tuohy MJ, LaSalvia MM, Procop GW. Pasteurella multocida urinary tract infection with molecular evidence of zoonotic transmission. Clin Infect Dis an Off Publ Infect Dis Soc Am. 2003 Feb;36(4):E58-60.
7. Peng Z, Wang X, Zhou R, Chen H, Wilson BA, Wu B. Pasteurella multocida: Genotypes and Genomics. Microbiol Mol Biol Rev. 2019 Nov;83(4).
8. Goldstein EJ. Bite wounds and infection. Clin Infect Dis an Off Publ Infect Dis Soc Am. 1992 Mar;14(3):633–8.
9. Dendle C, Looke D. Review article: Animal bites: an update for management with a focus on infections. Emerg Med Australas. 2008 Dec;20(6):458–67.
10. Martin TCS, Abdelmalek J, Yee B, Lavergne S, Ritter M. Pasteurella multocida line infection: a case report and review of literature. BMC Infect Dis. 2018 Aug;18(1):420.
11. Tena D, Romanillos O, Rodríguez-Zapata M, de la Torre B, Pérez-Pomata MT, Viana R, et al. Prosthetic hip infection due to Brucella melitensis: case report and literature review. Diagn Microbiol Infect Dis. 2007 Aug;58(4):481–5.
12. Gupta A, Berbari EF, Osmon DR, Virk A. Prosthetic joint infection due to Salmonella species: a case series. BMC Infect Dis. 2014 Nov;14:633.
13. Vasoo S, Schwab JJ, Cunningham SA, Robinson TJ, Cass JR, Berbari EF, et al. Campylobacter prosthetic joint infection. J Clin Microbiol. 2014 May;52(5):1771–4.
14. Gomez E, Kennedy CC, Gottschalk M, Cunningham SA, Patel R, Virk A. Streptococcus suis-related prosthetic joint infection and streptococcal toxic shock-like syndrome in a pig farmer in the United States. J Clin Microbiol. 2014 Jun;52(6):2254–8.
15. Griego RD, Rosen T, Orengo IF, Wolf JE. Dog, cat, and human bites: a review. J Am Acad Dermatol. 1995 Dec;33(6):1019–29.
16. Talan DA, Abrahamian FM, Moran GJ, Citron DM, Tan JO, Goldstein EJC. Clinical presentation and bacteriologic analysis of infected human bites in patients presenting to emergency departments. Clin Infect Dis an Off Publ Infect Dis Soc Am. 2003 Dec;37(11):1481–9.
17. Ferguson KB, Bharadwaj R, MacDonald A, Syme B, Bal AM. Pasteurella multocida infected total knee arthroplasty: a case report and review of the literature. Ann R Coll Surg Engl. 2014 Mar;96(2):e1-4.
18. Gabuzda GM, Barnett PR. Pasteurella infection in a total knee arthroplasty. Orthop Rev. 1992 May;21(5):601,604-605.
19. Antuña SA, Méndez JG, Castellanos JL, Jimenez JP. Late infection after total knee arthroplasty caused by Pasteurella multocida. Acta Orthop Belg. 1997 Dec;63(4):310–2.
20. Stiehl JB, Sterkin LA, Brummitt CF. Acute pasteurella multocida in total knee arthroplasty. J Arthroplasty. 2004 Feb;19(2):244–7.

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21. Ujvári B, Weiczner R, Deim Z, Terhes G, Urbán E, Tóth AR, et al. Characterization of Pasteurella multocida strains isolated from human infections. Comp Immunol Microbiol Infect Dis. 2019 Apr;63:37–43.
22. Jan L, Boute P, Mouawad F. Pasteurella multocida acute epiglottitis. Eur Ann Otorhinolaryngol Head Neck Dis. 2021 Mar;138(2):100–2.
23. Abreu F, Rodríguez-Lucas C, Rodicio MR, Vela AI, Fernández-Garayzábal JF, Leiva PS, et al. Human Pasteurella multocida Infection with Likely Zoonotic Transmission from a Pet Dog, Spain. Vol. 24, Emerging infectious diseases. United States; 2018. p. 1145–6.
24. Baykara Y, Dogon C, McCormick W, Siegert T, Hong T. Pasteurella Multocida Urinary Tract Infection in a Susceptible Patient with Non-Traumatic Feline Contact. R I Med J (2013). 2022 Feb;105(1):17–9.
25. Alaygut D, Engin A. Pasteurella aerogenes as an Asymptomatic Bacteriuria Agent. J Trop Pediatr. 2018 Feb;64(1):82–4.
26. Cortez JMC, Imam AA, Ang JY. Pasteurella multocida urinary tract infection in a pediatric patient with end-stage renal disease. Pediatr Infect Dis J. 2007 Feb;26(2):183–5.