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Source: Journal of Feline Medicine and Surgery Open Reports, 11(1)

Published By: SAGE Publishing

URL: https://doi.org/10.1177/20551169251313617

Case Report

jfms OPEN REPORTS

Journal of Feline Medicine and Surgery Open Reports
1–5

DOI: 10.1177/20551169251313617
journals.sagepub.com/home/jfmsopenreports

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Pleural and pericardial effusion associated with *Bartonella henselae* infection in a feline patient

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Abstract

Case summary A 7-year-old female spayed domestic shorthair cat was presented to our hospital with a 2-day history of anorexia, dyspnoea and lethargy. Blood tests revealed mild anaemia (packed cell volume [PCV] 22.4%) and the biochemistry panel was unremarkable. Thoracic radiographs and echocardiography showed the presence of pericardial effusion with cardiac tamponade as well as pleural effusion. During the initial attempt at pericardiocentesis, a small sample was obtained, sufficient only for fluid analysis and cytology. Subsequently, the pericardial effusion immediately resolved, presumably owing to the drainage of pericardial fluid into the pleural space. Thoracocentesis was then performed, yielding 50 ml of fluid. The analysis of the fluid was consistent with a protein-rich transudate associated with macrophagic-neutrophilic inflammation in both sampled areas. PCR was positive for *Bartonella henselae* in the pleural/pericardial fluid pool and peripheral blood. Bacterial culture was negative and feline coronavirus real-time PCR was negative. The patient was treated with marbofloxacin 5 mg/kg PO q24h for 5 weeks. No clinical signs were reported at this time; however, blood *B henselae* PCR remained positive. Treatment was changed to doxycycline at 5 mg/kg PO q12h for 6 weeks. The cat remained subclinical throughout the treatment, and a blood PCR after 6 weeks yielded negative results.

Relevance and novel information To the best of the authors' knowledge, the present clinical findings related to *B henselae* infection in a cat without concurrent heart failure have not been previously documented. This clinical case highlights the need to include *Bartonella* species as a differential diagnosis in cats with protein-rich transudate effusions associated with neutrophilic-macrophagic inflammation and fever.

Keywords: *Bartonella henselae*; pleural effusion; pericardial effusion; fever

Accepted: 26 December 2024

Introduction

Bartonellosis is a vector-borne zoonotic disease caused by species of the genus *Bartonella*.[1] *Bartonella* species infections are well documented in mammals, including cats, dogs and humans, and are associated with various clinical manifestations and disease severity.[1]

The cat is the main reservoir for *Bartonella henselae*, the aetiological agent of cat scratch disease in humans.[1–3] *B henselae* has been isolated with relative frequency in cavitary effusions in human and canine patients, being sometimes difficult to determine if it is an aetiological agent or an opportunistic pathogen.[1–4] This case report describes a cat with pleural and pericardial effusions likely caused by *B henselae* infection.

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Case description

A 7-year-old female spayed domestic shorthair cat presented with a 2-day history of dyspnoea, anorexia and lethargy. No previous diseases were reported and its retrovirus status was negative. The other cat in the household was admitted to our hospital 2 weeks earlier with fever. Investigations revealed a positive blood PCR for *Bartonella* species. Both cats had indoor/outdoor lifestyles.

A physical examination revealed pale mucous membranes, a grade II heart murmur, mild restrictive respiratory pattern (40 breaths/min), 170 beats/min, 40 rpm, fever (39.5°C), lethargy and a marked flea infestation. Blood tests showed mild normocytic normochromic non-regenerative anaemia (packed cell volume 22.4%) and a complete serum biochemistry revealed no abnormalities.

Thoracic radiographs revealed moderate pleural effusion (Figure 1), and echocardiography identified significant pericardial effusion with cardiac tamponade (Figure 2). Abdominal ultrasound showed mild ascites, but it was not sufficient enough to be sampled.

The cat was sedated with butorphanol (Torbugesic; Zoetis) at 0.3 mg/kg IV and dexmedetomidine (Dexdomitor; Ecuphar) at 1 µg/kg IV, and pericardiocentesis and thoracocentesis were performed.

A small sample was obtained during the initial attempt at pericardiocentesis, sufficient only for fluid analysis and cytology. Subsequently, the pericardial effusion immediately resolved, presumably owing to the drainage of pericardial fluid into the pleural space. Thoracocentesis was then performed, yielding 50 ml of fluid. The nucleated cell count and protein concentrations in the fluid from each location were consistent with a protein-rich transudate. Cytological examination revealed the presence of macrophages and non-degenerate neutrophils in similar numbers, with no evidence of microorganisms or neoplastic cells, consistent with macrophagic-neutrophilic inflammation in both sampled areas. Post-procedure echocardiography and ECG showed no structural, functional or cardiac rhythm abnormalities.

The mixture of pericardial/pleural fluid was submitted for aerobic/anaerobic bacterial and fungal cultures as well as RT-PCR for feline coronavirus (FCoV). Peripheral blood, and the mixture of pleural/pericardial effusions, were analysed in the Veterinary Clinical Hematology Service Laboratory of the Universitat Autònoma de Barcelona (UAB) by conventional and real-time PCR for *Bartonella* species.[5] A positive result was obtained in peripheral blood (conventional and real-time PCR) and pleural/pericardial effusions (real-time PCR). The PCR products were sequenced, analysed and compared using the GenBank database, and a 100% identity match with *B henselae* was obtained in both samples. No growth was obtained in the cultures and FCoV real-time PCR was negative.

The patient was hospitalised with marbofloxacin (5 mg/kg SC q24h, Marbocyl 1%; Vetoquinol) and amoxicillin–clavulanate (62.5 mg/cat IV q12h, amoxicillin–clavulanate 1000 mg/200 mg; Normon) along with flea treatments (first, fipronil spray [Frontline spray; Boehringer Ingelheim] and, later, imidacloprid and moxidectin spot-on [Advocate; Bayer]). Over the following days, the cat showed improvement and the fever resolved. After 3 days, follow-up radiography and echocardiography revealed no effusions, leading to the cat being discharged with marbofloxacin (5 mg/kg PO q24h, Marbocyl; Vetoquinol) and amoxicillin–clavulanate (62.5 mg/cat PO q12h, Clavaseptin; Vetoquinol). Amoxicillin-clavulanate was discontinued after the culture results came back negative, but marbofloxacin was continued.

One month later, the cat remained stable, with resolved anaemia and no effusions detected. However, a repeat blood PCR for *Bartonella* species, while the cat was still on marbofloxacin treatment, was positive. Marbofloxacin was discontinued and doxycycline was

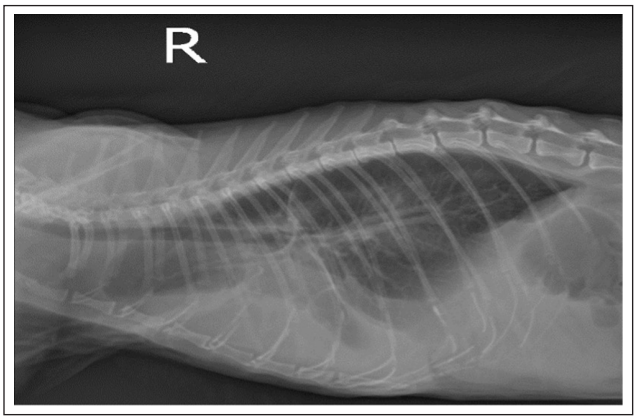

Figure 1 Right lateral thoracic radiograph showing pleural effusion

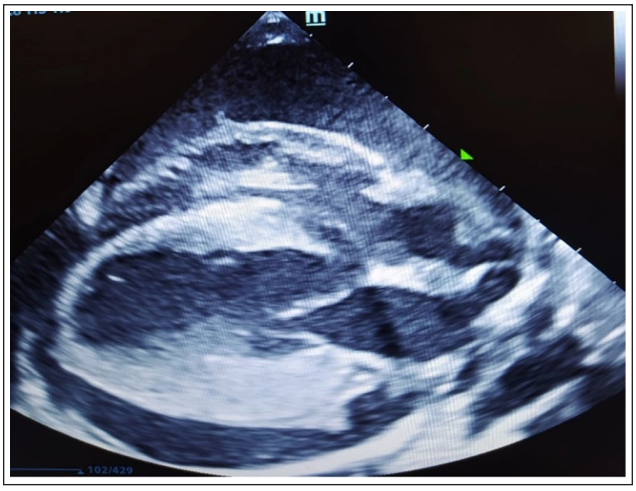

Figure 2 Echocardiography showing pericardial effusion

started (5 mg/kg PO q12h, Doxycare; Ecuphar). Six weeks later, while the cat was still receiving doxycycline, a follow-up blood PCR test for *Bartonella* species was negative; therefore, doxycycline treatment was stopped.

Three years later, the patient remained healthy and the recheck echocardiography indicated no pericardial or pleural effusions.

Discussion

Epidemiological studies indicate a high prevalence of *Bartonella* species infection in cats.[1,5] However, the few clinical cases described in the literature indicate that accurately diagnosing *Bartonella* species infections remains challenging.[1–4]

Clinical signs, lesions and laboratory abnormalities reported in association with *Bartonella* species infection in cats are fever, lymphadenomegaly, anaemia, eosinophilia, hyperglobulinaemia, thrombocytopaenia, diaphragmatic myositis, endocarditis, pyogranulomatous myocarditis, endocardial fibrosis complex, mild neurological signs, uveitis, conjunctivitis, keratitis, corneal ulcers, arthritis and osteomyelitis.[6] However, to the best of the authors' knowledge, pleural and/or pericardial effusion associated with *B henselae* infection has not been reported in cats without concurrent heart failure.[1,6,8]

One possible explanation for the pericardial effusion in our patient is infectious pericarditis caused by *B henselae*. Feline bacterial pericarditis is rarely documented, with a retrospective study of pericardial effusion in 146 cats finding no cases of septic pericarditis.[9] Another study of 83 cats with pericardial effusion identified hypertrophic cardiomyopathy, neoplasia and systemic infection as the main causes, and there have been few case reports of cats with bacterial pericarditis caused by bacteria other than *Bartonella* species.[8,10–13] This raises the question of whether *Bartonella* species could produce a similar clinical presentation.

The most common causes of pleural effusion in cats include congestive heart failure, feline infectious peritonitis (FIP), neoplasia, pyothorax or chylothorax.[14] Our patient presented with cardiac tamponade, which could explain the pleural effusion. Another possibility is pleuritis resulting from haematogenous spread or vasculitis due to *B henselae*-induced endothelial damage.[15–22]

In human medicine, *Bartonella* species infections have been associated with pericardial and pleural effusions.[15–19] In dogs, *B henselae* and *Bartonella vinsonii* subspecies *berkhoffii* have been identified in pleural and peritoneal effusions, though their pathogenic role remains unclear.[20–22] These observations suggest a comparable scenario might occur in cats. On the other hand, a PCR study for vector-borne pathogens in dogs with pericardial effusion did not detect *Bartonella* species.[23]

The effusions in our patient were classified as protein-rich transudates. An exudate typically indicates an inflammatory response to bacterial infection; however, this may not always apply to *Bartonella* species infections. The lipopolysaccharide of *Bartonella quintana* has demonstrated anti-inflammatory properties, while studies suggest that *B vinsonii* subspecies *berkhoffii* can lead to immunosuppression.[21,24,25]

Research on the pathophysiology of *Bartonella* species infection reveals their ability to invade endothelial cells, potentially increasing vascular permeability and leading to effusions without a significant inflammatory response. In addition, isolated cases in dogs have shown protein-rich transudate effusions where *Bartonella* species were detected.[21,24–26]

Fluid cytology analysis of the pericardial and pleural effusions revealed a protein-rich transudate with mixed macrophagic-neutrophilic inflammation. Common infectious agents associated with this type of inflammation in cats include FCoV, mycobacteria and systemic fungal infections, with occasional involvement from *Actinomyces*, *Nocardia*, *Rhodococcus*, *Streptomyces*, *Francisella*, *Bartonella* and *Leishmania* species, as well as rare immunomediated processes such as idiopathic sterile pyogranuloma.[27]

Although the FCoV real-time PCR (IDEXX Laboratory) results were negative, this test is not the gold standard, so a false negative is possible. However, given the patient's improvement and resolution of clinical signs, FIP is unlikely. In addition, culture and cytology tests did not reveal any fungal pathogens or other bacterial infections.

As a result of financial constraints, mycobacterial-specific culture and/or PCR, and *Leishmania* species PCR or serology, were not conducted. However, considering the patient's clinical presentation and disease progression with the given treatment, *Leishmania* species infection is unlikely.[28] In addition, considering the acute onset of clinical signs and outcome, a mycobacterial infection was also deemed unlikely, as mycobacterial infections usually only respond after prolonged periods with triple antibiotic therapy.

Bartonella species are difficult to detect directly in blood samples with traditional culture methods because of their low-level, intermittent bacteraemia and the requirement for prolonged incubation periods. Therefore, despite being the 'gold standard' method for diagnosing, a negative culture does not necessarily rule out their presence.[6,29,30]

The most reliable methods for confirming *Bartonella* species infection involve specialised culture techniques such as lysis centrifugation, cell culture isolation and insect-based growth enrichment.[1] *Bartonella* species can be cultured from reservoir hosts and occasionally from accidental hosts using agar plates with 5% defibrinated rabbit or sheep blood.[1] A combined method

using pre-enrichment liquid culture (Bartonella/alpha-Proteobacteria growth medium [BAPGM]), PCR and subculture on agar plates has been used to improve the detection and isolation of *Bartonella* species in cats, dogs and humans.[29] In this case, traditional culture media likely resulted in no growth from the pleural/pericardial effusion.

We obtained positive PCR results for *Bartonella* species in both peripheral blood (conventional and real-time PCR) and pleural/pericardial effusion (real-time PCR). While commercial veterinary laboratories offer conventional and quantitative PCR (qPCR) for detecting *Bartonella* species, the accuracy may vary depending on the primers and protocols used.[6]

Cats are natural reservoirs for *B henselae*, complicating serological diagnosis. Serology is primarily used for exclusion rather than confirmation; therefore, it was not performed for this patient.[1] A multimodal testing approach is advised for diagnosing feline bartonellosis, as one negative result is not conclusive.[29,30]

Recognising an active infection in cats can be challenging because they can be subclinically infected. Treatment is advised only for those cats suspected of exhibiting clinical signs due to *Bartonella* species or for those living with children or immunocompromised individuals owing to zoonotic risks.[1] In our case, the patient was not immunosuppressed, no other causes for the clinical signs were identified and flea infestation was noted.

There is no standardised treatment protocol for *Bartonella* species and the ideal therapy is still unknown.[1] Prolonged treatment is generally recommended, with recent trends suggesting a combination of fluoroquinolone and doxycycline, although in vitro studies have reported conflicting results on the need for multiple antibiotics.[1,6,7,31–35]

In our case, initial treatment with amoxicillin–clavulanate and marbofloxacin for 2 weeks, followed by 4 weeks of marbofloxacin alone, did not resolve the infection. However, after 6 weeks of doxycycline at 5 mg/kg PO q12h, a negative blood PCR was achieved. Although other doxycycline-responsive pathogens could not be completely ruled out, this was considered unlikely based on the type of inflammation present and clinical signs.

Amoxicillin–clavulanate and marbofloxacin were initially used for broad-spectrum coverage before confirming *B henselae*. Marbofloxacin was continued owing to the patient's positive response and the good response to fluoroquinolones seen in some studies.[7,32–34]

Conclusions

This case emphasises the importance of considering *Bartonella* species as a differential diagnosis in cats with protein-rich transudate effusions, neutrophilic-macrophagic inflammation and fever. The clinical signs were likely linked to *B henselae* infection, as no other causes were identified and the patient responded positively to treatment. Further research and case studies are needed to better understand the effects of this pathogen on healthy, non-immunocompromised cats and to characterise its morbidity. In addition, the importance of using combined diagnostic tools to detect or rule out the pathogen as the cause of clinical conditions is reinforced.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding The *Bartonella* species PCRs were carried out thanks to a UAB research project led by Laia Solano-Gallego and funded by Flag to Neil. Alejandra Álvarez-Fernández held a UAB research contract funded by Bayer Animal Health/Elanco.

Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognized high standards ('best practice') of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

Informed consent Informed consent (verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (experimental or non-experimental animals, including cadavers, tissues and samples) for all procedure(s) undertaken (prospective or retrospective studies). For any animals or people individually identifiable within this publication, informed consent (verbal or written) for their use in the publication was obtained from the people involved.

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References

1 Álvarez-Fernández A, Breitschwerdt E and Solano-Gallego **L. *Bartonella* infections in cats and dogs including zoonotic aspects.** *Parasites Vectors* 2018; 11: 624. DOI: 10.1186/s13071-018-3152-6.

2 Bergh K, Bevanger L, Hanssen I, et al. **Low prevalence of *Bartonella henselae* infections in Norwegian domestic and feral cats.** *APMIS* 2002; 110: 309–314.

3 Solano-Gallego L, Hegarty B, Espada Y, et al. **Serological and molecular evidence of exposure to arthropod-borne organisms in cats from northeastern Spain.** *Vet Microbiol* 2006; 118: 274–277.

4 Kordick D, Brown T, Shin K, et al. **Clinical and pathologic evaluation of chronic *Bartonella henselae* or *Bartonella clarridgeiae* infection in cats.** *J Clin Microbiol* 1999; 37: 1536–1547.

5 Álvarez-Fernández A, Maggi R, Martín-Valls GE, et al. **Prospective serological and molecular cross-sectional study focusing on *Bartonella* and other blood-borne organisms**

in cats from Catalonia (Spain). *Parasit Vectors* 2022; 15: 6. DOI: 10.1186/s13071-021-05105-6.
6 Taber R, Pankowski A, Ludwig AL, et al. **Bartonellosis in dogs and cats, an update.** *Vet Clin North Am Small Anim Pract* 2022; 52: 1163–1192.
7 Bradbury CA and Lappin MR. **Evaluation of topical application of 10% imidacloprid-1% moxidectin to prevent *Bartonella henselae* transmission from cat fleas.** *J Am Vet Med Assoc* 2010; 236: 869–873.
8 Davidson BJ, Paling AC, Lahmers SL, et al. **Disease association and clinical assessment of feline pericardial effusion.** *J Am Anim Hosp Assoc* 2008; 44: 5–9.
9 Hall DJ, Shofer F, Meier CK, et al. **Pericardial effusion in cats: a retrospective study of clinical findings and outcome in 146 cats.** *J Vet Intern Med* 2007; 21: 1002–1007.
10 LeBlanc N and Scollan KF. **Bacterial pericarditis in a cat.** *JFMS Open Rep* 2015; 1. DOI: 10.1177/2055116915603077.
11 Lobetti RG. **Anaerobic bacterial pericardial effusion in a cat.** *J S Afr Vet Assoc* 2007; 78: 175–177.
12 Brook I. **Pericarditis caused by anaerobic bacteria.** *Int J Antimicrob Agents* 2009; 33: 297–300.
13 Majoy SB, Sharp CR, Dickinson AE, et al. **Septic pericarditis in a cat with pyometra.** *J Vet Emerg Crit Care (San Antonio)* 2013; 23: 68–76.
14 König A, Hartmann K, Mueller R, et al. **Retrospective analysis of pleural effusion in cats.** *J Feline Med Surg* 2018; 21: 1102–1110.
15 Levy P, Fournier P, Carta M, et al. **Pericardial effusion in a homeless man due to *Bartonella quintana*.** *J Clin Microbiol* 2003; 41: 5291–5293.
16 Takeda N, Ishiwada N, Fukasawa C, et al. **Pediatric pneumonia, pleural effusion, and pericarditis following cat scratch disease and serological cross-reactions among *Bartonella henselae* and *Rickettsia japonica* determined by indirect fluorescence antibodies** [article in Japanese]**.** *Kansenshogaku Zasshi* 2007; 81: 206–209.
17 Kimura S, Hasegawa S, Yanagihara M, et al. **Cat-scratch disease with severe pleuritis in a 6-year-old girl.** *Pediatr Int* 2015; 57: 501–503.
18 Sodini C, Zani EM, Pecora F, et al. **A case of atypical Bartonellosis in a 4-year-old immunocompetent child.** *Microorganisms* 2021; 9. DOI: 10.3390/microorganisms 9050950.
19 Karanyi K. **Fever, back pain and pleural effusion in a four-year-old boy.** *Pediatr Infect Dis J* 1994; 13: 657–672.
20 Weeden AL, Cherry NA, Breitschwerdt EB, et al. ***Bartonella henselae* in canine cavitary effusions: prevalence, identification, and clinical associations.** *Vet Clin Pathol* 2017; 46: 326–330.
21 Cherry N, Diniz P, Maggi R, et al. **Isolation or molecular detection of *Bartonella henselae* and *Bartonella vinsonii* subsp.*berkhoffii* from dogs with idiopathic cavitary effusions.** *J Vet Intern Med* 2009; 23: 186–189.
22 Duncan A, Marr H, Birkenheuer A, et al. ***Bartonella* DNA in the blood and lymph nodes of golden retrievers with lymphoma and in healthy controls.** *J Vet Intern Med* 2008; 22: 89–95.
23 Tabar M-D, Movilla R, Serrano L, et al. **PCR evaluation of selected vector-borne pathogens in dogs with pericardial effusion.** *J Small Anim Pract* 2018; 59: 248–252.
24 Popa C, Abdollahi-Roodsaz S, Joosten LAB, et al. ***Bartonella quintana* lipopolysaccharide is a natural antagonist of Toll-like receptor 4.** *Infect Immununity* 2007; 75: 4831–4837.
25 Pappalardo BL, Brown TT, Tompkins M, et al. **Immunopathology of *Bartonella vinsonii (berkhoffii)* in experimentally infected dogs.** *Vet Immunol Immunopathol* 2001; 83: 125–147.
26 Dehio C. ***Bartonella* interactions with endothelial cells and erythrocytes.** *Trends Microbiol* 2001; 9: 279–285.
27 Giuliano A, Watson P, Owen L, et al. **Idiopathic sterile pyogranuloma in three domestic cats.** *J Small Anim Pract* 2018; 61: 202–205.
28 Pennisi MG, Cardoso L, Baneth G, et al. **LeishVet update and recommendations on feline leishmaniosis.** *Parasit Vectors* 2015; 8: 302. DOI: 10.1186/s13071-015-0909-z.
29 Duncan A, Maggi R and Breitschwerdt E. **A combined approach for the enhanced detection and isolation of *Bartonella* species in dog blood samples: pre-enrichment liquid culture followed by PCR and subculture onto agar plates.** *J Microbiol Methods* 2007; 69: 273–281.
30 Burzo M, Antonelli M, Pecorini G, et al. **Fever of unknown origin and splenomegaly: a case report of blood culture negative endocarditis.** *Medicine* 2017; 96. DOI: 10.1097/MD.0000000000009197.
31 Brunt J, Guptill L, Kordick DL, et al. **Panel report on diagnosis, treatment, and prevention of *Bartonella spp*. infections.** *J Feline Med Surg* 2006; 8: 213–226.
32 Perez C, Hummel JB, Keene BW, et al. **Successful treatment of *Bartonella henselae* endocarditis in a cat.** *J Feline Med Surg* 2010; 12: 483–486.
33 Kordick DL, Papich MG and Breitschwerdt EB. **Efficacy of enrofloxacin or doxycycline for treatment of *Bartonella henselae* or *Bartonella clarridgeiae* infection in cats.** *Antimicrob Agents Chemotherapy* 1997; 41: 2448–2455.
34 Podsiadly E, Zabicka D, Demkow U, et al. **Susceptibility of Polish *Bartonella henselae* strains.** *Polish J Microbiol* 2012; 61: 143–145.
35 Li T, Feng J, Xiao S, et al. **Identification of FDA-approved drugs with activity against stationary phase *Bartonella henselae*.** *Antibiotics* 2019; 8: 50. DOI: 10.3390/antibiotics8020050.