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Penicillium marneffei Isolated from a Thai AIDS Patient with Fungemia

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Penicillium marneffei was isolated from three blood cultures of a Thai woman with AIDS and then identified as such. The patient, 41 a year-old female from northeast Thailand came to Japan 10 years ago and married a Japanese man. She was reportedly the third patient infected with this fungal species in Japan, and considered to be the first case from whom the causative fungus was successfully cultured, which led to the diagnosis of penicilliosis marneffei. The colony of the isolate, which was cultured on Sabouraud dextrose agar at 25-27℃, was initially white and pannose, gradually turned in color from yellow to yellow-green, and diffused a deep red pigment into the medium. Conidial heads were divergent, and chains of conidia were formed from phialides. Colonies of the isolate, which was cultured on brain-heart infusion agar at 35℃, had a grayish white, membranous yeast-like form with fine plicae and microscopically consisted of short hyphae. Furthermore, 560 bases of the internal transcribed spacer (ITS) region of the ribosomal RNA gene including the 5.8S region (ITS1-5.8S-ITS2) (DDBJ accession number AB298970) were sequenced and allowed an unequivocal species identification.

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Exotic Small Mammals as Potential Reservoirs of Zoonotic *Bartonella* spp.

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To evaluate the risk for emerging human infections caused by zoonotic *Bartonella* spp. from exotic small mammals, we investigated the prevalence of *Bartonella* spp. in 546 small mammals (28 species) that had been imported into Japan as pets from Asia, North America, Europe, and the Middle and Near East. We obtained 407 *Bartonella* isolates and characterized them by molecular phylogenetic analysis of the citrate synthase gene, *gltA*. The animals examined carried 4 zoonotic *Bartonella* spp. that cause human endocarditis and neuroretinitis and 6 novel *Bartonella* spp. at a high prevalence (26.0%, 142/546). We conclude that exotic small mammals potentially serve as reservoirs of several zoonotic *Bartonella* spp.

The genus *Bartonella* includes a variety of gram-negative, fastidious, hemotrophic bacteria that are transmitted by blood-sucking arthropod vectors. The genus consists of 20 species and 3 subspecies; at least 11 of these species are known or suspected to be pathogenic for humans as causative agents of emerging zoonoses (*1*).

The following *Bartonella* spp. have been isolated from wild mice: *B. birtlesii* (*2*), *B. doshiae*, *B. grahamii*, *B. taylorii* (*3*), and *B. vinsonii* subsp. *arupensis* and subsp. *vinsonii* (*4*). In several countries, the following species have been carried by rats of the genus *Rattus*: *B. elizabethae* (*5*), *B. tribocorum* (*6*), *B. phoceensis*, and *B. rattimassiliensis* (*7*). In South Africa,

strains genetically related to *B. elizabethae* also have been isolated from mice of the genera *Aethomys* and *Tatera* (*8*). The main reservoir of *B. washoensis* is considered to be wild squirrels (*9*). Of these rodent-associated *Bartonella* spp., *B. elizabethae*, *B. grahamii*, *B. vinsonii* subsp. *arupensis*, and *B. washoensis* have been implicated in the human infections endocarditis (*10*), neuroretinitis (*11*), pyrexia and endocarditis (*4,12*), and myocarditis (*9*), respectively.

Previous studies have demonstrated high prevalence of infection with *Bartonella* spp. in wild and peridomestic small animals in Europe (*7,13–15*), North and South America (*5,16–19*), Asia (*20–23*), and Africa (*8*). Thus, these animals are thought to be reservoirs of several *Bartonella* spp. and sources of infection for humans.

Many exotic animals are traded as pets around the world and have been imported into Japan without quarantine. However, no data exist on the prevalence of infection with *Bartonella* spp., especially in exotic pet animals. Our study objectives were to 1) examine the prevalence of *Bartonella* spp. infection in exotic small mammals imported into Japan from various countries, 2) compare the diversity of these *Bartonella* strains by analyzing the partial sequence of the citrate synthase gene (*gltA*), and 3) evaluate the possibility that these mammals may serve as potential reservoirs of zoonotic *Bartonella* spp.

Materials and Methods

Animals and Samples

For this study, 546 exotic small mammals were purchased from trading companies. The animals represented 3 orders and included 6 families, 23 genera, and 28 species (Table 1). They had been imported into Japan as pets from June 2004 through October 2007 from 8 countries in 4 geographic regions: Asia (China, Thailand, and Indonesia), Europe (the Netherlands and Czech Republic), North America (United States), and the Middle and Near East (Egypt and Pakistan). Of the 546 animals, 367 had been captured in their natural environment and 179 had been bred in the exporting countries. Heparinized blood samples were aseptically collected from each animal (anesthetized with chloroform) and centrifuged at 3,000 rpm for 15 min. Plasma was removed and the blood sample pellets were kept at –80°C until examination.

Isolation of Bacteria

The blood sample pellets were thawed at room temperature, 100-μL supplemented Medium 199 (*24*) was added to each pellet, and each sample was mixed well. A 100-μL sample of each mixture was plated on 2 heart infusion agar (DIFCO, Sparks Glencoe, MI, USA) plates containing 5% defibrinated rabbit blood. The plates were incubated at 35°C under 5% CO_2. After 2 weeks of incubation, 2 or 3 colonies with genus *Bartonella* morphologic characteristics (small, gray or cream-yellow, round colonies) were picked from each plate, confirmed to be gram-negative pleomorphic bacteria, and subcultured using the same conditions used for the original cultures.

DNA Extraction and PCR

The genomic DNA of each isolate was extracted by using InstaGene Matrix (Bio-Rad, Hercules, CA, USA). The extracted DNA was used for PCR analysis of a 312-bp part of the *gltA* gene to confirm that the bacteria were from the genus *Bartonella*. PCR was performed by using an iCycler (Bio-Rad) with a 20-μL mixture containing 20 ng extracted DNA, 200 μM of each deoxynucleoside triphosphate, 1.5 mmol/L $MgCl_2$, 0.5 U Taq DNA polymerase (Promega, Madison, WI, USA), and 1 pmol of each primer. The specific primer pair and PCR conditions for *gltA* were as previously reported (*25*).

DNA Sequencing and Phylogenetic Analysis

The PCR products were purified by using a commercial kit (Spin Column PCR Products Purification Kit; Bio Basic, Markham, Ontario, Canada). Direct DNA sequencing of the purified PCR products was carried out by using dye terminator chemistry with specific primers (*25*) and a Model 3130 Genetic Analyzer (Applied Biosystems, Foster City, CA, USA). The 312-bp *gltA* sequences from the isolates and type strains of established *Bartonella* spp. in GenBank/EMBL/DDBJ were aligned with the Clustal X program (*26*), and a phylogenetic tree was drawn, based on the sequence data and using the neighbor-joining method (*27*) with the Kimura 2-parameter distance method (*28*) in MEGA 4 (*29*). Bootstrap analysis was carried out with 1,000 replications (*30*).

Statistical Analysis

The results were analyzed in 2×2 tables. Chi-square tests were used to examine the statistical significance; $p<0.05$ was considered significant.

Results

Prevalence of Bartonellae

The prevalence of bartonellae in the exotic small mammals examined was 26.0% (142/546). A total of 407 isolates were obtained from the 142 bacteremic animals (Table 1). The prevalence by animal origin was 37.3% (137/367) in captive animals and 2.8% (5/179) in animals from breeder facilities. A significantly higher prevalence of bartonellae was observed in captive animals than in animals from breeder facilities ($p<0.001$). In the captive animals, the prevalence by region varied up to 47.2% in Asia, which is higher than the 39.7% prevalence in North America. The prevalence of *Bartonella* isolates by corresponding taxonomic family of host animal ranged from 38.6% (49/127) in the family Muridae to 43.9% (69/157) in the family Sciuridae. No bartonellae were detected in animals in the families Octodontidae and Erinaceidae. Among animals from breeders, only 5 chipmunks (*Tamias sibiricus*) from China were found to be infected with bartonellae; no bartonellae were isolated from animals in the families Petauridae, Muridae, Octodontidae, or Dipodidae.

Bartonellae were isolated from 17 of the 28 animal species studied (Table 1). The prevalence by animal species varied from 9.7% (3/31) in the Cairo spiny mouse (*Acomys cahirinus*) to 100% (10/10) in the bushy-tailed jird (*Sekeetamys calurus*). Prevelances were considerably higher for the bushy-tailed jird, large Egyptian gerbil (*Gerbillus pyramidum*), greater Egyptian jerboa (*Jaculus orientalis*), and lesser Egyptian jerboa (*J. jaculus*) at 100% (10/10), 90.0% (9/10), 81.3% (13/16), and 75.0% (6/8), respectively.

DNA Sequences and Phylogeny of Isolates

The 407 isolates in this study were classified into 53 genotypes on the basis of DNA sequence analysis of a 312-bp fragment of their *gltA* genes. The sequence of a genotype from a Cairo spiny mouse was identical to that of the *B. elizabethae* type strain (GenBank accession no. Z70009) isolated from a human patient with endocarditis (*10*). The other 52 genotypes were found to be novel genotypes after comparison with known *Bartonella* spp. The phylogenetic tree of the *gltA* sequences shows that the 52 novel genotypes are clearly clustered in 10 genogroups, designated A to J (Figure).

Of the 52 novel genotypes, genogroup A, which consisted of 21 genotypes (AB444954 to AB444974) isolated from 7 squirrel species, was related to *B. washoensis* strain Sb944nv

(AF470616), which was isolated from a California ground squirrel (*Spermophilus beecheyi*) and was genetically identical to an isolate from a human patient with myocarditis (*9*). The sequence similarities of these genotypes and *B. washoensis* strain Sb944nv ranged from 94.2% to 97.4%. Genogroup A contained *B. washoensis*–like genotypes; the genotypes from each squirrel species formed a separate clade, except for the genotypes from Richardson's ground squirrels (*Sp. richardsonii*) and Columbian ground squirrels (*Sp. columbianus*), which formed a mixed clade (Figure).

In this study, 18 genotypes formed the 6 unique genogroups B to G. The DNA sequences of the genotypes in each genogroup showed relatively low similarity (82.4%–94.6%) to the type strains of known *Bartonella* spp., and sequence similarities between genogroups B to G were also low (87.5%–93.6%). The novel *Bartonella* genogroups B, C, D, and E were isolated from greater Egyptian jerboas, tricolored squirrels (*Callosciurus notatus*), fat-tailed gerbils (*Pachyuromys duprasi*), and golden spiny mice (*A. russatus*), respectively. The genotypes in group F were isolated from 6 animal species: large Egyptian gerbils, fat-tailed gerbils, fat sand rats (*Psammomys obesus*), lesser Egyptian jerboas, greater Egyptian jerboas, and bushy-tailed jirds; those in genogroup G were isolated from a bushy-tailed jird and a large Egyptian gerbil (Figure). In genogroup F, 3 of the 9 isolates from fat-tailed gerbils and the 14 isolates from fat sand rats had identical *gltA* DNA sequences. Furthermore, 5 of the 7 isolates from greater Egyptian jerboas and 2 of the 3 isolates from a lesser Egyptian jerboa also had identical sequences.

The 2 novel genotypes (AB444993 and AB444994) in genogroup H were also isolated from Siberian chipmunks, a Hokkaido squirrel (*Sciurus vulgaris* subsp. *orientis*), and Eurasian small flying squirrels (*Pteromys volans*). Their sequences showed high similarity (98.4%–98.7%) to *B. grahami* type strain (V2) (Figure).

The 10 novel genotypes in genogroup I were isolated from 9 animal species, and the sequence similarities between the genotypes (AB444995 to AB445005) and *B. elizabethae* type strain (F9251) ranged from 95.5% to 98.7%. The DNA sequences of *gltA* of the 3 isolates from a Cairo spiny mouse (AB445000) were identical to that of *B. elizabethae* (F9251). The sequences of the 13 isolates from lesser Egyptian jerboas were identical to those of the 16 isolates from greater Egyptian jerboas.

In genogroup J, a unique genotype (AB445006) was isolated from an American red squirrel (*Tamiasciurus hudosonicus*); it had 96.2% sequence similarity to *B. clarridgeiae* type strain (Houston-2), whose natural reservoir is cats (Figure).

Multiple Infections with Different *Bartonella* Genogroups and Genotypes

Of the 142 *Bartonella*-positive animals, 25 (17.6%) were found to be infected with different *Bartonella* genogroups or genotypes (Table 2). A lesser Egyptian jerboa carried 3 different genotypes in 2 genogroups; the other 24 animals carried 2 different genogroups or genotypes. Of these 24 animals, an American red squirrel carried a *B. washoensis*–like strain in genogroup A and *B. clarridgeiae*–like strains in genogroup J; 11 animals were infected with *B. elizabethae*–like strains in genogroup I and strains in genogroups B, C, D, E, F, or G, and the remaining 12 carried different genotypes in the same genogroup (Table 2).

Discussion

We report prevalence of bartonellae in exotic small mammals imported into Japan as pets. We found that 26.0% (142/546) of the animals examined had bartonellae in their blood. Prevalence among wild captive animal species was high (37.3%), significantly higher ($p<0.001$) than that among animals from breeder facilities. Of the 179 animals (representing 9 species) from breeder facilities, only 5 Siberian chipmunks imported from a Chinese breeder were found to carry bartonellae, and these were of the same genotype as bartonellae from wild captive animals. These results suggest that animals in breeder facilities may be maintained under hygienic conditions from birth to export, so they rarely have contact with wild animals or blood-sucking arthropod vectors.

Most isolates from animals in the family Sciuridae (58.7%; 122/208) were in genogroup A and showed high sequence similarity to *B. washoensis*. Kosoy et al. (*9*) have reported that *B. washoensis* is widely distributed in ground squirrels in the western part of the United States and that it was isolated from a human with myocarditis in Nevada, USA. Thus, captive squirrels carrying *B. washoensis*–like organisms could serve as a source of infection for humans.

Animals in the family Sciuridae were also found to be carrying several genotypes of bartonellae in genogroups C, *B. grahamii*–like strains in genogroup H, *B. elizabethae*–like strains in genogroup I, and *B. clarridgeiae*–like strains in genogroup J. The sequence similarities

between the genotypes and the related *Bartonella* spp. type strains ranged from 98.4% to 98.7% for *B. grahamii*, from 95.5% to 95.8% for *B. elizabethae*, and were 96.2% for *B. clarridgeiae*. In humans, *B. grahamii*, *B. elizabethae*, and *B. clarridgeiae* have been reported to cause neuroretinitis (*11*), endocarditis (*10*) and cat-scratch disease (*31*), respectively. These findings suggest that exotic squirrels also might be a potential source of *Bartonella* infections in humans. Although *B. clarridgeiae* has mainly been isolated from cats (*1*), *B. clarridgeiae*–like strains were isolated from an American red squirrel in this study. *B. clarridegeiae*–like organisms have also been isolated from yellow-necked mice (*Apodemus flavicollis*) in Sweden (*14*) and Greece (*15*).

The sequence similarity of the *gltA* sequence (312 bp) of the *B. clarridgeiae*–like genotype isolated in our study to that of the strain isolated from the yellow-necked mouse (AF391788) was relatively high (97.7%). Recently, *B. rochalimae*, a *B. clarridgeiae*–like organism, was isolated from a human patient with bacteremia, fever, and splenomegaly (*32*). The *B. clarridgeiae*–like strain from the American red squirrel in this study also showed high *gltA* sequence similarity (96.8%) with that of *B. rochalimae* strain BMGH. Studies will be required to clarify the pathogenicity of *B. clarridgeiae*–like organisms for humans. Such studies would include 1) evaluation of the organisms' ability to invade human erythrocytes and/or endothelial cells, 2) demonstration of the presence and expression of the genes of type 4 secretion systems (VirB/VirD4 or Vbh) and Trw, and 3) comparisons of the entire genome sequences of the organisms and with those of other human pathogenic *Bartonella* spp.

In this study, *Bartonella* genogroups D, E, and G were isolated from animals in the family Muridae, and *Bartonella* genogroup B was isolated from animals in the family Dipodidae. These findings suggest strict host specificity between the strains in these genogroups and the host animal family. However, findings also showed wide host species diversity; strains in genogroup F were isolated from 6 animal species, and strains from genogroup I (*B. elizabethae*–like) were isolated from 9 animal species. *Bartonella* strains in genogroup F were isolated from animals in the families Muridae and Dipodidae. Genogroup I (*B. elizabethae*–like) strains were also isolated from animals in the family Sciuridae. *B. elizabethae* has been isolated from different animal species, e.g., a human patient and genus *Rattus* rats (*5*,*10*), and *B. elizabethae* DNA has been isolated from a dog (*33*). In our study, 3 *Bartonella* isolates from a Cairo spiny mouse imported from Egypt had an identical *gltA* sequence to that of the *B. elizabethae* type strain. Thus, some

Bartonella spp., such as *B. elizabethae* and *B. washoensis*, infect host animals in diverse families and may have zoonotic potential.

In the present study, 17.6% (25/142) of exotic animals were infected with different *Bartonella* genotypes or genogroups. In particular, 3 isolates from a greater Egyptian jerboa were classified in 3 different genotypes. Of the 25 *Bartonella*-positive animals, 13 showed co-infection with different *Bartonella* genogroups. Of these 13 animals, 12 carried *B. elizabethae*–like strains in genogroup I. In contrast, strains with identical *gltA* sequences were isolated from 2 different animal species, such as greater Egyptian jerboas and lesser Egyptian jerboas, Siberian chipmunks and Hokkaido squirrels, and fat-tailed gerbils and fat sand rats. These findings suggest that some *Bartonella* species have a wide host range and may be transmitted horizontally by some blood-sucking arthropod vectors with low host specificity.

In summary, we examined the possibility that exotic small mammals may be reservoirs of zoonotic *Bartonella* spp. around the world. The animals in this study carried, at high prevalence, several *Bartonella* spp. that are human pathogens. Novel species were suggested by the fact that some of the genotypes in 6 genogroups (B to G) showed relatively low similarity (<94.6%) to known *Bartonella* spp. and formed independent clusters according to phylogenetic analysis based on partial *gltA* sequences. More taxonomic studies should sequence other housekeeping genes, such as *rpoB*, 16S rRNA, *ftsZ*, *groEL*, and *ribC*, to confirm whether these isolates are novel *Bartonella* spp. (*34*). To prevent human infections by *Bartonella* spp. carried by exotic small mammals, a quarantine system for these animals should be established as early as possible. Further studies will be necessary to clarify the route of transmission among exotic small mammals and to evaluate the pathogenicity for humans and animals of the isolates belonging to novel *Bartonella* genotypes found in this study.

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Table 1. Prevalence of *Bartonella* spp. among exotic small mammals imported into Japan as pets, June 2004–October 2007

Origin	Animal, taxonomic species	No. positive/no. tested (%)	Subtotal (%)
Wild-captive			
Asia			
China	*Spermophilus dauricus**	4/10 (40.0)	42/89 (47.2)
	Sciurus vulgaris subsp. *orientis**	2/10 (20.0)	
	*Tamias sibiricus**	12/29 (41.4)	
	*Pteromys volans**	5/10 (50.0)	
Thailand	*Callosciurus notatus**	19/30 (63.3)	
North America			
USA	*Tamiasciurus hudosonicus**	3/18 (16.7)	27/68 (39.7)
	*Glaucomys volans**	6/10 (60.0)	
Unknown	*Sp. columbianus**	6/20 (30.0)	
	*Sp. richardsonii**	12/20 (60.0)	
Europe			
The Netherlands	*Pachyuromys duprasi*†	13/18 (72.2)	13/47 (27.7)
The Netherlands, Czech Republic	*Octodon degus*‡,§	0/29 (0.0)	
Middle and Near East			
Egypt	*Mus minutoides*†	0/20 (0.0)	55/163 (33.7)
	Acomys cahirinus†	3/31 (9.7)	
	A. russatus†	8/13 (61.5)	
	Lemniscomys barbarus†	0/11 (0.0)	
	Psammomys obesus)†	6/10 (60.0)	
	Meriones tristrami†	0/4 (0.0)	
	Sekeetamys calurus†	10/10.(100)	
	Gerbillus pyramidum†	9/10 (90.0)	
	Jaculus orientalis¶	13/16 (81.3)	
	J. jaculus¶	6/8 (75.0)	
	Hemiechinus auritus#	0/10 (0.0)	
Pakistan	*Salpingotulus michaelis*¶	0/20 (0.0)	
	Subtotal	137/367 (37.3)	
Breeder facility			
Asia			
China	*Tamias sibiricus**	5/30 (16.7)	5/60 (8.3)
Indonesia	*Petaurus breviceps***	0/20 (0.0)	
Thailand	*Pe. breviceps***	0/10 (0.0)	
Europe			
The Netherlands	*Lagurus lagurus*†	0/9 (0.0)	0/99 (0.0)
	Pa. duprasi†	0/10 (0.0)	
	Mesocricetus auratus†	0/20 (0.0)	
	Phodopus roborovskii†	0/10 (0.0)	
The Netherlands, Czech Republic	*Ph. sungorus*†‡	0/30 (0.0)	
	O. degus‡§	0/20 (0.0)	
Middle and Near East			
Pakistan	*Sa. michaelis*¶	0/20 (0.0)	0/20 (0.0)
	Subtotal	5/179 (2.8)	
	Total	142/546 (26.0)	

*Member of the order Rodentia, family Sciuridae.
†Member of the order Rodentia, family Muridae.
‡Data for the Netherlands and Czech Republic are pooled because number of animals from these 2 countries was unknown.
§Member of the order Rodentia, family Octodontidae.
¶Member of the order Rodentia, family Dipodidae.
#Member of the order Insectivora, family Erinaceidae.
**Member of the order Diprotodonia, family Petauridae.

Table 2. Multiple infection of different *Bartonella* genotypes in exotic small mammals imported into Japan as pets, June 2004–October 2007

Host	No. animals	GenBank accession nos. of the isolates in 9 genogroups*								
		A	B	C	D	E	F	G	I	J
Daurian ground squirrel	1	4962								
		4963								
Siberian chipmunk	1	4965								
		4966								
	1	4964								
		4965								
Tricolored squirrel	2			4977					4995	
	1			4977					4996	
American red squirrel	1	4971								5006
Southern flying squirrel	1	4972								
		4973								
Columbian ground squirrel	1	4957								
		4958								
Richardson's ground squirrel	2	4959								
		4960								
	1	4954								
		4959								
	1	4954								
		4955								
Fat-tailed gerbil	3				4978				5003	
Golden spiny mouse	1					4979			4998	
Fat sand rat	1						4984		5002	
Bushy-tailed jird	1						4988			
							4989			
	1							4991	5004	
	1						4987			
							4989			
Large Egyptian gerbil	1						4981		5001	
Greater Egyptian jerboa	1		4975							
			4976							
	1						4986		5005	
Lesser Egyptian jerboa	1						4986		5005	
							4985			

*Genbank accession numbers all begin with AB44 and are abbreviated to the last 4 digits; e.g., AB444962 appears as 4962.

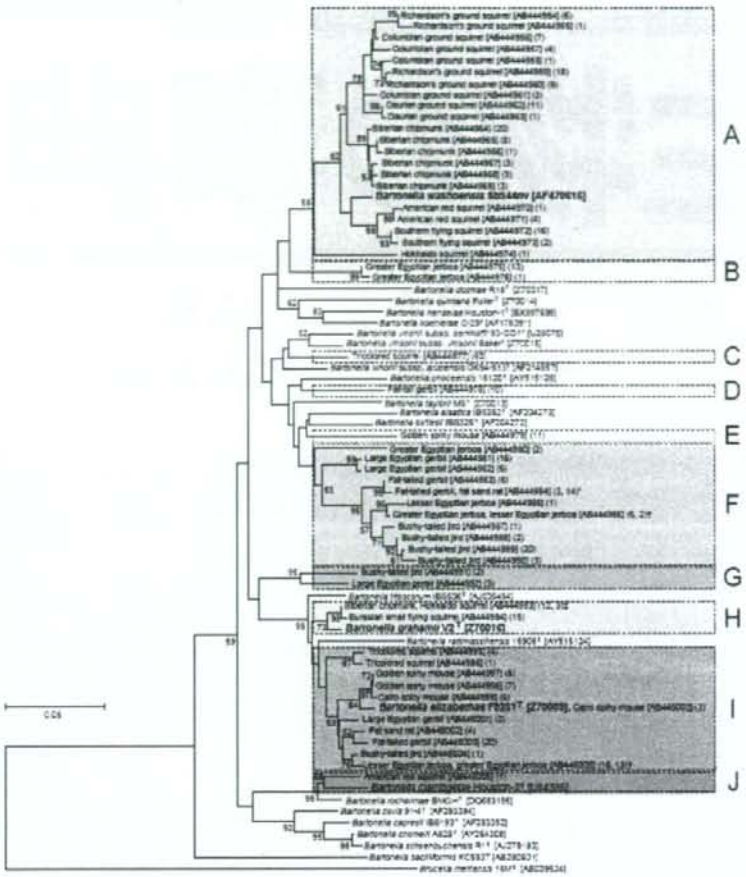
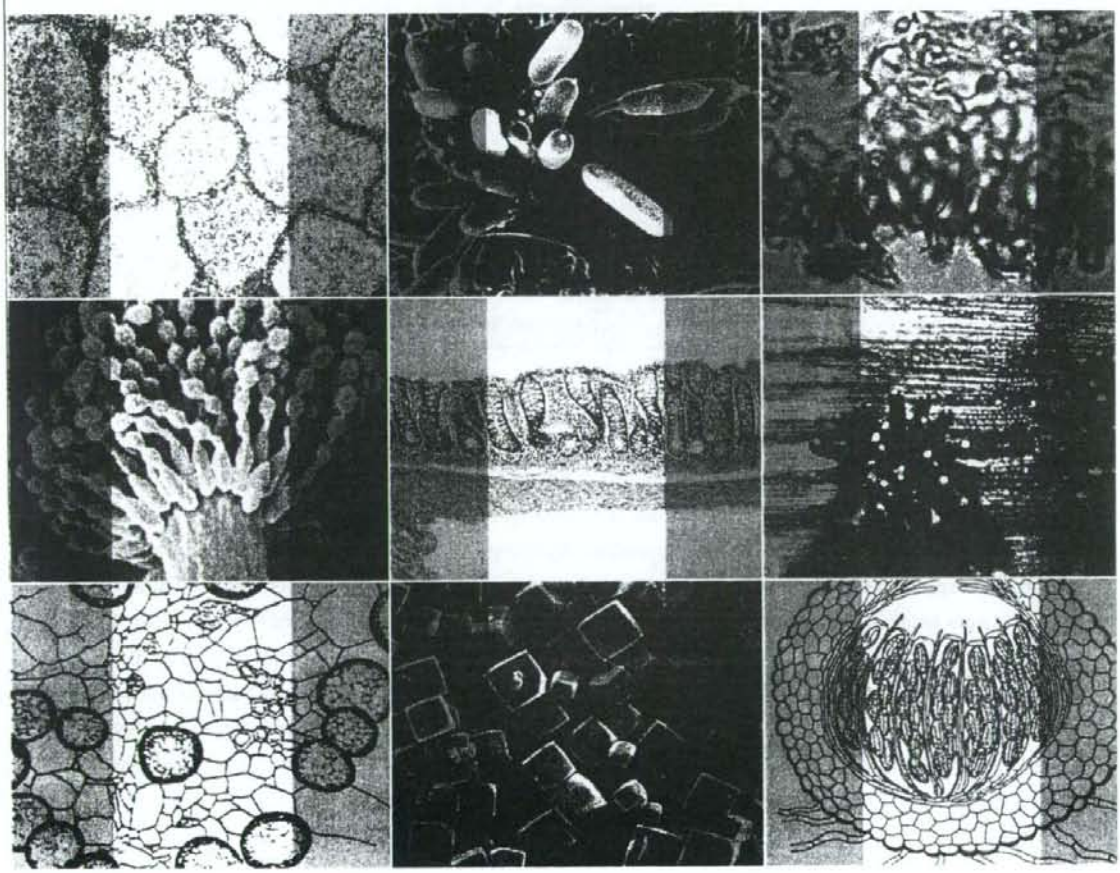


Figure. Phylogenetic tree based on a 312-bp region of the citrate synthase (*gltA*) gene sequence, constructed from *Bartonella* spp. isolates from 142 exotic small mammals imported into Japan as pets, June 2004–October 2007.Isolates from imported animals were compared with the type strains of known *Bartonella* spp. The phylogenetic tree was constructed by the neighbor-joining method, and bootstrap values were obtained with 1,000 replicates if values >50% were noted. The *Brucella melitensis* strain 16M sequence was used as an out-group. The GenBank accession number and the number of isolates are indicated in brackets and parentheses, respectively. The scale bar indicates 0.05 estimated nucleotide substitutions per site. Each colored column corresponds to genogroup A to G. Isolates showing identical genotypes were obtained from fat-tailed gerbils and fat sand rats (*), greater Egyptian jerboas and lesser Egyptian jerboas (†), and Siberian chipmunks and Hokkaido squirrels (‡).

微生物の事典

渡邉　信　　西村和子　　内山裕夫
奥田　徹　　加来久敏　　広木幹也
編



朝倉書店

（ii）　特異的な予防法　動物専用のウイルス病治療薬として承認されている製剤は少ない．ペットではネコのカリシウイルス感染症候群とイヌのパルボウイルス病にネコ組換えω型インターフェロンが，ネコのウイルス性鼻気管炎とカリシウイルス感染症候群に組換えネコ型キメラ抗体製剤が国内で承認されている．したがってヒトや他の産業動物と同じくウイルスに感染しないようにすることが肝要で，その最も有効な医療手段はワクチンによる予防接種である．イヌとネコのウイルス病予防用のワクチンを表Ⅷ.2.5に示す．国外には，例えばウサギのウイルス性出血病やフェレットのイヌジステンパーウイルス感染の専用予防用ワクチンが使われている地域もあるが，ウサギやフェレット，あるいはオウム・インコ類のウイルス病に対するワクチンのほとんどはいまだ実験・研究レベルである．

100％の有効性と安全性を示すワクチンは存在しない．したがって，獣医師と相談して必要なワクチンを必要なときに，指示通りに接種することが求められる．　〔望月雅美〕

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2.2　ペットの細菌病と予防

わが国では1200万頭のイヌ，約1000万頭のネコが飼育されているといわれている（2006年度現在）．この数字は，日本の人口を1億2000万人，4700万世帯（2001年度国勢調査）とすると，単純に計算しても，実に日本人の5.5人に1人，あるいは2世帯に1世帯がイヌあるいはネコを飼育していることを示している．イヌ，ネコ以外にも，小鳥，カメ，ヘビ，トカゲなどの爬虫類，カエル，イモリなどの両生類，熱帯魚（海水魚を含む）などの魚類をペットとして飼育している人もいる．この背景には，われわれの生活にイヌやネコなどのペットを飼う余裕ができたことや，核家族化，少子化の現象が進み，ペットが個人の愛情を向ける対象となってきたことがあげられる．また，ペットは小児の情操教育，ヒトの健康増進，生命延長あるいは精神衛生に深く関わっていることを示す意見から，最近ではこれらの動物をコンパニオンアニマルと呼ぶようにもなっている．特に，コンパニオンアニマルはヒトと濃密に接触する機会が多いため，人獣共通感染症に罹患していた場合，直接ヒトの健康にも影響を及ぼす場合がある．したがって，ペットの生態や習性はもちろんのこと，人獣共通感染症に対する正しい認識をもち，その発生を未然に防ぐことが重要である．

a.　ネコひっかき病

病原体はグラム陰性多形性細菌の*Bartonella henselae*で，ネコの赤血球内に寄生している．

本症は，その名の通りネコ，特に若齢のネコやネコノミが多く寄生したネコの掻傷や咬傷により感染することが多い．感染ネコの血液を吸血したノミが本菌をヒトへ伝播する可能性もある[2]．ネコ間ではけんかによる創傷や感染ネコの血液を吸血したネコノミにより感染は伝播する．

わが国では全国的な患者発生数に関する統計はないが，ネコの飼育頭数から推察して，かなりの数の患者が発生していると予想される．本症はすべての年齢層に発生するが，特に若齢者に多い．本症は7月から12月，あるいは秋から冬にかけて多発する．日本の飼育ネコの7～8％程度が本菌に感染している．若齢ネコ，ノミが寄生しているネコ，室外飼育のネコ，都市部のネコ，さらに南の温暖な地域のネコで高い感染率がみられている[1]（表Ⅷ.2.6）．

表Ⅷ.2.6　日本の飼育ネコの*Bartonella*保菌状況

道府県	検体数	保菌数（%）
北海道（札幌市）	50	0
宮城県（仙台市）	50	0
新潟県（上越市）	49	1（2.0）
神奈川県（藤沢市）	266	14（5.3）
京都府（京都市）	50	8（16.0）
大阪府（三島郡）	50	8（16.0）
兵庫県（三田市）	50	1（2.0）
島根県（簸川郡）	25	2（8.0）
鹿児島県（姶良郡）	50	6（12.0）
沖縄県（島尻郡）	50	10（20.0）
計	690	50（7.2）

（丸山ら：*J. Vet. Med. Sci.*, **62**, 273-279, 2000；一部改変）

ヒトが感染した場合，潜伏期は3～10日（まれに数週間）で，定型的なネコひっかき病では，菌の侵入部位（通常，手指や前腕）に虫さされに似た病変が形成され（図 VIII.2.1），丘疹から水疱に，また，一部では化膿や潰瘍に発展する場合もある．初期病変の形成から1,2週間後に局所のリンパ節（多くは鼠径部，鼠蹊あるいは頸部リンパ節）の腫脹が現れる（図 VIII.2.2）．リンパ節炎は，数週から数カ月間持続する．多くの症例で，発熱，悪寒，倦怠，食欲不振，頭痛などを示す．パリノー症候群（耳周囲のリンパ腺炎，眼球結膜炎など），脳炎，骨溶解性の病変，心内膜炎，肉芽腫性肝炎などの非定型のネコひっかき病が5～10%の割合で発生する．

B. henselae に感染したネコでは，ほとんど臨床症状は示さず，長期間（数カ月～数年）にわたり回帰性の菌血症を起こす．

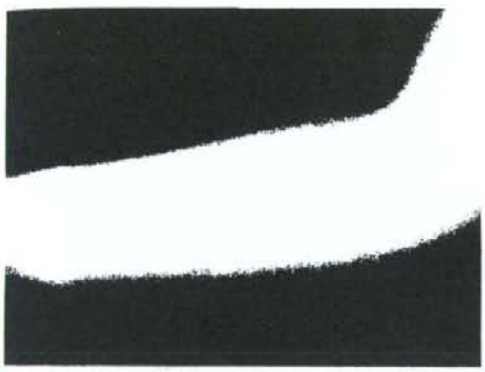

図 VIII.2.1 CSD 患者の前腕にみられたネコ受傷部の丘疹（受傷2週間後）

図 VIII.2.2 腋窩リンパ節の腫脹（鶏卵大）を示した子ども（6歳，男子）（公立八女総合病院 吉田 博氏提供）

ペットには性格の温厚な動物を選別し，咬傷や掻傷事故を未然に防止することが，予防上重要である．動物に接触した後は，手指をよく洗浄し，定期的な動物の爪の手入れと，ネコノミの駆除を励行する．動物から外傷を受けた場合，速やかに傷口を洗浄・消毒する．免疫不全状態，糖尿病などの基礎疾患のある人は，動物との接触や飼育は避けるべきである．

本症に罹患した場合，通常，特別な治療を受けなくとも2～3週間で自然に治癒する．定型的なネコひっかき病に対して各種の抗生物質による治療が試みられているが，その効果は高いとはいえない．ネコの菌血症に対しては，ドキシサイクリン，リンコマイシン，アモキシシリンなどの抗生物質を投与することである程度抑制できるが，血液中から完全に菌を排除することはできない．

b. パスツレラ症

主な病原体はグラム陰性細菌の *Pasteurella multocida* である．まれに，他の *Pasteurella* 属の細菌もイヌやネコに起因するパスツレラ症の原因となることがある．

感染経路は①動物の咬症，掻傷による感染，②動物からの非外傷性感染，③動物との接触歴が不明な感染に分けられる．このうち，動物，特にイヌやネコによる創傷感染が大部分を占める．また，①と②の患者をあわせると，パスツレラ症の約85%は直接あるいは間接的に動物の関与が明らかとなっている．

わが国のパスツレラ症患者の発生状況は不明であるが，イヌやネコの飼育頭数を考えると，相当数の患者が発生していると予想される．

イヌでは12～55%，ネコでは60～90%がその口腔内に，ネコの爪にも約20%の割合で *P. multocida* が保菌されているといわれている．

イヌやネコによる咬・掻傷によるパスツレラ症の場合，ほとんど例外なく傷口局所に発赤・腫脹が現れる（図 VIII.2.3）．早いものでは，受傷から数時間後には症状が現れるものもある．症例の約70%は1日以内に症状が現れる．3日以上経過して症状が現れることはまれである．発熱は約20%の患者でみられ，37～38℃のものが多く，38℃以上になることは少ない．局所の炎症に続いて傷口から漿液性の浸出液の漏出が多くの例でみられるが，化膿や蜂窩織炎が起こる割合は20～40%程度である．傷が軽い場合，傷害は局所のみで，血行を通じて全身感染にまで進むことはほと

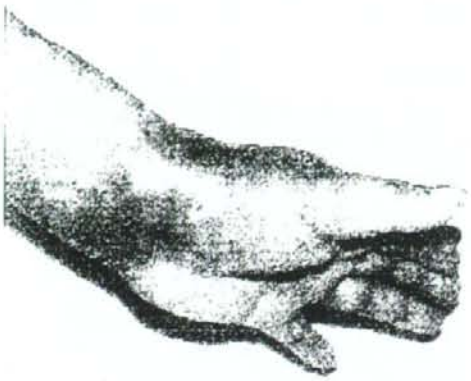

図 VIII.2.3　野良ネコによる手首の咬傷部の腫脹(男性)
(日本大学 荒島康友氏提供)

図 VIII.2.4　飼いイヌに咬まれて発症した肉芽腫と骨髄炎(男性)(日本大学 荒島康友氏提供)

んどない.

傷が深部に達したときは，炎症は速やかに深部組織まで達し，また，直接骨まで達するような傷の場合には，腱鞘炎や骨髄炎を起こすこともある（図 VIII.2.4）．このような場合でも，敗血症を起こすことは少なく，また全身感染に至ることもまれであるが，糖尿病などの基礎疾患のある患者では重篤な症状にまで発展する場合がある．

非外傷性の感染では，上部気道炎，気管支炎，肺炎などの呼吸器疾患が多くみられる．このような呼吸器感染例は，気管支拡張症や結核，悪性腫瘍などの疾患がある場合に発症しやすく，また，繰り返し感染することもある．日本ではこのような呼吸器感染を起こすパスツレラ症が多いといわれている．一般に，パスツレラ症の予後は良好であるが，後遺症として関節の機能不全や皮膚移植を必要とした例が報告されている．

イヌ，ネコの多くは健康保菌者であるが，ネコ同士のケンカで咬まれたり引っ掻かれたりして受けた傷が化膿し，蜂窩織炎を起こすことがある．また，まれに

表 VIII.2.7　*Brucella* の生物型，自然宿主，病[illegible]

生物型	自然宿主	ヒトに対[illegible]
B. abortus	ウシ	[illegible]
B. suis	ブタ	[illegible]
B. melitensis	メンヨウ，ヤギ	[illegible]
B. neotomae	野ネズミ	[illegible]
B. ovis	ヒツジ	不明
B. canis	イヌ	[illegible]

肺炎を起こすネコもいる．ウサギではスナ[illegible]炎，気管支炎，肺炎の俗称）の原因となる．

パスツレラ症の予防は，ネコひっかき[illegible]法で行う．動物の外傷がある場合は原因が明[illegible]るが，非外傷性の感染のパスツレラ症を[illegible]物を飼育していたり接触した履歴があれば，[illegible]そのことを医師に伝えることが重要である．

咬・掻傷を受けた場合，特に高齢者や[illegible]る患者では早期に適切な抗生物質を選別し，[illegible]を十分に行う必要がある．*P. multocida* は，[illegible]ン系，テトラサイクリン系，クロラムフ[illegible]セファロスポリン系に高い感受性を，アミノグリコ[illegible]ド系薬剤には中程度の感受性が認められる．[illegible]バンコマイシン，クリンダマイシンには[illegible]すので，抗生物質の選択には注意が必要となる．

c.　ブルセラ症（四類感染症）

グラム陰性細菌の *Brucella melitensis* が原因[illegible]る．本菌には，六つの生物型があり，それ[illegible]主となる動物や病原性が異なる（表 VIII.2.7）．[illegible]ペットとの関係ではイヌを自然宿主とする *B. canis* が重要である．

ヒトは本菌に汚染した食品，感染動物由来の[illegible]乳や乳製品が原因で感染する．*B. canis* に[illegible]ヌやその排泄物との接触によっても感染する．[illegible]他の感染動物の尿，流産胎児，悪露などに[illegible]れた飼料，自然環境などから感染する．また，[illegible]ウシ，ブタの死流産胎児や胎盤を食べて *B. abortus*，*B. suis* に感染する場合がある[4]．

わが国では，飼いイヌあるいは野犬の[illegible]*canis* に感染しているといわれている．2002 年に[illegible]京都で飼いイヌから感染したと思われる事例が報告[illegible]れている．また，2003 年に静岡県内のイヌの繁殖[illegible]設内で *B. canis* による感染が発生し，イヌ[illegible]児の臓器からは *B. canis* が分離されたが，[illegible]