

Evidence for vertical transmission of Lyme disease in animals

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Animal	Evidence for Maternal-Fetal (Vertical) Transmission of <i>Borrelia burgdorferi</i> in mammals.	Ref:
Mice - 1987	"One culture was obtained from a fetus of a pregnant white footed mouse from which spirochetes also were cultured from spleen and kidney tissues.'	1
Mice - 1992	'Spirochetes were also isolated from tissues from three of four still-born pups from two different inoculated dams (Table 2) A total of 76% of all the surviving pups born to both inoculated and uninoculated dams had <i>B. burgdorferi</i> spirochetes in their tissues at time of necropsy"	2
Mice - 1993	'Transplacental transmission of <i>B. burgdorferi</i> was demonstrated in a <i>M. musculus</i> and in a <i>P. leucopus</i> from Farm 2.	3
Mice - 1995	'A sensitive PCR technique detected <i>B. burgdorferi</i> in the uteri of acutely infected mice but did not detect DNA in uteri of controls or chronically infected mice. Spirochete DNA was only rarely detected in fetal tissues.'	4
Mice - 1997	"Among 49 infected from groups A and C, 5(10.2%) transmitted Bb to their pups either in-utero or intrapartum. Four of the litters from the mating pairs in group B had infected pups. The described mouse model with further modifications may provide a tool for studying such transmission modes and treatment strategies."	5
Mice/Rats - 1999	'Vertical transmission of B.b. was confirmed with B.b isolated from foetuses of <i>Apodemus agrarius</i> + <i>Rattus edwardsi</i> . The results showed that Lyme disease spirochetes, B.b., might be naturally maintained in an enzootic cycle by transplacental transmission.'	6
Cows - 1988	" <i>B. burgdorferi</i> was cultured from the blood of a newborn calf, and an aborted calf had antibodies to <i>B. burgdorferi</i> indicating in-utero infection. The findings of spirochetes in the blood of a cow that aborted and the high antibody levels in cows aborting also indicate that <i>B. burgdorferi</i> infection may cause reproductive disease in cows."	7
Cows - 1998	Detection of <i>B. burgdorferi</i> DNA from the tissues of stillborn calves, as well as spirochetemia in neonatal liveborn and stillborn calves, gives evidence for in-utero transmission of <i>B. burgdorferi</i> in naturally infected dairy cattle."	8
Horses - 1989	"The demonstration of antibodies in the serum of Foal 2 and the isolation of spirochetes from Foal 1 suggest infection took place in-utero."	9
Dogs - 1993	"Eight of 8 SI females that had litters delivered pups in which at least 1 had PCR detectable <i>B burgdorferi</i> DNA including 3 pups under 1 day of age (1 stillborn pup, and 1 that died at 30 minutes of age from female SI 3, and a 1 day old pup from SI female 10), providing evidence of in utero transmission."	10, 11
Dogs - 1993	"The finding of <i>B burgdorferi</i> specific DNA sequences by PCR in tissues from fetuses from 3/7 litters from females artificially inseminated with semen from spirochete inoculated males demonstrates that <i>B burgdorferi</i> can be transmitted in semen and that in utero infection of the fetuses occurs. These findings indicate that infected male dogs can transmit the organism to females during natural breeding. This could provide a means by which developing fetuses can become infected."	10
Foxes - 1993	"Transplacental transmission of <i>B burgdorferi</i> to fox kits was found to occur in 2 naturally infected vixens. This conclusion was based on the finding of spirochetes and PCR detectable <i>B burgdorferi</i> specific DNA sequences in tissues of 4 neonatal kits immediately destroyed by one vixen at birth and in tissues from a stillborn and 2 neonatal kits from the other vixen. "	10
Coyotes - 1989	"These findings show that <i>Borrelia</i> sp. (most probably <i>B. burgdorferi</i>) infection has been present in coyotes in Webb County, Texas, since 1984 and that transplacental infection can occur in infected coyotes."	12

Transplacental Transmission of Bb in natural populations of mice

'One culture was obtained from a fetus of a pregnant white footed mouse from which spirochetes also were cultured from spleen and kidney tissues.'

Anderson JF, Johnson RC, Magnarelli LA. Seasonal Prevalence of *Borrelia burgdorferi* in Natural Populations of White- Footed Mice, *Peromyscus leucopus*. Journal of Clinical Microbiology, Vol 25(8)Aug, 1987, p. 1564-1566.



'One *M. musculus* and one *P. leucopus* from Farm 2 were pregnant at the time of capture. Spirochetes were cultured from 2/5 fetuses from the *M. musculus* and 1 of 2 fetuses from the *P. leucopus*. The spirochetes from all three cultures were positive by PCR analysis.

'If fetuses can be infected in-utero with *B. burgdorferi*, as suggested by Anderson et al. (1987), and if they can survive transplacental transmission, this may be a means of maintaining the spirochete in the rodent population in the absence of ticks.'

Burgess EC, Wachal MD, Cleven TD. *Borrelia burgdorferi* infection in dairy cows, rodents, and birds from four Wisconsin dairy farms. Vet Microbiol. 1993 May;35(1-2):61-77. doi: 10.1016/0378-1135(93)90116-o. PMID: 8362496.

Transplacental Transmission of Bb in natural populations of mice and rats

> Wei Sheng Yan Jiu. 1999 Jan 30;28(1):7-9.

[Preliminary investigation on reservoir hosts of *Borrelia burgdorferi* in China]

[Article in Chinese]

K Wan ¹, Z Zhang, H Wang, X Hou

Affiliations + expand

PMID: 12712735

Abstract

From 1987 to 1997, the reservoir hosts of *Borrelia burgdorferi*(B.b.) were investigated in 16 provinces, municipalities and autonomous regions of China. Seroepidemiological findings indicated that cattle, sheep, dogs and rats from forest areas had a high antibody titer for B.b. (B31) with positive rates of 18.18%-32.61%, 17.12%-61.21%, 38.50-60.00% and 41.18%-86.05% respectively. Using BSK medium, 20 strains of B.b. were isolated from *Apodemus agrarius*, *Clethrionomys rufocanus*, *Eutamias sibiricus*, *Rattus coxingi*, *Rattus norvegicus*, *Rattus edwardsi*, *Rattus confucianus*, *Rattus fulvescens* and *Caprolagus sinensis*. These spirochetal strains were identified as B.b. by indirect immunofluorescence assay using species and genus specific monoclonal antibodies. Vertical transmission of B.b. was confirmed with B.b. isolated from foetuses of *Apodemus agrarius* and *Rattus edwardsi*. The results showed that lyme disease spirochetes, B.b., might be naturally maintained in an enzootic cycle by transplacental transmission. *Apodemus agrarius* and *Clethrionomys rufocanus* might serve as major reservoir hosts for B.b. in China.



- 'Vertical transmission of B.b. was confirmed with B.b isolated from foetuses of *Apodemus agrarius* + *Rattus edwardsi*. The results showed that Lyme disease spirochetes, B.b., might be naturally maintained in an enzootic cycle by transplacental transmission.'
- 'Lyme disease spirochetes were isolated from the fetuses of *Apodemus agrarius* and white-bellied rats, confirming that Lyme disease spirochetes can be transmitted vertically through the placenta, which is of great significance for the maintenance and expansion of the natural foci of Lyme disease.'

Hou X. [Preliminary investigation on reservoir hosts of *Borrelia burgdorferi* in China]. Wei Sheng Yan Jiu. 1999 Jan 30;28(1):7-9. Chinese. PMID: 12712735.

Table 2. Isolation of spirochetes in BSK culture media from tissues collected from still-born and unborn white mice pups from 10 dams inoculated with *Borrelia burgdorferi*.

ANIMAL NUMBER	T I S S U E S						
	Ear	Liver	Spleen	Kidney	Bladder	Eye	Heart
Still-born							
Wm-6a	-	-	-	-	-	-	-
8a	+	+	+	+	+	-	-
8b	-	-	-	+	+	-	+
9a	-	-	+	+	-	+	-
No. Pos.	1	1	1	3	2	1	1
Unborn							
Wm-3b	-	*	*	*	+	*	*
3c	-	*	*	*	-	*	*
3d#	-	*	*	*	-	*	*
3e	+	*	*	*	-	*	*
3f#	+	*	*	*	+	*	*
3g#	-	*	*	*	-	*	*
3h	-	*	*	*	-	*	*
3i	-	*	*	*	+	*	*
3j	-	*	*	*	-	*	*
3k	+	*	*	*	-	*	*
No. Pos.	3	*	*	*	3	*	*

- = negative for isolation; + = spirochetes; # = *B. burgdorferi* was also isolated from placental tissue; * = not tested due to the fact that all internal organs had been hemolyzed.

Experiment 1: Maternal-fetus, maternal-offspring transmission

Twenty two pregnant mice were chosen for the vertical transmission study.

- Ten dams were inoculated subcutaneously (sc) at day 15 on the average (ranging from day 10 to day 18) of pregnancy with approximately 50,000 spirochetes of a low- passaged isolate (NY90-14) . Ten dams were inoculated only with sterile BSK medium.
- At birth the newly born pups from each inoculated dam were switched with newly born pups from uninoculated dams in order to determine if transplacental and transmammary transmission occurs.
- Surrogate mothers of white laboratory mice readily accepted and cared for newly born pups.
- Two dams used as controls were inoculated with sterile BSK medium and cared for their own pups.
- Pups found dead that were born to inoculated dams and delivering dams that were found dead were immediately removed and tissue samples were obtained and placed in BSK media for isolation of *B. burgdorferi*.
- All surviving weanling mice and adoptive dams were euthanized with CO2 gas at 6 to 7 weeks post inoculation (PI) and samples from various tissues were aseptically removed and placed in BSK medium for isolation of spirochetes.
- Any culture in which spirochete-like organisms were observed by darkfield microscopy was tested with a direct fluorescent antibody (FA) test specific for the *Borrelia* genus.

Table 3. Isolation of *Borrelia burgdorferi* in BSK from tissues of pups born to 10 inoculated and 10 uninoculated dams at necropsy.

	<i>Borrelia burgdorferi</i>			%
	Positive	Negative	Total	
Born to inoculated dam, & raised by uninoculated dam	77	21	98	78.6
Born to uninoculated dam, & raised by inoculated dam	70	25	95	73.7
No. positive	147	46	193	76.2

Experimental and epizootiologic studies of Lyme disease Ubico-Navas, Sonya Renee, Ph.D. Colorado State University, 1992.

Results:

- 57% of the fetuses or still born pups from infected mothers were positive for Bb
- 79% of pups born to inoculated dams and raised by uninoculated dams were positive for Bb.
- 74% of the pups born to uninoculated dams and raised by inoculated dams were positive.
- Pups born to uninoculated dams became infected after being switched to and nursed by an inoculated dam
- 80% uninoculated dams became infected after caring for pups born to the inoculated dams.

'These results suggest that maternal-fetus transmission via the placenta and maternal-offspring transmission probably through contaminated saliva, colostrum or milk can occur.'

Unfortunately, it was not possible to separate transmammary transmission from direct contact transmission from infected mother to offspring. Surprisingly, the opposite direction of transmission from infected offspring to uninoculated mothers via contaminated urine, feces, or saliva and tissues was also observed.

Transplacental Transmission of Bb in a Murine Model

<i>Title:</i>	Transplacental Transmission of Bb In a Murine Model
<i>Authors:</i>	Altaie SS; Mookherjee S; Assian E; Al-Taie F; Nakeeb S; Siddiqui S
<i>Conference:</i>	10th Annual International Scientific Conference on Lyme Disease & Other Tick-Borne Disorders, National Institutes of Health, Bethesda, MD April 28-30, 1997
<i>Presenter:</i>	Sousan Sayahtaheri Altaie, Ph.D. Clinical Microbiology Review Officer U.S. Food and Drug Administration

Phase one studies: Males were infected and immediately mated. The day of coital plugging was established as day 1 of pregnancy. The pregnant mice were then infected during early- [day 6-7 postcopulation (PC)], middle-(day 9-10 PC) and late- (day 12-13 PC) gestation periods. Period mice were sacrificed 6 days post infection. Fetuses and their placentas were harvested and cultured for nine weeks in SKB II. No Bb was detected by culture, thus, PCR was performed on the cultures for detection of Bb DNA. There were no appreciable differences observed in transmission rates among the three Bb strains, therefore, the data were pooled.

Results:

- In groups A and C combined, **during early-gestation Bb was detected in 4/30 (13%) fetuses and 3/30 (10%) placentas.**
- During middle-gestation Bb was detected in 3/57 (5%) fetuses and 4/57 (7%) placentas.
- No Bb was detected in fetuses or placenta during late-gestation period.
- No Bb was detected in samples from group B.

Phase Two studies:

Mating pairs were assigned to groups A-D and were infected immediately prior to mating. The **pregnancies were allowed to go to term** and the pups were sacrificed at 1, 7, 14, and 21 days of age. The milk content of the stomach, sections from ear, skin, heart, liver, spleen, brain, bladder, and kidney of all pups were cultured for Bb. Milk was not cultured from sacrificed 21 day-old weanlings. Transmission to offspring was indicated when Bb was isolated from any tissue.

Results:

- Of 25 infected females, **2 (8%) transmitted Bb to their pups on day one via their milk.** No transmission was detected via milk on days 7 or 14.
- Among 49 infected females from groups A and C, **5(10.2%) transmitted Bb to their pups either in utero or intrapartum.** Two of the transmissions were detected on day 1, two on day 7, and one on day 14.
- From the 132 pups at risk for close contact infection in group B, **9 pups were infected resulting in a close contact transmission rate of 6.8%.**

This transmission model suggests that Bb can be transmitted in utero. Increasing the inoculum size and/or changing the route of inoculation to intrauterine or intra-amniotic may enhance infection rates. This model has the potential to be used to study intervention strategies for gestational LD.

Altaie SS, Mookherjee S, Assian E, Al-Taie F, Nakeeb SM, Siddiqui SY. Transplacental transmission of Bb in a Murine Model. 10th Annual International Scientific Conference on Lyme Disease and other Tick-Borne Disorders, National Institutes of Health, Bethesda MD April 28-30, 1997.

Altaie SS, Mookherjee S, Assian E, Al-Taie F, Nakeeb SM, Siddiqui SY. Transmission of Bb from Experimentally Infected Mating Pairs to Offsprings in a Murine Model. Abstract # I-17. FDA Science Forum, 1996.

Fetal Outcome in Murine Lyme disease - 1995

Outcome	Acutely infected mice n=39 (intradermal injection 4 days after mating)	Chronically infected mice n=18 (inoculated 3 weeks prior to mating)	Control mice N-25
Fetal death	46% suffered at least one fetal death	No fetal death	No fetal death
Bb in uteri (PCR)	Detected	Not detected	Not detected

Maternal infection/details	Bb uteri (PCR)	Bb identified in fetuses (PCR)	Bb (PCR) placenta (
8 C3H/HeN female mice mated with C57BL/6 males and infected day 4 gestation. Sacrificed 10-12 days later.	8/8	0/10 fetuses	1/8
C3H/HeN female mice mated w C3H/HeN males. Infected day 4 gestation.	+	none	none
4 C3H/HeN female mice mated with C57BL/6 males infected day 4 gestation and deliver spontaneously	-	0/8 fetuses	-
2 mice infected w Bb 5 days prior to mating and sacrificed day 14 of gestation.	-	Faint band of OspA DNA in 1/3 fetuses. 'Spirochete DNA in fetus did not correlate w fetal outcome.'	1/2

- These findings indicate an association between murine fetal death and acute infection with *B. burgdorferi* early in gestation but not with chronic infection.
- Our data suggest that fetal death is due to a maternal response to infection rather than fetal infection.
- These findings could provide an explanation for observations in humans in which sporadic cases of fetal death in women infected with *B. burgdorferi* during pregnancy have been reported, while previous infection has not been associated with fetal death.

Silver RM, Yang L, Daynes RA, Branch DW, Salafia CM, Weis JJ. Fetal outcome in murine Lyme disease. *Infect Immun.* 1995 Jan;63(1):66-72. doi: 10.1128/iai.63.1.66-72.1995. PMID: 7806385; PMCID: PMC172958.

TABLE 3. Cows from Which *B. burgdorferi* Has Been Isolated

Cow No. ^a	Antibody Titer ^b	<i>B. burgdorferi</i> Culture	Clinical Signs
1	512	+ blood	arthritis
2	neg	+ blood	arthritis
3	512	+ blood	arthritis
4	1024	+ blood	arthritis
5 ^c	neg	+ blood	none
6	256	+ blood	none
7	512	+ blood	none
8	1024	+ synovial fluid	swollen carpal joints
9	neg	+ colostrum	abortion
10	512	+ urine	none
11	512	+ urine	none

^aCows 1, 2, and 3 all from the same herd.

^bIndirect immunofluorescent IgG antibody titer given as reciprocal of end point dilution.

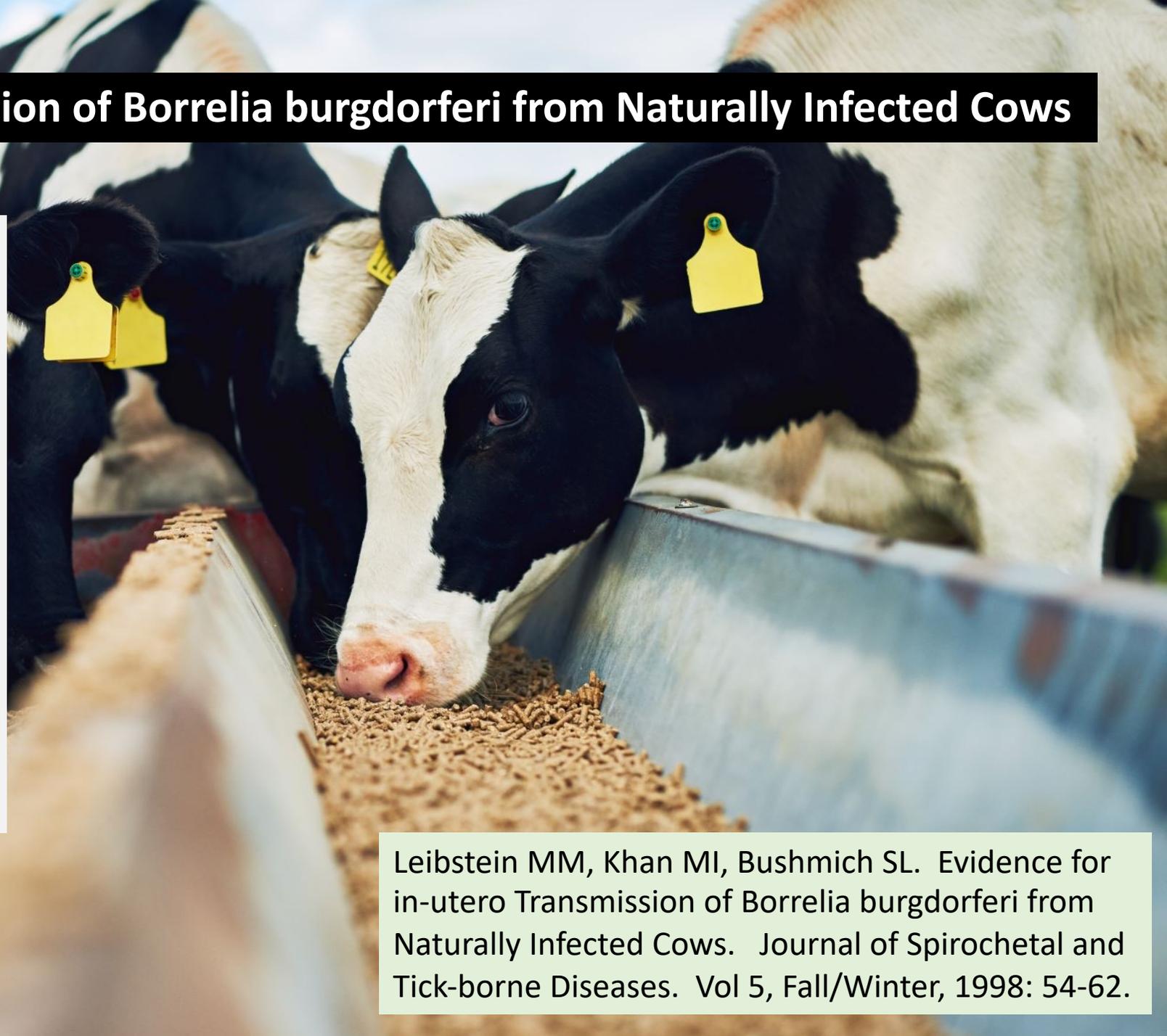
^cNewborn calf.

'Transplacental transmission of *B. burgdorferi* was demonstrated in the cows. *Bb* was cultured from the blood of a newborn calf, and an aborted calf had antibodies to *B. burgdorferi*, indicating in-utero transmission. There is no in utero maternal transfer of antibodies in cows. The findings of spirochetes in the blood of a cow that aborted and the high antibody levels in cows aborting also indicate that *B. burgdorferi* infection may cause reproductive disease in cows.'

Burgess EC. *Borrelia burgdorferi* infection in Wisconsin horses and cows. Ann N Y Acad Sci. 1988;539:235-43.

Evidence for in-utero Transmission of *Borrelia burgdorferi* from Naturally Infected Cows

- Cattle were first calf dairy heifers and their offspring n=15 from a Connecticut herd with a documented history of natural *B burgdorferi* infection.
- Heifers and neonatal offspring were evaluated for evidence of infection with *Bb* immediately after parturition before calves were given colostrum.
- Blood specimens were obtained from adult cows and calves after parturition for *Bb* serology (IFA, immunoblot) and antigen detection by PCR with *Bb* Osp A specific primers.
- Additional samples collected included placenta, uterine fluid and colostrum for culture in BSK media and/or PCR analysis.



Leibstein MM, Khan MI, Bushmich SL. Evidence for in-utero Transmission of *Borrelia burgdorferi* from Naturally Infected Cows. *Journal of Spirochetal and Tick-borne Diseases*. Vol 5, Fall/Winter, 1998: 54-62.

Table 2. Brief summary of data for cows naturally infected with *Borrelia burgdorferi* at parturition and stillborn calves.

COW ID	Spirochetemic (Bb PCR)		IFA Titer		# Bb Specific Antibodies		# Nonspecific Bb Antibodies	
	Dam	Calf	Dam	Calf	Dam	Calf	Dam	Calf
UC 378	(-)	NT	1:64	1:64	4/6	0	9/10	0
UC 380	(+)	(+)	1:64	1:64	3/6	1/6	9/10	1/10
UC 410 ¹	(+)	(+)	1:256	NEG	4/6	0	7/10	0

¹ = Bb PCR positive colostrum
 NT = sample not tested

3 of 15 calves (20%) were stillborn.

'3/15 (20%) calves were stillborn, two were spirochetemic and all showed evidence of disseminated Bb infection by detection of Bb by PCR in multiple tissues.'

Calf 378 had a low positive IFA titer (1:64) as did the mother.
 No specific or non-specific Bb antibodies
 PCR positive spleen, bladder, L carpus fluid, L hock fluid and heart.
Culture positive spleen

Calf 380 had was spirochemic (Bb in whole blood)
 Had a low positive IFA titer (1:64) as did the mother
 1/6 specific antibodies and 1/10 nonspecific Bb antibodies
 PCR positive spleen, L kidney and L carpus fluid

Calf 410 was spirochetemic (Bb in whole blood)
 negative by IFA; no specific or non-specific Bb antibodies
 Bb PCR positive colostrum in the heifer
 PCR positive L carpus fluid and tissue, PCR positive brain tissue and aqueous humor.
Culture and PCR positive R kidney

Table 3. Summary of data from organs and tissues collected from stillborn calves for culture or PCR analysis.

	CALF 378		CALF 380		CALF 410	
	PCR	CULTURE	PCR	CULTURE	PCR	CULTURE
Blood	(-)	(-)	(+)	(-)	(+)	(-)
Spleen	(+)	(+)	(+)	(-)	(-)	(-)
Urine	(-)	(-)	(-)	(-)	NT	NT
Bladder	(+)	(-)	(+)	(-)	NT	NT
L kidney	(-)	(-)	(-)	(-)	(-)	NT
R kidney	(-)	(-)	(-)	(-)	(-)	(+)(PCR+)
L carpus fluid	(+)	(-)	(+)	NT	(+)	(-)
L carpus tissue	NT	NT	(-)	NT	(+)	NT
L hock fluid	(+)	(-)	NT	NT	NT	NT
L hock tissue	(-)	NT	(-)	NT	NT	(-)
L hip-tissue	(-)	NT	NT	NT	NT	(-)
Liver	(-)	NT	NT	NT	NT	NT
Heart	(+)	NT	(-)	NT	NT	NT
Testes	(-)	NT	NT	NT	NT	NT
CSF	(-)	(-)	(-)	NT	(-)	(-)
Brain stem	NT	NT	NT	NT	(-)	(-)
Cerebrum	NT	NT	NT	NT	(+)	NT
Cerebellum	NT	NT	NT	NT	(-)	NT
Lung	NT	NT	NT	NT	(-)	NT
Aqueous humor	NT	NT	NT	NT	(+)	(-)

NT = sample not tested

Leibstein MM, Khan MI, Bushmich SL. Evidence for in-utero Transmission of *Borrelia burgdorferi* from Naturally Infected Cows. Journal of Spirochetel and Tick-borne Diseases. Vol 5, Fall/Winter, 1998: 54-62.

Table 1. Brief summary of data for cows naturally infected with *Borrelia burgdorferi* at parturition and liveborn neonatal calves.

COW ID	Spirochetemia (<i>Bb</i> PCR)		IFA Titer		# <i>Bb</i> Specific Antibodies		# Nonspecific <i>Bb</i> Antibodies	
	Dam	Calf	Dam	Calf	Dam	Calf	Dam	Calf
UC 359	(-)	(-)	1:32	NEG	3/6	0	7/10	0
UC 360	(-)	(-)	1:64	NEG	3/6	1/6	8/10	1/10
UC 376 ¹	(-)	NT	1:128	1:64	3/6	0	8/10	0
UC 382	(-)	NT	1:64	NEG	3/6	0	5/10	1/10
UC 385	(-)	(-)	1:64	1:128	3/6	2/6	8/10	6/10
UC 386	(-)	(-)	1:64	NEG	4/6	0	9/10	1/10
UC 388	(-)	(-)	1:64	NEG	3/6	0	6/10	0
UC 390 ¹	(-)	(-)	1:64	1:64	3/6	1/6	6/10	5/10
UC 392 ³	(+)	(-)	1:64	NEG	NT	NT	NT	NT
UC 933	(-)	(-)	1:32	NEG	2/6	0	5/10	0
UC 406	(+)	(+)	1:128	NEG	5/6	0	10/10	0
UC 408 ^{2,3}	(+)	(+)	1:64	NEG	3/6	0	6/10	0

1 = *Bb* culture positive placenta and uterine fluid

2 = *Bb* culture positive placenta

3 = *Bb* PCR positive colostrum

NT = sample not tested

Of liveborn neonatal calves:

2 calves (406 and 408) were spirochetemic, IFA negative and negative by immunoblot.

Leibstein MM, Khan MI, Bushmich SL. Evidence for in-utero Transmission of *Borrelia burgdorferi* from Naturally Infected Cows. *Journal of Spirochetal and Tick-borne Diseases*. Vol 5, Fall/Winter, 1998: 54-62.

'This study clearly demonstrates in-utero transmission of *Borrelia burgdorferi* from naturally infected cows to their calves.'

'Viable *Bb* was cultured from placenta and uterine fluid of two cows indicating disseminated infection with *Bb* at the time of parturition.'

'*Bb* DNA was detected in blood from adult cattle and their offspring at parturition indicating the calves were infected prior to parturition.'

'None of the cattle at parturition showed clinical signs commonly associated w *Bb* infection.'

Coyotes from southern Texas were sampled for antibodies to Bb from 1980-1986. Coyote fetuses, adult coyote kidneys were cultured for Bb in 1986.

Bb was isolated from kidneys of 1/5 coyote fetuses - the mother was seronegative.

‘The case of an antibody negative coyote having a Bb culture positive fetus might suggest a localized infection in the reproductive tract or that the female was infected recently and had insufficient time to develop antibodies.’

‘This could mean that a survey for Bb infection using the presence of antibodies alone as the method of detection may underestimate the prevalence of infection.’



**Foal Mortality Associated with Natural Infection of Pregnant
Mares with *Borrelia burgdorferi***

Elizabeth C. Burgess, Annette Gendron-Fitzpatrick, and Mark Mattison



Studied the effect of Bb on 7 naturally infected pregnant mares and 1 stallion (positive antibodies) from a breeding herd in an endemic area of Wisconsin.

'This herd had only 1 viable offspring by the end of one year of breedings from 1985.'

Pregnancy Outcome in 1986:

2 mares aborted or resorbed fetuses

3 foals died within days

2 mares had a live foal that survived, one of which was euthanized at one year due to neurologic disease.

Necropsy results:

Foal 1: Found dead next to placenta. Serum was antibody negative. Bb isolated from the kidney.

Foal 2: (twin 1) euthanized at 2 days age as unable to stand. Serum demonstrated antibodies to Bb. Bb isolated from kidney and brain and Bb demonstrated in kidney tissue by IFA.

Foal 3: (twin 2) died at 6 days of age. No lesions seen on histologic examination.

Foal 4: healthy when born, mare's colostrum had antibody titer of 1:256 but serum was negative. At six months of age foal had difficulty stepping up. Was euthanized as a yearling. Bb was isolated from kidney and liver.



10 female beagles inoculated intradermally w Bb. All were seronegative by IFA and WB before inoculation.

10 female control beagles inoculated w saline. remained IFA-WB negative and their tissues and their pups remained negative by PCR and culture.

Bred naturally.

Gustafson JM, Burgess EC, Wachal MD, Steinberg H. Intrauterine transmission of *Borrelia burgdorferi* in dogs. *Am J Vet Res.* 1993 Jun;54(6):882-90.

Intrauterine transmission of *Borrelia burgdorferi* in dogs

John M. Gustafson, DVM, MS; Elizabeth C. Burgess, DVM, PhD; Michael D. Wachal, BS; Howard Steinberg, VMD, PhD

- 10 infected females did not manifest clinical signs or infection during gestation, but a suggestion of increased dystocias and fetal resorptions was apparent.
- Of the 10 infected females, 8 delivered litters (3 to 7 pups) that had at least 1 neonatal or 6-week-old pup with *B burgdorferi* DNA-positive tissues (by PCR).
- Spirochetes were cultured from tissues from pups of 2 litters.
- Four pups of 3 separate litters (a stillborn, a neonate that survived to 30 minutes of age, a 20-hour-old, and a 48-hour-old) had *B burgdorferi*-positive tissues (by PCR), and the 20-hour-old pup was also culture-positive, **indicating intrauterine infection.**
- Further evidence of intrauterine exposure was the presence of IgM antibodies to *B burgdorferi* detectable by western blot in 3 of 7 one-day-old pups that did not receive colostrum, indicating a primary immune response.
- Pups that became infected, but they did not manifest clinical signs of infection, inflammatory response, or increased mortality
- Intrauterine infection with *B burgdorferi* is a mechanism by which pups can become infected in the absence of a vector.



Gustafson, John Michael, Ph.D. The in utero and seminal transmission of *Borrelia burgdorferi* in Canidae. The University of Wisconsin - Madison, 1993. PhD Thesis.

- ‘**Transplacental transmission of *Borrelia burgdorferi* was demonstrated in 2 foxes from a Wisconsin fox ranch.**’
- ‘Spirochetes were cultured from the tissues of 4 neonatal kits from fox vixen 1 and from a stillborn and a neonatal kit from fox vixen 2.’
- ‘Isolates from the liver and blood of one kit from vixen 1 were identified as *B burgdorferi* by indirect immunofluorescence using the H5332 monoclonal antibody specific for the 31 KDa protein.’
- ‘*B burgdorferi* specific DNA sequences were also detected in tissues from 2 kits in the vixen 1 litter and from 3 in the vixen 2 litter using polymerase chain reaction (PCR).’
- ‘The brain from vixen 1 and the spleen from vixen 2 also contained PCR detectable spirochetal DNA sequences.’
- ‘Both vixens were negative for antibodies using the indirect immunofluorescent antibody (IFA) test (a titer of 1:64 or less), but both had IgG antibodies to the 41 KDa and the 34 KDa *B burgdorferi* proteins by Western blot.’

**The *in utero* and seminal transmission of *Borrelia burgdorferi* in
Canidae**

Gustafson, John Michael, Ph.D.

The University of Wisconsin - Madison, 1993

‘It is surprising that the evidence presented for transplacental transmission has received little notice by investigators. It would seem that the clinical and epidemiological implications, if significant, could have an impact on current thinking and measures taken to manage the disease.’

‘It is possible that nonarthropod transmission could introduce the spirochete into populations outside of the geographical range of the tick vector. The apparent ease by which organisms can be transmitted by these mechanisms demands closer inspection if the overall epidemiologic and epizootiologic picture is to be understood.’

1. It is possible that non-arthropod transmission could introduce the spirochete into populations outside of the geographical range of the tick vector. **The apparent ease by which organisms can be transmitted by these mechanisms demands closer inspection if the overall epidemiologic and epizootiologic picture is to be understood.** – Gustafsen, 1993
2. If fetuses can be infected in-utero with *B. burgdorferi*, as suggested by Anderson et al. (1987), and if they can survive transplacental transmission, **this may be a means of maintaining the spirochete in the rodent population in the absence of ticks.** – Burgess, 1993
3. **'This could mean that a survey for Bb infection using the presence of antibodies alone as the method of detection may underestimate the prevalence of infection.'** – Burgess et al, 1989.
4. **'Intrauterine infection by B burgdorferi does occur in dogs and is a potential means by which the spirochete can be transmitted in a breeding population in the absence of a tick vector.'** – Gustafson et al, 1993
5. **'these results indicated that Bb can transmit by other modes than the tick bite.'** – Altaie et al, 1996
6. **'The findings of this study of natural B. burgdorferi infection in pregnant dairy heifers supports previous observations of both natural and experimental in-utero infections with B. burgdorferi in domestic animals and give further evidence of B. burgdorferi occurs during gestation in naturally infected cattle.'** – Bushmich et al, 1998
7. **'Vertical transmission of B.b. was confirmed with B.b isolated from foetuses of Apodemus agrarius + Rattus edwardsi. The results showed that Lyme disease spirochetes, B.b., might be naturally maintained in an enzootic cycle by transplacental transmission.'** - Wan et al, 1999.

Year	Vertical transmission NOT found	Other findings/notes	Citation
1990	'Infection did not affect reproduction or development of young born from infected dams, nor did spirochetes appear in the tissues of neonates.'	'Mice were susceptible to oral infection and transmitted infection to each through through direct contact.'	Wright SD, Nielsen SW. Experimental infection of the white-footed mouse with <i>Borrelia burgdorferi</i> . Am J Vet Res. 1990 Dec;51(12).
1991	'Five pregnant adult female Lewis rats were inoculated i.p. with spirochetes at 4 days gestation. Adult females seroconverted or had positive spleen cultures at 20 days gestation, placentas and fetuses were culture negative.'	'Venereal transmission from seven infected females or six infected males to uninfected rats of the opposite sex was not demonstrated.'	Moody KD, Barthold SW. Relative infectivity of <i>Borrelia burgdorferi</i> in Lewis rats by various routes of inoculation. Am Trop Med Hyg 44:135, 1991.
1991	'all 14 mother mice examined produced infected ticks and exhibited serum antibodies to Bb. However non of 28 offspring produced infected ticks and only a few had evidence of circulating antibody.'	In a separate experiment, no young CD-1 mice, born of infected mothers had IgM antibody to <i>B. burgdorferi</i> .'	Mather TN, Telford SR III, Adler GH. Absence of transplacental transmission of Lyme disease spirochetes from reservoir mice (<i>Peromyscus leucopus</i>) to their offspring. J Infect Dis 164:564, 1991.
1999	These experiments support the notion that the LD spirochete, <i>B. burgdorferi</i> , is not transmitted transplacentally, venereally, or via contact with urine or feces from infected hamsters.	However, although the hamster model is an excellent system to explore various tick/ <i>Borrelia</i> relationships, experimental data derived from it should be used cautiously in extrapolating to the murine model in nature.	Woodrum JE, Oliver JH. Investigation of Venereal, Transplacental, and Contact Transmission of The Lyme Disease Spirochete, <i>Borrelia burgdorferi</i> , in Syrian Hamsters. J. Parasitol., 85(3), 1999 p.426-430.

Vertical Transmission of Bb in Animals – Citations

- 1 Anderson JF, Johnson RC, Magnarelli LA. Seasonal Prevalence of *Borrelia burgdorferi* in Natural Populations of White-Footed Mice, *Peromyscus leucopus*. *Journal of Clinical Microbiology*, Vol 25(8)Aug, 1987, p. 1564-1566.
- 2 Ubico-Navas, Sonya Renee. Experimental and epizootologic studies of Lyme disease. Ph.D. Colorado State University, 1992.
- 3 Burgess EC, Wachal MD, Cleven TD. *Borrelia burgdorferi* infection in dairy cows, rodents, and birds from four Wisconsin dairy farms. *Vet Microbiol.* 1993 May;35(1-2):61-77. doi: 10.1016/0378-1135(93)90116-o. PMID: 8362496.
- 4 Silver RM, Yang L, Daynes RA, Branch DW, Salafia CM, Weis JJ. Fetal outcome in murine Lyme disease. *Infect Immun.* 1995;63(1):66-72. doi:10.1128/IAI.63.1.66-72.1995
- 5 Altaie SS, Mookherjee S, Assian E, Al-Taie F, Nakeeb SM, Siddiqui SY. Transplacental transmission of Bb in a Murine Model. 10th Annual International Scientific Conference on Lyme Disease and other Tick-Borne Disorders, National Institutes of Health, Bethesda MD April 28-30, 1997. ; Altaie SS, Mookherjee S, Assian E, Al-Taie F, Nakeeb SM, Siddiqui SY. Transmission of Bb from Experimentally Infected Mating Pairs to Offsprings in a Murine Model. Abstract # I-17. FDA Science Forum, 1996.
- 6 Hou X. [Preliminary investigation on reservoir hosts of *Borrelia burgdorferi* in China]. *Wei Sheng Yan Jiu.* 1999 Jan 30;28(1):7-9. Chinese. PMID: 12712735.
- 7 Burgess EC. *Borrelia burgdorferi* infection in Wisconsin horses and cows. *Ann N Y Acad Sci.* 1988;539:235-43. doi: 10.1111/j.1749-6632.1988.tb31857.x. PMID: 3190095.
- 8 Leibstein MM, Khan MI, Bushmich SL. Evidence for in-utero Transmission of *Borrelia burgdorferi* from Naturally Infected Cows. *Journal of Spirochetal and Tick-borne Diseases.* Vol 5, Fall/Winter, 1998: 54-62.
- 9 Burgess EC, Gendron-Fitzpatrick A, Mattison M. Foal mortality associated with natural infection of pregnant Mares with *Borrelia burgdorferi*. In *Proceedings, 5th Int Conf Equine Infectious Dis*, 1989, 217-220.
- 10 Gustafson, John Michael, Ph.D. The in utero and seminal transmission of *Borrelia burgdorferi* in Canidae. The University of Wisconsin - Madison, 1993. PhD Thesis.
- 11 Gustafson JM, Burgess EC, Wachal MD, Steinberg H. Intrauterine transmission of *Borrelia burgdorferi* in dogs. *Am J Vet Res.* 1993 Jun;54(6):882-90.
- 12 Burgess EC, Windberg LA. *Borrelia* SP. Infection in Coyotes, Black-Tailed Jack Rabbits and Desert Cottontails in Southern Texas. *Journal of Wildlife Diseases* 25(1), 1989, pp. 47-51.

Vertical transmission not identified in these studies

- Wright SD, Nielsen SW. Experimental infection of the white-footed mouse with *Borrelia burgdorferi*. *Am J Vet Res.* 1990 Dec;51(12):1980-7. PMID: 208522
- Mather TN, Telford SR III, Adler GH. Absence of transplacental transmission of Lyme disease spirochetes from reservoir mice (*Peromyscus leucopus*) to their offspring. *J Infect Dis* 164:564, 1991.
- Moody KD, Barthold SW. Relative infectivity of *Borrelia burgdorferi* in Lewis rats by various routes of inoculation. *Am Trop Med Hyg* 44:135, 1991.
- Woodrum JE, Oliver JH. Investigation of Venereal, Transplacental, and Contact Transmission of The Lyme Disease Spirochete, Bb, in Syrian Hamsters. *J. Parasitol.*, 85(3), 1999 p.426-430.