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FARAH

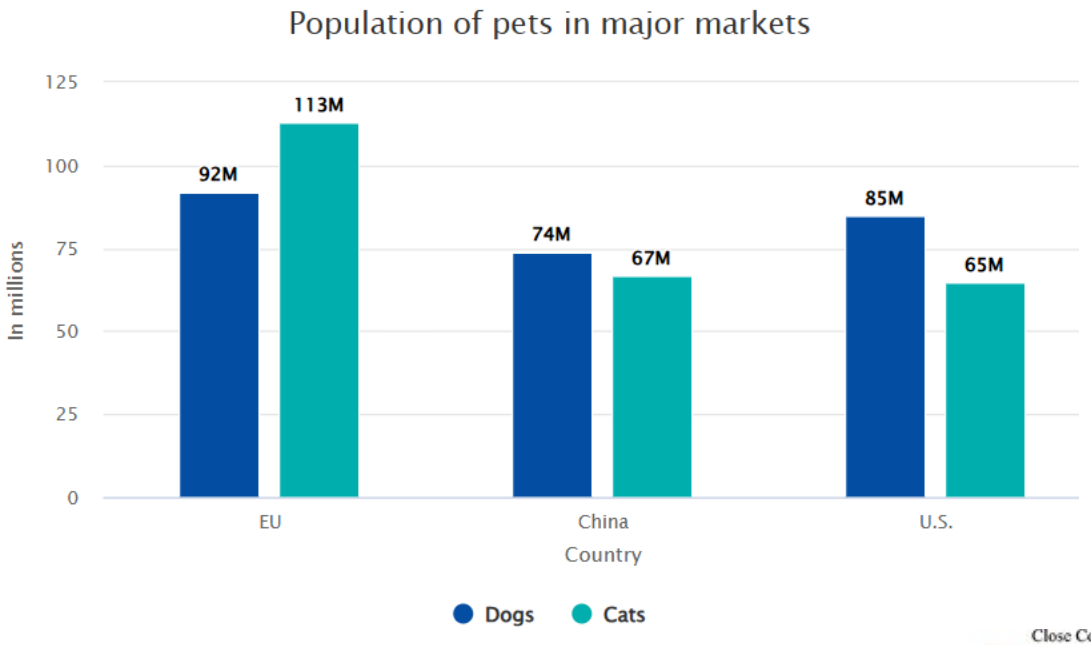
Phage therapy in companion animals: which way for an efficient treatment ?

Avoiding Antimicrobial Resistance: Veterinary use of Phages for Prevention, Therapy and Control of Bacterial Infections

November 19-20, 2024

Prof Damien THIRY, DVM, MVPH, PhD, Dipl ECVM
Veterinary bacteriology
FARAH Research Center
Faculty of Veterinary Medicine, Liège University, Belgium
damien.thiry@uliege.be

IABS



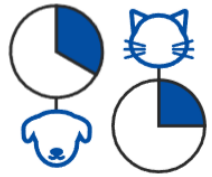
How many people own a pet?

Billions of households around the world are unified by a common theme – pet ownership. Sharing your home with a pet is a common language that cuts across country and culture.

More than half of the global population is estimated to have a pet at home. [22]

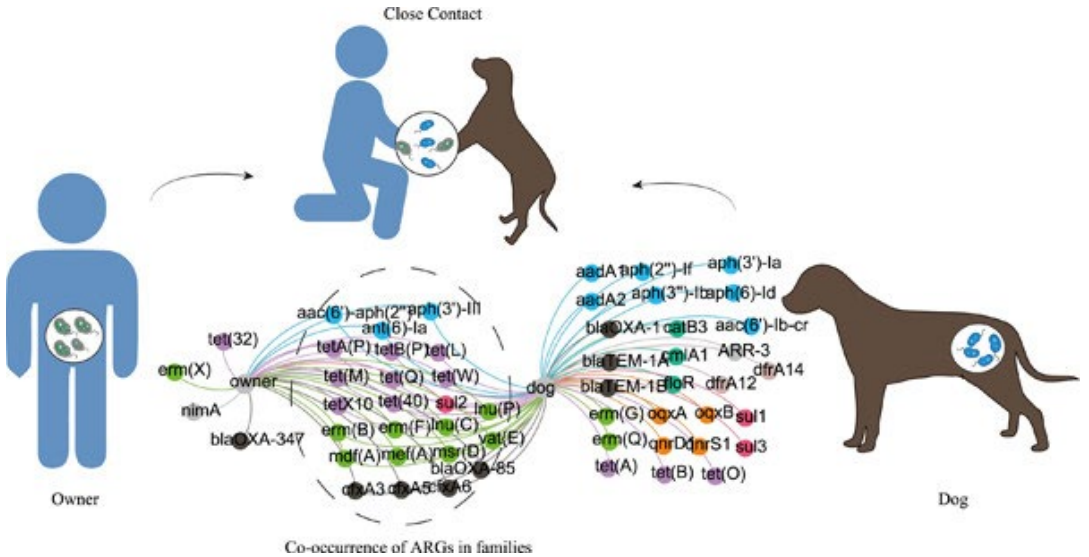
Families in the U.S., EU and China alone have over half a billion dogs and cats.

In the U.S., 70 percent of households owned a pet as of 2021 compared to 68 percent in 2016. [23]



Globally, dogs are the most popular pet, present in around one in three homes. Almost a quarter of pet owners have a cat. [24]

Health for Animals
global animal health association



(Zhao et al, 2022)

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phage therapy human

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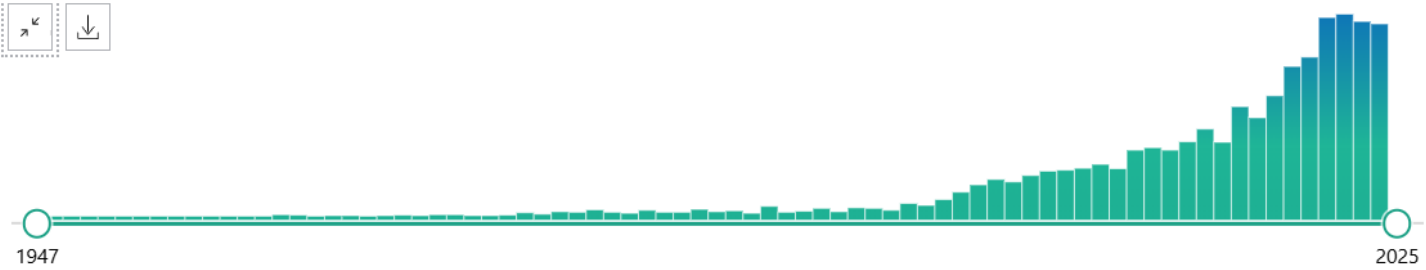
RESULTS BY YEAR

4,560 results

Page 1 of 456



PubMed®

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RESULTS BY YEAR

10 results

Page 1 of 1

PubMed®

phage therapy livestock

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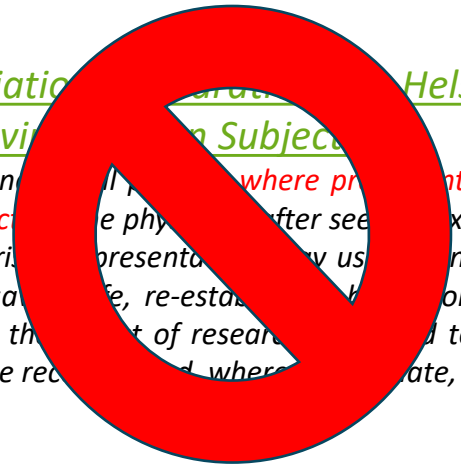
RESULTS BY YEAR

75 results

Page 1 of 8

Scarce literature compared to human and farm animals



World Medical Associatio[illegible] Helsinki – Ethical Principles for Medical Research Involvi[illegible]n Subject[illegible]

" 37. In the treatment of an in[illegible] where pr[illegible]nterventions do not exist or other known interventions have been ineffec[illegible]e phy[illegible]fter see[illegible]xpert advice, with informed consent from the patient or a legally authori[illegible]presenta[illegible]y us[illegible]nproven intervention if in the physician's judgement it offers hope of sa[illegible]fe, re-esta[illegible]h[illegible]or alleviating suffering. This intervention should subsequently be made th[illegible]t of resear[illegible]d to evaluate its safety and efficacy. In all cases, new information must be rec[illegible]d, where[illegible]ate, made publicly available."

Few research programs funded for companion animals

Scarce literature compared to human and farm animals

but

and
encouraging literature

Companion animals as *in vivo* models for human or farm animals

frontiers | Frontiers in Microbiology

TYPE Original Research
PUBLISHED 18 October 2022
DOI 10.3389/fmicb.2022.1031101

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EDITED BY
Yang Wang,
Henan University of Science and Technology, China

REVIEWED BY
Vathsala Mohan,
The New Zealand Institute for Plant and Food Research Ltd., New Zealand
Prasanth Manohar,
Zhejiang University-University of Edinburgh Institute, China

Topically applied bacteriophage to control multi-drug resistant *Pseudomonas aeruginosa*-infected wounds in a New Zealand rabbit model

Jinyu Wang, Wenxin Meng, Kaichuan Zhang, Jingyu Wang, Baochun Lu, Ruijie Wang and Kun Jia*

Contents lists available at ScienceDirect

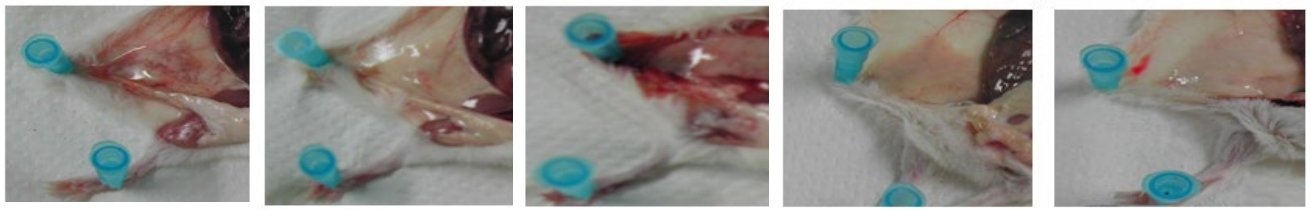
Journal of Global Antimicrobial Resistance

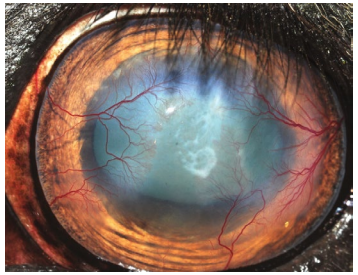
journal homepage: www.elsevier.com/locate/jgar

In vitro and in vivo assessment of phage therapy against *Staphylococcus aureus* causing bovine mastitis

C. Ngassam-Tchamba[a], J.N. Duprez[a], M. Fergestad[b], A. De Visscher[c,1], T. L'Abee-Lund[b], S. De Vliegher[c], Y. Wasteson[b], F. Touzain[d], Y. Blanchard[d], R. Lavigne[e], N. Chanishvili[f], D. Cassart[g], J. Mainil[a], D. Thiry[a]

Groups		OS001_ISP				OS001_marbo				OS001_PBS				ISP_PBS				PBS_PBS			
Hour post inoculation		HPI24		HPI48		HPI24		HPI48		HPI24		HPI48		HPI24		HPI48		HPI24		HPI48	
Mice		M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18	M19	M20
Bacterial titers (CFU/mg)	L4	$2,1.10^3$	$1,4.10^3$	-	-	-	$2,6.10^3$	-	-	$4,3.10^6$	$6,2.10^6$	69.10^8	$3,7.10^7$	-	-	-	-	-	-	-	-
	R4	$5,6.10^5$	$3,3.10^5$	-	2.10^4	-	-	-	-	$2,4.10^7$	$8,3.10^7$	$3,2.10^8$	7.10^7	-	-	-	-	-	-	-	-
Phage titers (PFU/mg)	L4	$3,4.10^2$	$1,2.10^3$	-	-	-	-	-	-	-	-	-	-	-	$5,8.10^5$	$1,3.10^2$	$1,4.10^2$	-	-	-	-
	R4	-	$2,3.10^2$	-	-	-	-	-	-	-	-	-	-	-	-	$3,4.10^3$	$1,9.10^2$	-	-	-	-

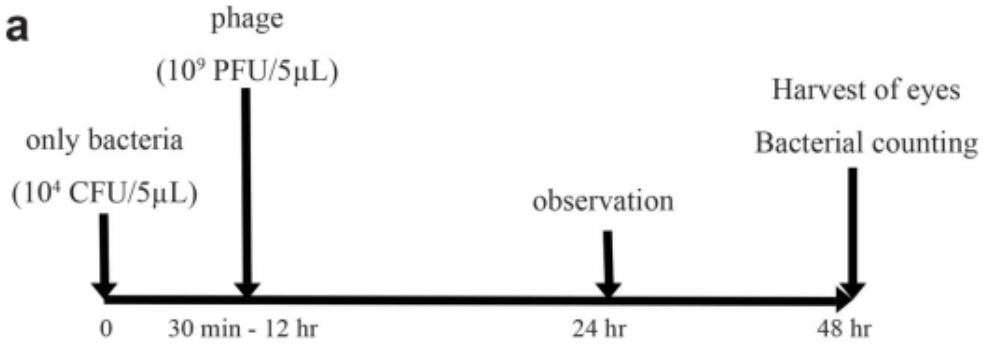


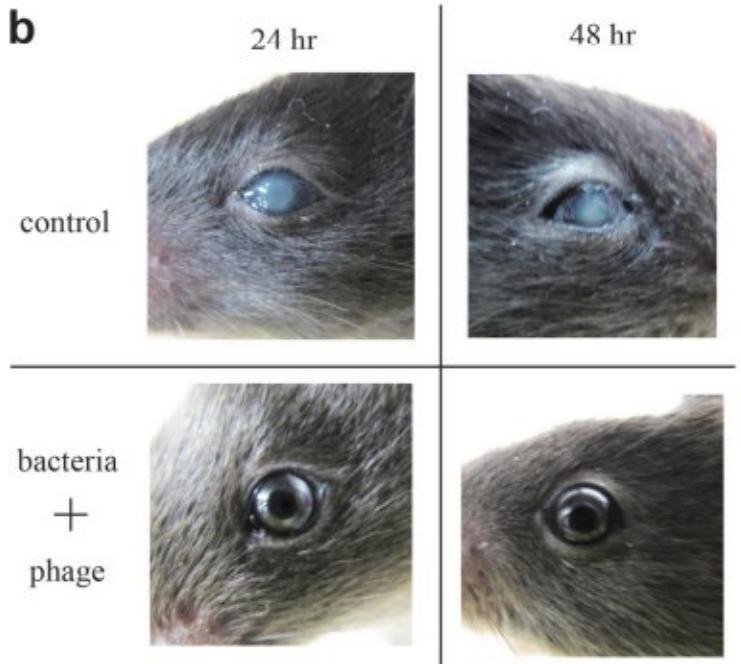


AMERICAN SOCIETY FOR MICROBIOLOGY | Applied and Environmental Microbiology

Phage Therapy Is Effective in a Mouse Model of Bacterial Equine Keratitis

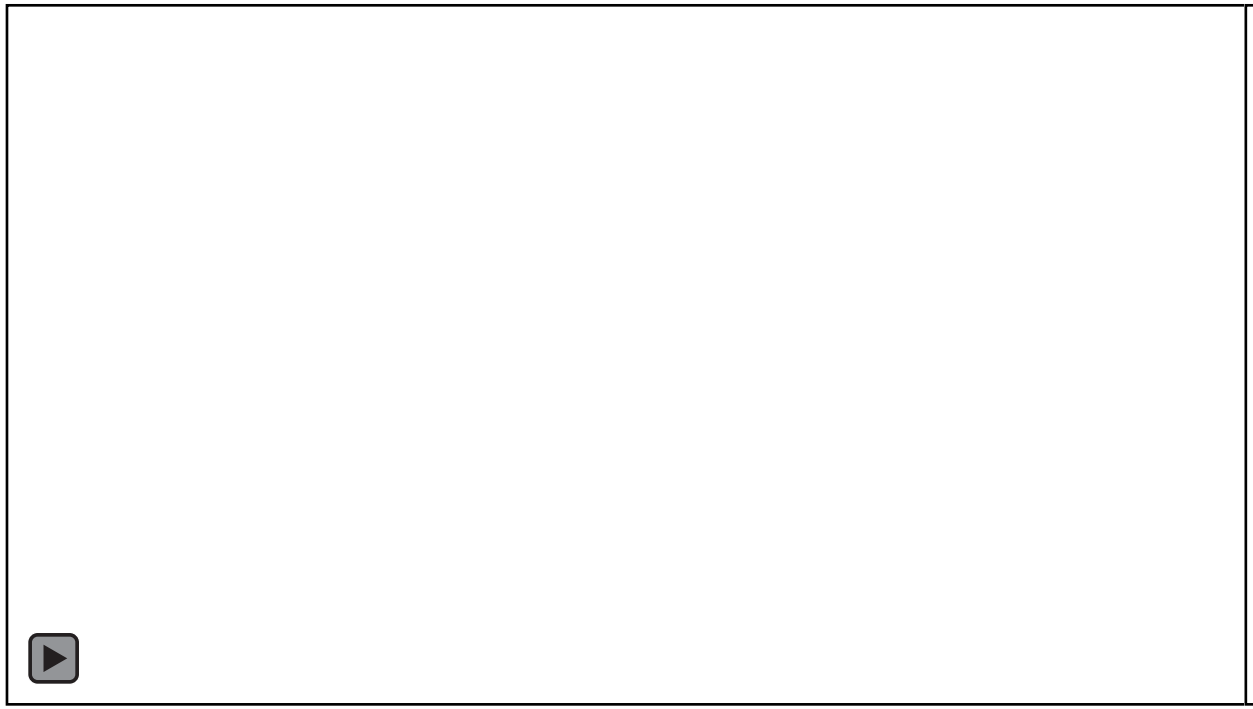
Takaaki Furusawa,[a] Hidetomo Iwano,[a] Yutaro Hiyashimizu,[a] Kazuki Matsubara,[a] Hidetoshi Higuchi,[b] Hajime Nagahata,[b] Hidekazu Niwa,[c] Yoshinari Katayama,[c] Yuta Kinoshita,[c] Katsuro Hagiwara,[d] Tomohito Iwasaki,[e] Yasunori Tanji,[f] Hiroshi Yokota,[a] Yutaka Tamura[g]

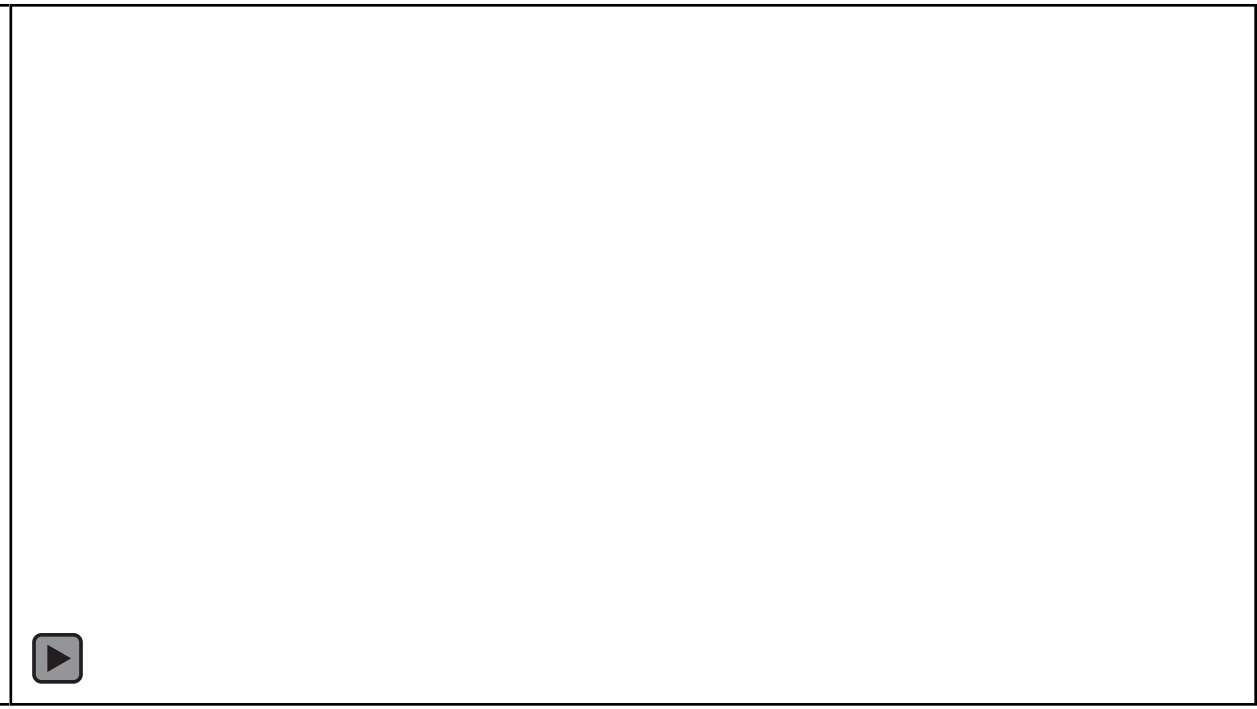




Dog otitis

Otitis in dog caused by *P. aeruginosa*





(Source: monvt.eu)

ELSEVIER

Burns

Volume 32, Issue 5, August 2006, Pages 644-646

Case report

Multiplication of therapeutically administered bacteriophages in *Pseudomonas aeruginosa* infected patients

J.A. Sivera Marza [a], J.S. Soothill [b], P. Boydell [c], T.A. Collyns [d]

Case:

- 5 years old atopic St Bernard dog
- Chronic bilateral otitis externa caused by ***P. aeruginosa***
- Failure of repeated topical and systemic treatment

Phage treatment:

- One phage
- Single application of 0,2mL of phage suspension at 400PFU/mL into external auditory canal

Observations:

- 27h post treatment: right ear was dry and no longer inflamed (left ear as control)
- Phage count: 1,6x 10^{e}8pfu / 0,032g of ear detritus ➔ phage replication
- Long term follow up: recurrent cycles of improvement-deterioration until a total recovery 9 months later (no *P. aeruginosa* isolated) without Ab

Dog’s ear before the phage treatment

Dog’s ear 27h post phage treatment

(Marza *et al*, 2006)

Veterinary Microbiology 146 (2010) 309–313

Contents lists available at ScienceDirect

Veterinary Microbiology

journal homepage: www.elsevier.com/locate/vetmic

Topical treatment of *Pseudomonas aeruginosa* otitis of dogs with a bacteriophage mixture: A before/after clinical trial

Catherine Hawkins [a], David Harper [a], David Burch [b], Erik Änggård [a], James Soothill [c,*]

[a] *Biocontrol Ltd., Suites 217-218, BioCity Nottingham, Pennyfoot Street, Nottingham, NG1 1GF, UK*
[b] *Octagon Services Ltd., The Round House, The Friary, Old Windsor, Berkshire, SL4 2NR, UK*
[c] *Level 4 CB Laboratories, Great Ormond Street Hospital, London, WC1N 3JH, UK*

Cases:

- Clinical trial
- 10 dogs with chronic otitis since > 3 months
- Failure of repeated Ab treatments (>3) and flushing
- *P. aeruginosa* sensitive to the used phages

Phage treatment:

- Cocktail of 6 phages against *P. aeruginosa*
- Single application of 0,2mL of phage suspension at 10^e5 PFU of each of the 6 phages into external auditory canal

Observations:

- Scoring (occlusion, erythema, discharge, …) ➔ before phage treatment and 48h post treatment
- Phage count 1 day post treatment
- Long term follow up: 18 months, incomplete but generally positive

Change in indicators from before to 48 h after bacteriophage treatment.

	Clinical condition		*P. aeruginosa*	Bacteriophage
	[a]Reduction in clinical score	Reduction in clinical score (%) (score on day 1 considered as 100%)	Reduction in *P. aeruginosa* count (%) (count on day 1 considered as 100%)	pfu/swab (6×10^5 pfu administered on day 1)
Dog 1	4	30.8	74	8×10^7
Dog 2	5	50	58.6	4.7×10^6
Dog 3	6	54.5	75.8	1.4×10^8
Dog 4	4.5	56.3	46	1.7×10^6
Dog 5	3	21.4	54	5.5×10^6
Dog 6	1.5	12.5	63.6	2.6×10^8
Dog 7	3	24	89	1×10^7
Dog 8	1	7.7	29.4	4.5×10^6
Dog 9 (L ear)	2	28.6	82.5	7.9×10^7
Dog 10 (R ear)	2.5	17.9	96.8	9.4×10^6
Mean (all dogs)	3.3	30.1	67	5.9×10^7

[a] Out of a total of 18, based on 5 clinical indicators where higher scores indicate worse condition.

(Hawkins *et al*, 2010)

The Journal of Veterinary Medical Science
This Journal For Authors Submissions

J Vet Med Sci. 2016 Feb 14;78(6):1035–1038. doi: 10.1292/jvms.15-0310

Bacteriophage can lyse antibiotic-resistant *Pseudomonas aeruginosa* isolated from canine diseases

Takaaki FURUSAWA [1], Hidetomo IWANO [1,*], Hidetoshi HIGUCHI [2], Hiroshi YOKOTA [1], Masaru USUI [3], Tomohito IWASAKI [4], Yutaka TAMURA [3]

Research in Veterinary Science 136 (2021) 598–601

Contents lists available at ScienceDirect

Research in Veterinary Science

journal homepage: www.elsevier.com/locate/rvsc

Efficacy assessment of PEV2 phage on *Galleria mellonella* larvae infected with a *Pseudomonas aeruginosa* dog otitis isolate

C. Antoine [a,b,1], F. Laforêt [a,b,1], B. Blasdel [c], T. Glonti [d], E. Kutter [e], J.P. Pirnay [d], J. Mainil [a], V. Delcenserie [b,2], D. Thiry [a,*,2]

pharmaceutics

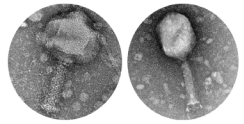
MDPI

Article

Isolation and Molecular Characterization of Two Novel Lytic Bacteriophages for the Biocontrol of *Escherichia coli* in Uterine Infections: In Vitro and Ex Vivo Preliminary Studies in Veterinary Medicine

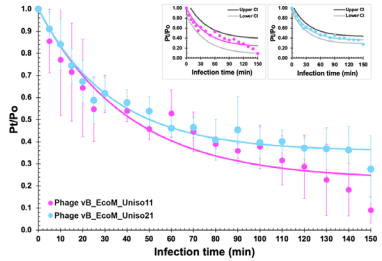
Victor M. Balcão [1,2,*], Bianca G. Belline [1], Erica C. Silva [1], Pablo F. F. B. Almeida [1], Denicezar Â. Baldo [1], Lara R. P. Amorim [3], José M. Oliveira Júnior [1], Marta M. D. C. Vila [1] and Fernando S. Del Fiol [1]

Uterine infection

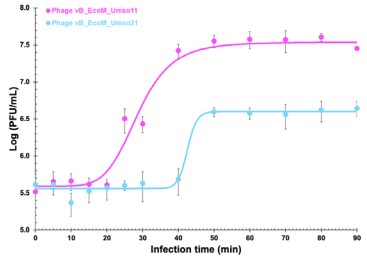


Phages ph0011 & ph0021

❶



Phage adsorption onto host cells



Phage growth parameters

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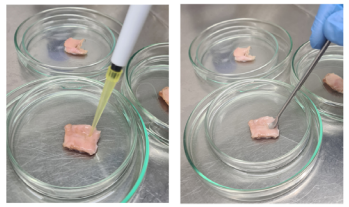

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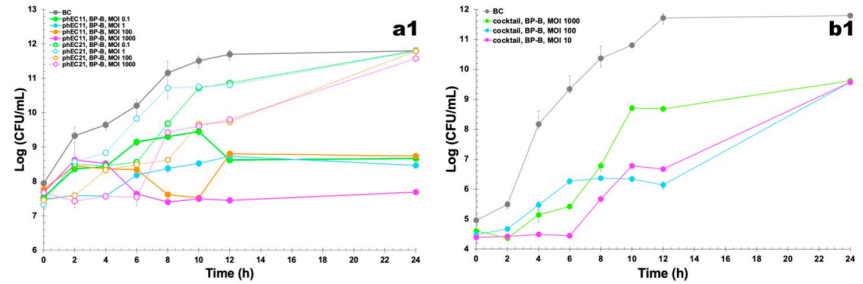
Preparation of uteri samples for ex vivo bacterial inactivation assays

❹



Ex vivo bacterial inactivation

(Balcão et al, 2022)

Food producing

Companion

Equine pyoderma

pathogens

MDPI

Article

Topical Bacteriophage Therapy for Staphylococcal Superficial Pyoderma in Horses: A Double-Blind, Placebo-Controlled Pilot Study

Kalie Marshall and Rosanna Marsella *

Abstract: Increased antimicrobial resistance highlights the need for alternatives to antibiotics. Bacteriophages, which are benign viruses that kill bacteria, are promising. We studied the efficacy of topical bacteriophages for treating equine staphylococcal superficial pyodermas. Eight *Staphylococcus aureus* isolates were tested against a bacteriophage bank, and a cocktail consisting of two bacteriophages was prepared. Twenty horses with clinical and cytological evidence of superficial pyoderma and confirmed *S. aureus* infection based on swabbed culture were enrolled in the study. Each horse received both the bacteriophage cocktail and the placebo at two different infection sites, once daily for four weeks. Clinical lesions and cytology were evaluated weekly by an investigator who was unaware of the treatment sites. All infection sites were swabbed and cultured at the end of the study. A linear mixed model showed no significant differences between the placebo and treatment sites in terms of clinical signs, cytological scores of inflammation, and bacterial counts at the end of the study. It is possible that the bacteriophage cocktail killed *S. aureus*, but cytology scores did not change as new populations of cocci took over. The study limitations included a small sample size and inconsistent control of the underlying causes of pyodermas.

Osteoarticular implant

VETERINARY QUARTERLY
2024, VOL. 44, NO. 1, 1–9
https://doi.org/10.1080/01652176.2024.2350661

Taylor & Francis
Taylor & Francis Group

CASE REPORT

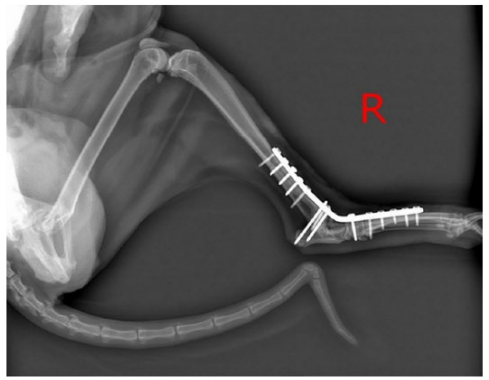
OPEN ACCESS Check for updates

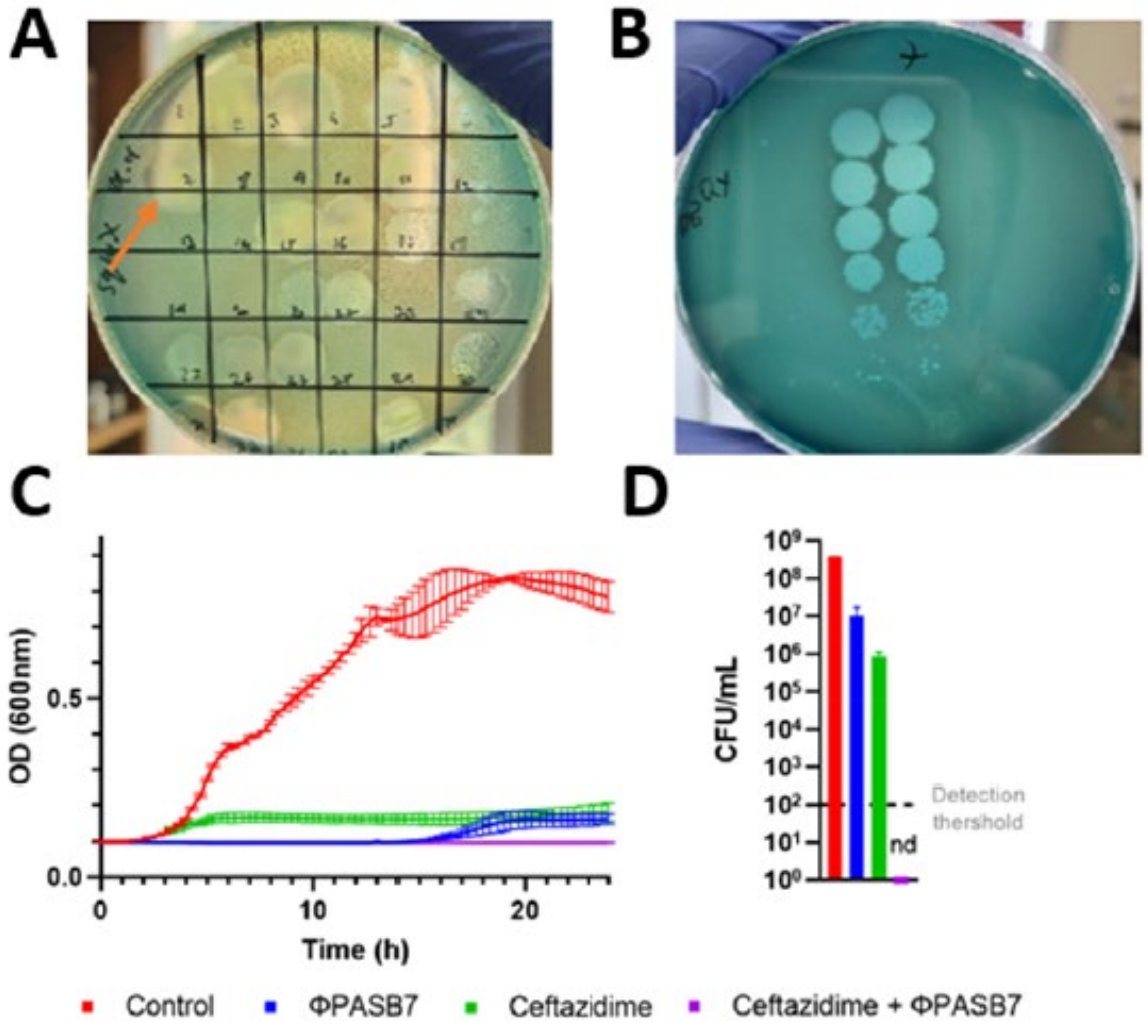
Successful phage-antibiotic therapy of *P. aeruginosa* implant-associated infection in a Siamese cat

Ron Braunstein[a], Goran Hubanic[b], Ortal Yerushalmy[a], Sivan Oren-Alkalay[a], Amit Rimon[a,c], Shunit Coppenhagen-Glazer[a], Ofir Niv[b], Hilik Marom[b], Alin Barsheshet[b] and Ronen Hazan[a]

Cases:

- Siamese cat, 5 years old
- Trauma with multiple comminuted fractures in both hind legs and impaired surrounding soft tissues
- Surgery: arthrodesis with internal fixation
- Two-weeks post surgery: necrosis and amputation of left hind leg and implant associated infection caused by *P. aeruginosa*
- Failure of several Ab treatment (4 months)

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0
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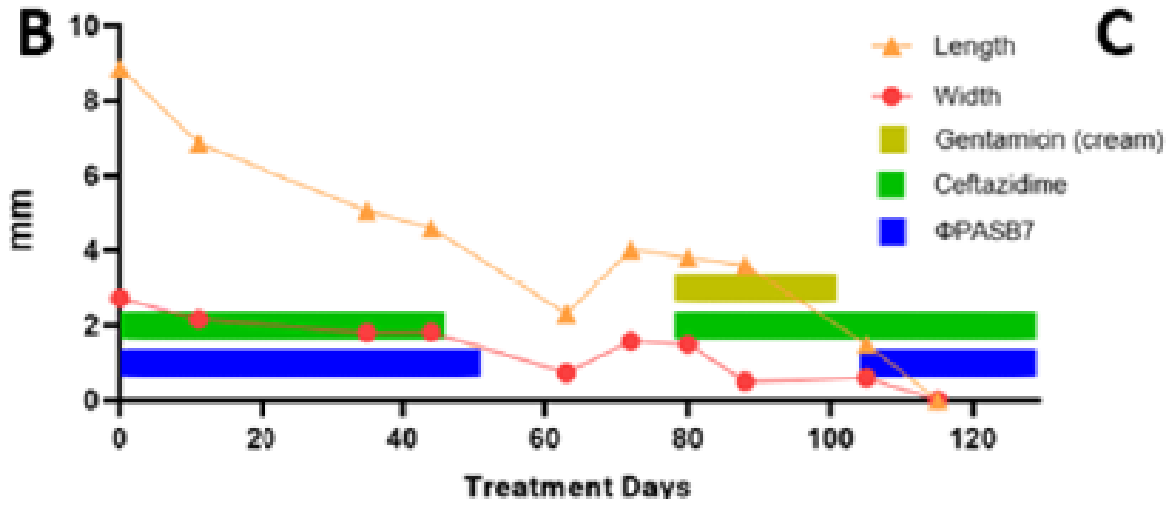
20
Time (h)
CFU/mL
10^9
10^8
10^7
10^6
10^5
10^4
10^3
10^2
10^1
10^0
Detection thershold
nd
Control
ΦPASB7
Ceftazidime
Ceftazidime + ΦPASB7

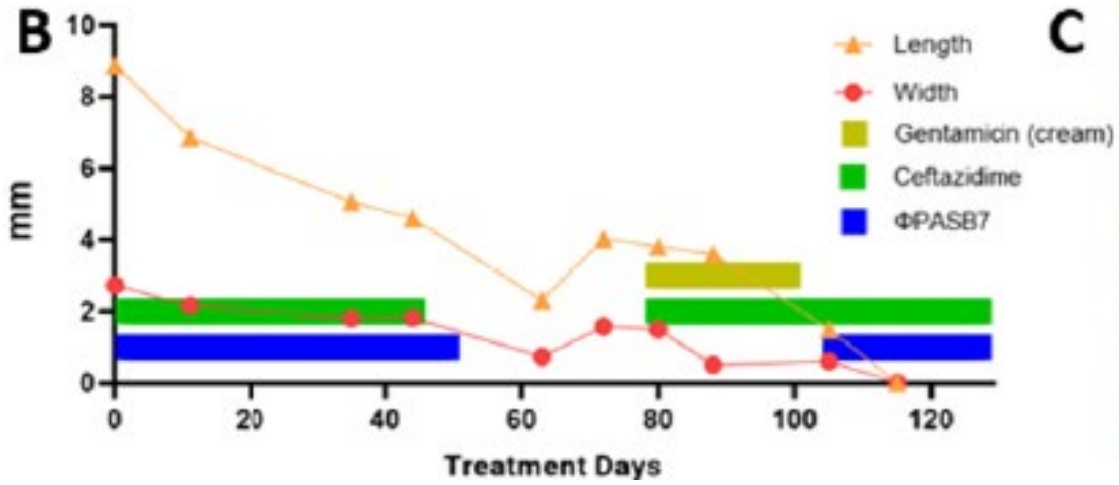
Phage treatment:

- 1st application, by a vet:
  - Bacteriophage PASB7, topical
  - Ceftazidime: 15 min later, IM

- Next applications, by the owner:
  - Bacteriophage: twice daily during the bandage changes
  - Ceftazidime: 4 times a day




A
Day 0
Day 11
Day 44
Day 80
Day 105
Day 115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mm
Length
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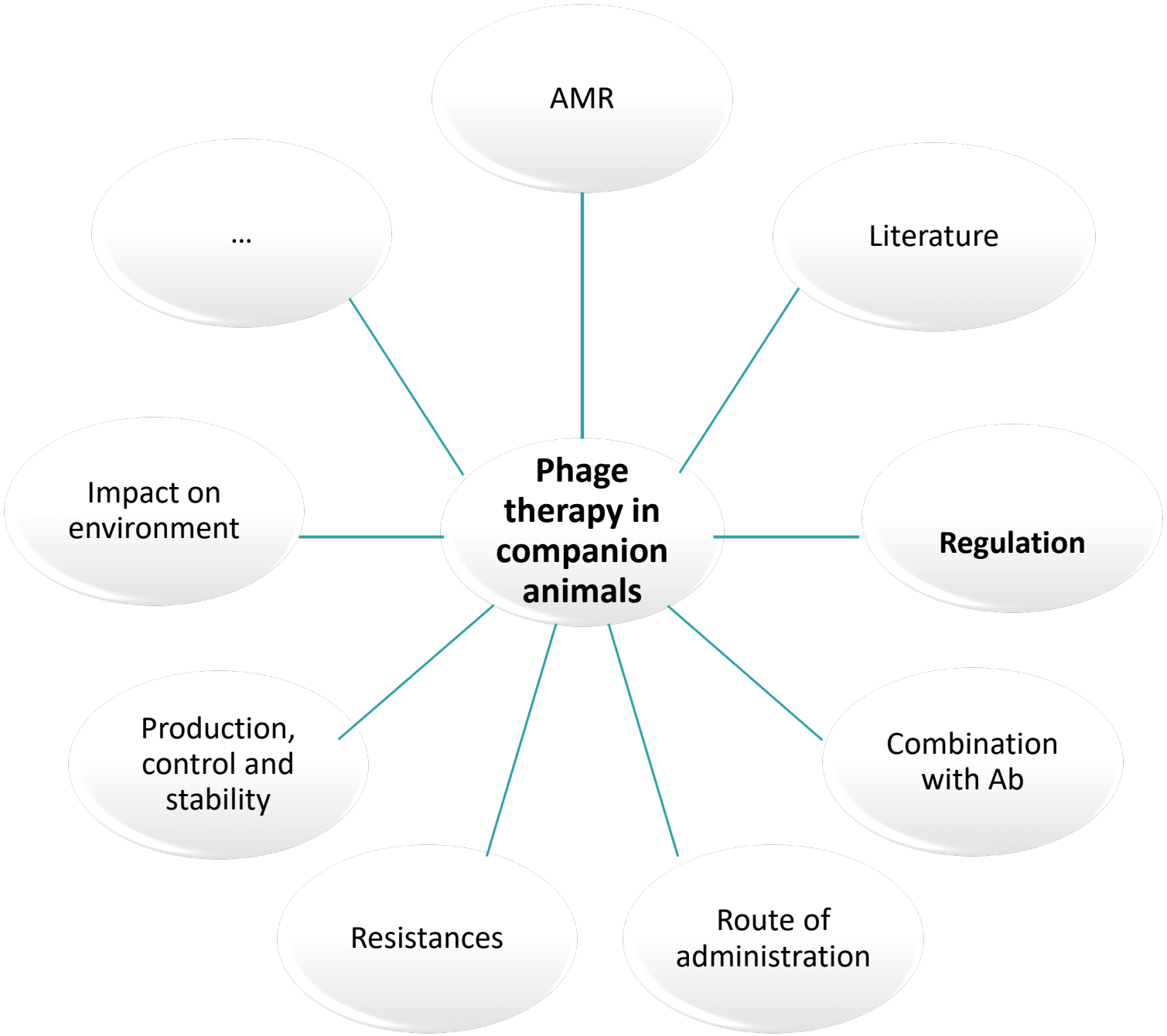
Gentamicin (cream)
Ceftazidime
ΦPASB7
Treatment Days


C
Eight months post phage therapy


AMR
Literature
Regulation
Combination with Ab
Route of administration
Resistances
Production, control and stability
Impact on environment
…
Phage therapy in companion animals

(*The New Yorker*, 2020)