

A Brief Study on Hemorrhagic Septicemia

Karunasree P*

GITAM University, Visakhapatnam, India

Review Article

Received: 22/07/2016

Accepted: 24/07/2016

Published: 25/08/2016

*For Correspondence

Karunasree P, MBA, GITAM University, Visakhapatnam, Andhra Pradesh, India.

E-mail:

karunasreepandiri@gmail.com

Keywords: Hemorrhagic Septicemia, *P. multocida*, Cattle, Dairy industries, Nasal release

ABSTRACT

Hemorrhagic septicemia (HS), an intense, lethal and septicemic disease of cattle and wild oxen is caused by *Pasteurella multocida*, is vital in tropical locales of the world, particularly in African and Asian nations. The pervasiveness of sickness has been very much reported with dominating detachment of *P. multocida* serotypes B:2 and E:2. Routine strategies for recognizable proof, for example, serotyping, antibiogram, biotyping determination and pathogenicity and in addition sub-atomic techniques (*P. multocida*-particular polymerase chain response (PCR), a serogroup B-particular PCR test, multiplex capsular writing framework and circle interceded isothermal enhancement methods) and portrayal (restriction endonuclease analysis, randomly amplified polymorphic DNA analysis, repetitive extragenic palindromic PCR and enterobacterial repetitive intergenic consensus PCR analysis) are connected in parallel for quick epidemiological examinations of HS flare-ups. Albeit a few antibody definitions including alum encouraged, oil adjuvant and various emulsion immunizations are financially accessible, the mission for appropriate extensively defensive HS antibodies with durable safety is on the upsurge. Simultaneously, endeavors are being made to disentangle the secrets of the pathogen and its destructiveness components, pathogenesis and determinants of defensive invulnerability and in addition differences among strains of *P. multocida*. This survey highlights the advances in these different parts of HS.

INTRODUCTION

Haemorrhagic septicaemia in cattle and buffaloes was previously known to be associated with one of two serotypes of *P. multocida*: B:2 and E:2 or 6:B and 6:E using different analytical systems [1-8]. The disease occurs mainly in cattle and buffaloes. It is an endemic disease mostly prevalent in African and Asian countries. As these continents mainly consist of Dairy industries, this disease is more prevalent in these areas than the European countries. Buffaloes are more susceptible to Haemorrhagic septicemia than any other animal [9-12].

CAUSATIVE ORGANISM

Pasteurella multocida is the causative organism which is causing Haemorrhagic septicemia in the cattle. *P. multocida* is a Gram-ve, non-motile bacterium which is sensitive to Pencillin. It causes a wide range of diseases in cattle mainly. This bacterium is a deadly organism which causes brain death in the cattle [13-15].

The serotyping techniques differentiate *Pasteurella multocida* into five capsular serogroups (A, B, D, E, and F) and 16 physical serotypes (1 to 16) [16-20]. The capsule and the liposaccharide are causing bacterial avoidance of phagocytosis and bacterial survival in the cattle. In the present study, we have built up a multiplex PCR test as a fast other option to the customary capsular serotyping framework.

Pasteurella is spread by means of direct contact, or by ingestion of food and water. Transmission of these is particularly effective when calves are swarmed or firmly bound (calf nursery). *P. multocida* is regularly connected with the more drawn out enduring instances of cow-like respiratory ailment [21-25]. The symptoms of this disease begin with melancholy, and diminished ravenousness. This advances to finish loss of hankering, cut head and hair, mucopurulent nasal release and a high fever and heavy breathing. If the treatment is not provided immediately, the lungs get infected which eventually leads to the death of the cattle.

SYMPTOMS

Heating of Conductors

The main symptoms include high temperature, loss of weight and feeling feeble, nasal release, salivation and heavy breathing, with swellings in the throat region spreading to the brisket area and to the forelegs [26-30].

The clinical signs include a temporary determination is imperative since preventive measures to control the spread of the ailment are required quickly, without sitting tight for the vital research facility affirmation [31-36]. At the most punctual opportunity, in any case, proper material ought to be gathered and dispatched to the closest research center. The simple segregation of *P. multocida* does not imply that Hemorrhagic septicemia was analyzed. From one perspective it ought to be placed in the epidemiological connection also, then again the disconnected strain must be serotyped [37-38]. *Bacillus anthracis*, blackquarter and, more particularly rinderpest (because of its conceivable ramifications in universal creature wellbeing) ought to dependably be considered when researching sudden passing's in dairy cattle and wild oxen.

EPIDEMIOLOGY

The three important factors of this epidemic are:

1. Climatic conditions: The climatic conditions regularly the storms with high moistness and at times with high temperatures.
2. Dairy practices: Dairy practices includes lack of fodder and the pressures of the work that animals do e.g. agriculture animals, crowded nurseries, dirty farm lands.
3. Species of the animal: Buffalos and calves are more susceptible than any other dairy cattle to this disease.

DIAGNOSIS

A complete conclusion of HS depends on separation of *P. multocida* serotype B:2 or E:2 (or different less regular serotypes perceived by the OIE as bringing on HS) from the blood and tissues of a creature with commonplace signs [39-44]. Different other *P. multocida* serotypes can bring about HS-like malady in dairy cattle and water bison, which must be separated from traditional HS. The aloof mouse insurance test utilizing particular B:2 and E:2 insusceptible rabbit sera has been utilized as a part of Asia and Africa to recognize these serotypes [45-49]. The PCR methods are most achievable for use in endemic ranges and can be utilized with different examples, including blood, tissues, or microorganisms from juices or plate societies.

TREATMENT AND PREVENTION

Cattle can be cured only if they have been treated in the very early phases of the attack. In Dairy farms, however, early detection and effective treatment are achieved only through regular checking temperatures of the animals. Generally chemotherapy resorts to either streptomycin or oxytetracycline managed by intramuscular course at genuinely high dose [50-56]. Penicillin, sulfonamides, tetracycline, chloramphenicol and ampicillin are also effective drugs to be administered [57-69]. Since hemorrhagic septicemia typically leads to acute death, control of the infection by treating them by using antibiotics and serum therapy has been futile and prevention is by vaccination [70-75].

Formaldehyde induced culture of *P. multocida* adsorbed on aluminum hydroxide gel is available for prophylactic vaccination against septicemia cows and buffaloes [76-82] with the following vaccination regimen:

Primary vaccination: Six months of age or above, followed by booster dose after one month.

Revaccination: Annually [83-88].

NOTE

Pastuerella multocida can easily infect humans and so while dealing with the cases related to these, proper care and preventive measures should be taken [89-100].

REFERENCES

1. Sugun MY, et al. Isolation of Uncommon *Pasteurella multocida* Strains from Cattle in North Central Nigeria. *J Vaccines Vaccin.* 2016;7:320.
2. Pandey N, et al. Conservation of Properties of Outer Membranes Protein across Host Genera of *Pasteurella multocida* Suggests Common Mechanism of Action. *Mol Biol* 2016;5:162.
3. Barghash SM, et al. Molecular Detection of Pathogens in Ticks Infesting Camels in Matrouh Governorate, Egypt. *J Bacteriol Parasitol.* 2016;7:269.
4. Pillai TG, et al. Bacterial Polysaccharides - Potential Candidate for Vaccine Development. *J Med Microb Diagn.* 2016;5:224.
5. Ali OS, et al. Haematological and Histopathological Vicissitudes Following Oral Inoculation of Graded Doses of *Pasteurella multocida* Type B: 2 and its Lipopolysaccharide in Mice. *J Veterinar Sci Technol.* 2015;6:220.
6. Sidhu PK, et al. Optimization of Dosage Regimen of Gentamicin against *Pasteurella multocida* in Bovines: Old Drug, New Approach. *J Veterinar Sci Technol.* 2014;5:199.
7. Khan A, et al. In Vitro Anthelmintic and Antimicrobial Activities of Methanolic Extracts of *Fumaria Indica*. *Clin Microbial.* 2014;3:161.
8. Annas S, et al. Distribution of *Pasteurella multocida* B:2 in the Respiratory, Gastrointestinal and Urinary Tracts of Buffaloes Following Experimental Subcutaneous Inoculation. *J Veterinar Sci Technol.* 2014;5:177.
9. Zhang YF, et al. Construction and Characterization of an Acapsular Mutant of *Pasteurella multocida* Strain P-1059 (A:3). *J Vaccines Vaccin.* 2013;4:184.
10. Elalouf O, et al. *Pasteurella* Endocarditis with Spine Involvement – A Case Report and Review of Literature. *J Clin Case Rep.* 2013;3:239.
11. Ramadan A, et al. Pharmacokinetics and Distribution of Florfenicol in Bronchial Secretions of Healthy and *Pasteurella multocida* Infected Calves. *Pharm Anal Acta.* 2011;2:117.
12. Ray SM, et al. Conferences: Development and evaluation of *Pasteurella multocida* B:2 marker vaccine for bovine hemorrhagic septicemia. *J Vaccines Vaccin.* 2015.
13. Lee JH. Conferences: Generation of an attenuated *Salmonella* expressing adhesins and toxins of *Pasteurella multocida* and *Bordetella bronchiseptica* for pig progressive atrophic rhinitis and evaluation of its immune responses. *J Vaccines Vaccin.* 2015.
14. Nagaleekar VK, et al. Conferences: 16s rRNA sequence analysis of Indian isolates of *Pasteurella multocida*. *J Biotechnol Biomater.* 2015.
15. Saxena HM and Qureshi S. Conferences: New marker vaccine and DIVA assays for hemorrhagic septicemia in cattle. *J Vaccines Vaccin.* 2015.
16. Qureshi S. Conferences: Isolation and characterization of a new broad acting lytic *Pasteurella*-phage. *J Infect Dis Ther* 2015.
17. Douthwaite S. Conferences: Isualizing novel macrolide antibiotics bound to their ribosomal target. *J Bacteriol Parasitol* 2015.

18. Arif J (2015). Conferences: Anti-idiotypic mimicking outer membrane proteins of *Pasteurella multocida* B:2 in the control of haemorrhagic septicaemia. *J Vaccines Vaccin*.
19. Chachra D, et al. Conferences: World Congress on Biotechnology. Isolation and morphological characterization of a brucellaphage against *Brucella abortus* strain S 19. *J Bioengineer Biomedical Sci* 2011.
20. Chachra D et al. Conferences: 2nd International Congress on Bacteriology & Infectious Diseases. Bactofection of mammalian cells by an attenuated derivatives of *Pasteurella multocida* B:2. *J Bacteriol Parasitol* 2014.
21. Alwakeel SS,. Conferences: 3rd International Conference on Clinical Microbiology & Microbial Genomics. Isolation and identification of fungal and bacterial specimens from the sand and seawater of the red sea coastline of Saudi Arabia. *Clin Microbial* 2014.
22. Borrathybay E, et al. Conferences: 3rd International Conference on Vaccines & Vaccination. Construction and characterization of an acapsular mutant of *Pasteurella multocida* strain P-1059 (A:3). *J Vaccines Vaccin* 2013.
23. Tizioto PC, et al. Immunological Response to Single Pathogen Challenge with Agents of the Bovine Respiratory Disease Complex: An RNA-Sequence Analysis of the Bronchial Lymph Node Transcriptome. *PLoS ONE*. 2015;10:e0131459.
24. Sacco RE, et al. Respiratory Syncytial Virus Infection in Cattle. *Veterinary Pathology*. 2014;51:427-436.
25. Gershwin LJ, et al. Single Pathogen Challenge with Agents of the Bovine Respiratory Disease Complex. *PLoS ONE*. 2015;10: e0142479.
26. Shaheen M, et al. A Treatise on Bovine Mastitis: Disease and Disease Economics, Etiological Basis, Risk Factors, Impact on Human Health, Therapeutic Management, Prevention and Control Strategy. *J Adv Dairy Res*. 2016;4:150.
27. Gupta BP, et al. Cholesterol Concentrations and Lipolytic Characteristics of Commercial Bovine and Caprine Milk Yogurts during Four Weeks Refrigerated Storage. *J Adv Dairy Res*. 2016;4:155.
28. Ahmadzadeh A, et al. Effect of Prostaglandin F₂ α on Growth of *Mycoplasma bovis* Associated with Bovine Mastitis. *J Adv Dairy Res*. 2015;3:142.
29. Zhang YR, et al. Molecular Characterization of Bovine SMO Gene and Effects of Its Genetic Variations on Body Size Traits in Qinchuan Cattle (*Bos taurus*). *Int J Mol sci*. 2015;16:16966-16980.
30. Magee DA, et al. DNA sequence polymorphisms in a panel of eight candidate bovine imprinted genes and their association with performance traits in Irish Holstein-Friesian cattle. *BMC genetics*; 2010;11:1.
31. Guerrero FD, et al. (2014) *Rhipicephalus (Boophilus) microplus* aquaporin as an effective vaccine antigen to protect against cattle tick infestations. *Parasites & vectors*. 2014;7:1.
32. Sasaki S, et al. Genetic variants in the upstream region of activin receptor IIA are associated with female fertility in Japanese Black cattle. *BMC Genetics*. 2015;16:123.
33. Xin T, et al. Assessment of a protein cocktail-based skin test for bovine tuberculosis in a double-blind field test in cattle. *Clinical and Vaccine Immunology*. 2013;20:482-490.
34. Utsunomiya YT, et al. Genome-wide association study for birth weight in Nellore cattle points to previously described orthologous genes affecting human and bovine height. *BMC Genetics*. 2013;14:1.

35. Gates MC, et al. Not all cows are epidemiologically equal: quantifying the risks of bovine viral diarrhoea virus (BVDV) transmission through cattle movements. *Veterinary Research*. 2014;45:1.
36. Bashitu L, et al. Sero-Prevalence Study of Bovine Brucellosis and its Associated Risk Factors in Debrebirhan and Ambo Towns. *J Adv Dairy Res*. 2015;3:131.
37. Samanidou V and Evaggelopoulou EN. HPLC Analysis of Penicillins in Veterinary Drugs. *Pharm Anal Acta*. 2015;6:e174.
38. Gopalakrishnan KK and Detchanamurthy S. Effect of Media Sterilization Time on Penicillin G Production and Precursor Utilization in Batch Fermentation. *J Bioprocess Biotechniq*. 2011;1:105.
39. Boadu RF, et al. *In vitro* Activity and Evaluation of Quality of Some Selected Penicillins on the Ghanaian Market using Developed HPLC Methods. *Med Chem*. 2105;5:001-014.
40. Sukumar M, et al. Penicillin Production from Transformed Protoplast of *Penicillium chrysogenum* by Fermentation. *J Pharmacogenomics Pharmacoproteomics*. 2010;1:102.
41. El-Hady AM, et al. Seroprevalence and Molecular Epidemiology of Brucellosis in Cattle in Egypt. *Adv Dairy Res*. 2016;4:153.
42. Hristov P and Radoslavov G. A Review of Methods for Genotyping Milk Proteins in Cattle. *J Adv Dairy Res*. 2015;3:144.
43. Fikru S. Assessment of Cattle Fattening and Marketing Practice in Harshin District of Somali Regional State, Ethiopia. *J Adv Dairy Res*. 2015;3:137.
44. Beriso K, eta I. Characterization of Smallholder Cattle Milk Production System in Aleta Chukko District, Southern Ethiopia. *J Adv Dairy Res*. 2015;3:132.
45. de Mello F, et al. Longevity in Dairy Cattle. *J Adv Dairy Res*. 2014;2:126.
46. Kishore A, et al. Single Nucleotide Polymorphism in Exon 4 and Promoter Regions of β -Lactoglobulin Gene in Native Cattle (*Bos indicus*) Breeds of India. *J Adv Dairy Res*. 2014;2:125.
47. De Mello F, et al. Progress in Dairy Cattle Selection. *Adv Dairy Res*. 2014;2:110.
48. Takahashi J. Bilateral Impact between Dairy Cattle and Global Warming. *Adv Dairy Res*. 2013;2:e104.
49. Mishra S, et al. (2016) Body Condition Scoring of Dairy Cattle: A Review. *J Vet Sci* 2: 1.
50. Widyastuti FR and Purwanto, Hadiyanto. Biogas Potential from the Treatment of Solid Waste of Dairy Cattle: Case Study at Bangka Botanical Garden Pangkalpinang. *Int J Waste Resources*. 2013;3:128.
51. Wilson DJ and Goodell GM. Comparison of Blood Strips, Milk Strips and Automated Milk Measurement of Beta-Hydroxybutyrate in Periparturient Dairy Cattle and Resultant Diagnoses of Ketosis. *J Veterinar Sci Technol*. 2013;4:136.
52. umar M, et al. Ameliorative Effect of Zinc Supplementation to Lead Exposed Goat Kids on Immune Status. *J Clin Cell Immunol*. 2012;3:119.
53. Liao DJ, et al. Egg Production of Paramphistomata in Dairy Cattle. *J Bacteriol Parasitol*. 2012;3:136.
54. Sulejmani Z, et al. Abuse of Pharmaceutical Drugs-antibiotics in Dairy Cattle in Kosovo and Detection of their Residues in Milk. *J Ecosyst Ecogr*. 2012;2:114.
55. Feye KM, et al. Abrogation of *Salmonella* and *E. coli* O157:H7 in Feedlot Cattle Fed a Proprietary *Saccharomyces cerevisiae* Fermentation Prototype. *J Vet Sci Technol*. 2016;7:350.
56. Jolly A, et al. Evaluation of Hyaluronic Acid in Cattle: Physiological Variations Related to Age, Periparturition and in Clinical Cases of Paratuberculosis. *J Vet Sci Technol*. 2016;7:342.

57. Sugun MY, et al. Isolation of Uncommon *Pasteurella multocida* Strains from Cattle in North Central Nigeria. *J Vaccines Vaccin.* 2016;7:320.
58. Hamamoto K, et al. Cytochrome P450 2D14 (CYP2D14) Gene Deletion Variants in the Japanese Black Cattle and Characterization of their Effects on Metoclopramide Pharmacokinetics. *J Veterinar Sci Technol.* 2016;7:318.
59. Singh J and Singh CV. Evaluation of Sires Using Different Sire Evaluation Methods on the Basis of First Lactation Traits in Sahiwal Cattle. *J Veterinar Sci Technol.* 2016;7:296.
60. Daouam S, et al. Evaluation of the Safety and Efficacy of a Live Attenuated Thermostable Rift Valley Fever Vaccine in Sheep, Goats and Cattle. *J Vaccines Vaccin.* 2015;6:295.
61. Allwin B, et al. Prevalence of Gastrointestinal Parasites in Gaur (*Bos gaurus*) and Domestic Cattle at Interface Zones of the Nilgiri Hills, Tamil Nadu, India. *J Veterinar Sci Technol.* 2015;7:280.
62. Jibril AH, et al. Survival of *Mycobacterium bovis* Following Heat Treatment of Infected Tissues obtained from Slaughtered Cattle in Sokoto Metropolitan Abattoir, Nigeria. *J Bacteriol Parasitol.* 2015;6:254.
63. Cheng Y, et al. Relationship of Bovine SLC11A1 (Formerly NRAMP1) Polymorphisms to the Risk of Bovine Tuberculosis in Holstein Cattle. *J Veterinar Sci Technol.* 2015;6:247.
64. Covarrubias AC, et al. Outbreak of *Dermatophilus congolensis* in Grazing Beef Cattle in Northeastern Mexico: First Report. *J Veterinar Sci Technol.* 2015;6:222.
65. Mengistu A, et al. Tuberculosis Infection in Cattle and Cattle Owners in North Eastern Parts of Ethiopia. *Biol Med (Aligarh).* 2015;7:241.
66. Bushara MOA and Abdelmahmod MKA. Efficiency of Selected Sudanese Cattle Markets: Multivariate Cointegration Approach (1995-2011). *Int J Econ Manag Sci.* 2015;4:264.
67. Sharma S, et al. Seroprevalence and Carrier Status for Leptospirosis in Cattle and Goats in Andaman Island, India. *J Veterinar Sci Technol.* 2014;5:205.
68. Akdouche L, et al. Importance of Yeasts in the Mammary Infection of the Cattle in the Region of Sidi M'Hamed Ben Ali, Wilaya of Relizane, Algeria. *J Veterinar Sci Technol.* 2014;5:172.
69. Shibata M, et al. Influence of Housing Density and Grazing on Heat Shock Protein 27 Expression in Skeletal Muscle of Beef Cattle. *J Fisheries Livest Prod.* 2014;2:117.
70. Beyene T, et al. Identification and Antimicrobial Susceptibility Profile of Salmonella Isolated from Selected Dairy Farms, Abattoir and Humans at Asella Town, Ethiopia. *J Veterinar Sci Technol.* 2016;7:320.
71. Rezaei M, et al. Determination of Polychlorinated Dibenzo Dioxin Levels in Fresh Milk from the Dairy Factories of Southwest Iran. *J Environ Anal Toxicol.* 2015;5:301.
72. Akbar Nikkhah. Botched Starch Serving: Avoidable Problems in Modern Dairying. *J Veterinar Sci Technol.* 2015;6:e119.
73. Ehsanul Haque Md. Rapid Detection of Subclinical Mastitis in Dairy Cow. *J Fisheries Livest Prod.* 2015;3:128.
74. Chollet M, et al. Beliefs and Concerns about Dairy Products in the Swiss Older Adult Population. *J Nutr Food Sci.* 2015;5:365.
75. Al-Shammari SB, et al. Treatment of Dairy Processing Wastewater using Integrated Submerged Membrane Microfiltration System. *J Anal Toxicol.* 2015.

76. Nikkhah A. Timely Provision of Different Feeds in Dairy Enterprises: A Circadian Science. *J Adv Dairy Res.* 2015;3:e116.
77. Givens DI and Hobbs DA. Milk and Dairy Products: Dietary Partners for Life? *Primary Health Care.* 2014;4:161.
78. Sivakumar MS And Asha B. A Study On Effect Of Volatile Fatty Acid On Anaerobic Bio Film Reactor Using Dairy Wastewater. *Journal of Industrial Pollution Control* 2012.
79. Rezaei M, et al. Determination of Polychlorinated Dibenzo Dioxin Levels in Fresh Milk from the Dairy Factories of Southwest Iran. *J Environ Anal Toxicol.* 2015;5:301.
80. Sugun MY, et al. Isolation of Uncommon *Pasteurella multocida* Strains from Cattle in North Central Nigeria. *J Vaccines Vaccin.* 2106;7:320.
81. Ali OS, et al. Haematological and Histopathological Vicissitudes Following Oral Inoculation of Graded Doses of *Pasteurella multocida* Type B: 2 and its Lipopolysaccharide in Mice. *J Veterinar Sci Technol.* 2015;6:220.
82. Sidhu PK, et al. Optimization of Dosage Regimen of Gentamicin against *Pasteurella multocida* in Bovines: Old Drug, New Approach. *J Veterinar Sci Technol.* 2104;5:199.
83. Annas S, et al. Distribution of *Pasteurella multocida* B:2 in the Respiratory, Gastrointestinal and Urinary Tracts of Buffaloes Following Experimental Subcutaneous Inoculation. *J Veterinar Sci Technol.* 2104;5:177.
84. Zhang YF, et al. Construction and Characterization of an Acapsular Mutant of *Pasteurella multocida* Strain P-1059 (A:3). *J Vaccines Vaccin.* 2013;4:184.
85. Ramadan A and Abd El-Aty AM. Pharmacokinetics and Distribution of Florfenicol in Bronchial Secretions of Healthy and *Pasteurella multocida* Infected Calves. *Pharm Anal Acta.* 2011;2:117.
86. Memoto S, et al. Mucosal Immune Responses Associated with NKT Cell Activation and Dendritic Cell Expansion by Nasal administration of α -galactosylceramide in the Nasopharynx. *Otolaryngology.* 2015;5:216.
87. Warg JV, et al. Detection and surveillance of viral hemorrhagic septicemia virus using real-time RT-PCR. II. Diagnostic evaluation of two protocols. *Diseases of aquatic organisms.* 2014;111:15-22.
88. Holm KO, et al. Complete genome sequence of *Vibrio anguillarum* strain NB10, a virulent isolate from the Gulf of Bothnia. *Standards in genomic sciences.* 2015;10:1.
89. Stepien CA, et al. Gene diversification of an emerging pathogen: A decade of mutation in a novel fish Viral Hemorrhagic Septicemia (VHS) substrain since its first appearance in the Laurentian Great Lakes. *PLoS one.* 2015;1:e0135146.
90. Alzaid A, et al. Cross Talk Between Growth and Immunity: Coupling of the IGF Axis to Conserved Cytokine Pathways in Rainbow Trout. *Endocrinology.* 2016;157:1942-1955.
91. Wilson AD and Baietto M. Advances in electronic-nose technologies developed for biomedical applications. *Sensors.* 2011;11:1105-1176.
92. Brooks-Pollock E and Wood JL. In: The Royal Society. Eliminating bovine tuberculosis in cattle and badgers: insight from a dynamic model. In *Proc R Soc B.* 2015; 282:20150374.
93. Braun U, et al. T-cell lymphoma in the nasal cavity of a Brown Swiss heifer. *Acta Veterinaria Scandinavica.* 2015;57:1.

94. Ghazali MF, et al. Alkaline phosphatase in nasal secretion of cattle: biochemical and molecular characterisation. *BMC veterinary research*. 2014;10:1.
95. Pan L, et al. Induction of mucosal immune responses and protection of cattle against direct-contact challenge by intranasal delivery with foot-and-mouth disease virus antigen mediated by nanoparticles. *International journal of nanomedicine*. 2014;9:5603.
96. Stenfeldt C, et al. The foot-and-mouth disease carrier state divergence in cattle. *Journal of virology J*. 2016;6:00388.
97. Gopal N, et al. The Prevalence and Control of Bacillus and Related Spore-Forming Bacteria in the Dairy Industry. *Frontiers in microbiology*. 2015;6.
98. Mitchell HM (2001) *Epidemiology of infection*.
99. Su F, et al. Protective Effect of Ginsenosides Rg1 and Re on Lipopolysaccharide-Induced Sepsis by Competitive Binding to Toll-Like Receptor 4. *Antimicrobial agents and chemotherapy*. 2015;59:5654-5663.
100. Jans C, et al. Phylogenetic, epidemiological and functional analyses of the Streptococcus bovis/Streptococcus equinus complex through an overarching MLST scheme. *BMC microbiology*. 2016;16:1.