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Research Article

Effectiveness of *Triticum Vulgare* and Nitrofurazone Combination in Secondary Infections Associated with Myiasis Wounds in Dogs

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ABSTRACT

Myiasis wounds have become increasingly common in recent years, posing challenges due to variable prognoses and Myiasis wounds have become increasingly common in recent years, posing challenges due to variable prognoses and complex treatments. This study evaluated the efficacy of the *Triticum vulgare* and Nitrofurazone combination for secondary infections caused by myiasis in dogs. Forty-two medium and large-breed dogs with myiasis wounds, aged 2 months to 5 years and weighing 5 to 56 kg, were included. Following the manual removal of larvae, a pomade comprised of 50 mg/g *Triticum vulgare* extract and 0.2 g Nitrofurazone was administered three times daily. Wound assessments were performed weekly for four weeks, including surface area measurements and contraction reeks. The most common wounds due to myiasis occur in Mongrels (47.6%) and Kangals (33.3%). Myiasis primarily affects the extremities (48%) and the genital area (28%), mainly occurring (66%) during the summer. The mean wound area significantly reduced, from 10.0 ± 2.5 cm^2 to 1.5 ± 0.8 cm^2 by week four, with an 85% wound contraction and healing rate. This study concludes that a combination of *Triticum vulgare* and Nitrofurazone is highly effective in managing secondary infections resulting from myiasis wounds in dogs.

Keywords: Myiasis, Nitrofurazone, *Triticum vulgare*, Wound

INTRODUCTION

Myiasis is caused by the larvae or eggs laid by flies on open wounds, skin ulcers, or other parts of the body in animals (1, 2). These infections can lead to severe wounds and general health disorders, causing significant health and economic problems (3). The World Health Organization lists myiasis as one of the major animal diseases in the Global Early Warning System (4). Although its prevalence is reported to be 37.4%, the infection rate can reach 100% in regions with high fly density or poor hygiene conditions (5). Cases of myiasis are primarily observed in cattle (46.4%), followed by dogs (15.3%), pigs (6%), horses (4%), and sheep (1%) (6). In these infections, the mechanical removal of the larvae and effective treatment usually provide favorable results (3). However, myiasis infections may result in death if an appropriate treatment protocol is not applied (3, 7, 8).

In veterinary medicine, there is a lack of sufficient data on the efficacy of wound treatment preparations for managing myiasis wound infections. In the relevant literature, the effectiveness of antiseptics such as creolin and sprays containing larvicidal pietrin, ivermectin derivative compounds, and insect growth regulators (IGR) has been reported in the treatment of myiasis wound infections (8). However, reports indicate that creolin is highly toxic to living tissues. Additionally, topical larvicidal products and other chemicals, while effective in killing larvae in treated wounds, delay the healing process (3, 9). These applications, the effectiveness of which has been reported in the literature, are currently of limited use. More research is needed to ensure that veterinarians are knowledgeable about the treatment of myiasis and to better understand the effectiveness of current applications used in the wound treatment of these lesions (7, 9).

Nitrofurazone is inexpensive, has a low risk of reaction compared to other drugs, and is frequently used to treat open wounds (10, 11). It has been reported that nitrofurazone does not cause maceration in tissues when applied locally and does not cause pain during application (12). *Triticum vulgare* is a cicatrizant agent that can be safely used with antibacterial drugs in wound treatments (13). When applied locally to the wound area, it induces the proliferation of fibroblasts and endothelial cells, accelerates repair, and promotes rapid healing and wound closure (14, 15, 16, 17). Several studies have examined the effects of these agents on wound healing. These studies have focused on healing wounds observed in human patients and those experimentally induced in rats or rabbits (13, 14, 18, 19, 20). Furthermore, biomedical studies have reported that these agents may be safely combined with different substances or used in various formulations (13, 18, 19, 21). However, there is limited literature in veterinary medicine regarding the efficacy

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of these agents in healing various wounds in other species.

Increasing temperatures due to global warming accelerate the life cycles of flies and boost their populations, which bears the potential for an increase in myiasis cases from year to year (22). Considering the effects of *Triticum vulgare* and Nitrofurazone reported in the literature, it is believed that these two agents may have significant effects on wound healing when combined. In this regard, the aim was to evaluate the efficacy of the combination of *Triticum vulgare*, a cicatricial agent used in open wound treatment, and the topical antibacterial Nitrofurazone in clinical practice for myiasis wound infections encountered in dogs, considering the deficiencies in the existing literature.

MATERIAL AND METHODS

Study group

The study included 42 dogs of varying breeds, ages, and genders admitted to the Surgery Clinic of Harran University Faculty of Veterinary Medicine Animal Hospital during the spring and summer months of 2023–2024, presenting with maggot-infested wounds of differing diameters across various body regions. Data on breed, age, sex, body weight, and the anatomical location of myiasis were systematically recorded. To standardize the cohort, only dogs aged 2–5 years were enrolled in the final analysis.

The study protocol was approved by the Local Ethics Committee on Animal Experiments, Harran University (Decision number: 2024 /008 /02).

Treatment procedure

Clinical and laboratory examinations were conducted on dogs that presented for treatment. Cardiopulmonary values and body temperature were measured during the clinical examination using a Mindray UMEC12VET bedside monitor (Shenzhen Mindray Bio-Medical Electronics Co, Shenzhen, China). Blood samples (2.5 ml) were obtained from the vena cephalica antebrachii for laboratory examination (23). The results of hematologic (WBC, RBC) (CFE 279, Hematology Analyzer, France) and biochemical (AST, ALT, CREA, BUN) (Arkray Inc., Kyoto, Japan) analyses were evaluated. Dogs whose clinical examination results were within the reference range and did not require additional drug treatment were included in the study. As part of the treatment protocol, wounds with myiasis were first cleaned with physiological saline (NaCl 0.9%, Polifarma, Turkey) without using any anesthetic. All visible larvae in the wound area were manually removed with the help of sterile forceps. Surgical debridement was performed in cases where necrotic tissue had developed in the wound area (3). After the larvae were removed, treatment continued with cleaning the area using a 10% povidone-iodine solution (Batiqonix Biyosidal, Turkey) diluted at 1:10 with physiological saline (NaCl 0.9%) (24). For the wound care, pet owners were provided with Fito cream® (50 mg/g, Tripharma, Istanbul), which contains *Triticum vulgare* extract, and Furacin® ointment (Sanofi, Istanbul), which comprises 2% Nitrofurazone. These two products were mixed in equal proportions to ensure complete coverage of the wound site with adequate quantities sufficient for a duration of four weeks use. Patients were informed of the need to apply this mixture three times daily to support complete wound closure (10). While bandaging was applied to the wounds after the initial application, the pet owners did not continue it. Furthermore, a single dose (0.4 mg/kg) of subcutaneous Moxidectin 1% (Cydectin®, Pfizer, New York, USA) was administered to the dogs on the first day as an antiparasitic (25). An Elizabethan collar was applied during the treatment to prevent the patient from licking the wound area. No systemic antibiotics were given to the dogs in this study, and all wounds were examined weekly. The borders of the wound area were carefully drawn on clean, transparent paper with a 0.3 mm-tipped drawing pen on day 0 and during weeks 1, 2, 3, and 4. These drawings were transferred to acetate paper marked with millimetric lines to measure the wound area in millimeters. CorelDRAW X5 and Golden Software Didger 3 were used to calculate the wound areas. The drawings on the acetate paper were transferred to the computer environment at a 1:1 scale using a scanner and saved as JPG format. Each wound area was drawn as a closed curve in the CorelDRAW X5 program and saved in the DXF file format. These files were opened using Didger 3 software for geological digitization, and the area of each closed curve was calculated in cm^2 (12, 26). The same investigator conducted all the procedures to ensure uniformity. The wound area and contraction rate were calculated from these measurements. (26, 27).

Statistical analysis

The initial wound dimensions and the time to complete wound closure were calculated as mean ± standard deviation (mean ± SD) in cm^2. The wound area (WA) and wound reduction (WC) following topical application were expressed as percentages (%). The wound surface areas (cm^2) of wounds treated with Nitrofurazone and *Triticum vulgare* were analyzed using the Kruskal-Wallis test and compared by week. The effect of topical application on the wound area (WA) percentage and wound shrinkage (WC) percentage was analyzed with the Kruskal-Wallis and the Mann-Whitney U test for intergroup comparisons. All statistical analyses were performed using SPSS 22.1 (IBM Corporation, Armonk, NY, USA), and the significance level was established at $p < 0.05$.

RESULTS

The average age of the dogs included in the study was 19 ± 11 months, and their body weights ranged from 5 to 56 kg. The clinical and laboratory examination results for the dogs are presented in Tables 1 and 2. Forty-two dogs (36 males and six females) were identified at ages of 24 ± 14 months (for males) and 11 ± 7 months (for females) respectively. Upon examining the breed distribution records of the dogs in the study, it was observed that the majority of the cases were mixed-breed dogs (20), followed by Kangal (14), German Shepherd Dog (2), Belgian Malinois (2), Pomeranian (2), and Rottweiler (2). Regarding the localization and frequency of myiasis cases, 20 (48%) cases occurred in the extremities, 8 (19%) in the head and neck region, 2 (5%) in the abdomen, and 12 (28%) in the genital region (Figure 1). In terms of seasonal distribution, myiasis cases were recorded in all seasons; however, the highest number of cases occurred in the summer (66%) (Figure 2).

Treatment findings

Wound areas of all animals were debrided, and *Triticum vulgare* and Nitrofurazone were applied equally. A single subcutaneous dose of Moxidectin (0.4 mg/kg) was administered to dogs (25). During the treatment period, the pet owners came regularly for clinical controls every week, and four weeks of the control process were completed (Figure 3). It was confirmed that the treatment applications were conducted by each patient owner who brought the control. The animal owners were informed that no maggots had been observed in the wound area after the first intervention. During the control period, no general condition disorders were detected in any of the animals, and no larvae were found in the wound areas. No exudate or signs of inflammation were detected in the lesions of the dogs brought in for control one week after the start of treatment (Figure 4). After the first week, prominent granulation tissue was observed in dogs with wound sizes of approximately 5 cm^2 or less, while re-epithelialization (proliferative phase) became evident in the second week (Figure 5). Granulation tissue began to form during the first week in

Table 1. Some haematological and biochemical parameters of the dogs included in the study (mean ± SD).

Parameter	WBC (x103/µL)	RBC (x106/µL)	AST (U/L)	ALT (U/L)	CREA (mg/dL)	BUN (mg/dL)
Value	13.6±7.5	6.74±1.8	14.1±2.2	59.5±41.2	0.90±0.26	17.6±2.1

WBC: White blood cell, RBC: Red blood cell, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CREA: Creatinine, BUN: Blood urea nitrogen

Table 2. Some clinical examination results for the dogs included in the study (mean ± SD).

Parameter	WBC (x103/µL)	RBC (x106/µL)	AST (U/L)	ALT (U/L)	CREA (mg/dL)	BUN (mg/dL)
Value	13.6±7.5	6.74±1.8	14.1±2.2	59.5±41.2	0.90±0.26	17.6±2.1

HR: Heart rate, T: Temperature, RR: Respiratory rate, SpO2: Oxygen saturation

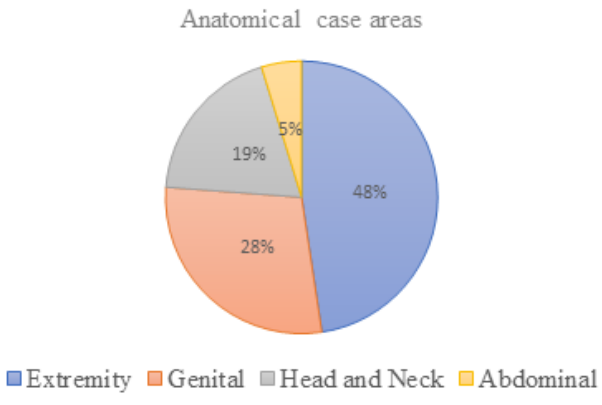

Figure 1: Anatomical distribution of myiasis wounds in dogs by region

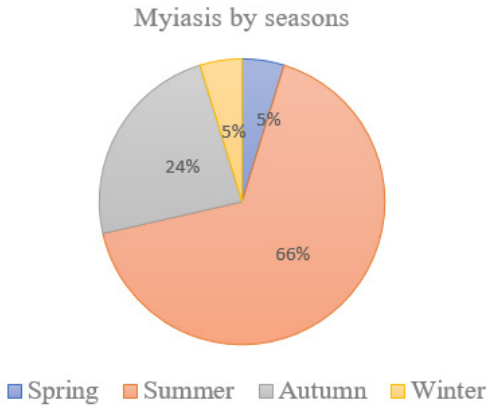

Figure 2: Seasonal distribution of myiasis wounds in dogs

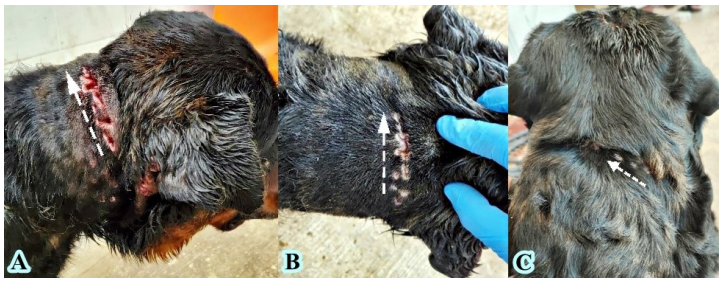

Figure 3: A. Wound myiasis area in the neck of a Rottweiler dog at the 1st week control, B. 2nd week wound area of the same dog, C. 4th week wound area of the same dog (white arrow) (Case 2).

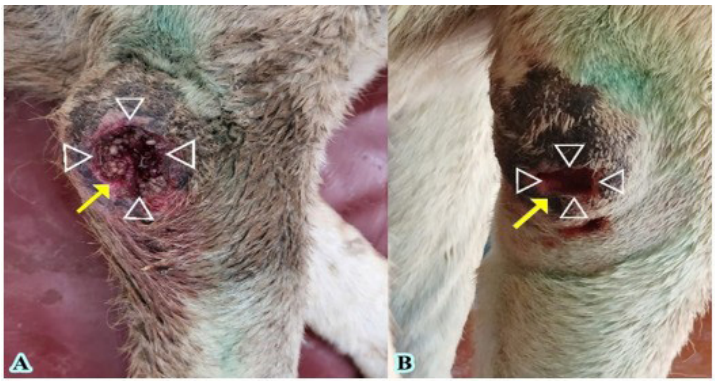

Figure 4: A. Myiasis of a wound in the extremity of a mongrel dog. B. Wound area (white arrowhead) during the first week follow-up of the same case (Case 15).

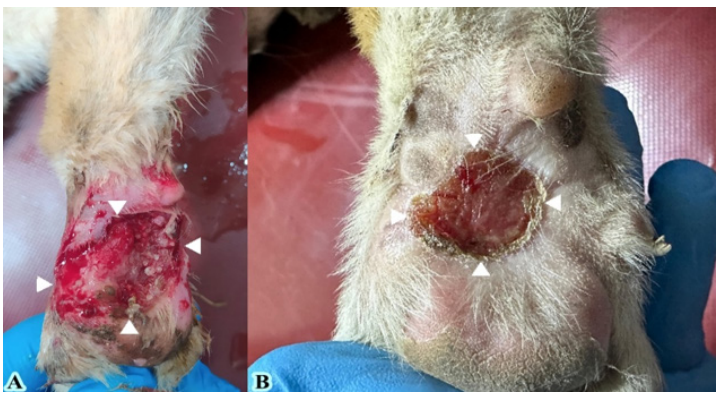

Figure 5: A. Wound myiasis in the extremity of a mongrel dog. B. Wound area (white arrowhead) at the 2nd week follow-up of the same case. (Case 40).

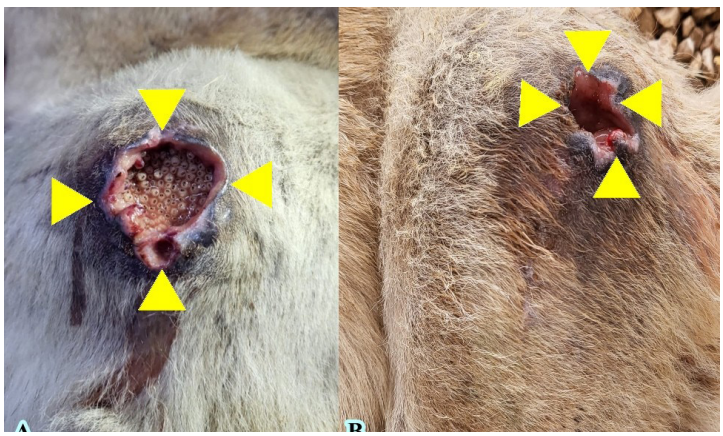

Figure 6: A. Wound myiasis in the extremity of a Kangal dog, B. Wound area of the same case during the 1st week (yellow arrow-head) (Case 41).

dogs with larger wounds (Figure 6). All treated wounds healed without re-infestation of larvae since the start of treatment, and no complications, such as fistula or purulent discharge, were observed. No overall reduction in the wound surface area was noted until complete re-epithelialization occurred. The fastest healing was observed in the first week, while the slowest was noted in the fourth week, depending on the wound surface area. The mean wound surface size was 10.0 ± 2.5 cm². The wound surface areas at the first (1), second (2), third (3), and fourth (4) weeks following topical application were 7.5 ± 2.0 cm², 5.0 ± 1.8 cm², 3.0 ± 1.5 cm², and 1.5 ± 0.8 cm² respectively. While the wound area was determined to be 100% in the first instance, it was statistically significant that this area decreased to 15% in the fourth week, demonstrating a shrinkage rate of 85%. The wound measurements and contraction rates are presented in Tables 3 and 4 respectively.

Table 3. Effect of topical application on changes in wound size (mean ± SD).

Week	0	1	2	3	4	P
Wound surface area (cm2)	10.0 ± 2.5	7.5 ± 2.0	5.0 ± 1.8	3.0 ± 1.5	1.5 ± 0.8	0.012

0: initial, 1: first week, 2: second week, 3: third week, 4: fourth week

Table 4. The effect of topical application on wound area (WA) and wound contraction rate (WC).

Week	0	1	2	3	4	P
WA (%)	100	75	50	30	15	0.045
WC (%)	0	25	50	70	85	0.02
p	0.001	0.041	0.063	0.011	0.034	

0: initial, 1: first week, 2: second week, 3: third week, 4: fourth week.

DISCUSSION

Myiasis wounds are frequently encountered in dogs and heal with the completion of biological processes such as inflammation, cell migration, collagen accumulation, angiogenesis, and re-epithelialization, as with other wound types (3, 27). Although the efficacy of various herbal and chemical drugs contributing to the acceleration of these biological processes in different types of wounds has been reported, information regarding the treatment of myiasis wounds is insufficient (15, 28, 29). Within the scope of this study, when examined at the clinical level using a combination of Triticum vulgare and Nitrofurazone after the removal of larvae in the treatment of myiasis wounds in dogs, near-complete wound closure was achieved in 42 cases, including deep and extensive wounds, within 4 weeks, and successful results were obtained.

In the relevant literature, myiasis cases were mostly observed in the summer months (22, 30). In the present study, most cases were noted in the summer months due to the increase in the fly population with rising temperatures in Şanlıurfa Province. This indicates that myiasis cases may be more common in provinces with hot climates and that fly control should be managed more meticulously in these regions.

Studies on myiasis wounds in animals found that these wounds resulted from traumatic injuries, particularly in large-breed male dogs (22, 30). Specifically, Johnson et al. reported that 24 of 29 dogs (82.8%) in their study were large-breed male mongrel dogs, followed by breeds such as Boerboel and Rottweiler (31). In the present study, myiasis wounds were primarily encountered in male mongrel dogs, followed by Kangal dogs. The hormonal nature of male dogs may lead them to exhibit more aggressive and active behaviors than female dogs, which can result in injuries. It could also be argued that keeping small-breed dogs in a home environment, unlike large-breed dogs, may reduce the risk of such injuries. In addition, the high incidence of myiasis wounds in Kangal dogs is attributed to the adaptation of these dogs to our region. Another study on myiasis wounds in dogs reported the anatomical area of the body where more wounds were observed. In a study conducted by Orfanou et al., it was reported that myiasis wounds were observed in the abdominal region at a rate of 44.8% and in the extremities at a rate of 6.9% (25), while another study reported that they were observed in the extremities at a rate of 44.4% (31). The findings obtained in this study showed that the most common lesion in dogs was observed in the extremities, with a rate of 49%. This difference can be attributed to variations in the environmental factors to which dogs are exposed and their interactions with others dogs. Ectoparasitic applications are recommended as supportive treatments for myiasis wounds (9).

In a study examining the efficacy of ectoparasitic applications alongside the treatment of myiasis wounds in dogs, lotilaner, which belongs to the chemical class of isoxazoline, demonstrated effectiveness rates of 80.5%, 93%, and 100% for larval expulsion in myiasis cases at 2, 6, and 24 hours after oral administration, respectively (32). In another study, sarolaner was administered orally, and all larvae died (33). In addition to ectoparasitic applications, systemic antibiotic and anti-inflammatory treatments were applied in these two studies, yielding effective results obtained. The difference of the present study is that, in addition to tropical Triticum vulgare and Nitrofurazone, subcutaneous moxidectin (0.4 mg/kg) was also used as an ectoparasitic application, and favorable results were obtained in all cases. According to the information obtained from the patient owners and weekly controls, no larvae were found in the wounds cleaned of larvae after topical application. In this respect, ectoparasitic applications should be performed for the treatment of wounds with myiasis.

Studies on *Triticum Vulgare* (wheat extract) and Nitrofurazone are currently available, having been primarily investigated in various wounds affecting humans, as well as in experimental models using rats or rabbits (13, 14, 18, 19, 20, 34). The present study examined the effects of Triticum Vulgare (wheat extract) and Nitrofurazone on wounds caused by myiasis in dogs. It revealed important results at the clinical level, noting that these agents positively affect the acceleration of wound healing. These findings align with the results of several studies that support wound healing

by these two agents. In studies conducted by Souza et al. and Silva et al., *Triticum Vulgare* accelerated wound healing and promoted the re-epithelialization process (35, 36). These studies suggest that *Triticum Vulgare* promotes rapid healing of the wound area and may play a significant role in restoring tissue integrity. Moreover, Bedir et al. reported positive results in wound healing after 21 days when applied in cream form to experimental wound models in diabetic rats (16). In another study, almost complete healing was observed in 50 human patients with diabetic foot ulcers after 29 days (19). Considering these studies, it can be concluded that *Triticum Vulgare* has favorable effects on chronic wounds. In studies conducted with Nitrofurazone, favorable results have been reported, particularly regarding the prevention of bacterial contamination and the elimination of larvae. Lima et al. reported that Nitrofurazone eliminated larvae within three days, and wound healing was completed within four weeks in two patients with oral myiasis. In their studies on experimental wound models in rabbits, Pişkin et al. and Shahzad et al. reported that the combination of Momordica Charantia (bitter gourd) and Nitrofurazone, a herbal product, along with the local application of Jacobaea Maritima (ash flower) and Nitrofurazone, accelerated wound healing (20, 37, 38). Shahzad et al. reported that complete healing with nearly 100% closure was achieved in 24 days (38). These results are consistent with the rapid healing process observed in the present study. Other studies on the accelerating effect of herbal products on the healing process of wounds with myiasis are also noteworthy. In a pioneering study using neem oil and St John's wort oil on 44 domestic animals, including dogs, wounds with myiasis healed within 10 to 32 days (3). Similarly, in the present study, it was observed that the combination of herbal *Triticum Vulgare* and Nitrofurazone had positive effects on wounds with myiasis, which presented a potential worsening prognosis, and the wound healing process was completed within a range of 7-28 days. The clinical significance of our study is that a treatment protocol involving a plant-based agent and an antibacterial agent may provide an alternative to conventional approaches for treating wounds with myiasis. Clinicians may find *Triticum Vulgare* and Nitrofurazone attractive options due to their low side effect profiles and their ability to accelerate wound healing.

CONCLUSION

In conclusion, this study demonstrates the effects of *Triticum Vulgare* and Nitrofurazone combined with ectoparasitic applications on the healing rate of myiasis wounds in dogs. Moreover, myiasis wounds, which are more frequently observed in male dogs and certain breeds, are influenced by environmental and hormonal factors, and this should be taken into consideration regarding both veterinary practice and animal adoption. Thus, clinicians believe that this combination can be used successfully.

DECLARATIONS

Availability of Data and Materials: The data that support the findings of this study are available on request from the corresponding author.

Funding Support: There is no any funding support.

Ethical Statement: This study was completed in accordance with the procedures and principles of Harran University Animal Experiments Local Ethics Committee (Session Number: 2024/008/02).

Competing Interests: The authors declare that there is no competing of interest regarding the publication of this article.

Declaration of Generative Artificial Intelligence: The authors of the current study declare that the article and/or tables and figures were not written/created by AI and AI-assisted technologies.

Authors' Contributions: All authors contributed to this present work: KY, ÜY, and AH designed the study. KY, KDI, MSK and MSH performed the experiments, KY, KDI, MSK and MSH collected data, KY, ÜY and AH analyzed the data. KY, KDI, MSK and MSH drafted the manuscript. All authors revised the manuscript. All authors read and approved the final manuscript.

REFERENCES

1. Bambaradeniya YTB, Magni PA, Dadour IR: Traumatic sheep myiasis: A review of the current understanding. Vet Parasitol, 314: 1-12, 2023. DOI: 10.1016/j.vetpar.2022.109853
2. Pezzi M, Scapoli C, Chicca M, Leis M, Marchetti MG, Del Zingaro CNF, Vicentini CB, Mamolini E, Giangaspero A, Bonacci T: Cutaneous myiasis in cats and dogs: Cases, predisposing conditions and risk factors. Vet Med Sci, 7 (2): 378-384, 2021. DOI: 10.1002/vms3.370
3. Carnevali F, Franchini D, Otranto D, Giangaspero A, Di Bello A, Ciccarelli S, Szpila K, Valastro C, Van der Esch AS: A formulation of neem and hypericum oily extract for the treatment of the wound myiasis by Wohlfahrtia magnifica in domestic animals. Parasitol Res, 118: 2361-2367, 2019. DOI: 10.1007/s00436-019-06375-x
4. WHO, 2007. http: //www.who.int/zoonoses/outbreaks/glews/en/index.html. Accessed on 24/11/2020.
5. Papadopoulos E, Himonas C, Boulard C: The prevalence of bovine hypodermosis in Greece. Parasitologia, 39 (4): 431-433, 1997.
6. Sergio EB, José DE, Angel BC, Franklin C, Janina S, Sabina B, Enrique M: Incidence of myiasis in Panama during the eradication of Cochliomyia hominivorax (Coquerel 1858, Diptera: Calliphoridae) (2002-2005). Memórias do Instituto Oswaldo Cruz, 102 (6): 675-679, 2007. DOI: 10.1590/s0074-02762007005000074
7. Oliveira PC, Moraes PA, Scott FB, Verocai GG, Correia TR, Fernandes JI: Efficacy of spinosad on the treatment of myiasis caused by Cochliomyia hominivorax (Diptera: Calliphoridae) in dogs. Vet parasitol, 258: 53-56, 2018. DOI: 10.1016/j.vetpar.2018.06.006
8. Giangaspero A, Traversa D, Trentini R, Scala A, Otranto D: Traumatic myiasis by Wohlfahrtia magnifica in Italy. Vet Parasitol, 175: 109-112, 2011. DOI: 10.1016/j.vetpar.2010.09.028
9. Correia TR, Scott FB, Verocai GG, Souza CP, Fernandes JI, Melo RMPS, Vieira VPC, Ribeiro FA: Larvicidal efficacy of nitenpyram on the treatment of myiasis caused by Cochliomyia hominivorax (Diptera: Calliphoridae) in dogs. Vet Parasitol, 173: 169-172, 2010. DOI: 10.1016/j.vetpar.2010.06.019
10. Erdur B, Ersoy G, Yilmaz O, Ozkutuk A, Sis B, Karcioglu O, Parlak İ, Ayrık C, Aksay E, Guryay M: A comparison of the prophylactic uses of topical mupirocin and Nitrofurazone in murine crush contaminated wounds. Am J Emerg Med, 26 (2): 137-143, 2008. DOI: 10.1016/j.ajem.2007.03.030
11. Liu X, Shen B, Shen C, Zhong R, Wang X, Yuan H: Nanoparticle-loaded gels for topical delivery of Nitrofurazone: effect of particle size on skin permeation and retention. J Drug Deliv Sci and Technol, 45: 367-372, 2018. DOI: 10.1016/j.jddst.2018.04.005
12. Kurt Özkaya N, Gümüş N, Yılmaz S, Mesci BL, Çınar Z: Topikal Olarak Uygulanan Nitrofurazon ve Rifampisinin Kısmi Kalınlıkta Yara İyileşmesi Üzerine Etkileri. Turk Plast Surg, 23 (3): 113-117, 2015.
13. Tito A, Minale M, Riccio S, Grieco F, Colucci MG, Apone F: A Triticum vulgare extract exhibits regenerating activity during the wound healing process. Clin Cosmet and Investig Dermatol, 13: 21-30, 2020. DOI: 10.2147/CCID.S216391
14. Gölgeli Bedir A, Yanmaz LE: The effects of cream-based Triticum vulgare with and without therapeutic ultrasound on excisional wound healing in diabetic rats. Cutan Ocul Toxicol, 42(2): 61-67, 2023. DOI: 10.1080/15569527.2023.2201833.
15. Sanguigno L, Minale M, Vannini E, Arato G, Riccio R, Casapullo A, Monti MC, Riccio R, Formisano S, Di Renzo G, Cuomo O: Oligosaccharidic fractions derived from Triticum vulgare extract accelerate tissutal repairing processes in in vitro and in vivo models of skin lesions. J Ethnopharmacol, 159: 198-208, 2015. DOI: 10.1016/j.jep.2014.10.051
16. Sanguigno L, Casamassa A, Funel N, Minale M, Riccio R, Riccio S, Bosna F, Brancaccio P, Pollina LE, Anzilotti S, Di Renzo G, Cuomo O: Triticum vulgare extract exerts an anti-inflammatory action in two in vitro models of inflammation in microglial cells. PLoS One, 13(6): 1-14, 2018. DOI: 10.1371/journal.pone.0197493
17. D'Agostino A, Pirozzi AVA, Finamore R, Grieco F, Minale M, Schiraldi C: Molecular mechanisms at the basis of pharmaceutical grade Triticum vulgare extract efficacy in prompting keratinocytes healing. Molecules, 25 (3): 1-14 2020. DOI: 10.3390/molecules25030431
18. Romano E, Campagnuolo C, Palladino R, Schiavo G, Maglione B, Luceri C, Mennini N: Technical Evaluation of a New Medical Device Based on Rigenase in the Treatment of Chronic Skin Lesions. Bioengineering, 10: 10-22, 2023. DOI: 10.3390/bioengineering10091022
19. Romanelli M, Macchia M, Panduri S, Paggi B, Saponati G, Dini V: Clinical evaluation of the efficacy and safety of a medical device in various forms containing Triticum vulgare for the treatment of venous leg ulcers - a randomized pilot study. Drug Des Devel Ther, 27 (9): 2787-2792, 2015. DOI: 10.2147/DDDT.S82712
20. Pişkin A, Altunkaynak BZ, Tümentemur G, Kaplan S, Yazıcı ÖB, Hökelek

M: The beneficial effects of Momordica charantia (bitter gourd) on wound healing of rabbit skin. J Dermatolog Treat, 25(4): 350-357, 2015. DOI: 10.3109/09546634.2012.713459
21. Gupta A, Upadhyay NK, Parthasarathy S, Rajagopal C, Roy PK: Nitrofurazone-loaded PVA–PEG semi-IPN for application as hydrogel dressing for normal and burn wounds. J Appl Polym Sci, 128: 4031-4039, 2013. DOI: 10.1002/app.38594
22. Dik B, Uslu U, Işık N: Myiasis in animals and humanbeings in Turkey. Kafkas Uni Vet Fak Derg, 18 (1): 37-42, 2012. DOI:10.9775/kvfd.2011.4654
23. Hayat A, Bulut S: Köpeklerde Halotan ve sevofluranın bazı hematolojik ve biyokimyasal değerler ile anestezinden uyanma üzerine etkilerinin karşılaştırılması. Vet Bil Derg, 19 (3-4): 49-54, 2003
24. Moshaverinia A, Mehrjerdi HK: Canine myiasis and its causal agents in Northeastern Iran. Iran J Parasitol, 11 (1): 91-97, 2016.
25. Orfanou DC, Papadopoulos E, Cripps PJ, Athanasiou LV, Fthenakis GC: Myiasis in a dog shelter in Greece: Epidemiological and clinical features and therapeutic considerations. Vet Parasitol, 181 (2-4): 374-378, 2011. DOI: 10.1016/j.vetpar.2011.04.006
26. Yavuz Ü, Temamoğulları F, Yığın A, Yumuşak N: Diyabetik Tavşanlarda Tam Kat Deri Yaralarında Topikal Centarium Erythraea'nın Etkilerinin Araştırılması. Dicle Üniv Vet Fak Derg, 13 (2): 92-98, 2020. DOI: 10.47027/duvetfd.735544
27. Han MC, Durmuş AS, Sağlıyan A, Günay C, Özkaraca M, Kandemir FM, Çomaklı S, Öztopalan DC: Effects of Nigella sativa and Hypericum perforatum on Wound Healing. Turk J Vet Anim Sci, 41: 99-105, 2017. DOI: 10.3906/vet-1603-26
28. Chaturvedi A, Meswani R, Shah S, Deasi S, Lele J, Mehta P: An Indian clinical trial to assess wound healing activity and safety of Fitostimoline 15%+ 1% cream as topical treatment of different type of wounds. Journal of Plastic Dermatology, 6 (3): 1-8, 2010.
29. Serafini G, Saponati G: Attività e tollerabilità degli estratti di Triticum Vulgare nelle affezioni flogistico-distrofiche. Dental Clinics, 3 (1): 35-39, 2012. DOI:10.12691/js-3-1-3
30. Farkas R, Hall MJR: Prevalence of traumatic myiasis in Hungary: a questionnaire survey of veterinarians. Vet Record, 143 (16): 440-443, 1998.
31. Johnson SAM, Gakuya DW, Mbuthia PG, Mande JD, Afakye K, Maingi N: Myiasis in dogs in the Greater Accra Region of Ghana. Vector-Borne Zoonotic Dis, 16 (1): 54-57, 2016. DOI: 10.1089/vbz.2015.1811
32. Do Vale TL, Costa AR, Miranda LM, Silva GF, Silva NCS, Lima TB, Chaves DP, Sager H, Lasmar PVF, Costa–Junior LM: Efficacy of lotilaner against myiasis caused by Cochliomyia hominivorax (Diptera: Calliphoridae) in naturally infested dogs. Parasit Vectors, 16 (1): 1-5, 2023. DOI: 10.1186/s13071-023-05661-z
33. De Oliveira PC, De Almeida GPS, Cardoso JD, Tavares RB, Fernandes JI, Correia TR, Verocai GG, Scott FB: Efficacy of sarolaner on the treatment of myiasis caused by Cochliomyia hominivorax (Diptera: Calliphoridae) in dogs. Vet Parasitol, 276: 1-4, 2019. DOI: 10.1016/j.vetpar.2019.108966
34. Della Pepa G, Lombardi G, Gianfrancesco S, Piccolo R, Chirico G, Pellegrino M, Santella L, Tecce N, Volpicelli A, Sollo E, Bozzetto L, Masulli M, Riccardi G, Rivellese AA, Saldalamacchia G: Triticum vulgare extract and Polyhexanide (Fitostimoline® hydrogel/Fitostimoline® plus gauze) versus saline gauze dressing in patients with Diabetic foot ulcers: results of a randomized controlled trial. J Clin Med, 12 (10): 1-11, 2023. DOI: 10.3390/jcm12103596
35. Souza DW, Machado TSL, Zoppa ALV, Cruz RSF, Gárague AP, Silva LC: Experimental study of topical use of Triticum vulgare cream in induced skin wounds in horses. Rev Bras Plantas Med, 8 (3): 9-13, 2006.
36. Silva TDP, Rabelo RE, Oliveira SL, Santana FJF, Leao HF, Sousa PF, Pleffhen HBO: Uso do Triticum vulgare como auxiliar na cicatrização de feridas cutâneas cirurgicamente induzidas em cães. In: Congresso De Pesquısa, Ensıno E Extensão Da Ufg - Conpeex, 3 Goiânia. Anais eletrônicos do XIV Seminário de Iniciação Cientifica [CD-ROM], Goiânia: UFG, 2006.
37. Lima MS, Asprino L, Prado AP, Moreira RWF, Moraes M, Piracicaba SP: Oral myiasis caused by Cochliomyia hominivorax treated nonsurgically with Nitrofurazone: report of 2 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 109 (3): 70-73, 2010. DOI: 10.1016/j.tripleo.2009.11.014.
38. Shahzad R, Kousar S, Gull I, Bukhari M, Fatima M, Malik R: Evaluation of wound healing activity of hydromethanolic extract of Jacobaea maritima leaves in rabbits. Pak J Pharm Sci, 37 (5): 1053-1061. 2024.

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Research Article

The Effect of Kanamycin on Biochemical Parameters Following Repeated Intramuscular Administrations in Chukar Partridges (*Alectoris Chukar*)

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ABSTRACT

Kanamycin is an aminoglycoside antibiotic widely used to treat infections caused by aerobic gram-negative bacteria in animals. The chukar partridge plays an important role in the nutrition and hunting industries. The study aimed to determine the effect of repeated intramuscular administration of kanamycin at doses of 15 and 100 mg/kg on biochemical parameters in chukar partridge. A total of 18 partridges were randomly divided into three equal groups: control (n=6) and kanamycin groups. Saline solution was administered to the control group. In the other groups, 15 and 100 mg/kg of kanamycin were administered intramuscularly, respectively. Kanamycin was administered once daily for 5 days, and blood samples were taken at 24, 72, and 120 hours. Kanamycin at a 15 mg/kg dose increased albumin (ALB) at 120 h and aspartate transaminase (AST) at all sampling times. The administration of kanamycin at a 100 mg/kg dosage resulted in a notable elevation in ALB, AST, alkaline phosphatase, and cholesterol levels. No difference was observed in other parameters at both dose levels. The results show that kanamycin, at a dose of 100 mg/kg, can cause liver and lipid metabolism damage in chukar partridges. In the future, further studies on histopathological and molecular techniques are required to delineate the organ damage caused by kanamycin.

Keywords: *Alectoris Chukar*, Biochemical parameters, Kanamycin

INTRODUCTION

Aminoglycosides are bactericidal antibiotics, especially against gram-negative bacteria and some gram-positive bacteria. They show their effects by binding irreversibly to the 30S subunit of the bacterial ribosome and inhibiting protein synthesis (1). Aminoglycosides have the advantages of being cheap and having a long post-antibiotic effect. Still, they have the disadvantages of having a narrow therapeutic index and causing adverse effects such as nephrotoxicity, ototoxicity, and neurotoxicity (1,2). Kanamycin is an aminoglycoside antibiotic obtained from *Streptomyces kanamyceticus*. It is effective against gram-negative bacteria such as *Escherichia coli, Salmonella enteriditis, Pseudomonas aeruginosa, Helicobacter pylori, Moraxella, Proteus mirabilis, Enterobacter, Klebsiella pneumoniae,* and *Serratia marcescens.* Kanamycin is frequently used parenterally and orally in veterinary medicine. However, as with other aminoglycosides, kanamycin is a polar and cationic compound, so its oral bioavailability is very low (1%), and it should only be used orally in digestive system diseases (3,4,5).

Partridge is a medium-sized, short-winged, and short-tailed bird species in the Phasianidae family, well-known in Anatolia. One of the most important partridge species is the chukar partridge (*Alectoris chukar*) (6). It is produced for partridge meat or hobby purposes in special hunting grounds. To meet the increasing demand, partridge production on farms has become widespread. However, poor maintenance conditions and stock density on farms have led to the spread of bacterial infections. Bacterial infections in poultry are caused by gram-negative bacteria, especially *E. coli, Klebsiella, Pseudomonas, Salmonella, Citrobacter, Proteus,* and *Serratia* species (7,8). Antibiotics such as enrofloxacin, trimethoprim/sulfamethoxazole, and amoxicillin/clavulanate are commonly used in infections caused by gram-negative bacteria in poultry (7). However, it has been reported that resistance to these antibiotics has developed, and alternative antibiotic options are needed (9). Therefore, kanamycin can be used in infections caused by gram-negative bacteria in chukar partridges.

No research was found on the usage and safety of kanamycin in partridges. Assessing the safety of pharmaceuticals in the target species is crucial for the efficacy of the treatment. Kanamycin can be used in bacterial infections caused by gram-negative bacteria in partridges; therefore, establishing its reliability is essential for widespread use. The aim of this study was to determine the effects of repeated (every 24 hours for 5 days) intramuscular administration of kanamycin at 15 and 100 mg/kg doses to chukar partridges on biochemical parameters.

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MATERIAL AND METHODS

Animals

The study utilized eighteen chukar partridges (*Alectoris chukar*) with weights ranging from 0.4 to 0.6 kg, which had not been administered any medication in the prior two months. The partridges were evaluated as healthy based on physical examination, starvation, and behavior, and housed in groups of three within stainless steel cages. The birds were fitted with numbered rings on their feet for better identification. They were provided with a drug-free diet, and water was made available ad libitum. The research was performed following a two-week acclimatization phase. All study protocols were approved (2017/71) by the Ethics Committee of the Faculty of Veterinary Medicine (University of Selcuk, Konya, Türkiye).

Experimental design

A total of 18 partridges were divided into three equal groups to receive different doses of kanamycin and a control. The control group received intramuscular injections of sterile saline solution. The other two groups were administered kanamycin intramuscularly at 15 and 100 mg/kg, respectively. Drug administration to partridges continued every 24 hours for 5 days. Following drug administration, 0.5 ml blood samples were collected from the jugular vein at 24, 72, and 120 hours. Serum samples were obtained by centrifuging blood samples at 4000 x g for 10 minutes and stored at -80 °C until analysis.

Biochemical analysis

The measurements of albumin (ALB), alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST), blood urea nitrogen (BUN), cholesterol (CHOL), creatinine (CRE), gamma glutamyl transpeptidase (GGT), total bilirubin (TBIL), total protein (TP) and triglyceride (TRIG) values from serum samples were performed on an auto-analyzer using commercial kits.

Statistical analysis

Biochemical parameters were presented as mean±SD. Analyses were performed using the SPSS program (22.0 software; IBM). Statistical comparison of biochemical parameters was performed using one-way analysis of variance (ANOVA) and post-hoc Tukey test. Statistical significance was accepted as $P<0.05$.

RESULTS

No differences were observed in the behavior, appetite, and movement of partridges after intramuscular administration of kanamycin at doses of 15 and 100 mg/kg once daily for 5 days. The effects of repeated administration of kanamycin to chukar partridges on biochemical parameters are presented in Table 1. The administration of kanamycin at a dosage of 15 mg/kg resulted in elevated ALB levels at 120 hours and increased AST levels at 24, 72, and 120 hours. In contrast, a 100 mg/kg caused increased levels of ALB, AST, ALP, and CHOL. No difference was observed in the values of ALP, ALT, BUN, CREA, GGT, TBIL, TP, TRIG, and CHOL at the 15 mg/kg dose and in the values of ALT, BUN, CREA, GGT, TBIL, TP, and TRIG at the 100 mg/kg dose.

DISCUSSION

For the first time, this study established the effects of repeated intramuscular kanamycin treatment at doses of 15 and 100 mg/kg on biochemical parameters in Chukar partridges. Notable hepatic and lipid metabolism alterations were seen in the 100 mg/kg dose group relative to the 15 mg/kg dose. The information obtained in this study is important for the safe use of kanamycin in chukar partridges.

While kanamycin applications to chukar partridges did not cause any difference in ALP, ALT, BUN, CREA, GGT, TBIL, TP, and TRIG values, differences were observed in ALB and AST levels in the 15 mg/kg dose group and ALB, AST, ALP, and CHOL levels in the 100 mg/kg dose group. Surprisingly, despite repeated application of kanamycin, no difference was observed between the groups in BUN and CRE values, which are indicators of kidney damage. There may be more than one reason underlying this situation. The physiological and functional structure of the poultry kidney is quite different from that of the mammalian kidney. While the perfusion of the kidneys of mammals, where nephrotoxic effects are seen at the same doses, is provided by a single renal artery, there are three renal arteries feeding the poultry kidneys (10). The kidneys of poultry possess a renal-portal system that improves their blood flow (11). These perfusion differences between the mammalian and avian kidneys may have provided a better blood supply to the avian kidneys and thus facilitated the rapid removal of kanamycin from the kidneys before damage occurs. Another reason might be that the 100 mg/kg dose cannot cause nephrotoxic effects. This conclusion is supported by the fact that kanamycin causes toxic effects at doses >200 mg/kg in other species (12,13,14,15).

Aminoglycosides cause nephrotoxic effects because they accumulate in the kidney tissue. These drugs accumulate in the liver tissue and the kidneys (16). Aminoglycosides can bind to cell membranes and intracellular organelle membranes, such as lysosomes/mitochondria. Aminoglycosides have a very high affinity for lysosomes and inhibit phospholipase A1 and sphingomyelinase enzymes, preventing intracellular reactions and stopping intracellular events, leading to cellular damage (17,18,19). In addition, histopathological examinations have shown that aminoglycosides cause damage to the liver (20).

Both kanamycin doses in chukar partridges caused elevated ALB and AST, but the 100 mg/kg dose increased ALP. ALB is produced by the liver and is the most common protein found in the blood, and it plays a vital role in body development and tissue repair (21). ALB may be elevated as a defense mechanism to repair damage to the liver. Additionally, aminoglycosides may increase or decrease urination frequency to varying degrees between individuals (3). Therefore, the increased serum ALB levels may be due to the blood's reduced fluid. ALP is a protein enzyme found in various tissues in the body, including the liver, bone, intestines, and kidneys, but 95% of its measured amount in the blood comes from the liver and bone. High ALP levels generally indicate liver and bone damage. AST is an enzyme found in different tissues in the body, such as the liver, heart, muscle, kidney, and brain. Although its specificity for liver damage is lower than other parameters, it is generally accepted as a parameter indicating liver damage with the increase in the enzymes found in the liver in the blood (22). When all these results are evaluated, it can be said that repeated administration of kanamycin may cause liver damage in chukar partridges. Previous studies have also reported liver injury due to aminoglycosides (23,24,25).

CHOL is an enzyme produced by the liver, plays a role in synthesizing some hormones and vitamins D and E, and contributes to synthesizing bile acids with cell/organelle membranes (26). It has been reported that oral administration of aminoglycosides (kanamycin, neomycin, paramomycin) reduces the blood's CHOL level in humans (27). However, parenteral administration to rats and rabbits did not cause any change in CHOL levels (28,29). In this study, the CHOL value increased after intramuscular application of kanamycin. These results indicate that the effect of kanamycin on CHOL varies depending on the route of administration.

Table 1: Effect of kanamycin (15 or 100 mg/kg, intramuscular, every 24 h for 5 days) in chukar partridge on biochemical parameters (n = 6, mean ± SD)

Parameters	Groups	Sampling time (Mean ± SD)		
		24 hours	72 hours	120 hours
ALB (g/dL)	Control	0.85±0.13	0.88±0.10b	0.90±0.08b
	15 mg/kg	1.00±0.16	1.23±0.33ab	1.30±0.24a
	100 mg/kg	1.28±0.43	1.33±0.17a	1.38±0.21a
ALP (U/L)	Control	140.00±30.16b	170.25±60.98b	149.75±46.00b
	15 mg/kg	260.75±78.13ab	259.50±92.41ab	436.25±177.24ab
	100 mg/kg	344.25±96.00a	566.50±79.24a	624.75±242.34a
ALT (U/L)	Control	2.00±0.82	1.50±0.48	1.50±0.58
	15 mg/kg	1.75±0.96	1.50±0.58	2.50±0.58
	100 mg/kg	1.75±0.96	1.50±0.58	1.50±0.58
AST (U/L)	Control	201.75±29.90b	212.00±25.07b	208.75±17.76b
	15 mg/kg	515.25±132.77a	772.25±148.50a	787.75±83.84a
	100 mg/kg	617.50±147.84a	809.50±138.90a	881.50±94.04a
BUN (mg/dL)	Control	2.15±0.85	2.14±0.33	2.02±0.50
	15 mg/kg	2.30±0.82	2.33±0.38	2.22±1.04
	100 mg/kg	2.45±1.03	2.21±0.45	2.10±0.27
CHOL (mg/dL)	Control	94.00±21.15	96.50±21.27b	103.00±21.95b
	15 mg/kg	109.00±19.25	133.00±24.64ab	132.50±22.84ab
	100 mg/kg	151.75±48.02	167.75±24.74a	174.00±21.18a
CRE (mg/dL)	Control	0.44±0.04	0.49±0.05	0.47±0.03
	15 mg/kg	0.42±0.05	0.46±0.13	0.50±0.05
	100 mg/kg	0.40±0.07	0.48±0.07	0.48±0.04
GGT (U/L)	Control	4.75±0.96	5.00±1.41	5.75±1.71
	15 mg/kg	4.25±0.50	5.75±1.26	5.50±1.29
	100 mg/kg	5.00±0.82	6.00±1.41	6.25±1.26
TBIL (mg/dL)	Control	0.08±0.03	0.08±0.01	0.09±0.04
	15 mg/kg	0.12±0.03	0.08±0.02	0.08±0.02
	100 mg/kg	0.11±0.02	0.10±0.04	0.09±0.01
TP (g/dL)	Control	3.90±0.89	4.15±0.93	4.33±0.56
	15 mg/kg	3.70±0.48	4.43±0.79	4.63±0.78
	100 mg/kg	4.18±1.19	4.35±0.64	4.48±0.81
TRIG (mg/dL)	Control	106.00±30.14	118.50±9.38	113.75±32.38
	15 mg/kg	150.25±40.61	178.00±83.36	152.50±38.92
	100 mg/kg	161.00±64.22	182.00±65.63	165.00±27.65

Different letters (a, b) in the same column are statistically significant ($P<0.05$).
ALB; albumin, ALP; alkaline phosphatase, ALT; alanine aminotransferase, AST; aspartate aminotransferase, BUN; blood urea nitrogen, CHOL; cholesterol, CRE; creatinine, GGT; gamma-glutamyltransferase, TBIL; total bilirubin, TP; total protein, TRIG; triglyceride.

In conclusion, repeated intramuscular administration of kanamycin to chukar partridges at doses of 15 and 100 mg/kg did not cause any difference in markers of kidney damage but caused liver damage. The liver adverse effects of kanamycin were dose-dependent. Therefore, observing the adverse effects of repeated intramuscular application of kanamycin at a dose of 100 mg/kg in partridges is necessary. In addition, further studies with histopathological and molecular techniques are needed to understand better the damage caused by kanamycin to organs.

DECLARATIONS

Availability of Data and Materials: The data that support the findings of this study are available on request from the corresponding author (O.A.).

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Ethical Statement: The experiment was approved (2017/71) by the Local Ethics Committee of the Faculty of Veterinary Medicine (University of Selcuk, Konya, Türkiye).

Competing Interests: The authors declare that there is no competing of interest regarding the publication of this article.

Declaration of Generative Artificial Intelligence: The authors of the current study declare that the article and/or tables and figures were not written/created by AI and AI-assisted technologies.

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REFERENCES

1. Block M, Blanchard DL: Aminoglycosides. In, StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541105/
2. Wargo KA, Edwards JD: Aminoglycoside-induced nephrotoxicity. J Pharm Pract, 27(6): 573-577, 2014. https://doi.org/10.1177/0897190014546836.
3. CVMP 2003: Kanamycin summary report. EMEA/MRL/886/03. European medicines agency London, United Kingdom.
4. Asif M: Role of aminoglycoside antibiotics in the chemotherapy of Mycobacterium tuberculosis. J Pharm Phytother, 2(1): 1-16, 2013.
5. Archer M, Bastow T, Steinvoort C, Larson B, Oderda G: Drug Class Review. Aminoglycoside Agents. Final Report, 2014.
6. Yardimci SB, Sakin F, Corum O: Pharmacokinetics, tissue residues, and withdrawal times of florfenicol in chukar partridges (Alectoris chukar). J Vet Pharmacol Ther, 48(2): 94-102, 2025. https://doi.org/10.1111/jvp.13484
7. Tian M, He X, Feng Y, Wang W, Chen H, Gong M, Liu D, Clarke JL, van Eerde, A: (2021). Pollution by antibiotics and antimicrobial resistance in livestock and poultry manure in China, and countermeasures. Antibiotics, 10(5): 539, 2021. https://doi.org/10.3390/antibiotics10050539
8. Doneley RJ: Bacterial and parasitic diseases of parrots. Vet Clin North Am Exot Anim Pract, 12(3): 417-432, 2009. https://doi.org/10.1016/j.cvex.2009.06.009
9. Foti M, Rinaldo D, Guercio A, Giacopello C, Aleo A, De Leo F, Fisichella V, Mammina, C: Pathogenic microorganisms carried by migratory birds passing through the territory of the island of Ustica, Sicily (Italy). Avian Pathol, 40(4): 405-409, 2011. https://doi.org/10.1080/03079457.2011.588940
10. Buyse K, Stein K, De Spiegelaere W, Cornillie P, Clauss M, Janssens GP: On the function and origin of the avian renal portal shunt and its potential significance throughout evolution. Biol Rev, 100(1): 351-361, 2025. https://doi.org/10.1111/brv.13144
11. Blackburn R, Prashad D: The avian renal portal system: a model for studying nephrotoxicity of xenobiotics. Toxicol Lett, 53(1-2): 219-221, 1990. https://doi.org/10.1016/0378-4274(90)90131-5.
12. Yeary RA: Systemic toxic effects of chemotherapeutic agents in domestic animals. Vet Clin North Am, 5(1): 51-69, 1975.
13. Kitasato I, Yokota M, Inouye S, Igarashi M: Comparative ototoxicity of ribostamycin, dactimicin, dibekacin, kanamycin, amikacin, tobramycin, gentamicin, sisomicin and netilmicin in the inner ear of guinea pigs. Chemotherapy, 36(2): 155-168, 1990. https://doi.org/10.1159/000238762.
14. Hashino E, Tanaka Y, Salvi RJ, Sokabe M: Hair cell regeneration in the adult budgerigar after kanamycin ototoxicity. Hear Res, 59(1): 46-58, 1992. https://doi.org/10.1016/0378-5955(92)90101-R.
15. Xiang ML, Mu MY, Pao X, Chi FL: The reinnervation of regenerated hair cells in the basilar papilla of chicks after kanamycin ototoxicity. Acta Otolaryngol, 120(8): 912-21, 2000. https://doi.org/10.1080/00016480050218636.
16. Kornuguth ML, Kunin CM: Distribution of gentamicin and amikacin in rabbit tissue. Antimicrob Ag Chemother, 11: 97-4, 1977. https://doi.org/10.1128/aac.11.6.974.
17. Le TA, Hiba T, Chaudhari D, Preston AN, Palowsky ZR, Ahmadzadeh S, Shekoohi S, Cornett EM, Kaye AD: Aminoglycoside-related nephrotoxicity and ototoxicity in clinical practice: a review of pathophysiological mechanism and treatment options. Adv Ther, 40(4): 1357-1365, 2023. https://doi.org/10.1007/s12325-023-02436-x
18. Chen LC, Chen HH, Chan MH: Calcium channel inhibitor and extracellular calcium improve aminoglycoside-induced hair cell loss in zebrafish. Archiv Toxicol, 98(6): 1827-1842, 2024. https://doi.org/10.1007/s00204-024-03720-7
19. Kim YR, Baek JI, Lee KY, Kim UK: Berberine chloride protects cochlear hair cells from aminoglycoside-induced ototoxicity by reducing the accumulation of mitochondrial reactive oxygen species. Free Radic Biol Med, 204: 177-183, 2023. https://doi.org/10.1016/j.freeradbiomed.2023.04.017
20. Mirazi N, Baharvand F, Moghadasali R, Nourian A, Hosseini A: Human umbilical cord blood serum attenuates gentamicin-induced liver toxicity by restoring peripheral oxidative damage and inflammation in rats. Basic Clin Pharmacol Toxicol, 128(2): 268-274, 2021. https://doi.org/10.1111/bcpt.13502.
21. De Simone G, di Masi A, Ascenzi P: Serum Albumin: A Multifaced Enzyme. Int J Mol Sci, 22(18): 10086, 2021. https://doi.org/10.3390/ijms221810086.
22. Anadón A, Castellano V, Martínez-Larrañaga MR: Biomarkers in drug safety evaluation. In: RC Gupta (eds.), In: Biomarkers in Toxicology, 923-945, 2014.
23. Webster CM, Shepherd M: A mini-review: environmental and metabolic factors affecting aminoglycoside efficacy. World J Microbiol Biotech, 39(1): 7, 2023. https://doi.org/10.1007/s11274-022-03445-8
24. Dinev T, Zapryanova D, Lashev L: Changes in some blood biochemical and haematological parameters in goats after aminoglycoside and aminocyclitol treatment at therapeutic doses. Turk J Vet Anim Sci, 31(3): 179-188, 2007.
25. Nisly SA, Ray SM, Moye RA: Tobramycin-induced hepatotoxicity. Ann. Pharmacother, 41(12): 2061-2065, 2007. https://doi.org/10.1345/aph.1K266.
26. Craig M, Yarrarapu SNS, Dimri M: Biochemistry, Cholesterol. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK513326/
27. Rivetti S, Romano A, Mastrangelo S, Attinà G, Maurizi P, Ruggiero A: Aminoglycosides-Related Ototoxicity: Mechanisms, Risk Factors, and Prevention in Pediatric Patients. Pharmaceuticals, 16(10): 1353, 2023. https://doi.org/10.3390/ph16101353.
28. Fisher ER: Effect of neomycin on cholesterol atherosclerosis in rabbit. Proc Soc Exp Biol Med, 103: 857-860, 1960. https://doi.org/10.3181/00379727-103-25696.
29. Broitman SA, Kinnear DG, Gottlieb LS, Bezman AL, Vitale JJ, Zamcheck N: Effect of neomycin alteration of the rat intestinal flora on serum cholesterol and valvular sudanophilia. Transl Res, 55(1): 55-59, 1960.

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Review Article

Herpesviral Infections of the Nervous System in Ruminants: BoHV-1, BoHV-5, PRV, MCFV

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ABSTRACT

Bovine Herpesvirus-1 (BoHV-1), Bovine Herpesvirus-5 (BoHV-5), Pseudorabies Virus (PRV), and Malignant Catarrhal Fever Virus (MCFV) are significant viral pathogens that cause respiratory, neurological, and immunological system diseases in cattle. This review aims to provide a comparative evaluation of these viruses based on current literature regarding etiology, epidemiology, clinical manifestations, diagnostic methods, treatment options, and preventive strategies. BoHV-1 is a globally prevalent virus that can be effectively controlled through vaccination, whereas BoHV-5 primarily affects young calves by causing severe CNS infections and is associated with high mortality rates. Although originating from swine, PRV can lead to peracute and fatal neurological syndromes in cattle. It has been established that MCFVs, transmitted from various reservoir species, are the causative agents of lymphoproliferative and vasculitic disease courses in ruminants. The agents' ability to cross species barriers, establish latent infections, and induce neurological signs complicates their control. Practical diagnostic tests, strict biosecurity protocols, and the development of new-generation vaccines are the main approaches to controlling these infections.

Keywords: BoHV-1, BoHV-5, MCFV, Neurological disease, PRV, Ruminants

INTRODUCTION

Herpesvirus infections in ruminants have been demonstrated to cause significant health and economic losses in the livestock sector, primarily due to the pathologies they cause on the central nervous system (CNS) (1). The primary agents responsible for CNS involvement are bovine herpesvirus type 1 (BoHV-1), bovine herpesvirus type 5 (BoHV-5), malignant catarrhal fever viruses (MCFV) and pseudorabies virus (PRV). These viruses have been observed to induce severe neurological findings, including encephalitis, meningoencephalitis, ataxia and paralysis, often resulting in high mortality rates, particularly among juvenile animals (2).

The latent infection ability of these pathogens results in their persistence within herds for extended periods, thereby hindering effective control and eradication efforts (3). It has been demonstrated that the reactivation of BoHV-1 is exceptionally responsive to stress and immunosuppression. Furthermore, it has been observed that latently infected animals have the potential to become virus shedders. MCFV infections have the potential to induce fatal clinical manifestations when transmitted from subclinical carrier species (e.g., sheep) to susceptible species (cattle, deer) (4).

The consequences of such infections are twofold, impacting animal health and animal husbandry productivity. A plethora of indirect losses have been identified, including but not limited to: a decline in milk yield; a decline in fertility; growth retardation; an increase in labor and treatment costs; and the replacement of animals removed from the herd (1). Furthermore, in the event of outbreaks, measures such as trade restrictions, quarantine practices, and animal movement prevention can result in significant economic repercussions (5).

In this review, the etiology, epidemiology, pathogenesis, clinical findings, diagnosis and treatment approaches of BoHV-1, BoHV-5, MCFV and PRV infections were analyzed in the light of current literature.

BOVINE HERPESVIRAL MENINGOENCEPHALITIS (BOVINE ALPHAHERPESVIRUS 1 and 5)

Etiology, epidemiology and pathogenesis

Bovine herpesviral meningoencephalitis (BHM) is an infectious disease characterized by neurological signs, usually seen in young calves and rare in adult cattle. BoHV-5 and BoHV-1 mainly cause the disease, but BoHV-1 can also cause meningoencephalitis. It is impossible to distinguish these two agents using conventional laboratory tests because they are genetically and antigenically closely related (1). It has been demonstrated that both BoHV-1 and BoHV-5 manifest neurotropic effects, with BoHV-5 reaching the frontal regions of the brain and causing neurological diseases

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that are frequently fatal. In contrast, BoHV-1 is rarely responsible for bovine encephalitis. (6).

The order *Herpesvirales* consists of 3 families: *Alloherpesviridae* (frog and fish herpesviruses), Malacoherpesviridae (oyster herpesviruses) and *Orthoherpesviridae* (mammalian, reptile and avian herpesviruses). The *Orthoherpesviridae* family contains three subfamilies: *Alphaherpesvirinae, Betaherpesvirinae* and *Gammaherpesvirinae*. All ruminant herpesviruses are classified in the subfamilies *Alphaherpesvirinae* or *Gammaherpesvirinae*. BoHV-1 and BoHV-5 are in the subfamily *Alphaherpesvirinae*, genus *Varicellovirus* (1). According to the classification by the International Committee on Taxonomy of Viruses (ICTV), BoHV-1 and BoHV-5 share high genetic similarity (>80% amino acid identity) (2,7).

Herpesviruses are linear DNA viruses and their genomes are 120-250 nm in diameter, double-stranded, contain 135.3 kilobase pairs (kbp) and are high in guanine and cytosine (GC) content (1,3). Surrounded by an icosahedral protein capsid of 162 capsomers, viral DNA encodes approximately 200 genes. (3). The nucleocapsid is embedded in an amorphous protein tegument originating from the host cell and surrounded by an envelope consisting of a double lipid layer covered with viral glycoproteins. Herpesviruses (especially those of the *Alphaherpesvirinae* family) can cause acute or latent infection (1). The site of latency is sensory neurons in the trigeminal ganglia, but it has also been observed in lymphoid tissues (6).

All BoHV-1 strains belong to a single viral species but are divided into three subtypes based on antigenic and genomic analysis: BoHV-1.1, -1.2a and -1.2b. Subtype 1 virus strains, the causative agent of infectious bovine rhinotracheitis (IBR), are typically found in the respiratory tract and aborted fetuses. Strains of this type are prevalent in Europe and North and South America. Subtype 2a infections are associated with various clinical symptoms in the respiratory and genital systems. This type causes infectious pustular vulvovaginitis (IPV), infectious balanoposthitis (IPB) and abortions. Subtype 2b has been identified in Australia and Europe and is linked to respiratory diseases, IPV and IPB. However, it has been demonstrated not to be the causative agent of abortions (3).

BHM was first reported in Australia in 1963 (5). Due to its shared virion morphology, cytopathic effect in cell culture, and antigenic properties, the virus was categorized as a neuropathogenic variant of BoHV-1. This categorization resulted in the designation of bovine encephalitis herpesvirus (BEHV) or BoHV-1 subtype 3. Subsequently, based on restriction site mapping of viral DNA and cross-reaction with monoclonal antibodies, BEHV was detected as a separate strain with distinct genomic and antigenic properties. Therefore, in 1992, the ICTV recognized BEHV as a separate virus species, namely BoHV-5 (5).

BoHV-5 is the primary etiologic agent of non-suppurative, necrotic meningoencephalitis, which is usually fatal in calves (6). BoHV-5 has been shown to trigger fatal meningoencephalitis or a meningitis-like illness after intravaginal infection or intranasal vaccination. Neurological symptoms begin with severe depression, loss of appetite, jaw clenching and excessive salivation (9). Animals vaccinated by the intraconjunctival route develop hyperthermia with nasal replication of the virus but do not show any neural signs (10). BoHV-5 is divided into 5a, 5b and 5c subtypes (2). The only strain classification to subtype b was recognized as a natural recombinant between BoHV-1 and BoHV-5 (6). BoHV-5 cases are highly prevalent in South America, especially in Brazil and Argentina, but sporadic disease in some countries (11).

Although data on the factors affecting BoHV-5 transmission are limited, viral DNA and infectious viruses have been detected in the semen of subclinically infected bulls (10). For BoHV-1, viral transmission occurs directly or indirectly between animals. The virus's initial replication occurs in the epithelial cells of the oral, nasal, oropharyngeal and ocular mucosa, where the virus spreads through local invasion of nerve endings and/or viremia. Approximately 7 days after infection, the entry of viruses into the CNS occurs via retrograde axonal transport along the cranial nerves, particularly the olfactory nerves. In the CNS, a new cycle of viral replication leads to either meningoencephalitis (the primary manifestation of the disease) or lifelong latent infection (1).

The prevalence and incidence of BoHV-1 infection varies worldwide (12). During the latent period, a new reactivation, often triggered by stressful conditions, enables the virus to disseminate and infect other individuals. Several factors have been identified as causative to the propagation of viruses within a herd. These include the reduction of passive immunity, the weaning of calves during this period, large numbers of animals, transport, the introduction of cattle from outside the herd, alterations to feed, paddock changes, vaccination, ear numbering, cauterization and castration. Decreased maternal immunity is associated with an increased risk of infection and seroconversion. This condition leads to a higher prevalence of antibodies to BoHV-1 in adult cattle, where the seroconversion rate is lower due to herd immunity (1,12). Early weaning of calves has been documented in 75% of BoHV-5-induced investigations on farms with BHM cases; however, a possible failure of passive transfer of immunity has not been confirmed. The effect of passive immunity was confirmed by experimental studies showing that calf groups that did not receive colostrum developed meningoencephalitis and respiratory disease after BoHV-5 and BoHV-1 vaccinations, respectively (1).

Latent viruses can be detected by polymerase chain reaction (PCR) or in situ hybridization. Viral particles produce a latency-associated gene, but no viral proteins or infectious particles are produced. The viral DNA is localized in the nucleus of latently infected neurons. Sites of latent infection in cattle include the trigeminal nerve or sensory root ganglia, olfactory bulbs, telencephalic cortex, midbrain, pons, cerebellum and medulla oblongata (1). Reactivation of BoHV-1 after a latent period is necessary for virus transmission. During this period, immune responses are temporarily suppressed, and the integrity of mucosal surfaces is disrupted, but it does not cause serious recurrent diseases. Therefore, reactivation during the latent period may accelerate secondary bacterial infections in the lower respiratory tract and lead to pneumonia (13).

There is a strong association between BoHV-1 infection and bovine respiratory disease complex (BRDC), which causes losses of approximately US$1 billion annually. These economic losses have led to the widespread adoption of vaccination against BoHV-1. Natural or vaccine-induced immunity to BoHV-1 protects animals against BoHV-1 and BoHV-5, which may explain the lower prevalence of BHM cases in Europe and North America. In countries where vaccination against BoHV-1 is less frequent, outbreaks of neurological diseases are more common (1).

Factors affecting the survival, transmission and dispersal of BoHV-1 include temperature and humidity. BoHV-1 remains stable at 4°C for up to 1 month, but stability decreases with increasing temperature. The infectivity of the virus decreases 106-fold in 50 days at 22°C, 10 days at 37°C and 21 minutes at 56°C. High humidity is conducive to virus reproduction because it survives longer and spreads rapidly in high humidity. The virus can survive up to 30 days in a cold environment with a humidity of more than 90% and 5-13 days in a warmer environment. Aerosol dispersion has been demonstrated over short distances of up to 4 m, but transmission is estimated to occur over distances of up to 8 km. The virus can be detected in contaminated feed for up to 30 days. BoHV-1 is sensitive to many disinfectants, such as quaternary ammonium, phenol and formalin (14).

Clinical signs

Lethargy and loss of consciousness are typical clinical symptoms of BHM in endemic areas and are important indicators of the disease. Infected cattle move away from the herd and remain immobile with a low head posture. As the disease progresses, mucoid and mucopurulent serous nasal and ocular discharge is observed. Cerebrocortical symptoms include behaviors such as teeth grinding, muscle tremors, circling, blindness, incoordination, pressing the head against objects, nystagmus and seizures. Some cattle may remain lying down and unable to get up. Aggression is a rare clinical symptom. Non-specific symptoms include dehydration, weight loss, hard hair, fever, abdominal pain, anorexia, tachycardia and tachypnea. Some affected individuals may develop complications from inpatient treatment, such as bacterial bronchopneumonia (1).

The course of the disease caused by BoHV-1 is influenced by factors such as virus-specific virulence properties, infected tissue type, presence of secondary bacterial infections, host age and resistance factors. Clinical signs of BoHV-1 in cattle usually include fever, apathy, cough, persistently increased respiratory rate and anorexia. In adult dairy cows, there is a severe decline in milk yield. Primary infection occurs in the turbinates of the nose and trachea, while mucopurulent discharge from the nostrils and eyes is associated with pustular lesions of the nasal mucosa and conjunctivitis (3). BoHV-5 meningoencephalitis usually affects cattle as young as 18 months, but older animals can also be affected. Clinical symptoms of the disease include tremors, rotation, incoordination, depression, loss of visual, hearing or skin reflexes, blindness, mandibular trismus, bruxism, nystagmus, opisthotonos, paresis, permanent recumbency, pedaling movements, tetany, convulsions. BoHV-5 meningoencephalitis is characterized by low morbidity and high mortality. Death can occur in 4-15 days, along with clinical symptoms. (15).

Diagnosis

Current diagnostic methods for BoHV-1 infection include virus neutralization test (VNT), serological tests such as enzyme-linked immunosorbent assay (ELISA), virus isolation, detection of viral DNA and antigens. Madin Darby Bovine Kidney (MDBK) cell line has been successfully used for virus isolation (9).

Purification, amplification and detection of DNA is expensive and time-consuming. PCR testing is a rapid method for the diagnosis and/or typing. However, viral DNA detection techniques such as PCR and real-time PCR require specialized instruments and trained personnel. Therefore, they are not suitable for searching for viruses in large numbers of samples.

BoHV-1 or BoHV-5-specific herpesviral differentiation can be done with a PCR test directed against the glycoprotein C (gC) region. PCR detection of the glycoprotein B (gB) gene region confirms herpesviral infection but does not distinguish between species. In cases of neurological disease, serological methods are of little use as cattle are often dead or lethargic at the time of sample selection. Furthermore, this serological method is expensive and requires high-quality antisera as it is severely affected by improper sampling and autolysis. Immunohistochemistry (IHC) can be used to diagnose BoHV infection routinely. However, IHC is unreliable for diagnostic confirmation as immunolabelling is often inconsistent in diagnostic cases. These methods cannot perform rapid detection of clinical samples. Immunochromatography assays (ICAs) are sensitive, specific, rapid, easy to perform, and accurate diagnostics, which are next-generation detection technologies for detecting and controlling bovine diseases. ICAs have been widely applied in clinical diagnosis, food chemistry and environmental monitoring (1,16,17). Clinical signs and necropsy findings are important for the diagnosis of BHM. As a differential diagnosis, diseases such as polioencephalomalacia and rabies, which affect the CNS of cattle with neurological, should be considered. The hallmark of BHM that distinguishes it from other non-viral cerebral cortical diseases, such as polyencephalomalacia, lead poisoning, salt toxicity and vitamin A deficiency, is the absence of blindness in BHM. (14,15).

Treatment

Better identification of infectious disease prevention and effective treatment strategies is based on a thorough understanding of the replicative cycle of the pathogen. As BoHV-1 is a latent virus that remains in organisms for life, it is important to understand the entry route and develop ways to intervene. There is no specific or effective treatment for cattle in cases of BHM. Treatments for BHM are supportive (1,18). Antiviral research is continuous, and its efficacy is being investigated. Although it is known that non-toxic antiviral agents are not available for BoHV-1 infection, the use of non-toxic zinc oxide (ZnONPs), silver nanoparticles (AgNPs) and flavonoid derivatives are also being investigated (19,20). Plant and fungal extracts are of great interest for developing new antiviral drugs. More specifically, peptides derived from a strain of *Scytalidium sp*., macrolides derived from an unidentified fungus belonging to the Pleosporales, and lactones derived from a strain of *Aspergillus terreus* have shown inhibitory activity against herpesviruses (21). To date, a potential antiviral effect against BoHV-1 is due to traditional synthetic drugs (acyclovir, fenbendazole, famciclovir, ivermectin) administered alone or in combination with natural agents. Few medicinal compounds without toxicity have been identified to treat BoHV-1 infection. Examples include polyphenols, which are known to have anti-herpesvirus activity. Polyphenols and flavonoids have been shown to have in vitro antiviral activity in MDBK cells, and *Thymus capitata*, a plant rich in these substances, provides antiviral activity by interfering with the early stages of viral adsorption and replication and inhibiting viral replication. Another substance that shows a strong antiviral effect against virus replication is kaempferol. Genistein, a soy isoflavone, inhibits BoHV-1 replication; curcumin, a component of the spice turmeric, inhibits the entry of BoHV-1 into MDBK cells. (19).

Although antiviral studies on BoHV-5 are minimal, the activity of three antiherpes drugs (acyclovir, ganciclovir and foscarnet) was tested in vitro using plaque reduction assay and it was revealed that foscarnet might be effective against herpesviral infections. (22).

In conclusion, various antiviral agents are being investigated to treat BoHV-1 infections in BHM cases. Investigation of the efficacy of these agents against BoHV-5 and the development of new treatment approaches may provide new literature on specific antiviral treatment options for BoHV-5 because there is limited literature on the treatment of BoHV-5.

Prevention

In endemic areas, control and prophylactic measures are implemented to reduce economic losses caused by respiratory, reproductive and neurological diseases. These are determined using serology to determine whether infection is present in the herd or in individuals to be included in the herd. Potentially stressful situations should be minimized and affected individuals should be isolated in cases of clinical illness to detect the disease early, prevent its spread and develop control strategies. In endemically infected herds, high immunity levels also provide adequate protection against disease. In particular, genetically modified vaccines produce antibodies that can be distinguished from those produced by natural infection, giving them an advantage over conventional vaccines (1).

Commercial BoHV-1 vaccines can be classified as modified

live (MLV) or inactivated. MLV was developed on cell cultures and evokes a high humoral and cellular immune response due to attenuated virus replication. Existing MLVs establish latency and can periodically reactivate from latency, allowing the virus to spread and infect pregnant cows and cause abortions. MLV vaccines have been reported to be pathologic in calves whose immune systems are not fully developed because they are immunosuppressive. Inactivated vaccines, which consist of viruses inactivated by chemical processes, usually contain all viral particles. The effectiveness of these vaccines depends on establishing a protective neutralizing antibody titer, which requires multiple vaccinations.

Furthermore, inactivated vaccines do not consistently induce cellular immune responses. Marker vaccines are vaccines prepared by removing virulence-related genes from the virus genome. These vaccines can distinguish between vaccinated animals and animals infected with the field strain. Two types of commercial marker vaccines are currently available. The first involves the deletion of the glycoprotein E (gE) gene. The second type involves deleting the gE and the viral thymidine kinase (TK) gene. The gE gene encodes a protein required for anterograde transport from the TG to the ocular surfaces and nasal cavities. Therefore, if a gE marker virus establishes latency, reactivation from latency should not occur easily. The viral TK gene encodes a protein that phosphorylates thymidine and plays an important role in viral replication in non-dividing cells. Although deleting TK in the context of the gE gene further reduces the chance of reactivation from the latent stage, a thymidine kinase BoHV-1 mutant has been reported to reactivate from the latent stage and cause abortions. Therefore, mutating the viral TK gene alone is insufficient to produce a safe and effective BoHV-1 MLV (23).

Current vaccines used in BoHV-1 or BoHV-5 infections can reduce the clinical symptoms of the disease but cannot routinely prevent its latency. Another study reported that calves fed colostrum were protected against BoHV-1 and BoHV-5 encephalitis (14).

PSEUDORABIES VIRUS-PRV (AUJESZKY DISEASE)

Etiology, epidemiology and pathogenesis

PRV is also named Aujeszky disease virus or Suid alphaherpesvirus 1 (SuHV-1). PRV belongs to the *Orthoherpesviridae* family, subfamily *Alphaherpesvirinae*, genus *Varicellovirus*. It contains 143 kb of double-stranded, enveloped linear DNA. PRV can encode more than 70 proteins and has an approximately 74% GC content (24-26). Tegument proteins between the capsid and envelope provide various functions during virus entry, replication and exit. Glycoproteins enable the virus to attach to host cells, fuse to cell membranes, and enter the cell (27). Like other members of the Varicellovirus genus, PRV is neurotropic and can cause latent infection in the peripheral nervous system (28). Genetically, the PRV strains prevalent worldwide are divided into two genotypes, and the majority of PRV strains in China belong to genotype II (29). This genotype can be further divided into classical and variant strains (30).

A Hungarian veterinarian first documented PRV as the causative agent of Aujeszky's disease in 1902. Wild boars and pigs are the primary natural hosts of PRV (31). Neurological disorders in newborn piglets and reproductive problems in sows can be observed after infection (28). Firstly, respiratory symptoms, fetal death, abortion in pregnant sows, or both may occur in older pigs. In piglets and more susceptible species, PRV infection is usually fatal due to CNS disorders (25). Although pigs are known to be the only reservoir of PRV, they can infect many animal species, including sheep, cattle, dogs, foxes, tigers, bears, rats, raccoons, panthers, mink, Iberian lynx, wolves, bats, and cats. In addition, the zoonotic potential of PRV infection is also a threat to public health (31). PRV infection can cause retinal vasculitis, endophthalmitis and encephalitis in humans (25,26).

PRV infection was first described as 'mad itch' in cattle in America in 1813 (28). PRV infection is enzootic and widespread in Eurasian wild boars. As wild boar populations expand their range, the risk of disease transmission increases, which may affect the health of humans, domestic pigs, and wildlife conservation. Characterization of PRV from wild boars helps understand population diversity and can trace back the infection pathway. In Europe, phylogenetic analysis of partial sequences of the gC gene shows that wild boar isolates can be differentiated into A and B clades. Clade A isolates originate from Austria, France, Germany, Hungary, Italy and Slovakia, while clade B isolates originate from south-western Europe, including Germany, France and Spain. Thus, clades A and B isolates geographically overlap in Central Europe, Germany and France. PRV isolated from the USA was distinct from European isolates and closely related to domestic swine isolates. It may represent a transmission from domestic to feral pigs (31).

PRV infection usually begins with viral replication in epithelial cells of the nasal and oropharyngeal mucosa. It then spreads to the neurons of the peripheral nervous system that innervate the infected epithelium. Viral particles are carried by retrograde transport to the sensory and autonomic peripheral ganglia. It causes a latent infection in this region and infects the host for life. When reactivation occurs, PRV particles multiply by replication. It returns to the mucosal surfaces, where infection begins in an anterograde direction along the sensory nerves. In addition, PRV infection can spread from the primary replication site to other organs of the pregnant host, such as the uterus, by viremia associated with peripheral blood mononuclear cells. Then, secondary replication can occur in the endothelial cells of these organs. As a result of this replication, vasculitis and multifocal thrombosis may occur, leading to pregnancy loss (26).

Although the disease was initially controlled worldwide in 1961 with the gE-negative vaccine Bartha-K61 from Hungary, PRV reemerged. The mutated variant of PRV spread rapidly and the conventional vaccine provided only partial protection against this new variant. It has been highlighted that PRV variant strains may be more virulent to animals and humans than classical strains. In addition, due to the latent persistent infection pattern of PRV, infected animals can become lifelong carriers and latent shedders of the virus (26).

Cattle are more resistant to PRV than other domestic species and can be infected by direct or indirect contact with pigs. Transmission is mainly airborne but can also occur through skin or mucous membrane injuries. In rare cases, rodents or biting flies can also cause infection. Due to the neurotropic properties of the virus, a small amount of virus production occurs in the fascia at the bite site and reaches the brain via the peripheral nerves. PRV replicates intensively in the brain and causes encephalomyelitis. This situation leads to death within a short time. Although the gastrointestinal tract does not usually play a significant role, infection can occur after ingesting contaminated feed. In cases of close contact, severe itching and death in the hindquarters of cattle due to sniffing and biting by pigs, especially in the perineum, are also significant. Experimental infection of cattle is possible through intranasal, intramuscular, subcutaneous, intravenous, and intradermal routes. Since transmission from cattle to cattle does not occur, they appear to be the final host (32,33).

Sheep and goats infected with PRV usually do not shed. Infection usually results in CNS disease, often severe itching and death. Although the natural incidence of infection in sheep is low, mortality rates due to PRV can be as high as 60% and cause

significant losses to sheep flocks. The source of infection in sheep is always infected pigs. Sheep and goats are most commonly infected by aerosol but are also highly susceptible to percutaneous infection. Small ruminants shed very little virus and are not transmitted between each other as in cattle. However, lambs can shed as much virus as piglets through nasal secretions just before and during the onset of clinical signs. Horizontal transmission of PRV from lambs to pigs has been demonstrated. Generally, goats are more susceptible than sheep and clinical signs are more pronounced (30,32).

Clinical signs

The disease is always fatal in all hosts except pigs. Excessive itching is characterized by a mortality rate approaching 100% and severe clinical signs in the CNS (32).

PRV in cattle begins with a fluctuating fever with a temperature of up to 42°C until shortly before death. Characteristic signs of PRV are behavioral disturbances and CNS signs (severe itching, convulsive restlessness followed by paralysis). Other symptoms include incoordination, unsteady gait, circling, howling, drooling, jaw paralysis, grunting, self-mutilation (auto-mutilation), head banging against the wall, and floppy ears with friction at the base of the ear. Initially, there were only jerky twitches of individual muscle groups in the head, neck, and back. The animals lick or gnaw at various body parts, most commonly the knee joint area, the inside of the hind legs, the udder or the base of the tail and the perineum. Death occurs 6-48 hours after the onset of clinical signs due to paralysis (32,33).

Infection with the PRV has been demonstrated to affect sheep of all age groups, with the resultant clinical signs including degeneration and paralysis of the CNS. This form of CNS paralysis is characterized by paresis, recumbency, pharyngeal paralysis, dyspnoea and rumen atony. The main clinical signs are fever, restlessness and movement disorders. Excessive pruritus, characteristic of cattle, is also seen in sheep. Lambs become recumbent and die acutely. Fever is not always high, may occur early in the disease and is not severe (32). Pathological examination revealed hemorrhagic pneumonia, hemorrhagic lymphadenopathy syndrome, cerebral hyperemia and hemorrhages in dead goats (29).

Diagnosis

For definitive diagnosis, anamnesis, clinical findings, and hematologic and biochemical parameters should be evaluated and supported by laboratory diagnosis. Various direct and indirect tests are used for laboratory diagnosis (immunofluorescence, immunoperoxidase, IHC, PCR, VNT, latex agglutination, or ELISA). The most commonly used diagnostic methods are immunofluorescence and immunoperoxidase. Virus isolation is difficult and time-consuming and requires experienced personnel and equipment. The immunoperoxidase test is the most preferred method (33).

Clinical diagnosis in cattle, sheep and goats is based on clinical signs and history of direct contact with pigs. In cases where pruritus is not prominent, it is difficult to differentiate from other causes of viral encephalitis. Severe neurological lesions are not usually seen. Microscopically, diffuse non-suppurative inflammation with perivascular congestion and focal neuronal necrosis observed in the brain and spinal cord. Intranuclear inclusion bodies are rarely seen. Serological diagnosis in cattle, sheep, or goats is ineffective because most infected animals die before antibodies can be detected in serum. In surviving and latently infected adult animals, diagnosis can be made by VN or antibody ELISA tests. Serological tests form the basis of most testing and culling programs for pseudorabies eradication. False-positive results are rare (14).

Treatment

No effective treatment for PRV in cattle, sheep and goats has been reported. In latently persistently infected animals, reactivation and shedding of the virus often occur after a stressor. Stress factors include micro-infection, transport, poor husbandry, parturition and treatment with immunosuppressive agents (e.g., corticosteroids) (34). There are currently no drugs available for PRV infection, and vaccination remains the main method of disease prevention. The combination of acyclovir and ribavirin has been shown to inhibit PRV replication in vitro. In addition, several synthetic diaminopurine-based acyclic nucleoside phosphonate analogs have been reported to have anti-PRV activity. Natural plant extracts, including kumazasa extract, *Duabanga grandiflora* leaf extract and *Houttuynia cordata,* can suppress PRV replication in vitro at high concentrations of isobavachalcone and resveratrol (35).

Prevention

Vaccines against PRV have been developed primarily to prevent disease caused by wild-type virus infection. The vaccine is intended to activate the body's natural defense mechanisms and develop immunity against disease or infection caused by field viruses. The use of inactivated and attenuated live vaccines to control PRV is widespread. Simultaneously, more effective and safer recombinant vaccines are being developed (36,37).

Although vaccines can effectively control the spread of PRV, they do not protect against the latency of the wild-type virus. Since 2011, outbreaks of new PRV variants have been reported in pigs vaccinated with the Bartha-K61 strain. The variability of viral strains and the inability to safely use attenuated vaccines pose a serious threat to the pig industry (37).

This disease causes significant economic losses to the pig industry each year, and vaccination with classical live attenuated PRV or inactivated PRV vaccines has been one of the main methods used to prevent and control the disease. Many European countries, such as New Zealand and the United States of America, have implemented strict national eradication programs based on compulsory vaccination, culling positive pigs, and establishing PRV-free pig herds (25).

MALIGNANT CATARRHAL FEVER-MCF (CORIZA GANGRENOZA BOVUM-CGB)

Etiology, epidemiology, and pathogenesis

MCF or Coriza Gangrenoza Bovum (CGB) affects a wide range of susceptible hosts, including hoofed animals from the order *Artiodactyla*, such as cattle, water buffalo, bison, deer, antelope, elk, and reindeer. It is a sporadic but often fatal disease in ruminants (4,38). Rarely pigs may also be affected, and experimental infections have been demonstrated in rabbits, guinea pigs, and hamsters. The causative agents of MCF are herpesviruses from the genus *Macavirus*, within the subfamily *Gammaherpesvirinae*, of which at least six are known to be pathogenic under natural conditions. Ovine gammaherpesvirus 2 (OvHV-2) is the most widespread globally. MCF is endemic in sheep and can cause sheep-associated MCF in various ruminant and pig species. Alcelaphine gammaherpesvirus 1 (AlHV-1) is endemic in antelope and is responsible for antelope-associated MCF outbreaks in domestic cattle in sub-Saharan Africa. Caprine gammaherpesvirus 2 (CpHV-2) is endemic in domestic goats and has been reported to cause MCF in particular deer species and water buffalo. White-tailed deer and red deer are susceptible to Malignant Catarrhal Fever Virus (MCFV-WTD - malignant catarrhal fever virus–white-tailed deer), which domestic goats carry. Ibex MCF virus (Ibex-

MCFV) has been identified in the bongo antelope and anoa, a buffalo species. The virus is known to be carried by the Nubian ibex. Alcelaphine herpesvirus 2 (AlHV-2), carried by the hartebeest and topi antelopes, has been reported to cause MCF in Barbary red deer and, experimentally, in bison (4).

MCFVs are both antigenically and genetically related. The presence of the 15-A antigenic peptide of gB and a high degree of homology in the DNA polymerase gene sequence characterize them. Simultaneous infections with multiple MCFV strains in a single host are possible (39). While these viruses typically cause subclinical infections in their natural hosts, they can lead to clinical disease in susceptible species such as cattle, deer, bison, and pigs (38).

MCFVs are present wherever clinically susceptible hosts are close to their wildlife reservoirs. The earliest described forms of MCF are the European and African forms. The African form (associated with AlHV-2) has been primarily reported from sub-Saharan African countries such as Kenya, Tanzania, and South Africa, where antelopes represent a significant component of the native wildlife. Blue and black wildebeests (Connochaetes spp.) serve as carriers and reservoir hosts for AlHV-1. The annual migration of these antelopes through the Maasai Mara and Serengeti regions threatens cattle populations in these areas. Approximately 10% of cattle herds in Kenya are lost annually due to the African form of MCF. Outside of Africa, OvHV-2 is the primary causative agent of MCF in domesticated animals, with domestic sheep acting as the primary reservoir hosts. The European form, or sheep-associated MCF caused by OvHV-2, is most commonly observed in domestic livestock, captive ruminants, and wildlife populations outside Africa. The disease occurs sporadically but is widely distributed across Europe, North and South America, the Middle East, Asia, Africa, and New Zealand. The American bison (Bison bison) is approximately 1,000 times more susceptible to clinical disease caused by OvHV-2 than domestic cattle (Bos taurus and Bos indicus), which show a high degree of resistance. Water buffalo are also more susceptible to OvHV-2 than cattle. Diseases associated with CpHV-2 have been reported not only in cervids but also in buffalo (38).

MCFV is a lymphoproliferative disease characterized by lymphoid cell accumulation in non-lymphoid organs, vasculitis, and T-lymphocyte hyperplasia in lymphoid tissues. Histological examination reveals necrosis in the respiratory, digestive, and urinary epithelial tissues. This necrosis is considered to be a consequence of systemic vasculitis affecting the brain and blood vessels. Vasculitis is a prominent pathological feature of MCF across all affected species. It is believed to result from immune dysregulation, leading to the accumulation of lymphocytes (4). The complex epidemiology and pathogenesis of MCF contribute to the challenges in fully understanding the disease. Like most gammaherpesviruses, MCFVs can establish latent, persistent infections in lymphoid tissues during the early stages of infection. The incubation period varies across species: approximately 14 days in rabbits, 21–90 days in rodents, and 16–29 days in cattle. Among affected cattle, approximately 95–100% succumb to the disease within 4–7 days after the onset of clinical signs (38).

OvHV-2 is primarily transmitted through direct contact or aerosol from lambs under one year of age. Lambs typically acquire the virus via aerosol exposure from other flock members between 3 and 6 months of age and begin actively shedding the virus between 6 and 9 months. Viral shedding decreases around 10 months and occurs at significantly lower levels in adults than in adolescents. Adult sheep can also become infected with OvHV-2 through natural contact and may intermittently shed large quantities of the virus. Clinically susceptible species usually acquire the virus via inhalation; however, ingesting virus-contaminated secretions through contaminated feed or water may also represent a transmission route. Colostrum and milk samples from infected sheep have tested strongly positive for OvHV-2 DNA, suggesting that mammary secretions may serve as an important source of infection for newborn lambs. High levels of OvHV-2 DNA have also been detected in ram semen, raising the possibility that vertical transmission may play a significant role in disease spread (40).

Clinical signs

MCF is a progressive, lymphoproliferative, and typically fatal disease. The main clinical signs include fever, profuse nasal discharge, ophthalmia, corneal opacity, generalized lymphadenopathy, upper respiratory tract erosions, and gastrointestinal tract leukopenia. Affected animals typically die within days or weeks following the onset of clinical signs. The clinical outcome can vary depending on the species and their level of susceptibility, and symptoms may also be species-specific (39). The disease may manifest in several clinical forms, including peracute, head and eye, alimentary, neurologic, and cutaneous forms. In susceptible Cervidae species, the clinical course is shorter than in cattle, and sudden death can occur. Highly susceptible species often present with the peracute form of the disease. In cattle, MCF generally follows an acute course, with the head and eye form being the most commonly observed. Affected animals may exhibit swelling of limb joints and a significant decrease in milk production. Some animals show neurological symptoms such as hyperesthesia, incoordination, and nystagmus. Approximately 25% of infected cattle may develop the chronic form of the disease, and mortality can reach up to 95%. Severe ocular lesions such as panophthalmitis and hypopyon are commonly observed in deer and bison. Infected animals may also display aggressive and violent behavior. The average time from onset to death is approximately 48 hours in deer, 3 days in bison, and 1 week in cattle (38).

Diagnosis

The diagnosis of MCF is based on clinical signs, histopathological features, and the detection of viral DNA via PCR. Histopathological confirmation includes evidence of vasculitis, lymphoid tissue hyperplasia, and the accumulation of lymphoid cells in non-lymphoid organs such as the brain, kidneys, and liver. A history of exposure to pastures recently grazed by sheep or antelopes often supports the diagnosis. However, the extended incubation period can complicate the clinical presentation. In cattle, the disease manifests sporadically and disseminates slowly within the herd. In conjunction with a history of contact with sheep or antelopes, the characteristic lesions and signs observed frequently serve as sufficient evidence for a presumptive diagnosis.

Nevertheless, the wide range of clinical manifestations may make differential diagnosis challenging, particularly for diseases such as Bovine Viral Diarrhea, Foot-and-Mouth Disease, Lumpy Skin Disease, and Infectious Bovine Rhinotracheitis. Given the prevalence of MCF in regions such as Southern Africa and Northern Europe, differentiation from Bluetongue virus infection is also critical. Both diseases can present with similar clinical signs, including lachrymation, stomatitis, coronitis, sloughing of the skin on the udder and mouth, and diarrhea. Therefore, laboratory confirmation through diagnostic testing is essential for a definitive diagnosis (38).

Treatment

Although no specific treatment for MCF exists, symptomatic therapies are commonly applied. These include using anti-inflammatory steroids, antibiotics to prevent secondary infections, and supportive fluid therapy. Oxytetracycline, sulfadimidine, procaine penicillin, and ceftiofur sodium can be administered

parenterally to prevent secondary bacterial infections. Supportive treatment may also include the administration of flunixin meglumine and vitamin A (38,40). Although recovery has been observed in some animals following treatment, it remains unclear whether these recoveries can be directly attributed to therapeutic intervention. Despite ongoing research over the past six decades, no effective commercial vaccine is available for AlHV-1. However, a field study using an attenuated AlHV-1 virus vaccine demonstrated a 56% reduction in infection rates in cattle exposed to antelope contact (38).

Prevention

The primary control strategy for MCF is to prevent interaction between susceptible and non-susceptible host species. This situation minimizes the risk of virus transmission from reservoirs and carrier animals to susceptible species (39). There is currently no commercially available effective vaccine. In addition to maintaining species separately, control programs may include preventing lambs from contacting infected sheep before they reach two months of age to produce OvHV-2-free flocks. Only seronegative animals should be introduced into herds. Maintaining the maximum possible separation between sheep and susceptible species is crucial; even in confined environments, a minimum distance of 1,000 meters should be maintained between them (40).

CONCLUSION

Herpesvirus infections pose significant threats to the cattle industry, leading to substantial health issues and economic losses due to their complex etiologies, wide host ranges, and variable clinical outcomes. This review focuses on BoHV-1, BoHV-5, PRV and MCFV as major pathogens affecting the respiratory, nervous and immune systems. The review examines the acute and subacute courses of the pathogens in particular species and the potential progression to peracute and fatal forms. Critically, these viruses can establish latent, persistent infections in ruminants, allowing them to persist for life and transform their hosts into long-term carriers. Their widespread distribution, capacity for latency, the high mutation potential of PRV, and their ability to cross species barriers collectively make control and eradication particularly challenging. Despite considerable progress in diagnostic methods, particularly through the utilization of PCR, serological analyses, virus isolation and histopathology, there is an urgent requirement to develop rapid, reliable and portable diagnostic tools suitable for field conditions. Treatment remains supportive mainly, as the availability of virus-specific antiviral agents is still limited. As a result, preventive veterinary practices remain paramount in managing these diseases. Vaccination is currently an effective control strategy for BoHV-1; however, the lack of effective and commercially available vaccines for BoHV-5, PRV, and MCFVs remains a significant concern. This underscores the importance of strict herd isolation, minimizing contact with reservoir hosts, and implementing comprehensive biosecurity measures. Future studies should focus on understanding virus-host interactions, preventing interspecies transmission, and developing next-generation vaccines, particularly for MCFVs and BoHV-5. In this regard, interdisciplinary approaches are promising for enabling more sustainable livestock health management under field and laboratory conditions.

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REFERENCES

1. Santos BS, Lemos RAA, Rech RR, Barros CSL, Rissi DR: Bovine herpesviral meningoencephalitis: Large case study and literature review. J Vet Diagn Invest, 37(3), 417–428, 2025. DOI: 10.1177/10406387251319804
2. Can-Sahna K, Abayli H, Ilgin M, Aksoy M: Investigation of some neuroinfectious viral agents in Turkish cattle: First detection and molecular characterization of bovine herpesvirus type 5 (BoHV5). Pak Vet J, 44(3), 896–902, 2024. DOI: 10.29261/pakvetj/2024.211
3. Ostler JB, Jones C: The bovine herpesvirus 1 latency-reactivation cycle, a chronic problem in the cattle industry. Viruses, 15(2), 552, 2023. DOI: 10.3390/v15020552
4. Saura-Martinez H, Al-Saadi M, Stewart JP, Kipar A: Sheep-associated malignant catarrhal fever: Role of latent virus and macrophages in vasculitis. Vet Pathol, 58(2), 332–345, 2020. DOI: 10.1177/0300985820978310
5. Kumar N, Chander Y, Riyesh T, Khandelwal N, Kumar R, Kumar H, Tripathi BN, Barua S: Isolation and characterization of bovine herpes virus 5 (BoHV5) from cattle in India. PloS One, 15(4), e0232093, 2020. DOI: 10.1371/journal.pone.0232093
6. Marin M, Burucúa M, Rensetti D, Rosales JJ, Odeón A, Pérez S: Distinctive features of bovine alphaherpesvirus types 1 and 5 and the virus-host interactions that might influence clinical outcomes. Arch Virol, 165, 285–301,2020. DOI: 10.1007/s00705-019-04494-5
7. International Committee on Taxonomy of Viruses. 2025. ICTV. https://ictv.global/
8. Johnson LAY, McGavin MD, Simmons GC: Diseases of the bovine central nervous system in south east Queensland. Aust Vet J, 38(10), 397–403, 1962. DOI: 10.1111/j.1751-0813.1962.tb04013.x
9. Oberto F, Carella E, Caruso C, Acutis PL, Lelli D, Bertolotti L, Masoero L, Peletto S: A qualitative PCR assay for the discrimination of bubaline herpesvirus 1, bovine herpesvirus 1 and bovine herpesvirus 5. Microorganisms, 11(3), 577, 2023. DOI: 10.3390/microorganisms11030577
10. Del Médico Zajac MP, Ladelfa MF, Kotsias F, Muylkens B, Thiry J, Thiry E, Romera SA: Biology of bovine herpesvirus 5. Vet J, 184(2), 138–145, 2010. DOI: 10.1016/j.tvjl.2009.03.035
11. Verma A, Kamboç H, Handelwal N, Kumar R, Riyeş T, Kumar N: Genome sequencing of bovine herpesvirus 5 (BoHV-5) isolated from India. Microbiol Resour Announc, 14, e00950-24, 2024. DOI: 10.1128/mra.00950-24
12. Raaperi K, Orro T, Viltrop A: Epidemiology and control of bovine herpesvirus 1 infection in Europe. Vet J, 201(3), 249–256, 2014. DOI: 10.1016/j.tvjl.2014.05.040
13. El-Mayet F, Jones C: Stress can induce bovine alpha-herpesvirus 1 (BoHV-1) reactivation from latency. Viruses, 16(11), 1675, 2024. DOI: 10.3390/v16111675
14. Callan RJ, Van Metre DC: Viral diseases of the ruminant nervous system. Vet Clin North Am Food Anim Pract, 20(2), 327–vii, 2004. DOI: 10.1016/j.cvfa.2004.02.001
15. Pinheiro IAB, Dias BP, Ferreira JM, Dos Santos AJF, Moron SE, Silva GMDL, de Lima LBD, de Cordova FM: Bovine herpesvirus meningoencephalitis in the State of Tocantins, Brazil. Braz J Vet Med, 46, e004023, 2024. DOI: 10.29374/2527-2179.bjvm004023
16. Jiang L, Zhang G, Wang P, Niu X, Liu Q, Zhang S, Gao W, Li Y: Simultaneous detection of bovine viral diarrhea virus (BVDV) and bovine herpesvirus 1 (BoHV-1) using recombinase polymerase amplification. Sci Rep, 14, 10169, 2024. DOI: 10.1038/s41598-024-56869-7
17. Liu W, Zhang K, Cheng J, Yu S, Cheng C, Jiang B, Zhou L, Li Y: Development and evaluation of a time-resolved fluorescence labelled immunochromatographic strip assay for rapid and quantitative detection of bovine herpesvirus 1. Front Microbiol, 15, 1371849, 2024. DOI: 10.3389/fmicb.2024.1371849
18. Pastenkos G, Lee B, Pritchard SM, Nicola AV: Bovine herpesvirus 1 entry by a low-pH endosomal pathway. Virol J, 92, e00839-18, 2018. DOI: 10.1128/jvi.00839-18
19. Cerracchio C, Amoroso MG, Piccolo M, Ferraro MG, Nocera FP, De

Martino L, Serra F, Irace C, Tenore GC, Novellino E, Santamaria R, Fiorito F: Antiviral activity of Taurisolo® during bovine alphaherpesvirus 1 infection. Virus Res, 336, 199217, 2023. DOI: 10.1016/j.virusres.2023.199217
20. Zeedan GS, El-Razik KA, Allam AM, Abdalhamed AM, Zeina HA: Evaluations of potential antiviral effects of green zinc oxide and silver nanoparticles against bovine herpesvirus-1. Am J Anim Vet Sci, 8(4), 433–443, 2020. DOI: 10.17582/journal.aavs/2020/8.4.433.443
21. Fiorito F, Cerracchio C, Salvatore MM, Serra F, Pucciarelli A, Amoroso MG, Nicoletti R, Andolfi A: Antiviral property of the fungal metabolite 3-O-Methylfunicone in bovine herpesvirus 1 infection. Microorganisms, 10(1), 188, 2022. DOI: 10.3390/microorganisms10010188
22. Dezengrini R, da Silva SC, Weiss M, Kreutz LC, Weiblen R, Flores EF: Activity of three antiviral drugs against bovine herpesviruses 1, 2 and 5 in cell culture. Pesq Vet Bras, 29(1), 19–24, 2009. DOI: 10.1590/S0100-736X2009000100004
23. Righi C, Franzoni G, Feliziani F, Jones C, Petrini S: The cell-mediated immune response against bovine alphaherpesvirus 1 (BoHV-1) infection and vaccination. Vaccines, 11(4), 785, 2023. DOI: 10.3390/vaccines11040785
24. Bo Z, Li X: A review of pseudorabies virus variants: Genomics, vaccination, transmission, and zoonotic potential. Viruses, 14(5), 1003, 2022. DOI: 10.3390/v14051003
25. Ye N, Feng W, Fu T, Tang D, Zeng Z, Wang B: Membrane fusion, potential threats, and natural antiviral drugs of pseudorabies virus. Vet Res, 54, 39, 2023. DOI: 10.1186/s13567-023-01171-z
26. Zheng HH, Fu PF, Chen HY, Wang ZY: Pseudorabies virus: From pathogenesis to prevention strategies. Viruses, 14(8), 1638, 2022. DOI: 10.3390/v14081638
27. Chen X, Yu Z: Insight into the interaction mechanism of pseudorabies virus infection. Biology, 13(12), 1013, 2024. DOI: 10.3390/biology13121013
28. Liu Q, Kuang Y, Li Y, Guo H, Zhou C, Guo S, Tan C, Wu B, Chen H, Wang X: The epidemiology and variation in pseudorabies virus: A continuing challenge to pigs and humans. Viruses, 14(7), 1463, 2022. DOI: 10.3390/v14071463
29. Tan Lei, Xu K, Yang S, Wang W, Lin G, Yang L, Yao J, Wang A: First report of variant pseudorabies virus infection in goats in China: a neglected infectious disease to ruminants. Authorea. 2024. DOI: 10.22541/au.170664805.56815073/v1
30. Duan Y, Liu N, Tan L, Gao L, Zhu G, Tao Z, Liu B, Wang A, Yao J: Isolation and biological characterization of a variant pseudorabies virus strain from goats in Yunnan Province, China. Vet Res Commun 49, 149, 2025. DOI: 10.1007/s11259-025-10703-1
31. Liu A, Xue T, Zhao X, Zou J, Pu H, Hu X, Tian Z: Pseudorabies virus associations in wild animals: Review of potential reservoirs for cross-host transmission. Viruses, 14(10), 2254, 2022. DOI: 10.3390/v14102254
32. Sehl J, Teifke JP: Comparative pathology of pseudorabies in different naturally and experimentally infected species—A review. Pathogens, 9(8), 633, 2020. DOI: 10.3390/pathogens9080633
33. Yıldırım S, Özkan C, Yener Z, Cetin M, Kozat S: Immunohistochemical Diagnosis of Pseudorabies (Aujeszky's Disease) in a Cow in Van, Turkey. Kafkas Univ Vet Fak Derg, 23(1), 173-176, 2017. DOI: 10.9775/kvfd.2016.16071
34. Pomeranz LE, Reynolds AE, Hengartner CJ: Molecular Biology of Pseudorabies Virus: Impact on Neurovirology and Veterinary Medicine. Microbiol Mol Biol Rev69, 2005. DOI: 10.1128/mmbr.69.3.462-500.2005
35. Wang G, Chen R, Huang P, Hong J, Cao J, Wu Q, Zheng W, Lin L, Han Q, Chen Y, Xia N: Adefovir dipivoxil efficiently inhibits the proliferation of pseudorabies virus in vitro and in vivo. Antiviral Res, 186, 105014, 2021. DOI: 10.1016/j.antiviral.2021.105014
36. Freuling CM, Müller TF, Mettenleiter TC: Vaccines against pseudorabies virus (PrV). Vet Mic, 206, 3–9, 2017. DOI: 10.1016/j.vetmic.2016.11.019
37. Li L, Wang R, Hu H, Chen X, Yin Z, Liang X, He C, Yin L, Ye G, Zou Y, Yue G, Tang H, Jia R, Song X: The antiviral activity of kaempferol against pseudorabies virus in mice. BMC Vet Res, 17, 247, 2021. DOI: 10.1186/s12917-021-02953-3
38. Sharma B, Parul S, Basak G, Mishra R: Malignant catarrhal fever (MCF): An emerging threat. J Entomol Zool Stud, 7(3), 26–32, 2019.
39. Bianchessi L, Rocchi MS, Maley M, Piccinini R, Turin L: Molecular tools to identify and characterize malignant catarrhal fever viruses (MCFV) of ruminants and captive Artiodactyla. Viruses, 14(12), 2697, 2022. DOI: 10.3390/v14122697
40. Meravi P, Tiwari A, Singh B, Mourya A, Baghel PRS: Emerging threats of sheep-associated malignant catarrhal fever in India: A review. J Pharmacogn Phytochem, 8(5), 844–848, 2019.

CURRENT VETERINARY SCIENCE

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Current Veterinary Science

Review Article

Common Errors in Breeding Management and Incubation Practices of Geese Raised by Local Geese Farmers

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ABSTRACT

This review was written to identify common errors encountered in breeder selection and incubation management in geese raised under local farming conditions. Goose farming is a low-cost and high-return form of animal production, particularly prevalent in rural areas. In these regions, goose farming is mostly based on traditional methods. This reliance on traditional practices and a lack of knowledge often leads to poor incubation outcomes and negatively affects overall productivity. Notable issues include the insufficient consideration of genetic structure, age, body condition, and sex ratio during breeder selection. During the incubation period, mistakes are frequently observed in the collection, storage, and turning of eggs, as well as in maintaining appropriate temperature and humidity levels. This review is based on direct field observations. In light of these observations, it is recommended that training activities aimed at raising awareness among farmers be increased to reduce the problems local goose farmers face. Furthermore, farmers should be encouraged to adopt incubator use instead of traditional practices and natural incubation methods, and necessary equipment support should be provided.

Keywords: Breeder selection, Goose farming, Incubation errors, Traditional practices

INTRODUCTION

When examining the goose population in Türkiye, the Eastern Anatolia Region ranks first at the regional level. Within this region, the provinces of Kars, Ardahan, and Muş account for approximately 55% of the country's total goose population (1). The geographical structure, climate, and cultural characteristics of Eastern Anatolia strongly support goose farming. In addition to the vast pasture and meadow areas, the presence of water resources such as streams and the region's cold climate make goose farming particularly advantageous in this area (2, 3). In the regional ranking, the Central Anatolia Region comes second due to the goose population in provinces such as Yozgat, Konya, Ankara, and Çankırı. The Southeastern Anatolia Region ranks third, followed by the Black Sea Region in fourth place (1).

In some countries today, goose farming is carried out at a highly significant economic scale, whereas in Türkiye, commercial-level goose production has not yet been established. The main reason for this is a narrowly regional culture of goose meat consumption that has persisted in Türkiye until recent years. Historically, goose farming in Türkiye has been practiced at a regional level and within small family farms, primarily using local goose genotypes. The characteristics of these indigenous geese raised in Türkiye have not yet been fully identified or documented (4, 5).

The aim of this review is to examine the common husbandry errors encountered in breeder management and incubation practices in goose flocks raised by local farmers, based on existing literature, and to reveal the impacts of these errors on production performance. This study serves as a guide to help local producers identify and avoid frequent mistakes while offering practical solutions to address these issues. Additionally, it aims to highlight the lack of education and technical support, to contribute to the sustainability of goose farming.

ERRORS IN BREEDER MANAGEMENT

In recent years, the increasing introduction of foreign goose genotypes in Türkiye and their uncontrolled crossbreeding with local breeds have led to significant problems in goose farming. This situation has particularly resulted in the disruption of genetic homogeneity, inconsistencies in performance traits, and difficulties in flock management. Some farms raise multiple foreign-origin goose genotypes within a single mixed flock to obtain higher egg and gosling yields from breeders, which leads to unplanned crossbreeding. However, production with a single genotype is much more appropriate in maintaining reliable performance monitoring and ensuring more accurate intra-flock control and comparisons. One of the most fundamental mistakes made by farmers across the country is the random crossbreeding of foreign genotypes with

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each other or local geese. Therefore, guiding producers toward using a single genotype is crucial for preserving genetic integrity and enhancing production efficiency (6, 7).

Breeder management is one of the most critical factors affecting productivity and flock quality in poultry farming. In goose production, factors such as breeder selection, age, nutrition, housing, and maintaining an appropriate sex ratio play a decisive role in egg production and incubation characteristics (6, 8). However, field observations and producer experiences indicate that various errors in breeder management are quite common.

The body condition of breeder individuals is of great importance in production performance. Selecting individuals who are either excessively thin or overweight can negatively affect reproductive performance and lead to reduced fertility rates (8). In goose farming, determining an appropriate sex ratio is crucial for effective flock management. In particular, an incorrect ratio between male and female breeders can directly impact fertility rates. The generally recommended male-to-female ratio is 1:3–4 or 1:5–6 (8). However, in field practices, failure to adhere to this ratio or the absence of a sufficient number of healthy males in the flock often increases the number of unfertilized eggs, thus causing production losses. Additionally, an excessive number of female individuals and the use of inexperienced male geese can also lead to a decline in productivity (6).

Breeder age in poultry is an essential factor affecting egg production and fertility. Using very young or old individuals negatively impacts fertility rates and egg yield. Selecting healthy and reproductively active individuals within the optimal production age is crucial for sustainable production success (9). Nutrition of breeding geese directly influences reproductive performance and health, with deficiencies in energy, protein, calcium, and vitamins adversely affecting egg production and fertility. A balanced feeding program appropriate to age, physiological condition, and season is essential for sustainable and efficient farming (10, 11).

ERRORS MADE BEFORE INCUBATION PROCEDURES

One of the most critical factors affecting incubation performance is the accuracy of the procedures carried out before the incubation process begins. Mistakes at this stage can negatively impact embryonic development, reducing fertility rates and lowering hatchability. In particular, failure to collect fertile eggs under appropriate conditions and neglecting temperature, humidity, and hygiene requirements during transportation and storage increase embryo losses. Therefore, thoroughly implementing hygienic and technical measures to preserve egg quality before starting incubation procedures is a fundamental requirement for a successful incubation process (6, 8, 10).

Timely collection and proper storage of hatching eggs are critical for embryonic development and incubation success. Delayed collection increases the risk of contamination and microbial infection (12, 13, 14), while high temperatures and prolonged storage negatively affect embryo viability. Therefore, it is recommended that eggs be stored at 15–18°C with 55–65% relative humidity. The storage period should not exceed 7–10 days (6, 8).

Washing hatching eggs damages the protective cuticle layer on the eggshell surface, increasing the risk of microbial contamination and adversely affecting embryo health. Using chemical cleaning agents or hot water can increase shell permeability, creating an unsuitable gas exchange environment for the embryo (12, 15). Therefore, dirty eggs should be gently wiped or lightly cleaned with a dry cloth or soft brush. Eggs from breeder flocks should be collected several times a day. Infrequent egg collection can accelerate broodiness in females, reducing egg production and increasing the number of dirty and cracked eggs in the flock (13).

ERRORS MADE DURING INCUBATION PROCEDURES

Accurate adjustment of environmental parameters during the artificial incubation process is crucial for healthy embryo development and high hatchability rates. One of the most common errors encountered in this process is improperly regulating temperature and humidity levels. The optimal incubation temperature for goose eggs during development is 37.8°C, at which the best embryonic growth is achieved (16). The humidity inside the incubator is reported to need to be between 65-75% (8, 17, 18, 19) and increased to 80% during the hatching period. An 80% humidity level during hatching helps the eggshell to crack. Relative humidity inside the machine, either too low or too high, negatively affects incubation outcomes. Environmental conditions outside these ranges can slow embryo development, cause deformities, and lead to embryonic mortality (20, 21, 22).

Failure to turn the eggs at regular intervals or insufficient turning frequency can cause the embryo to adhere to the membranes and eggshell surface, leading to circulatory disorders and hatching difficulties (8, 23). On the other hand, inadequate ventilation results in carbon dioxide accumulation and oxygen deficiency in the incubation environment, negatively affecting embryo development. Considering all these factors, careful control of fundamental environmental parameters such as temperature, humidity, turning, and ventilation in artificial incubation systems is essential to achieve a successful hatching (24).

Unlike many commonly raised poultry species, goose eggs undergo cooling and spraying treatments during certain periods of the incubation process. The cooling and spraying procedures begin on the 5th day of incubation. Initially, the cooling is applied for about 5 minutes daily, but this duration gradually increases, and from the 15th day onward, it is applied for 30 to 35 minutes. If the cooling process is not performed adequately, hatchability rates can decrease by up to 20% (8).

Goose breeding in Türkiye has not yet reached the desired levels compared to leading countries worldwide. Although goose breeding is carried out in almost every province, its development has some obstacles. One of the most critical problems is that the goose meat market is limited only to the regions where production occurs and is not sufficiently promoted. Another issue is that goose breeding is mainly conducted in small, low-capacity family farms, and commercial enterprises are lacking. To establish commercial enterprises, there is a need for farms engaged in breeding stock production and incubation facilities that can increase the number of animals. The slaughtering conditions in small farms are inadequate. The slaughterhouse problem for small enterprises must be resolved. Additionally, large enterprises need support to establish incubation facilities, slaughterhouses, and cold storage warehouses (25).

CONCLUSION

Although Türkiye is among the countries with high potential for goose breeding, modern and commercial breeding has not yet been carried out. The production, primarily carried out in rural areas by local farmers using traditional methods, limits productivity and hinders sectoral development. Effective training programs for producers and increased government support are of great importance for the improvement and economic efficiency of goose breeding. Resolving the problems faced by breeders is necessary for the sustainability of the sector. Additionally, comprehensive and widespread training programs are essential to minimize errors during the breeding process.

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REFERENCES

1. TÜİK (2024): Türkiye İstatistik Kurumu http://www.tuik.gov.tr. Hayvansal Üretim İstatistikleri. Erişim Tarihi: 20.05.2025.
2. Kırmızıbayrak T, Önk K, Yazıcı K: Kars ilinde serbest çiftlik koşullarında yetiştirilmiş yerli ırk kazların kesim ve karkas özellikleri üzerine yaş ve cinsiyetin etkisi. Kafkas Univ Vet Fak Derg, 17(1): 41-45, 2011. DOI:10.9775/kvfd.2010.2375
3. Demir P, Kırmızıbayrak T, Yazıcı K: Socio-economic importance of goose breeding. Ankara Univ Vet Fak Derg, 60(2): 129-34, 2013. DOI: 10.1501/Vetfak_0000002566
4. Tilki M, Saatcı M: Dünyada ve Türkiye'de kaz yetiştiriciliği. Turk Klin J Reprod Artif Insemin-Spec Top, 2(1): 7-14, 2016.
5. Önk K, Kırmızıbayrak T: Kars ili yetiştirici koşullarındaki kazların (Anser anser) yumurta verimi, kuluçka, büyüme, kesim ve karkas özellikleri (I. yumurta verimi ve kuluçka özellikleri). Turk J Agric Food Sci Technol, 7(3): 543-549, 2019. DOI: 0000-0002-5618-2988
6. Karadağ S: Egg Production and Characteristics and Hatching Characteristics of Gray Hungarian Geese and Mast Geese Crossbreeds in a Family Farm in Kars Province, Kafkas University, Institute of Health Sciences, Department of Zootechnics, PhD Thesis, Kars, 2023.
7. Kırmızıbayrak T, Karadağ S, Kuru BB: Slaughter and carcass traits of Gray Hungarian and German Mast Geese. Van Vet J, 35(1): 64-69, 2024. DOI: 10.36483/vanvetj.1386149
8. Salamon A: Fertility and hatchability in goose eggs: a review. İnt J Poult Sci, 19(2): 51-65, 2020. DOI: 10.3923/ijps.2020.51.65
9. Drzazga BB, Banaszewska D, Charuta A, Koncerewicz A: Influence of age on egg characteristics and reproduction features of Coluda White Geese. Europ Poult Sci, 80(142), 2016. DOI:10.1399/eps.2016.142
10. Kingori A: Review of the factors that influence egg fertility and hatchability in poultry. Int J Poult Sci, 10(6): 483-492, 2011.
11. Ogbu O, Oguike M: Hatchability of fertilite egg in poultry industry. J Agric Sustain, 12(1): 107-123, 2018.
12. Eroglu M, Erisir Z, Simsek UG, Mutlu S I, Baykalir Y, Gungoren A, Adiyaman G: Effects of washing dirty eggs of geese with boric acid and vinegar on hatchability and microbial loads. J Anim Plant Sci, 35(2): 354-363, 2025. DOI:10.36899/JAPS.2025.2.0029
13. Wales A, Davies R: Review of hatchery transmission of bacteria with focus on Salmonella, chick pathogens and antimicrobial resistance. World's Poult Sci J, 76(3): 517-536, 2020. DOI: 10.1080/00439339.2020.1789533
14. Salamon A: The reproductive behaviour of geese and its implications on production and welfare. World Poult Sci J, 81(1): 103-116, 2025. DOI: 10.1080/00439339.2024.2437173
15. Coulibaly F, Onbaşılar EE, Bakır B, Sarıçam İnce S: The effects of using UV light instead of formaldehyde in disinfection of hatching eggs on shell microbial load, embryo development, hatchability, and chick characteristics. Int J Environ Health Res, 34(8): 2852-2862, 2024. DOI: 10.1080/09603123.2023.2276361
16. Lourens A, Vanden Brand H, Meijerhof R, Kemp B: Effect of eggshell temperature during incubation on embryo development, hatchability, and posthatch development. Poult Sci, 84(6): 914-920, 2005. DOI: 10.1093/ps/84.6.914
17. Biesiada B, Banaszewska D, Koncerewicz A, Jóźwik A, Horbańczuk J: Examination of changes in selected external and internal egg traits during the geese laying season and their effect on gosling hatching results. Europ Poult Sci, 79, 1-11, 2015. DOI: 10,1399/Eps. 77
18. Kucharska J, Adamski M, Kuzniacka J, Kowalska E: Influence of the weight of hatching eggs on the hatchability indices and on the body weight of geese in rearing and after fattening with oats. Acta Sci Pol Zootechnica, 15, 67-82, 2016. DOI:10.21005/asp.2016.15.3.06
19. Amantai S, Omarkhozha N, Kazhgaliev NJ, Saginbaeva MB, Arney D: Hatchability and hatchling sex ratio depending on holding period and physical parameters of hatching eggs. Eur Poult Sci, Vol. 82, 228, 2018. DOI: 10.1399/eps.2018.228
20. Nakage ES, Cardozo JP, Pereira GT, Boleli IC: Effect of temperature on incubation period, embryonic mortality, hatch rate, egg water loss and partridge chick weight (Rhynchotus rufescens). Braz J Poult Sci, 5, 131-135, 2003. DOI: 10.1590/S1516-635X2003000200007
21. Tainika B, Abdallah N, Damaziak , Waithaka Ng'ang'a, ., Shah T, Wójcik W: Egg storage conditions and manipulations during storage: effect on egg quality traits, embryonic development, hatchability and chick quality of broiler hatching eggs. World's Poult Sci J, 80(1): 75-107, 2024. DOI: 10.1080/00439339.2023.2252785
22. Fulla ST, Gebreslassie AH: Evaluation of Egg Production, Fertility, Hatchability, Embryonic Mortality and Chick Quality of Different Chickens. Int J Anim Sci Technol, 8(3): 55-65, 2024. DOI: 10.11648/j.ijast.20240803.14
23. Salamon A, Kent JP: Manual egg turning is necessary for optimal hatching in geese. Int J Poult Sci, 15(2): 57, 2016. DOI: 10.3923/ijps.2016.57.61
24. Çopur G: Damızlık yetiştiriciliğinde kuluçka aksaklıkları. Hayvansal Üretim, 45(1): 31-35, 2004.
25. Karadağ S, Kırmızıbayrak T: Goose as an Increasingly Popular Poultry in Türkiye. VII. International Halich Congress on Multidisciplinary Scientific Research, p. 1095-1101, 2024. ISBN: 978-625-367-639-1

CURRENT VETERINARY SCIENCE

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Current Veterinary Science

Case Report

Surgical Treatment of Mammary Melanoma in a Mare: A Case Report

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ABSTRACT

Mammary tumors are exceptionally uncommon in horses, whereas melanomas are frequently observed in gray horses. Limited information is available regarding the treatment options and corresponding success rates for such cases. This case report aims to describe the surgical treatment of a malignant melanoma in a gray mare. A 5-year-old dark gray mare weighing 440 kg was referred to Kafkas University Animal Health Education Research and Practice Hospital due to a slowly growing pigmented mass located in her right peri-mammary region. Detailed clinical examination and lung X-ray did not reveal any specific metastatic findings. Ultrasonography (USG) and Doppler examination showed an oval solid hypoechoic mass with a well-defined hyperechoic margin and limited vascularization. Surgical extraction of the mass was successfully performed under inhalation anesthesia. Histopathological examination of the removed tumoral mass revealed numerous spindles or epithelioid-shaped neoplastic cells containing large brownish-black granular melanin pigments in their cytoplasm, which were widely distributed throughout the mass. This case demonstrates that careful post-operative monitoring can lead to successful outcomes in the surgical management of rare conditions such as mammary gland melanoma/carcinomas in mares. However, further studies are needed to conduct long-term follow-ups of survival rates.

Keywords: Mare, Melanoma, Surgical treatment.

INTRODUCTION

Melanomas are cutaneous tumors originating from pigment-producing melanocytes. In horses, melanomas have a prevalence of 4-15% and are among the most commonly diagnosed tumors in horses with gray hair (1, 2). Although many melanocytic lesions initially appear as slow-growing or benign, a significant number of them develop malignant features over time, increasing local invasiveness and constituting a risk of systemic metastasis (1, 3). Melanoma in horses is a common neoplasm, particularly in older horses with a genetic predisposition resulting from mutations in specific regulatory genes, which creates challenges in tumor treatment planning (4, 5). Although tumor extirpation by surgical excision has long been considered the mainstay of treatment for localized melanoma, it is difficult to obtain complete and oncological safe resection margins in areas with anatomically specific challenges such as the perianal region, tail, and mammary glands, resulting in high local recurrence rates (1, 6).

It is generally accepted that the diagnosis of melanocytic tumors in horses can be established reliably from macroscopic appearance and clinical findings. Reported case studies and retrospective studies show that promising results have been obtained with surgical methods, but they also present some challenges. In one reported case, a mare underwent resection for an intraocular neuroepithelial tumor followed by evidence of metastatic mammary carcinoma, suggesting that in multifactorial cases, surgical intervention on a tumor at a single anatomical site may sometimes not adequately control recurrences (7). In addition to surgery, innovative techniques provide important complementary approaches to enhance the efficacy of treatment when complete excision is technically challenging. Moreover, the integration of precise imaging modalities such as three-dimensional ultrasonography into preoperative planning has contributed to improved surgical results by ensuring a more accurate definition of tumor margins (6, 8). Although some studies have focused on topical treatments or intratumorally administered chemotherapeutics, surgical intervention remains the primary treatment modality when total resection is possible (2, 9).

In the present case report, the application of the surgical excision approach in treating melanoma in the mammary region of a mare, including the determination of resection margins supported by preoperative planning and modern imaging techniques, as well as post-operative care and follow-up after diagnosis, is considered in detail.

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CASE HISTORY

This case summarizes the clinical diagnosis and treatment of a tumorous mass in a 5-year-old, 440 kg, gray-skinned mare that was brought to the Kafkas University Animal Health Education, Research, and Training Hospital and was diagnosed with a pigmented mass in the right mammary region. The anamnesis reported that the mass had started as a small lump over the last 10 months and had grown slowly, but recently reached a size larger than the palm. It was determined that the mare was regularly monitored. Its general condition and feed consumption were normal. There were no issues, such as a decline in body condition or respiratory problems. The mass caused the animal to experience restlessness and anxiety due to its constant contact with its hind limbs and abdominal area, and a decrease in work performance as it was used as a work animal.

Clinical and ultrasonographic examination

In general, clinical examination determined that the patient's overall condition and attentiveness to the environment were normal. The vital signs (respiration, pulse, body temperature) were within physiological limits, and the hair coat was normal. In the detailed clinical examination and thoracic radiography, no specific metastatic findings were observed. Clinical inspection revealed a single solid mass in the right mammary area, larger than the palm, with irregular contours and dense black pigmentation on the surface facing the ground (Figure 1a-b). On palpation, the mass was found to have a hard structure connected to the skin of the right mammary lobe and to penetrate subcutaneously, originating from a specific region. No other mass was found in the region.

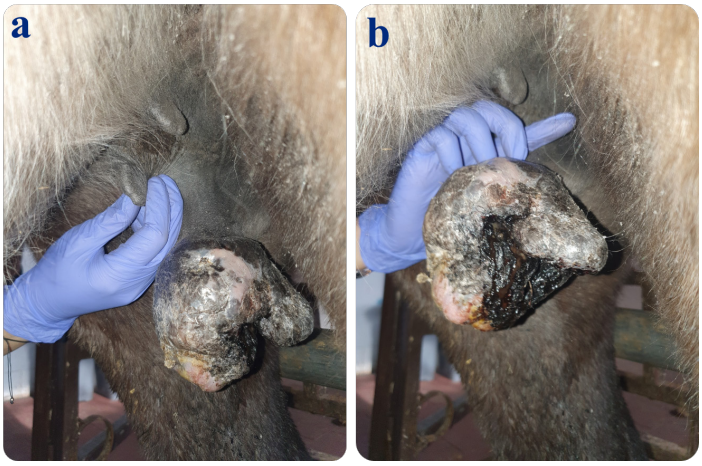

Figure 1: Clinical appearance of an irregular tumoral lesion in the mammary gland (a-b).

Ultrasonographic (USG) and Doppler examination revealed an oval, solid, hypoechoic mass with a well-defined hyperechoic border and poor vascularization (Figure 2).

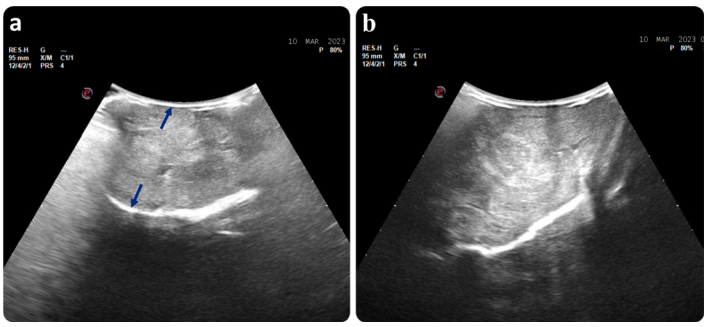

Figure 2: B-mode ultrasonography of the tumoral mass from different directions and hyperechoic capsule (a-b, dark blue arrows).

Surgical treatment

The preoperative clinical examination of the case revealed normal cardiovascular and respiratory values (pulse rate 37 bpm, respiratory rate 12/min). Pre-anesthesia was induced with detomidine hydrochloride (Dormosedan®, 20 µg/kg IV, Zoetis Animal Health, Florham Park, NJ) for about 10 minutes, and the mare was restrained by the Berlin method and placed on the operation mat. After sedation, rapid induction was achieved with ketamine hydrochloride (Ketasol 10%, 2 mg/kg IV, Interhas, VetViva Richter GmbH, Austria) in the pre-induction phase. An endotracheal tube was administered, and general anesthesia was maintained with sevoflurane (Sevoflurane-Baxter, Baxter Healthcare Corp., Puerto Rico, USA) inhalation anesthesia. After standard surgical procedures were performed, the tumor was extirpated by controlled dissection of the mass, whose borders were determined by clinical and USG examinations. Subsequently, the subcutaneous connective tissue was closed using an absorbent suture (PGLA, 0, 2/0 Trusynth Healthium Medtech, India) to minimize tissue gaps. Finally, the operation was completed with a simple continuous suturing technique to preserve the aesthetic and functional integrity of the skin (Figure 3a-b).

Figure 3: Surgical procedure (a-b) and post-operative scar region at 3 months (c, arrowheads).

Meloxicam 0.6 mg/kg, IV (Maxicam, Sonavel Türkiye) was used as an analgesic for post-operative pain management, and 10,000 IU benzyl penicillin procaine/day and 10 mg dihydrostreptomycin/kg, IM (Reptopen, Ceva Animal Health, France) were administered for 5 days for broad-spectrum prophylactic treatment. Nitrofurazone (Furacin 0.2%, Sanofi Türkiye) was applied topically to prevent infection at the incision site. At the end of the three-month clinical follow-up, the patient had recovered with no complications (Figure 3c), and no recurrence was found in the tumor resection area or other parts of the body during the post-operative follow-up period.

Histopathological diagnosis

In the prepared tissue (Figure 4a), the tumoral lesions taken from the mare were fixed in 10% formaldehyde solution, and after routine tissue follow-up procedures, 5-micron-thick sections were prepared from the paraffin blocks obtained, and Hematoxylin & Eosin staining was performed. Neoplastic cells containing intensive, large, brownish-black granular melanin pigments in their cytoplasm were observed spread over a large area of the tumoral mass (Figure 4b). There was a significant nuclear-to-cytoplasmic ratio, heterogeneous nuclei, and sometimes multiple mitotic figures. Furthermore, the band-like arrangement of melanoma cells in the dermis layer was determined to be an essential criterion for confirming the diagnosis and also indicates the tumor's invasive potential and tendency to infiltrate surrounding tissues. Accompanied by these histopathological findings, the diagnosis was confirmed by supporting the classical melanoma histomorphology, and the intensity of melanin pigmentation provided certainty to the diagnosis.

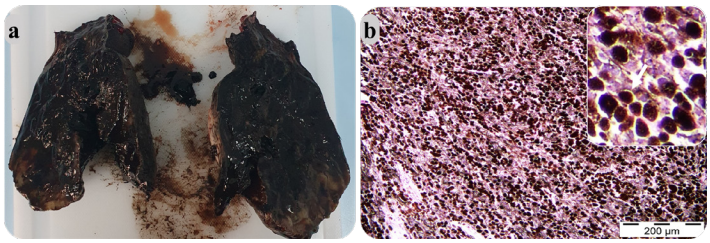

Figure 4: Macroscopic section of the tumor (a), histopathologic observation of neoplastic cells (b, thick white arrow).

DISCUSSION

It was reported that melanocytic tumors constitute 6-15% of all equine cutaneous tumors and 34% of total neoplasms in horses (10). Statistical analyses reveal that there is a marked predisposition to the formation of melanocytic tumors (EMT: Equine Melanocytic Tumors) especially in horses with gray hair (63.27%, $P < 0.01$) and the prevalence of the most malignant EMT types is significantly increased in horses over 15 years of age (70%, $P < 0.05$). These tumors may be benign in the beginning, but data from the literature suggest that all EMTs have the potential to undergo a malignant transformation and even develop distant metastases (11). A black color characterizes EMTs, but (especially high-grade anaplastic melanomas) may range from pale pink to white or marble-like in color. In addition to the more common occurrence of EMT in gray horses, these tumors can also develop in other horses. Typical areas of localization include the ventral side of the tail, perianal region, perineum, external genitalia, parotid gland region, mammary gland, periocular region, and lips (3, 10, 12, 13). The presented case was a gray-brown mare; the anatomical location of the mass and clinical findings were evaluated, resulting in a preliminary diagnosis of melanoma, consistent with the literature information.

Equine melanomas account for approximately 15% of all cutaneous neoplasms; however, their incidence increases sharply in gray hair horses, where progressive hair loss is often accompanied by the gradual appearance of multiple melanocytic masses that grow, coalesce, and sometimes undergo malignant transformation, highlighting the critical need for lifelong dermatologic monitoring and early intervention (14, 15, 16, 17). Although congenital lesions are rare in young horses, melanoma development begins around 6 years of age, when graying of the coat starts, and this risk can be as high as 80% in gray horses over 15 years of age (17, 18, 19). Furthermore, the clinical course of melanoma in horses is slower than in other species, such as humans and dogs, with lower rates of invasion and metastasis (20, 21, 22, 23, 24). Moreover, the effects of the time factor on the clinical course of equine melanomas have been clearly demonstrated. The observed 11.2-fold increase in tumor size over time (25) and an increase in the number of tumors carried by each horse (26) suggest that patients may require more invasive and challenging surgical techniques in the event of late intervention. Accordingly, late intervention results not only in the growth of the current tumor but also in an increased risk of new lesions appearing in the future. Similarly, a review of the clinical course of EMT has demonstrated that early diagnosis and surgical excision significantly reduce the risk of progressive invasive complications and distant metastasis by preventing an increase in tumor size and tumor number. Surgical excision of tumors located in the perianal, perirectal, and ventral surface of the tail has been reported to be locally curative, and recurrence has been emphasized to be minimal (6, 27). Furthermore, the simultaneous presence of two rare tumors affecting the eye and mammary gland, intraocular neuroepithelial neoplasm and metastatic mammary carcinoma, which are diagnosed in horses in a short period (e.g. within 9 months), reveals the vital importance of early intervention and points out that post mortem and immunohistochemical (IHC) evaluations provide diagnostic certainty (6, 7 ,28).

In the presented case, the pigmented mass, initially appearing as a small lump in the right mammary region, developed significantly over time, causing the animal to become restless and negatively affecting its work performance. In the light of clinical, ultrasonographic, and Doppler examinations, the lesion was demarcated and its malignant potential was considered low. The surgical operation was performed meticulously following standard procedures from preoperative preparations to anesthesia administration, from controlled dissection to at least 2 cm additional removal of surrounding tissue, and this approach is in line with the treatment options reported by Groom and Sullins (6), where systemic effects are rarely observed and local control is achieved.

Veterinary pathologists have had difficulty accurately predicting the biological behavior of EMT using existing classification systems for many years; therefore, the combined evaluation of clinical staging and histopathological classification has become indispensable in providing prognostic information (10, 13, 19, 25, 29, 30, 31). Histopathologic examination of the tissue samples, stained with hematoxylin and eosin, revealed the classic features of the tumor tissue, including intense melanin pigmentation, spindle or epithelioid cellular morphology, a high nuclear-to-cytoplasmic ratio, and a band-like cellular distribution. These findings confirm the invasive potential of the tumor and its tendency to infiltrate surrounding tissues, which are critical in clarifying the diagnosis and determining prognosis (32).

In the presented case, early surgical treatment, USG-guided excision of the tumor within clearly defined surgical margins, and careful management of appropriate anesthesia and post-operative care protocols resulted in a significant improvement in the patient's clinical prognosis. No recurrence was observed at the excision site during the three-month follow-up period. Histopathological evaluations confirmed the classical melanoma features of the tumor, demonstrating its invasive potential and indicating that early intervention is successful in these neoplasms. These results, which are in line with the literature data, support that the progressive complications of equine melanomas and the need for invasive surgery can be minimized with timely and correctly planned intervention. Thus, by providing reliable, evidence-based advice to horse owners, veterinarians can take important steps in preserving patients' quality of life and working performance through early diagnosis and surgical excision (6, 25, 26, 27, 33).

It is believed that melanoma cases can be effectively controlled through a surgical approach, and the difficulties and recurrence rates reported in the current literature can be reduced with the use of appropriate techniques and a multidisciplinary methodology. However, long-term follow-up is required to determine survival rates.

DECLARATIONS

Authors' Contributions: The operative procedure was performed under the management of DK, SK, and CŞE. MSK managed the post-operative clinical follow-up, and EK made a histopathological diagnosis. DK and MAK prepared and wrote the manuscript.

Conflict of Interest: The authors declare that there is no conflict of interest regarding the publication of this manuscript.

Ethical Statement: Informed consent was obtained from the patient's owner for this case report.

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REFERENCES

1. Johnson PJ: Dermatologic Tumors (Excluding Sarcoids). Vet Clin North Am: Equine Pract, 14: 625-658, 1998. https://doi.org/10.1016/S0749-0739(17)30190-6
2. Weber LA, Delarocque J, Feige K, Kietzmann M, Kalbitz J, Meißner J, Paschke R, Cavalleri JM: Effects of Topically Applied Betulinic Acid and NVX-207 on Melanocytic Tumors in 18 Horses. Animals, 11: 3250, 2021. https://doi.org/10.3390/ani11113250
3. Valentine BA: Equine Melanocytic Tumors: A Retrospective Study. J Vet Intern Med, 9: 291-297, 1995. https://doi.org/10.1111/j.1939-1676.1995.tb01087.x
4. Pielberg GR, Golovko A, Sundström E, Curik I, et al: A cis-acting regulatory mutation causes premature hair graying and susceptibility to melanoma in the horse. Nat Genet, 40: 1004-1009, 2008. https://doi.org/10.1038/ng.185
5. Sundström E, Imsland F, Mikko S, Wade C, et al: Copy number expansion of the STX17 duplication in melanoma tissue from grey horses. BMC Genomics, 13: 365, 2012. https://doi.org/10.1186/1471-2164-13-365
6. Groom LM, Sullins KE: Surgical excision of large melanocytic tumours in grey horses: 38 cases (2001–2013). Equine Vet Educ, 30: 438-443, 2018. https://doi.org/10.1111/eve.12767
7. Brocca G, Centelleghe C, Padoan E, Stoppini R, Giudice C, Castagnaro M, Zappulli V: Case Report of a Mare Diagnosed with a Metastatic Mammary Carcinoma after the Excision of a Recurrent Intraocular Neuroepithelial Tumor. Animals, 10: 2409, 2020. https://doi.org/10.3390/ani10122409
8. Faustino-Rocha A, Oliveira PA, Pinho-Oliveira J, et al: Estimation of rat mammary tumor volume using caliper and ultrasonography measurements. Lab Anim, 42: 217-224, 2013. https://doi.org/10.1038/laban.254
9. Jeong H, Kwon YS: Topical Chemotherapy Using Cisplatin for Treatment of Malignant Melanoma in a Grey Horse. Pak Vet J, 40 (1): 130-132, 2019. DOI: 10.29261/pakvetj/2019.072
10. Knottenbelt DC: Melanocytic neoplasms. In, Patterson-Kane JC, Snalune KL (Eds): Clinical Equine Oncology. 237-245, Elsevier Health Sciences, UK, 2015.
11. Malá A, Kopecká A, Jahn P, Linhart P, Frgelecová L, Škorič M: Prevalence and histopathological classification of equine melanocytic tumours in the Czech Republic and Slovakia. Acta Vet Brno, 93 (3): 269-274, 2024. https://doi.org/10.2754/avb202493030269
12. Fleury C, Bérard F, Balme B, Thomas L: The study of cutaneous melanomas in Camargue-type gray-skinned horses (1): clinical-pathological characterization. Pigment Cell Res, 13: 39-46, 2000. https://doi.org/10.1034/j.1600-0749.2000.130108.x
13. MacGillivray K, Sweeney R, Del Piero F: Metastatic melanoma in horses. J Vet Intern Med, 16: 452-456, 2002. https://doi.org/10.1111/j.1939-1676.2002.tb01264.x
14. Rosengren Pielberg G, Golovko A, Sundström E, Curik I, Lennartsson J, Seltenhammer MH, Druml T, Binns M, Fitzsimmons C, Lindgren G, Sandberg K, Baumung R, Vetterlein M, Strömberg S, Grabherr M, Wade C, Lindbald-Toh K, Pontén F, Heldin CH, Sölkner J, Andersson L: A cis-acting regulatory mutation causes premature hair graying and susceptibility to melanoma in the horse. Nat Genet, 40: 1004-1009, 2008. https://doi.org/10.1038/ng.185
15. Curik I, Druml T, Seltenhammer M, Sundström E, Pielberg GR, Andersson L, Sölkner J: Complex Inheritance of Melanoma and Pigmentation of Coat and Skin in Grey Horses. PLoS Genet, 9: e1003248, 2013. https://doi.org/10.1371/journal.pgen.1003248
16. Teixeira RBC, Rendahl AK, Anderson SM, Mickelson JR, Sigler D, Buchanan BR, Coleman RJ, McCue ME: Coat Color Genotypes and Risk and Severity of Melanoma in Gray Quarter Horses. J Vet Intern Med, 27: 1201-1208, 2013. https://doi.org/10.1111/jvim.12133
17. Cavalleri JM, Mählmann K, Steinig P, Feige K: Aetiology, Clinical Presentation and Current Treatment Options of Equine Malignant Melanoma—A Review of the Literature. Pferdeheilkunde, 30: 455-460, 2014.
18. Foley G, Valentine B, Kincaid A: Congenital and Acquired Melanocytomas (Benign Melanomas) in Eighteen Young Horses. Vet Pathol, 28: 363-369, 1991. https://doi.org/10.1177/030098589102800503
19. Pimenta J, Prada J, Cotovio M: Equine melanocytic tumors: A narrative review. Animals, 13: 247, 2023. https://doi.org/10.3390/ani13020247
20. Seltenhammer MH, Heere-Ress E, Brandt S, Druml T, Jansen B, Pehamberger H, Niebauer GW: Comparative Histopathology of Grey-Horse-Melanoma and Human Malignant Melanoma. Pigment Cell Res, 17: 674-681, 2004. https://doi.org/10.1111/j.1600-0749.2004.00192.x
21. Resende L, Moreira J, Prada J, Queiroga FL, Pires I: Current Insights into Canine Cutaneous Melanocytic Tumours Diagnosis. In: Melanoma—Current Clinical Management and Future Therapeutics. Intech, Rijeka, Croatia, 2015. https://doi.org/10.5772/59480
22. Nishiya AT, Massoco CO, Felizzola CR, Perlmann E, Batschinski K, Tedardi MV, Garcia JS, Mendonça PP, Teixeira TF, Dagli MLZ: Comparative Aspects of Canine Melanoma. Vet Sci, 3: 7, 2016. https://doi.org/10.3390/vetsci3010007
23. Wong K, van derWeyden L, Schott CR, Foote A, Constantino-Casas F, Smith S, Dobson JM, Murchison EP, Wu H, Yeh I, et al: Cross-Species Genomic Landscape Comparison of Human Mucosal Melanoma with Canine Oral and Equine Melanoma. Nat Commun, 10: 353, 2019. https://doi.org/10.1038/s41467-018-08081-1
24. Deleon M: Cutaneous Melanoma: A Comparative Study between Gray Horses, Canines, and Humans. Iowa State Univ, Ames, IA, USA, 2021.
25. Moore JS, Shaw C, Shaw E, Buechner-Maxwell V, Scarratt WK, Crisman M, Furr J, Robertson J: Melanoma in horses: Current perspectives. Equine Vet Educ, 25:3 144-151, 2013. https://doi.org/10.1111/j.2042-3292.2011.00368.x
26. Knottenbelt DC: The equine melanoma. Equine Health, 40: 23-26, 2018. https://doi.org/10.12968/eqhe.2018.40.23
27. Rowe EL, Sullins KE: Excision as treatment of dermal melanomatosis in horses: 11 cases (1994–2000). J Am Vet Med Assoc, 225: 94-96, 2004. https://doi.org/10.2460/javma.2004.225.94
28. MacEachern KE, McKay JS, Hewicker-Trautwein M: Malignant mammary melanoma in a young mature thoroughbred mare. Equine Vet Educ, 13 (2): 68-71, 2001. https://doi.org/10.1111/j.2042-3292.2001.tb01888.x
29. Metcalfe LV, O'Brien PJ, Papakonstantinou S, Cahalan SD, McAllister H, Duggan VE: Malignant melanoma in a grey horse: case presentation and review of equine melanoma treatment options. Ir Vet J, 66: 22, 2013. https://doi.org/10.1186/2046-0481-66-22
30. Sullins KE: Melanocytic Tumours in Horses. Equine Vet Educ, 32: 624-630, 2020. https://doi.org/10.1111/eve.13159
31. Seltenhammer MH, Simhofer H, Scherzer S, Zechner R, Curik I, Sölkner J, Brandt SM, Jansen B, Pehamberger H, Eisenmenger E: Equine melanoma in a population of 296 grey Lipizzaner horses. Equine Vet J, 35: 153-157, 2003. https://doi.org/10.2746/042516403776114234
32. Billi T, Karadima V, Tyrnenopoulou P, Apostolopoulou EP, Brellou GD, Diakakis N: Surgical excision of a malignant metastatic melanoma located in a skeletal muscle of the lateral thorax of a horse. Vet Med Sci, 7 (2): 297-302, 2021. https://doi.org/10.1002/vms3.366
33. Pimenta J, Prada J, Pires I, Cotovio M: The Impact of Excision Interval on Equine Melanoma Progression: Time Matters? Animals, 14 (8): 1244, 2024. https://doi.org/10.3390/ani14081244