VETERİNER İÇ HASTALIKLARI KONULARI

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yaz
yayınları

Veteriner İç Hastalıkları Konuları

Editör

Dr. Fatma ATLI

yaz yayınları

2025

Veteriner İç Hastalıkları Konuları

Yazar: Dr. Fatma ATLI

E_ISBN 978-625-5547-91-0

Mart 2025 – Afyonkarahisar

Dizgi/Mizanpaj: YAZ Yayınları

Kapak Tasarım: YAZ Yayınları

YAZ Yayınları. Yayıncı Sertifika No: 73086

M.İhtisas OSB Mah. 4A Cad. No:3/3
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İÇİNDEKİLER

BABESIOSIS IN SHEEP

Fatma ATLI[1]

1. INTRODUCTION

The most significant hemoparasitic tick-borne illness affecting small ruminants is called "ovine babesiosis," and it is brought on by Babesia ovis, Babesia motasi, and B. Crassa (Aydin et al., 2013). In regions where Rhipicephalus bursa is present, sheep babesiosis, which is brought on by Babesia ovis (Babes, 1892), is a significant economic concern (Canestrini and Fanzago, 1887). Hemoprotozoan parasites carried by ticks are common in tropical and subtropical regions. Babesiosis-related morbidity and mortality in sheep and goat herds grazing in enzootic environments closely correlate with the vector R. bursa's seasonal activity. Ixodid ticks, especially those belonging to the genus Ixodes (Homer et al., 2000), are the vectors of the diseases, and their global expansion is reliant on the geographic availability of capable vectors (Young et al., 2019). The castor bean tick (Ixodes ricinus), black-legged tick (Ixodes scapularis), and taiga tick (Ixodes persulcatus) are the three most significant tick vectors of zoonotic Babesia. Particularly in sheep, B. ovis and Babesia sp. Xinjiang are extremely harmful and produce serious infections that manifest as fever, anemia, icterus, and hemoglobinuria (Aydin et al., 2013).

Human babesiosis in Europe is mostly caused by B. divergens, which is of bovine origin (Gray et al., 2010); in North America, B. microti, which is of rodent origin (Herwaldt et al.,

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2012); and in Asia and other regions of the world, B. venatorum. Depending on the Babesia species involved and other host-related factors like age (Chang et al., 2019), immunocompromised conditions (Gonzalez et al., 2015), and spleen condition (Centeno-Lima et al., 2003), human babesiosis can range from asymptomatic infections to severe disease and death. In 1956, B. divergens caused the first human babesiosis case in a young Croatian herdsman who was asplenic. Two weeks later, the young man died (Skrabalo and Deanovic, 1957; Karshima et al., 2021).

The current study was carried out to evaluate the epidemiology of babesiosis, clinical aspects, pathology and effect on several blood parameters in sheep, taking into account the financial losses caused by the disease.

2. EPIDEMIOLOGY

The bio-ecology of R. bursa, the tick vector, is intimately linked to the epidemiology of ovine babesiosis caused by B. ovis. Ovine babesiosis exhibits a notable seasonal incidence trend. Every year, during the adult tick stage's activity phase, the disease strikes regions infested with R. bursa (Yeruham et al., 1998). Together with the animal infestation rate of R. bursa ticks, the incidence of babesiosis peaked in May. It then declined and vanished entirely by the end of July.

Two weeks after adult R. bursa ticks are found in the field, ovine babesiosis develops (Yeruham et al., 1998). This time frame gives an indication of how long it takes for the vector to become active and start looking for a host before the host develops a clinical illness. Despite being permanent in the enzootic area, babesiosis in sheep might recur annually in the same flocks, according to the knowledge currently available. The recognized enzootic stability in bovine babesiosis is not the same as this epizootiological pattern (Chang et al., 2019). Outside of

the primary season of adult R. bursa tick activity, and at the same time as few adult ticks are visible, sporadic clinical instances of babesiosis have been documented.

3. THE BLOOD PARASITE

According to Suleimanov (1976) and Habela et al. (1990), the adult double pyriform parasites and the single ring were the most prevalent erythrocytic types. Four hoggets were found to have a cross-form parasite that resembled the B. crassa that was discovered in Iran (Yeruham et al., 1998). These animals also tested positive for the B. ovis antigen. No prior descriptions of such B. ovis cross forms exist. There is both stage-to-stage and transovarial transmission.

4. PATHOGENESIS

Host-mediated diseases are brought on by this infection. Anaemia is caused by a mix of extravascular and intravascular hemolysis from several processes, such as increased osmotic fragility of the blood vessels, intracellular parasite proliferation that lyses red blood cells, via intravascular hemolysis, biogenic amine activation, and oxidative alterations in erythrocytes (Villanueva-Saz et al., 2022). Even if there aren't any other pathophysiological mechanisms that have been identified in sheep, there may be other comparable mechanisms in animal species like dogs, about which more scientific data is known. The development of abnormal anti-erythrocyte membrane antibodies is one of the possible pathogenic processes that lead to immune-mediated hemolytic anemia (Solano-Gallego et al., 2016). In diseased animals like dogs (Wozniak et al.i 1997) and cattle (Mahmoud et al., 2015), erytrophagocytosis can be seen in smears from the liver and spleen. Since sheep do not exhibit overt clinical

symptoms but instead exhibit a strong humoral reaction, they have been considered as an experimental animal model of bovine babesiosis produced by B. divergens. The spleen plays a vital role in managing clinical illness and splenectomized animals with experimental infection quickly develop parasitemia and clinical symptoms (Moreauet al., 2009). When B. rossi (Henning et al., 2020) or B. canis causes canine babesiosis, a similar circumstance is seen.

Although high parasitemia is generally associated with severe clinical symptoms and laboratory abnormalities, there is also varying evidence regarding the relationship between parasite load and severity, taking into account each species of Babesia that affects sheep (Sevinc et al., 2013).

Some writers, however, believe that certain species of Babesia are not harmful because parasitemia levels may vary according on the species that is present. More severe symptoms are likely to appear in animals who are infected for the first time. But after sheep were experimentally infected with B. ovis, the parasite burden, antibody response, and latent infection duration were all kept low (Uilenberg, 2006).

The protozoan parasites attach to the red blood cell membrane and enter the red blood cells after infected ticks have consumed sheep blood. Following that, merozoite development and red blood cell lysis are signs of hemoparasite growth. Because of intravascular and extravascular hemolysis as well as cell membrane fragility, this condition is accompanied by lesions of the blood cell membrane. New hemoparasites infiltrate fresh erythrocytes in the bloodstream following the loss of red blood cells and the huge growth of the parasites within the cell, hence sustaining the parasite's widespread proliferation (Ganzinelli et al., 2018).

Hypoxia may develop in organs and tissues in certain people with severe acute babyesiosis and a substantial decrease in red blood cells. Clinical symptoms related to the afflicted tissues could result from it (Villanueva-Saz et al., 2022). The acute form of sheep babesiosis is sometimes associated with the risk of disseminated intravascular coagulation syndrome and glomerular basal membrane damage. In the past, autoimmune anemia has been identified as being connected to babesiosis in both dogs and humans (Narurkar et al., 2017). However, there is no proof that ruminants exhibit this kind of anemia.

5. CLINICAL SIGNS

Babesia species' intracellular invasion of the erythrocytes causes clinicopathological symptoms. In this regard, the animal may exhibit clinical symptoms like fever, hemoglobinuria, jaundice, and anemia as a result of these parasites. This final indication appears in 30 to 50 percent (Alessandra and Santo, 2012). Clinical signs and symptoms, however, vary depending on the pathogenic virulence of the Babesia species that is causing the illness. Furthermore, other variables like immunosuppressive state, parasite load, immune system function, concomitant disease presence, and vulnerability could all have a direct impact on how severe the clinical illness is.

When the acute form occurs naturally, symptoms like fever, anorexia, tachypnea, jaundice, hemoglobinuria, diarrhea, anemia, and ultimately mortality might be identified. In an experimental circumstances, a B. motasi infection in sheep might result in weight loss, anorexia, and fever (Henning et al., 2020). Lastly, the chronic version describes cough, oedema, and poor health (Alessandra and Santo, 2012). Assessing immunology and other clinicopathological factors, aside from experimental infection, is a persistent challenge in the research of immune

response in sheep under natural conditions (Moreauet al., 2009). When hemolytic anemia is present in certain animals, the enormous intracellular parasite growth in the red blood cells may result in more severe clinical symptoms, including changes to hemostasis (Rahbari et al., 2008).

Several effects of B. ovis, including elevated liver parameters, can be identified by laboratory methods. Because of the renal damage brought on by glomerulonephritis, an increase in renal parameters is seen. Due to the hepatopathy issue and renal failure-induced urine loss, hypoalbuminemia and a reduction in total protein are found. All of these lab changes suggest that the primary lesion target organs. The kidney and liver are involved (Yeruham et al., 1998). Additionally, the infection can impact total serum proteins, serum glutamic pyruvic acid transaminases, unconjugated and conjugated bilirubin, and other biochemical markers that are typically elevated (Rahbari et al., 2008).

While macrocytic and hyperchromic anemia can be found in sheep with chronic course disease, hypochromic microcytic anemia is the most frequent laboratory change in sick animals. Additionally, there is a decline in hemoglobin levels and the identification of when disseminated intravascular coagulation is present, thrombocytopenia (Sevinc et al., 2013). Furthermore, sheep have been shown to exhibit neutrophilia when experimentally infected with B. motasi.

6. DIAOGNOSIS

Clinical symptoms and microscopic analysis of Giemsa-stained blood smears are used to diagnose babesiosis in acute cases (Yin et al. 2003). Following infection, babesiosis-infected animals become porters, and the population importance of these animals is crucial for disease epidemiology. It has been suggested that microscopic techniques are inadequate, and that serological

approaches for diagnosing porter animals have produced false-positive and false-negative findings (Aydin et al., 2013). Because of these factors, epidemiological investigations have required the use of molecular diagnostic techniques to identify Babesia infections (Heidarpour Bami et al. 2009).

Molecular techniques such as the polymerase chain reaction (PCR)-based reverse line blotting method (RLB), which can diagnose multiple agents at once and identify new species and genotypes, have been used in recent years to evaluate parasitic DNA for the diagnosis of subclinical Theileria and Babesia infections. Due to the inability to detect many species at once, new diagnostic procedures have been developed that enable the simultaneous detection of multiple agents in blood as needed. In 1995, the RLB technique was created to distinguish between four species of Borrelia in ticks (Rijpkema et al. 1995). This technique has shown effective in diagnosing Theileria and Babesia species, and its application in parasitological research is growing.

The primary method for diagnosing piroplasm infections in vertebrate hosts has been microscopic analysis of blood smears. Nonetheless, the morphological characteristics of piroplasms are identical. Low parasitemia rates and mixed infected animals can be detected and differentiated using PCR-based molecular methods. Furthermore, RLB can identify many parasites in a single sample (Inci et al. 2010).

7. DISCUSSION

The health and production of sheep and goats are seriously threatened by small ruminant babesiosis, a serious protozoan illness spread by ticks and brought on by Babesia species (Liu et al., 2007). There are six species of Babesia that are known to be infectious for cattle and buffalo worldwide: B. bigemina, B. bovis, B. divergens, B. major, B. ovata, and B. orientalis. Babesia

species that infected small ruminants, on the other hand, have not been the subject of as extensive taxonomic research (Ulucesme et al., 2024). Three Babesia species—B. ovis, B. motasi, and B. crassa—that infect tiny ruminants were acknowledged as legitimate species until recently. Nonetheless, new Babesia species and genotypes have been identified throughout the last 20 years, including Babesia Xinjiang, B. motasi-like variations [Babesia sp. BQ1 (Lintan), Babesia sp. BQ1 (Ningxian), and, lastly, B. Aktasi (Niu et al., 2009). Of them, B. motasi is more common in goats and has milder clinical signs, but B. ovis mostly affects sheep and causes clinical symptoms such fever, anemia, jaundice, and hemoglobinuria (Lewis et al., 1981).

With the exception of the detection of parasite DNA using the molecular method (loop-mediated isothermal amplification) in the second and third weeks following parasite inoculation, clinical and parasitological findings were seen in immune-suppressed lambs in a prior study assessing the virulence of Babesia sp. Xinjiang in sheep (Guan et al., 2009). No findings were found in spleen-intact lambs. In the same investigation, Babesia sp. Xinjiang was also found to infect an immune-compromised calf that was observed for 60 days; however, microscopic analysis revealed no parasite piroplasm. According to these results, Babesia sp. Xinjiang is infectious for sheep with weakened immune systems but not for cattle.

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VIRAL DISEASES IN SHEEP AND GOATS ASSOCIATED WITH SKIN LESIONS

Fatma ATLI[1]

1. INTRODUCTION

Parapoxviruses (PPVs) infection in sheep and goats is widespread and causes severe economic loss under the names sore mouth, ORF, Contagious Pustular Dermatitis (CPD), and Contagious Ecthyma (CE) (Shehata et al., 2022).

Lumpy skin disease (LSD), goat pox (GTP) and contagious ecthyma (CE) are viral skin diseases of animals hat have been documented globally (Nawathe et al., 1982; Adedeji et al., 2018). The OIE lists LSD and GTP as transboundary illnesses because of their capacity to spread quickly over international borders and reach epidemic levels, which results in trade restrictions (Tuppurainen et al., 2017). LSD virus (LSDV), whereas GTP virus (GTPV) is responsible for lumpy skin condition. These DNA viruses belong to the Capripoxvirus genus and are related to one another (Tulman et al., 2002). Although GTPV affects goats and sheep, lumpy skin disease only affects cattle, buffalo, and other closely related wild ruminants (Tuppurainen et al., 2017). Clinically noticeable lumpy skin disease is distinguished by lymphadenopathy and big, firm

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nodular skin lesions. According to Babiuk et al. (2008), goat pox is associated with significant economic losses, including reduced milk output, in areas where it is endemic. weight loss, miscarriage, damage to fleece, and in affected flocks of sheep and goats. According to Bhanuprakash et al. (2011), GTP outbreaks can cause 100% morbidity and 49.5% mortality, particularly in naive animals. Contagious ecthyma is a crippling disease that affects sheep and goats. It is caused by the Orf virus (ORFV), a DNA virus that is a member of the genus Parapoxvirus and family Poxviridae (Nandi et al., 2011). Bovine Papilloma (BP) is brought on by the BP virus (BPV), a DNA virus that is a member of the Papillomaviridae family (Ogawa et al., 2004). In order to confirm cases of these viral skin infections in animals, laboratory tests are crucial. Polymerase Chain Reaction (PCR) is a highly dependable method for the confirmation diagnosis of LSD, GTP, CE, and BP (Torfason & Guonadottir, 2002; Ifende et al., 2019).

Economically speaking, viral skin diseases lower the trade value of infected animals by causing morbidity, death, skin damage, and other symptoms (Gambo et al., 2018).

2. CONTAGIOUS ECTHYMA

Orf illness is an acute, economically, and highly contagious significant viral disease that affects sheep, goats, and several domesticated and wild ruminants with zoonotic importance (Nandi et al., 2011; Akkaya et al., 2021). Contagious ecthyma and contagious pustular dermatitis are other names for this condition, sore mouth, or scabby mouth (Shehata et al., 2022). The World Organization for Animal Health claims that,

orf is a zoonosis that must be reported and poses a concern to humans working with animals (Scagliarini et al., 2012). Although the morbidity rate is higher than the mortality rate, lambs are more susceptible to the disease and their mortality is much higher (Kumar et al., 2015). Poor growth rates in mastitis and lambs in ewes due to orf result in financial loss for the sheep business (Lovatt et al., 2012). A live orf vaccine is currently available with the capability to control this disease. But it poses a possible harm to the environment and heightens the dangers to other creatures (Esmaeili et al., 2021). The main driver of disease transmission within some flocks has been recognized by the introduction of additional animals, which may be orf virus carriers (Nettleton et al., 1996). However, it has been discovered that this does not significantly affect the illness prevalence in ewes and lambs (Esmaeili et al., 2021).

The disease is brought on by the linear dsDNA Orf virus (ORFV), a prototype of the Parapoxvirus genus and a member of the Poxviridae family's Chordopoxvirinae subfamily. The structure of the viral genome typically consists of a conserved central section and changeable terminal portions that encode the components needed for viral interactions with host cells (Shehata et al., 2022). The B2L gene, which codes for a significant immunogenic envelope protein that is a homologue of the virus vaccinia, is one of numerous genes involved in the core conserved region that are involved in viral replication (Olivero et al., 2018).

Neonate and young lambs around the age of two weeks exhibit severe clinical manifestations of the disease. Clinically, ORFV mostly affects the skin surrounding the lips, oral and nasal mucosa, and udders, and is linked with cutaneous lesions that

show through various stages as maculopapular, vesicular pustules, and scabby proliferative lesions. The traditional method for diagnosing ORFV in a lab involved examining the distinctive clinical symptoms and then confirming the diagnosis through viral isolation, histology, and electron microscopy of negatively stained scabs with the distinctive ovoid-shaped virion. As a precise and sensitive approach for virus detection today, PCR is widely utilized all over the world (Chan et al., 2007).

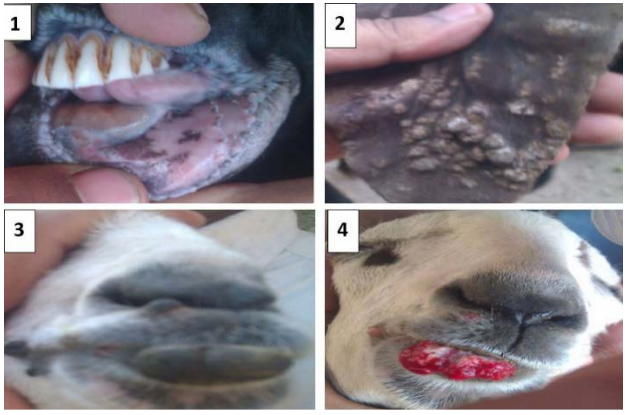

Fig.1: Gross pathological injuries in goats and sheep. (1) Hemorrhages and ulcerations on the oral cavity's delicate tissues. (2) The growth of lumps on the sheep's, external ear pinnae. (3) Lower lip warts and goat commissure. (4) Blood oozing and ulceration after wart excision (Ghani et al., 2019).

Sheep with no apparent skin lesions are the carriers of disease that spread it across a herd. For many months, dry scab material in buildings can retain the viability of an illness, which is probably why an infection persists year after year on the same land. Therefore, thorough cleaning and disinfection of lambing accommodations may aid in preventing the yearly occurrence of sickness. Although it is challenging to measure the control after

scarification using a live vaccination, it is a common practice in many flocks in the UK. Never administer a vaccination to a flock that has never had orf. In order to administer the vaccination, the inner thigh of lambs and the axillary region of ewes are scarified. The vaccination should be administered around 6 weeks before the sickness is expected to manifest. The live vaccination must be treated with caution because it is sensitive to high temperatures and is rendered inactive by disinfectants (Ghani et al., 2019).

3. SHEEPPOX AND GOATPOX

The two are goatpox virus (GTPV) and sheeppox virus (SPPV), species that make up the Capripox genus (Capx) of the Poxviridae. These two double stranded DNA viruses each have a 150 kbp genome and 147 putative genes in common (Haegeman et al.,2020). With conserved core genes in the center region and host-specific and cellular genes in the terminal portions, the chordopoxviral genomes are colinear across the subfamily (Krotovaet al., 2022). By biting mosquitoes of the genera Culex and Aedes, biting flies of the genera Stomoxys and Biomyia, and Ixodes ticks—all of which are regarded as mechanical carriers of the infectious the virus that causes lumpy skin disease (LSD) is known to spread (Hakobyan et al., 2023). Because SPPV and GTPV can selectively infect both mammalian hosts and produce comparable clinical symptoms in each one, they are frequently referred to as a single infectious agent. The latter includes pneumonia, fever, enlarged lymph nodes, skin and mucous membrane lesions, and swelling. (Krotovaet al., 2022).

Fig.2: Clinical indication of the malignant form of goat and sheep pox. (Hurisa et al., 2018).

In terms of severe morbidity, mortality, damage to hides, and limits on international trade, goatpox and sheeppox are the most significant illnesses, and as a result, they must be reported to OIE (Bhanuprakash et al., 2011). The disease has a substantial negative economic impact on the farming community in Northern Africa, Europe, Asia, and the Middle East (Venkatesan et al., 2018).

Depending on the epidemiological condition, different requirements for sensitivity and specificity may be imposed. The highest specificity and sensitivity are necessary in a region (or nation) free of capripox, whereas these qualities may be less important during an outbreak. The choice may also be affected by the accessibility of specialized lab equipment and the capacity to purchase consumables (such PCR probes). The overall cost of the analysis should also be considered, especially when numerous samples need to be checked for numerous diseases. Therefore, it is crucial to choose diagnostic instruments that are appropriate for the situation at hand (Venkatesan et al., 2018).

In order to minimize SPP outbreaks and subsequently prevent disease-related expenses in affected nations, vaccination is thought to be the only economically viable strategy (Babiuk et al., 2009). The indigenous Bakirköy strain is used in Turkey to vaccinate sheep, while the Romanian and Yugoslavian RM65 SPPV vaccine strains are used in Morocco, Senegal, Egypt, Algeria, and the Romanian Fenner as well as the Srinagar vaccine strains are used in India. Russia, Kazakhstan, and other former Soviet Union nations employ the NISKHI SPPV vaccine strain to immunize sheep, goats, and cattle. (Krotova et al., 2022; Uzar et al., 2022).

Without the need for additional testing or confirmation, SPPV and GTPV have been successfully distinguished and identified from clinical samples of infected small ruminants using the Real-Time and traditional PCR based PRO30 gene. The nucleic acid extraction by unique modified microwave method made it possible to isolate DNA from scab biopsy samples and CAM positive samples, and it offers inexpensive quick extraction methods. The best quality DNA was extracted in less than five minutes (Zeedan et al., 2020).

4. ULCERATIVE DERMATOSIS-OVINE VENERAL DISEASE

Parapoxviruses (PaPVs) are members of the genus Parapoxvirus and the family Poxviridae (Das et al., 2022). The four species of PaPVs are: Pseudocowpox virus (PCPV), red deer parapoxvirus in New Zealand (PVNZ), bovine papular stomatitis virus (BPSV), and orf virus (ORFV). Worldwide, ruminants

(cattle, sheep, and goats) infected with PCPV or BPSV are the primary hosts of PaPVs. All PaPVs share a similar appearance, are genetically and antigenically closely related, and have indistinguishable virulence mechanisms. The clinical disease of PaPV is characterized by fever, sores, ulceration sores and raised or elevated skin are symptoms of proliferative dermatitis on the leg, mouth, teats, lips, nose, gums, and tongue. PaPV infections are frequently minor. This viruses are typical ruminant pathogens that affect sheep, goats, and cattle.

Fig. 3: The scrotum and hind legs of animals with ulcerative dermatosis. (https://anipedia.org/resources/ulcerative-dermatosis/1079)

Parapoxvirus infections in livestock are endemic viral illnesses that were initially described by Jenner in 1798 (Fenner,

1979). Humans may contract parapox illnesses by coming into touch with infected material. After exposure to the pseudocowpox or paravaccinia virus from cattle, or the orf virus from goats or sheep, or less frequently after contact with other hoofed animals like moose, reindeer, or camels, the zoonosis typically manifests in humans as a milker's nodule. The viral infection can manifest in animals as an undetectable, localized, or widespread infection. Cheilitis appears as seeping, crust-covered erythematous papulopustules and nodules on the lips (Chua et al., 2011).

Mixed infections of foot and moth disease virus (FMDV) or capripox virus (CaPV) with other viruses in ruminants have been documented (Chua et al., 2011; Das et al., 2022). These viruses include PaPV, the blue tongue virus (BTV), the peste des petits ruminant virus (PPRV) (Kumar et al., 2015). Due to the highly similar clinical symptoms linked to CaPV, PaPV, and FMDV, diagnosing mixed infections involving these viruses can be difficult. Finding and differentiating PaPV from FMDV and CaPV is essential in suspected animals in places where PaP is endemic while CaP and FMD are not. In nations where all three viruses are endemic, differential diagnosis of these viruses is more difficult (Das et al., 2022).

The 139-kbp Parapox ovis virus (PPOV) infects sheep and goats and, with its primary localization in the mouth and nostrils, creates a highly contagious pustular dermatitis (Robinson and Balassu, 1981). The first research on the immunostimulating potential of inactivated Parapox ovis virus (iPPOV) was published in 1978 and suggested that the PPOV vaccination strain D1701 could reduce the mortality rate in mice infected with Pseudomonas aeruginosa. (Mayr et al., 1981). Comprehensive

research on the immunostimulating potential of iPPOV in swine has shown that its use may help prevent economically significant stress-mediated illnesses. These include wasting pig syndrome, post-weaning diarrhea syndrome, and mastitis metritis agalactia syndrome (Kyriakis et al., 1998; Fachinger et al., 2000).

5. PRINCIPLES OF THERAPY

For any viral disease to be diagnosed, the underlying causes must be found quickly. Isolating the causative virus from the field samples is the best diagnostic step. Molecular science presents the possibility of more dependable and effective methods of diagnosing viral infection in the case that virus isolation is not feasible. Immunization against each virus, effective quarantine protocols, hygienic practices, and vector control are essential components of the control program. The use of immunomodulators to enhance non-specific defense systems should be considered while treating viral infections. However, it's crucial to monitor the efficacy of therapies for viral diseases and investigate any inconsistencies. The adverse effects of the medication and the duration of its presence in meat and milk are further considerations. Since antiviral drugs are ineffective in treating most viral illnesses, treating the symptoms is essential.

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