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MYCOPLASMATIC (ENZOOTIC) PNEUMONIA OF PIGS AS A HEALTH PROBLEM IN FATTENING UNITS

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Abstract

Mycopasmatic or enzootic pneumonia is the most common disease of the respiratory system under in the intensive pig production. It is clinically manifested by coughing, a chronic inflammatory process in the lungs, high morbidity and a relatively low percentage of deaths. The infection can be transmitted horizontally and vertically. *Mycoplasma hyopneumoniae* invades the epithelial cells of the trachea, bronchi, bronchioles and alveoli and disrupts the function of the ciliary body. Evagination of epithelial cells occurs, so that the cleansing of the airway mucosa by the mucociliary apparatus is inhibited. As a result, bacterial complications (*Pasteurella, Bordetella, Klebsiella, Actinobacillus, Hemophilus*) are common.*M.hyopneminia* can play imortant role in PRDC. The development of *Mycoplasma hyopneumoniae* is favoured by large congregations of pigs in small spaces, inadequate environmental conditions (microclimate), parasitic infections and inadequate nutrition. *Mycoplasma hyopneumonia* can be a significant health problem on the fattening farm, exacerbated by the influence of non-specific factors as well as the spread of other bacterial pathogens.

Key words: *Mycoplasma, pneumonia,* fattening, pigs, intensive breeding

After completion of the rearing phase, the further technological process in intensive pig breeding comprises several production lines: fattening, rearing of female breeding material (gilts) to maintain the parity structure and repair the udder, and rearing of boars to obtain semen for artificial insemination. Pig fattening is the finnish phase of meat production. The piglets arrive at the fattening center facilities at the age of 10 weeks and with a body weight of about 25 kg. They remain in the fattening center until they reach their final body mass. (Mrvaljević, 1995).

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Successful fattening depends on numerous factors, such as genetic potential, balanced nutrition, microclimatic or zoohygienic conditions, and general health of the sow. On the quality of external and internal biosecurity measures and health management depends the extent of direct and indirect damage caused by health disorders in fattening farms (Bojkovski et.al. 2011,2022, Prodanović et al. 2021; Prodanov-Radulović et al., 2020a). One of the most common diseases in fattening is mycoplasmatic or enzootic pneumonia. Mycoplasmatic or enzootic pneumonia is a multifactorial disease of the respiratory tract of pigs whose primary pathogen is *Mycoplasma hyopneumoniae* and in which a number of so-called risk factors are involved. The source of infection is sick pigs, which transmit the pathogens to individual pigs by direct contact. Piglets are most commonly infected through contact with an infected sow or contaminated

environment (aerogenic infection). The horizontal route of transmission is particularly pronounced in chronically infected pigs. After infection, an immune reaction occurs and specific antibodies and sensitized lymphocytes are produced. All previous studies have shown that sensitized lymphocytes play an important role in the defense against mycoplasma infection. All the above facts should be taken into account in the program to control enzootic pneumonia. This is especially important since vaccination has been shown to be the most effective control method in many countries. In addition, an effective strategy to control enzootic pneumonia would have to include correction of management, housing conditions, microclimate, all-in/all-out pig manipulation, strategic medication, and, of course, implementation of effective vaccine programe.Each of the above measures should be adapted to the specific conditions, especially the type of farm, the production system, the origin of the infection, the time of its occurrence, and other non-specific factors (Prodanov-Radulović, 2020b). *M. hyopneumoniae* is sensitive to light, high temperatures, and drying. Most disinfectants and detergents quickly inactivate it. Under humid and cold conditions, it can be maintained in an infectious state for 2-3 days. The bacterial species *Mycoplasma hyopneumoniae* has spread worldwide and causes major economic losses in intensive pig farming. Studies have shown that total production losses can be as high as 25%, even in the absence of secondary infections *(*Stevenson, 1998, Bojkovski et.al.2021). Damage results from reduced daily gains, weaker feed conversion, and individual growth retardation, which together extend the time it takes for the animal to reach adequate body weight. Because of the difference in growth rates, animals on infected farms must be sorted multiple times, which increases the cost of fattening. Infection with the *M. hyopneumoniae* species also leads to an increased likelihood of lung infections with other microorganisms that further complicate the inflammatory processes in the lungs and increase mortality.
As mentioned earlier, mycoplasmas can live as commensals on the mucous membranes of organs and cause disease under certain conditions, such as a decrease in the body's defenses. Mycoplasmas are transmitted transovarially by direct contact between animals, cohabitation, coitus, through the secretions and excretions of infected individuals. Whether infection occurs depends on numerous factors that interact, but the most important is certainly the resistance of the animal. Prolonged, direct and indirect contact between animals is sometimes required for infection with mycoplasma to develop. Bronchial secretions, urine, milk, fetal fluids, joint contents may be contaminated with mycoplasma. The possibility of transmission of the pathogen through food is not excluded, but the infection is most often introduced through the purchase and introduction of new animals with unknown health status.

Epizootiology

The source of infection for the youngest categories of pigs are sows and older gilts. Infection is predominantly by droplet infection and is transmitted by airborne or direct contact with nasal discharge. The infection spreads relatively quickly from litter to litter. The youngest categories of pigs are also most susceptible to infection, although in most cases latent infection occurs in the youngest pigs. In piglets, the infection may rarely cause lesions on the teat. When pigs are in pre-fattening, when they are exposed to other micro-organisms due to the mixing of animals from different farms and when non-specific factors are present, bronchopneumonia may occur in a larger number of animals. Since the pathogen is already in the pig's body, the housing conditions and the immune status of the animal play an important role in the development of the disease. Air, frequent temperature changes, mixing or bringing in animals from other areas, unbalanced diet, possible parasite infestation and other unfavourable conditions contribute to the occurrence of the disease (Pavlović, et al., 2007, Došen, 2007)

Pathogenesis

M. hyopneumoniae colonizes the upper part of the respiratory system of swine and adheres to the ciliated epithelium of the bronchi and bronchioles, where it remains without further invasion of the cells or parenchyma. It adheres exclusively to the cilia of the ciliated epithelium, and in some cases structures resembling adhesion pili have been observed to attach the mycoplasma by using cells. When mycoplasmas are taken up by cells, they damage the cell membrane using metabolites (H_2O_2)., In this case the infected cells lose the ability to degrade hydrogen peroxide. The pathogen spreads and colonizes the respiratory system by ingesting the ciliated epithelial cells of the trachea and bronchi in the cranioventral parts of the lung (Sarradell et al., 2003). During evolution, mycoplasmas have lost all genes involved in the biosynthesis of amino acids, fatty acids, and vitamins, so they obtain all of the above substances from the host cell in which they parasitize. Furthermore, *M. hyopneumoniae* disrupts the cellular receptors and transport mechanisms of the cell to which it binds, causing additional damage through toxic metabolites. Because of the aforementioned actions, the activity of the cilia ceases, they become blind, and eventually the affected cells die and slough off. The consequence dysfunctionality the ciliated epithelium is the accumulation of mucus and inflammatory exudate and the obstruction of the airways. In the acute phase of the disease, neutrophils and macrophages accumulate in the airways and surrounding tissues. As the disease progresses, the peribronchial and perivascular areas are densely infiltrated with mononuclear cells (lymphocytes and macrophages), resulting in hyperplasia of the lymphoid tissue associated with the bronchi (BALT - "Bronchi alveolar lymphoid tissue"). Cytokines secreted by macrophages (IL -1, IL -6, IL -8, prostaglandin E2, TNF) stimulate the activation and accumulation of inflammatory cells, but also have a cytotoxic effect on the endothelium of the alveoli and the epithelium of the airways. The accumulation of mucus and inflamed exudate due to the loss of function of the ciliated epithelium, the increased activity of the glandular cells of the mucosa, bronchoconstriction due to the action of chemical mediators of the inflamed cells, and the increased pressure of the lymphoid tissue lead to airway constriction and atelectasis of the surrounding alveoli. Secondary infections with microorganisms that are physiologically present either on the mucosa or in the immediate environment are common. The most common infection is the bacterium *Pasteurella multocida*, which potentiates the pathological process and doubles the lung surface area affected by the changes. In addition to this bacterium, other microorganisms can also act as agents of secondary infections; the most common are *Actinobacillus pleuropneumoni, Haemophilus parasuis, Streptococcus suis*; some viruses (PRRS - "Porcine Reproductive and Respiratory Syndrome", SIV - "Simian immunodeficiency virus") or other species of mycoplasma *(M. hyorhinis*) *(*Ciprian et al. 1988). If the infection with *M. hyopneumoniae* is not complicated by common infections with the already mentioned microbes, the changes on the lungs may remain localized and gradually detach from the healthy tissue, but they remain permanent (scarring changes are most often found on the slaughter line) (Burch, 2004 , Ivetić et al. 2005).

Clinical picture

Enzootic swine pneumonia caused by the bacterium *M. hyopneumoniae* is characterized by high morbidity and low mortality; secondary infections are common and complicate the course, increasing the number of deaths, i.e., mortality. The course of disease can be acute or chronic. The acute form of the disease occurs only when animals first exposed to the *M. hyopneumoniae* species become infected. The incubation period lasts 2-8 weeks (Zimmereman 2012 Šamanc, 2009,). Severe acute pneumonia may occur, with respiratory distress, painful and nonproductive but audible coughs, dehydration, elevated body temperature, apathy, and clumsiness, and mortality is high in all age groups. It is not uncommon for the disease to manifest with only mild pneumonia. The chronic form often occurs in farms where the M. hyopneumoniae species has been present for some time, i.e., it is an enzootic infection of the sputum. Symptoms may occur for several weeks or even months and are more frequent and intense when animals are disturbed (e.g., during morning feeding, rehousing, etc.); in addition to coughing, weaker feed conversion and consequently reduced growth are observed. If the primary infection is not complicated by additional bacterial infections, the sick pigs recover spontaneously. Despite the clinical improvement, this disease, i.e. its causative agent, persists in breeding, so the cure, i.e. eradication of this disease from breeding, is problematic.(Šamanc, 2009 , Fano et.al. 2005,

Zimmereman 2012).It is manifests in from of increased body temperature, fatigue, inappetence, dyspnea, and in the most severe cases, death. Subclinical infections, where the disease progresses without visible clinical signs (carriers), are very common and therefore represent a major problem in intensive pig farming.

Pathological changes

The first changes in the lungs are seen on the 7. to 10. day of infection and peak after four weeks. They consist of clearly demarcated areas of purple to gray consolidated lung tissue, the extent and distribution of which depend on the stage of the disease, the resistance of the individual animal, the virulence of the causative species, and possible secondary infections. The apical and cranial lobes are most commonly affected, and changes in the caudal lobes are found only in severe cases of disease and complicated secondary infections (Prodanov-Radulović et al., 2020a; Vicca, 2005). Macro pathologically, the cross-section shows a large amount of catarrhal exudate from the trachea, bronchi, and bronchioles, and the tissue is edematous and fleshy in consistency. The bronchial and mediastinal lymph nodes are often markedly enlarged. Three to five weeks after infection, the small airways in the affected portions of the lungs become visible as white spots, which is a consequence of the severe peribronchial inflammation. In cases where there is no secondary infection, the changes are resolved after 12 to 14 weeks. Affected areas become gray, have a hard consistency, are atelectatic, and have even greater demarcation. After cessation of the disease, gray scars remain visible, and in milder cases, healing may be complete, with no visible scars on the lung tissue (*Leneveu et al., 2005*). In the initial phase of the disease caused by the *M. hyopneumoniae*, following histological changes: Loss of airway ciliated epithelium, flaking of ciliated epithelium, and accumulation of neutrophils and macrophages in the lumen and around the airways). In cases where the disease or infection progresses,following changes can be seen: catarrhal bronchointerstitial pneumonia of the cranioventral parts of the lung, peribronchial, peribronchial and perivascular infiltration of lymphoid cells, formation of lymphoid follicles, thickening of the alveolar septa and obliteration of the bronchiolar lumen, and atelectasis of the adjacent alveoli. Hyperplasia of airway lymphoid tissue (BALT "bronchus-associated lymphoid tissue") is the most significant histologic change in enzootic pneumonia and consists of macrophages, dendritic cells, T and B lymphocytes, plasma cells, CD4 cells, and some CD8 cells (*Sarradell et al ., 2003*). Histopathologic findings can be further complicated by secondary infections. For example, necrotic pneumonia is found in infection with the bacterium *P. multocida*, fibrinous-hemorrhagic-necrotic pneumonia, pleural adhesions of yellowish color and massive fibrinous infiltration in infection with the species *Actinobacillus pleuropnumoniae*, and secondary infection with the species *M. Hyorhinis* as well as *Haemophilus parasuis* manifests as catarrhal pneumonia, pleurisy, pericarditis, and polyserositis (Prodanov-Radulović et al, 2020a).

Diagnostic

Epizootiologic control and anamnestic approach are the first steps in suspecting *M. hyopneumonia*e infection in a farm. Enzootic pneumoniae usually occurs in previously uninfected breeding animals after the purchase of new animals and after the mixing of fattening piglets of different origins when a new farm is established. The diagnosis of enzootic pneumonia is difficult to make on the basis of the clinical picture, because the signs of the disease are sparse and often without characteristic symptoms. Despite its obvious advantages (ease of performance, low cost, no burden), clinical surveillance without other diagnostic methods is not sufficient to objectively diagnose enzootic pneumonia. This is confirmed by studies that have shown that in 30% of infected farms, the presence of the disease could not be detected by clinical surveillance alone (*Levonen, 2000*). Macropathological and pathohistological findings are characteristic. However, they are not pathognomonic. The cranioventral distribution of pulmonary changes is also seen in *Streptococcus suis* infection, and subacute infection with porcine influenza virus can produce changes similar to those seen in the early phase of enzootic pneumonia (Zimmermann et.al.2012*)*. Lung lesions caused only by the *M. hyopneumoniae* species are resolved by 5-6 weeks, and by 2 months after infection, the changes may no longer be apparent (Morris et al., 1995). Diagnosis of enzootic pneumonia by isolation and culturing of the pathogen is very difficult and time consuming..Clinical material for laboratory examination should be collected and transported as soon as posible. The age of the pathologic process also affects the success of isolation, in the chronic course of the disease, secondary bacterial infections isolation of *M. hyopneumoniae often is* unsuccesful. Special culture media are used for laboratory detection and isolation of *M. hiopneumoniae*, and an atmosphere with elevated

CO_2 concentration is required. Colonies grow after 7-10 days, they are about 5 mm in size; they only exceptionally have a denser center grown into the substrate, and the appearance of "film and spots" is weak. Because of its slow growth, other microoganisms often cover it most commonly by the species *M. hiorhinis* and *M. flocculare*. The species *M. flocculare* is considered part of the physiological microflora of the respiratory system of healthy pigs, while *M. hyorhinis* often settles in the inflamed, altered lung tissue after primary infection with the species *M.hyiopneumoniae*. In many diagnostic laboratories, immunofluorescence with labeled polyclonal antibodies is used as the standard method for detecting *M. hyopneumoniae*. The disadvantage of this method is the frequent cross-substitution with the species *M. flocculare and M. hyorhinis*. The immunohistochemical method on lung specimens fixed in formalin is also available for the detection of the species *M. hyiopneumoniae*, but it is not sensitive enough (Rautiainen, 1998). Of the serological methods, RVK and ELISA are used and are considered the most sensitive, but still not sufficiently specific, methods for the diagnosis of enzootic pneumonia. Special antigen preparation avoids cross-reactions with the bacterial species *M. hyorhinis* and *M. flocculare*. In addition to blood serum, antibodies can also be detected in colostrum. The advantages of using colostrum are that it is easy to collect and the test is very sensitive, since colostrum has a higher concentration of antibodies than sow serum in the first 24 hours after farrowing. The disadvantage of antibody detection methods is that it is not always possible to distinguish diseased from vaccinated animals based on the results, and they cannot be used for early diagnosis of this disease because of the long period required for seroconversion. With advances in molecular biology, new diagnostic methods have emerged, the most important of which is the polymerase chain reaction (PCR), which has been shown to be highly specific, sufficiently sensitive, and rapid. To date, various PCR methods have been developed (single PCR, multiplex PCR, realtime PCR). Currently, the so-called "nested PCR" is used in most laboratories. This involves two consecutive PCR procedures, where the PCR product of the first procedure is immediately used as starting material for the second PCR procedure. This method is suitable when an extremely small amount of mycoplasma is expected in the test material, which cannot be detected by the usual PCR method (*Baumeister et al., 1998*), *Caron et al., 2000*). Material for the detection of *M. hyopneumoniae* can be lung tissue, if it is a dead animal, or swabs of the nasal mucosa, i.e. bronchoalveolar lavage from live animals*(*Otagiri et.al.200*5).*

Therapy

Despite the variety of antibiotics and chemotherapeutic agents used in the treatment of enzootic pneumonia in pigs, it is very difficult to cure the disease completely and to remove *M. hyopneumoniae* from the cultures. Because *M. hyopneumoniae* colonises the surface of the ciliated epithelium without penetrating the tissue, accessing and achieving a therapeutic dose of the drug is difficult. An additional obstacle to antibiotics is the accumulation of infected cells and the constriction of blood vessels in the affected area. An additional problem with on-site treatment is the simultaneous presence of animals in different stages of disease. The drugs used today to control and treat enzootic pneumonia in pigs are: tetracyclines, macrolides (tylosin, tilmicosin), lincosamides (lincomycin, clindamycin), pleuromutilins (tiamulin, valnemulin), fluoroquinolones (enrofloxacin, flumequin, danofloxacin, ciprofloxacin), aminoglycosides (streptomycin, gentamicin, tobramycin) and fluorfenicol (Prodanov-Radulović et al., 2020b; Vicca, 2005). Of the above-mentioned preparations, tetracyclines, macroloid antibiotics and pleuromutilins are most frequentlyused. The combination of chlortetracycline and valnemulin and chlortetracycline and tiamulin proved to be particularly effective. Fluoroquinolones and aminoglycosides are the only ones that have a mycoplasmicidal effect, which is why their use is recommended in programmes to eradicate enzootic swine pneumonia. The susceptibility of field isolates of *M.hyopneumoniae* to various antimicrobial preparations has been studied only rarely and on a small number of isolates, due to the difficult cultivation of this microorganism and the lack of standardised procedures (Burch, 2004). It is particularly important to emphasize that the stand-alone use of antibiotics under in vivo conditions cannot eliminate all microbes, especially when dealing with co-infection with viruses (PRSV and PCV_2), which significantly weaken the pig's immune system. Thus, treatment with antibiotics not only fails to kill the pathogen *(M. hyopneumoniae),* but also allows the emergence of resistant strains that can cause disease of epidemic proportions. The emergence of species resistant to certain antimicrobial preparations to which they were previously sensitive has also been noted; isolates of *M.hyopneumoniae* moderately sensitive to oxytetracycline have been isolated in Japan, and several authors noted reduced sensitivity of

certain species to chlortetracycline. They were the first to demonstrate acquired resistance of certain field isolates to macroloides (tylosin and tilmicosin), lincosamides (lincomycin) and fluoroquinolones (flumequine and enrofloxacin) (Vicca et al. 2005). The mechanism of resistance emergence is based on the high frequency of mutations in the genes encoding the target site to which antibiotics bind, which is a consequence of the low amount of genetic information destined for DNA repair systems. The frequency of occurrence of resistant *M. hyopneumoniae* species under field conditions is probably low, and some of the possible reasons for this are: the inability to transfer this type of resistance between different species, the instability of the gene mutation causing the resistance, and the more difficult spread of resistant species *(Bojkovski, et al. 1997 ., Vicca, 2005*).As enzootic pneumonia is a disease of intensive pig production, animals are usually treated in groups. Parenteral administration of the drug is usually used only in animals with an acute form of the disease for the first three days, after which therapy is continued (usually by one drug if water-soluble preparations are used for group therapy). For the most common, chronic form of the disease, all animals in the breeding are treated. Antibiotics are added to the drinking water. The problem with this application is the weak appetite of the sick animals. To prevent this, feed intake must be carefully monitored. Similar difficulties arise when antibiotics, which is an effective form of group therapy, are administered in the drinking water, as consumption is closely related to temperature, feed composition and many other factors. When selecting an antibiotic and its dose, many other factors must be taken into account (absorption of the antibiotic after oral administration and its distribution in the target tissue, solubility, secondary infections). Therefore, the focus of control of enzootic pneumonia should be on prophylaxis and control measures.

Prophylaxis

Prophylactic measures can be divided into those carried out in areas where infection with *M. hyopneumoniae* has not yet been detected and those carried out when this pathogen is already present in the herd. One of the preventive measures is the purchase and introductioninto the herd new animals that are free from *M.hyopnemoniae* and formation of a new mycoplasma-free herd.. Similarly, it would be good to introduce only animals from single source animals with , tested breeding farm, as mixing animals of different origins and health status reared on different farms increases the possibility of disease outbreaks. Whether farms remain free of the pathogen depends on the location of the farm itself. Thus, if there is an infected farm within a radius of three kilometers, it is only a matter of time before the infection spreads to healthy farms. Therefore, in areas with developed pig farming, it is almost impossible to keep the farm free of infection. By applying external biosecurity measures, the possibility of introducing mycoplasmas can be reduced. Uninfected farms should be kept as closed as possible, genetic material should only be introduced by artificial insemination, and newly arrived pigs must be quarantined for a period of eight weeks. Among the quarantined pigs, some animals from the own breeding should be placed and tested at the beginning of the quarantine and after five weeks. All animals in quarantine should be serologically tested and, in case of death, tissue samples should be submitted for molecular diagnostics. For farms raising only fattening animals, the "all in all" husbandry system should be applied. out ". In farms where *M.hyopnoniae* is already present and in areas where safe husbandry is not possible, the following measures are taken: Compliance with prescribed zootechnical conditions, vaccination and strategic medication. New animals introduced into farms where *M.hyopneumoniae* is already present may be infected with this bacterium, but should be free of other diseases such as swine dysentery or PRRS. If animals are free of the pathogen causing enzootic pneumonia and they are planned to be introduced into farms where this disease is already present, it is recommended to add antibiotics to the feed during the first weeks. Measures to reduce the risk of spread or clinical manifestation of the disease include: 1. avoiding overcrowding of the house, 2. ensuring good ventilation and air circulation, 3. maintaining a high level of hygiene, 4. reducing the amount of biologically active dust, micro-organisms, CO_2 and ammonia in the air, 5. reducing unnecessary manipulation of the animals and other stress factors, 6. Maintaining an optimal air temperature according to the pig categories, 7. Ensuring a balanced and high quality diet, 8. Avoiding dietary changes at sensitive life stages, 9. Monitoring the presence of other respiratory disease agents (PRRSV, SIV). Numerous vaccines have come onto the market in the last decade and are used with varying degrees of success in most countries with developed pig farming. When planning a vaccination programme, each breed should be considered as an individual case. In order for the expected outcome of vaccination to be as successful as

possible, the dynamics of the spread of infection at the level of a particular farm, the presence of competing diseases and the relationship between cost and expected gain should be taken into account. Vaccinating sows in the last stage of pregnancy provides protection for piglets in the first weeks of life. Most of the antibodies are absorbed by the piglets in the first six hours after colostrum intake, and the antibody level in the piglets' serum is the same as that of the sow about 24 hours after farrowing. The half-life of the antibodies is about 15 days, so that in piglets with a high initial titre, significant amounts of antibodies can still be detected 60 days after farrowing. In such piglets, infection is possible at a later stage of rearing and the disease usually occurs at the end of fattening. In contrast, in piglets with a low initial titer, a relatively low antibody level is observed after only 30 days. *(Burch, 2004, Hodgins et.al.2004*). It has been found that piglets with a high maternal antibody titre show a significantly weaker response to vaccination (interference phenomenon). In such cases, it is better to vaccinate 6-8 weeks after farrowing to allow a natural decline of maternal antibodies (passive immunity) and to achieve an adequate immune response in most vaccinated animals (active immune response). Piglets without maternal antibodies or with low titers can be vaccinated as early as one week after farrowing, as the age of the piglets has been shown to have no significant influence on the effect of the vaccination(Thackeret.al. 2000,Siugzdaite et.al.2002, Meyns et.al.2006,Valčić,2007)..

Control of Mycoplasma pneumonia in pigs in the Republic of Serbia

Respiratory diseases have become one of the biggest problems in modern pig production. Within this disease complex, *Mycoplasma pneumonia and Actinobacillus pleuropneumonia* occupy a prominent place. For this reason, the following was carried out: Examination of pig blood serum for the presence of antibodies against *Mycoplasma hyopneumoniae* and *Actinobacillus pleuropneumoniae* by ELISA. Blood samples were collected from sows, gilts, boars and piglets from 5 pig farms and analysed. The tests were performed by the indirect ELISA method using the following diagnostic kits: Herd Chek *M.hyo*: *Mycoplasma hyopneumoniae*, antibody test kit, and Chekit APP –Apx IV*: Actinobacillus pleuropneumo*niae (App) antibody test kit. A total of 1100 pig blood sera were tested, including 458 sera from sows, 434 sera from gilts, 88 sera from boars and 120 sera from piglets. Antibodies against *Mycoplasma hyopneumonia* were found in 176 (38.42 %) sow sera, 217 (50 %) gilts sera, 36 (40.90 %) boars sera and 30 (25 %) piglets sera. The percentage of positive sera varied between farms, ranging from 21-80 % in gilts, 17-65 % in sows, 16.67-100 % (10/10) in boars and 0-60 % in piglets. Antibodies against *Actinobacillus pleuropneumoniae* were found in 320 (69.86 %) sera from sows, 333 (76.72 %) sera from gilts, 43 (48.86 %) sera from boars and 66 (55 %) sera from piglets. The percentage of positive sera between farms ranged from 60.32-79.64% for sows, 64.54-89.58% for gilts, 34.09-72.73% for boars and 51.43-60% for piglets. The test results show that infection with *Mycoplasma hyopneumonia*e and *Actinobacillus pleuropneumoniae* is present in pigs in all 5 farms tested. The intensity of infection differs between farms and also between production and technology categories of animals. We highlight here gilts as a category in which the highest percentage of positive sera was found for *M. hyopneumoniae* with 80% and for *A. pleuropneumoniae* with 89.58%. (Žutić M, 2009, Žutić J.2008).

Successful control of *Mycoplasma pneumoniae and Actinobacillus pleuropneumoniae* depends on effective prevention of transmission of the pathogen both between farms and between certain categories of animals on the same farm. Good results can be achieved by strict application of reliable serological methods. Serological control of gilts is particularly important to detect infected animals before insemination and to remove them as such from the herd, as dams transmit the infection to their offspring after farrowing.

Control of Mycoplasma pneumonia in pigs in North Macedonia

In the studyconducted by Angelovski et.al.2023,antibody against *M.hyopneumoniae* were detecte3d in 58%(145/250) of pigs with highest seroprevalence observedin finishing pigs(86%,43/50). Lowest seroprevalence was detected in youngest pigs at 6 weeks of age(26%,13/50). In the same study ,high precentage (91,2%) of lungas with enzootic pneumonia like3 lesions was observed during slaugheter checks in finishing pigs.(Angjelovski et.al. 2023*).*

CONCLUSION

Enzootic pneumonia is widespread throughout the world and causes major economic losses in intensive pig farming. the pathogen type *M. hyopneumoniae* is found exclusively in pigs and is mainly transmitted by carriers or airborne. In farms where the pathogen is enzootic, the disease is chronic, and the constant occurrence of cramp-like, unproductive coughing on the farm, weaker feed conversion and consequently lower growth are often the only signs of the disease. Additional problems are caused by very frequent secondary infections with bacteria and viruses. The acute course of the disease occurs in pigs first exposed to *M. hyopneumoniae* and the visible signs of the disease are either very mild changes in the respiratory system to severe acute pneumonia associated with high mortality. Clearly demarcated, purple to grey areas of consolidated lung tissue, usually distributed over the apical and cranial lobes, are characteristic pathoanatomical findings for enzootic pneumonia in pigs. ELISA, polymerase chain reaction (PCR) and RT - PCR (real life polymerase chain reaction) have proven to be the most reliable methods for diagnosing enzootic pneumonia Antimicrobials most commonly used today to control and treat this disease are: Oxytetracycline, Chlortetracycline, Florfenicol, Macrolide antibiotics, Pleuromutilins and Fluoroquinolones. After treatment, *M. hyopneumoniae* can still be detected in the lungs and relapses are very common. Disease suppression and eradication measures include compliance with external and internal biosecurity rules, adherence to prescribed zoohygienic conditions, vaccination and, depending on the farm technique, the use of strategic medication .

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