Proceedings 5th World Rabbit Congress, 25-30 July 1992, Corvallis – USA, 1515-1523.

NATURAL HISTORY OF *PASTEURELLA MULTOCIDA* INFECTION IN RABBITS

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Abstract

In rabbit colonies with *Pasteurella multocida* infection, the prevalence of infection increases with age. The rate of infection is usually low in preweanlings, whereas most adults are infected. Higher rates of infection in younger rabbits may be related to late weaning, vaginal infection in dams, and prevalence of infection in the colony. The main routes of transmission are by direct contact, airborne spread, and fomites. The potential for transmission may depend on the severity of infection in rabbits, as shedding may be greatest during periods of upper respiratory tract disease. The nares are infected soon after exposure suggesting that the portal of entry is respiratory. The incubation period is probably days to weeks and infection usually persists. The organism has a predilection for the upper respiratory tract and contiguous tissue sites. It can usually be recovered from the nasal passages. Sites of frequent dissemination and persistence include the paranasal sinuses and middle ears. The nasopharynx and oropharynx may be colonization or transit sites. The vagina is the only non-respiratory site of colonization. Infection is usually endemic in conventional rabbit colonies, but outbreaks of severe respiratory tract disease may occur.

Infection in Relation to Age, Sex, and Breed

In a study (Hagen, 1958; Hagen, 1959) of 3 pregnant does killed 3 to 7 days prior to parturition, *P. multocida* was not isolated from blood of the lungs or heart of the fetuses. In 2 litters of 2-day-old rabbits, blood samples from lungs and heart were culture-negative for *P. multocida*. However, *P. multocida* was recovered from the lungs of 4 rabbits 11 to 17 days old. No information relative to *P. multocida* infection in the dams was provided. Holmes *et al.* (1984) found that 3 of 5 litters, 0 to 5 days old, from does with *P. multocida* infection of the nares and acute rhinitis prior to kindling, had *P. multocida* recovered from oropharyngeal swabs or somatic tissues. Similarly, 3 of 5 litters, from does with nasal *P. multocida* infections but without rhinitis, had *P. multocida* isolated from the nares and oropharynx at 3 to 10.5 weeks old. DiGiacomo *et al.* (1983) obtained nasal swabs from nine litters of rabbits, prior to weaning at 8 weeks of age, in a commercial colony. While 4 of the does had *P. multocida* infection, none of the litters acquired infection. In 29 breeding does, either with nasal *P. multocida* infection or antibodies to *P. multocida*, 10 (34%) had progeny which were infected when sampled at 2 to 10 weeks old (Glass and Beasley, 1989). Of 50 rabbits sampled from the 10 litters, *P. multocida* infection was detected in 14 (28%) rabbits.

Deeb *et al.* (1990) reported that the prevalence of infection increased from 22% in rabbits 5 to 6 weeks old to 51% in rabbits 13 to 14 weeks old; the prevalence in does > 6 months old was 73%. Hagen (1967) reported that 29 of 46 (63%) weaned (8 weeks old)

rabbits had *P. multocida* infection whereas 6 of 7 (85%) adult rabbits were infected. Duclos *et al.* (1986) found that 0 of 16 weaned (5 to 12 weeks old) rabbits had *P. multocida* infection whereas 9 of 19 (47%) adult rabbits were infected. Nakagawa *et al.* (1986) reported the prevalence of infection in 6 age categories from <1 to >5 months in 2 rabbit colonies. The prevalence of infection increased steadily with age, from 4% in preweanlings (<1 month old) to 94% in adults (>5 months old). Lu *et al.* (1978) reported the prevalence of *P. multocida* by the weight of rabbits. In rabbits from 1 vendor, 2 of 27 (7%) juveniles (1.8-2.7 kg) and 29 of 49 (59%) adults (2.8-4.1 kg) had *P. multocida* infection, while in rabbits from another vendor, 7 of 49 (14%) juveniles and 4 of 10 (40%) adults were infected.

Both Hagen (1958) and Hinton (1979) reported isolation of *P. multocida* from pneumonic lungs of rabbits 0 to 8 weeks old. *P. multocida* was also isolated frequently from pneumonic lungs of rabbits 8 to 12 weeks old (Percy *et al.*, 1988). Flatt (1971a) found that about 20% of 3,967 healthy rabbits, 8 to 10 weeks old, had pneumonia at slaughter. Of 113 pneumonic lungs examined bacteriologically, *P. multocida* was isolated from 51 (45%) (Flatt *et al.*, 1971b). Fox *et al.* (1971) reported the isolation of *P. multocida* from the middle ears of rabbits 3 weeks to 30 months old with otitis media. Similarly, Flatt *et al.* (1977) recovered *P. multocida* from rabbits 8 to 10 weeks old with otitis media. Of 2,001 rabbits examined, 87 (4%) had otitis media and *P. multocida* was isolated from 60 to 61 rabbits cultured. Examination of 583 culled breeding females revealed that 188 (32%) had otitis media. Similarly, 10 of 31 (32%) rabbits with upper respiratory tract disease had otitis media from which *P. multocida* was isolated (Snyder *et al.*, 1973).

Few studies have reported the influence of sex or breed of rabbits on *P. multocida* infection. Lu *et al.* (1978) found that 1 of 17 (6%) males and 1 of 10 (10%) females, 1.8 to 2.7 kg, newly received from a commercial vendor had *P. multocida* infection. However, in rabbits 2.8 to 4.1 kg, 9 of 24 (38%) males and 20 of 25 (80%) females had *P. multocida* isolated from nasal swabs. Webster (1927) reported the influence of breed on the occurrence of pasteurellosis in a commercial rabbitry. The prevalence of rhinitis and mortality due to *P. multocida* was considerably lower in the Blue Beveren than in the Chinchilla or Havana breeds. Similarly, the carriage of *P. multocida* in the nares of normal rabbits was significantly greater in rabbits of the Chinchilla than the Blue Beveren breed; 60 of 142 (42%) of the former were infected compared to 20 to 76 (20%) of the latter breed. Hence, of the 3 breeds, the Blue Beveren was most resistant to infection and disease caused by *P. multocida*. Alexander *et al.* (1952) reported mortality from pneumonia due to *P. multocida* in 11 rabbit strains at The Jackson Laboratory (U.S.A.). The mortality, by strain, ranged from 0 to 100%. In strains with at least 15 rabbits observed, strains Ach and III had the highest mortality, 21% and 20%, respectively, whereas strains OS and DRD had the lowest mortality, 5% and 3%, respectively. A group of miscellaneous strains, which might be considered a comparison group, had a mortality of 13%. Fox *et al.* (1971) determined the incidence of otitis media, due to *P. multocida*, in 11 rabbit strains at The Jackson Laboratory (U.S.A.). Strains C, ACCCR (Y), and ACCR (B) had high rates, 8.3, 4.6, and 4.1, respectively, whereas strains ACEP, A, AX, and X had low rates (0.3 to 0.5). A miscellaneous group of rabbit strains had a rate of 0.8. Data from 3 rabbit strains (X, OS, III) reported in both studies were not relatively similar.

Transmission

Transmission of *P. multocida* between infected and *Pasteurella*-free rabbits was examined by Lelkes and Corbett (1983). Six uninfected rabbits in direct contact with infected rabbits all acquired infection, 5 within 3 weeks after initial contact. Seven of 8 uninfected rabbits housed in the same cage rack, but in cages 4 inches removed from cages containing infected rabbits contracted infection within 4 weeks. Six uninfected rabbits housed in a rack 10 feet away from infected rabbits failed to acquire infection after 12 weeks of exposure. DiGiacomo *et al.* (1987) assessed contact and airborne transmission of *P. multocida* in an artificially controlled environment. In one experiment, only 1 of 4 rabbits acquired infection after 3 weeks of contact with 2 naturally infected rabbits. In a second experiment, 3 of 3 rabbits acquired infection after 8 days of contact with rabbits experimentally infected. Two of 3 rabbits in contact for 9 days with the 3 rabbits that acquired their infections from the experimentally infected rabbits also acquired infection. *P. multocida* was detected in air samples during the second experiment only. However, uninfected rabbits, caged 75 cm away from infected rabbits in both experiments, failed to become infected. While infection of rabbits by airborne exposure did not occur, the duration of exposure was only 3 weeks. DiGiacomo *et al.* (1991) reported that 5 of 41 (12%) rabbits in 12 litters, 5 to 8 weeks old, acquired *P. multocida* infection, when housed for 3 months in a building with *Pasteurella*-infected adult rabbits, presumably by aerosol transmission. Six of 13 (46%) additional rabbits in 3 of the litters also contracted infection, 5 within 1 to 3 weeks, presumably by direct contact with the rabbit initially infected in the litter. Similarly, during 3-1/2 months, 11 of 62 (18%) 8-week-old rabbits, initially free of *Pasteurella* infection, acquired infection when housed in the same building with *Pasteurella*-infected adult rabbits (DiGiacomo *et al.*, 1983). Scharf *et al.* (1981) reported that 23 of 134 (17%) young adult rabbits, purchased as *Pasteurella*-free but maintained under conventional conditions for 3 to 6 months, contracted *P. multocida* infection. In both of these latter reports, aerosol transmission was assumed. This mode of transmission suggests respiratory escape, airborne conveyance by infected droplet nuclei and a respiratory portal of entry.

McKennedy and Shillinger (1938) noted that females bred to the same buck developed either an acute hemorrhagic septicemia or a purulent discharge of the reproductive tract that resulted in sterility. Examination revealed an enlarged left testicle, and a testicular abscess due to *P. multocida* was diagnosed. The buck was mated with 11 does. Two does died of septicemia within 3 days after breeding, and the other does developed a purulent discharge from the reproductive tract 9 to 42 days later. *P. multocida* was isolated from vaginal swabs or blood. Five does, brought to the buck's cage but prevented from mating remained uninfected. Fomite spread of *P. multocida* was reported by Smith (1927). A group of 15 rabbits infected with *P. multocida* were brought to a facility holding rabbits which had been free of *P. multocida* for over 2 years. Infected rabbits were isolated from the colony and maintained for 5 months. Through error, infected rabbits were placed in transport cages normally reserved for the *P. multocida*-free rabbits for several hours. The cages were subsequently used without being sterilized, presumably within hours. Within a week, several of the 22 *P. multocida*-free rabbits were sneezing and *P. multocida* was isolated from affected rabbits. In a study designed to evaluate environmental contamination in cages of *P. multocida*-infected rabbits, Holmes *et al.* (1983) reported that 29 of 36 (81%) water valves

were contaminated with *P. multocida* in cages of rabbits with rhinitis. However, in cages containing infected rabbits without clinical signs, 20 of 37 (54%) water valves were contaminated. While the possibility of fomite transmission existed, it was not evaluated by exposure of *P. multocida*-free rabbits to the valves.

Incubation Period and Persistence

Alexander *et al.* (1952) noted that *P. multocida* was isolated from the nares of apparently healthy rabbits 1 to 2 weeks prior to development of pneumonia. However, it was not stated whether previous nares specimens had been culture-negative. DiGiacomo *et al.* (1983) monitored the onset of rhinitis in relation to *P. multocida* infection in 13 weanling rabbits. Three rabbits had rhinitis 1 to 2 weeks before isolation of *P. multocida*. In 2 rabbits, isolation was concurrent with onset of clinical signs; in 8 rabbits, rhinitis developed 1 or more weeks after isolation of *P. multocida*. Of the 8 rabbits, 7 had rhinitis 2 or more weeks after infection was detected. In a similar study of 10 weanling rabbits, 4 rabbits developed rhinitis 0 to 4 weeks after isolation of *P. multocida*, however, 6 rabbits had rhinitis 1 to 4 weeks prior to detection of nasal infection (DiGiacomo *et al.*, 1991). Jaslow *et al.* (1981) conducted a therapeutic trial in 28 rabbits infected with *P. multocida* that had clinical signs of rhinitis for 60 days or more. During a 40-day observation period, rabbits with chronic rhinitis improved clinically with or without treatment. However, infection with *P. multocida* persisted.

Sites of Infection

In transmission studies (Lelkes and Corbett, 1983; DiGiacomo *et al.*, 1987) rabbits recently infected with *P. multocida* were detected by cultures of nasal swabs. Glass and Beasley (1989) cultured several sites in rabbits killed at 2 to 10 weeks old and *P. multocida* was isolated from the paranasal sites in 11 of 14 (79%) infected rabbits, however, the nares were not cultured. In addition, *P. multocida* was recovered from the trachea of 5 rabbits, the middle ears of 3 rabbits, and the lungs of 1 rabbit. Holmes *et al.* (1984) reported that in 4 of 6 infected rabbits 39 to 70 days old, *P. multocida* was isolated from the nasopharynx. *P. multocida* was also isolated from the oropharynx of 3, the middle ears of 2, the nares of 1, and the paranasal sinuses of 1 of these 4 rabbits. Two rabbits had *P. multocida* isolated from the middle ears only. Nakagawa *et al.* (1986) cultured various sites at necropsy in 54 *P. multocida*-infected rabbits >3 months old. *P. multocida* was recovered from the paranasal sinuses in 53 (98%) rabbits and from the nares in 49 (91%) rabbits. The frequency of isolation from other organs was as follows: 28 (52%) from the trachea, 26 (48%) from the middle ears, 9 (17%) from the conjunctiva, 9 (17%) from the lungs, 7 (13%) from the heart, and 1 (2%) from the spleen. One rabbit had *P. multocida* isolated from the middle ears only. In 69 rabbits, >6 months old with nasal *P. multocida* infection, the organism was also recovered from the paranasal sinuses in 60 (87%) rabbits and the middle ears in 55 (80%) rabbits (Deeb *et al.*, 1990). In 26 rabbits without nasal infection, *P. multocida* was recovered from the paranasal sinuses of 5 (19%) rabbits and the middle ears of 9 (35%) rabbits. Lukas *et al.* (1987) cultured the nares and middle ears of 7 mature rabbits with antibodies to *P. multocida*. *P. multocida* was isolated from the nares of 5 rabbits and from the middle ears only of 2 rabbits. Holmes *et al.* (1986) reported that *P.*

multocida was recovered from the naso-oropharynx and middle ears of 13 of 14 nasal-culture negative rabbits, 5 to 6 months old, with antibodies to *P. multocida*. The 1 other rabbit had a subcutaneous abscess from which *P. multocida* was isolated. Okuda and Campbell (1974) recovered *P. multocida* from the conjunctival sac of 1 of 54 rabbits without signs of external ocular or upper respiratory tract diseases. Concurrent cultures of other sites (nares) were not reported. Jacques *et al.* (1986) cultured the vagina, cervix, and uterus of 35 does 4 to 5 months old and failed to recover *P. multocida*. McKennedy and Shillinger (1938) isolated *P. multocida* from the vagina of only 1 of 50 (2%) breeding does. Holmes *et al.* (1983a) recovered *P. multocida* from the vagina of 18 of 73 (25%) junior and working does. No significant difference in the prevalence of infection between the 2 groups was found. Fourteen of the 18 rabbits also had *P. multocida* isolated from the nares.

Prevalence of Infection in Colonies

During the past 25 years, the prevalence of *P. multocida* infection in New Zealand White rabbit colonies has been determined in a number of studies (Hagen, 1967; Weisbroth and Scher, 1969; Lu *et al.*, 1978; Mraz *et al.*, 1980; Garlinghouse *et al.*, 1981; Scharf *et al.*, 1981; DiGiacomo *et al.*, 1983; Holmes *et al.*, 1983a; Holmes *et al.*, 1983b; Duclos *et al.*, 1986; Nakagawa *et al.*, 1986; Holmes *et al.*, 1986; Lukas *et al.*, 1987). The prevalence of *P. multocida* in the nares of apparently healthy rabbits, without signs of upper respiratory tract disease, ranged from 31% to 94%. All studies reported data from mature (>5 months old) rabbits and used cultural techniques to detect *P. multocida* from nasal swab specimens. Weisbroth and Scher (1969) detected a 90% carrier rate in an institutional colony, using an indirect fluorescent antibody assay on smears of nasal swabs. However, the sensitivity and specificity of the assay was not directly compared to standard cultural or serologic tests in rabbits. There was insufficient data to determine whether the prevalence of infection differed between institutional and commercial colonies. A recent serologic survey of 9 institutional colonies revealed that 34% to 100% of rabbits sampled had antibodies to *P. multocida* (Zaoutis *et al.*, 1991).

Outbreaks of Disease in Colonies

Smith (1927) reported an outbreak of lower respiratory disease in a population of rabbits previously unexposed to *P. multocida*. A colony of 22 rabbits of mixed Belgium hare breed had been maintained free of *P. multocida* for over 2 years. Rabbits were subsequently exposed to infected rabbits brought into the facility. Within a week after exposure, several rabbits were sneezing, and between 18 to 33 days after exposure, 7 of the 22 rabbits had died of pneumonia. *P. multocida* was isolated from the lungs and pleural fluid. All remaining rabbits developed mucopurulent rhinitis from which *P. multocida* was recovered. Alexander *et al.* (1952) noted that The Jackson Laboratory (U.S.A.) experienced a 50% mortality in a colony of about 1,000 inbred rabbits. Mortality was due to pneumonia and *P. multocida* was isolated in pure culture from pneumonic lungs. Sato *et al.* (1967) reported that 50 of approximately 300 adult rabbits in an institutional holding colony either died or were euthanatized with respiratory tract disease over a 4-month period. Rabbits exhibited a purulent nasal discharge, labored breathing and emaciation. Fibrinous pneumonia was found, and severe cases had purulent pleuropneumonia and pyothorax. Some rabbits had a

fibrinopurulent pericarditis and peritonitis. *P. multocida* was isolated from the lungs in pure culture. An outbreak of pasteurellosis was reported from a commercial rabbitry by DiGiacomo *et al.* (1983). Pasteurellosis, characterized by mucopurulent rhinitis, was endemic in the colony. A survey of healthy adult rabbits in the breeding program revealed that 27 of 45 (60%) had *P. multocida* infection. During the early phase of the outbreak, there was an increase in the prevalence of rhinitis in weanlings and young adults. Affected rabbits were culled from the colony, resulting in a decline in morbidity. However, this had only a temporary effect on the outbreak, because it began anew, first in weanlings, then in young adults, and finally in adults. Preweanlings were not affected. The outbreak gradually abated by the culling of affected rabbits, although some breeding stock were treated. During the outbreak, *P. multocida* was isolated from the nares of 11 of 14 (79%) adult rabbits with rhinitis. The major phase of the outbreak lasted for about 9 months. The increased morbidity was not associated with increased mortality.

Conclusion

This review summarizes current knowledge of various aspects of the natural history of *P. multocida* infection in rabbits. This infection is widespread in rabbit colonies, resulting in significant morbidity and mortality in rabbits. An understanding of the natural history of infection is an essential prerequisite for the control of pasteurellosis in rabbits.

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