



When bacteria infect nursing does and / or their kits ...

Michel Gruaz, Arie van Praag and Esther van Praag

Rabbits are naturally clean animals. They regularly groom their fur and perineal region by licking the hair with their tongue or by licking their paws before cleaning their ears or face.

The goal of meticulous grooming and daily detangling of the fur is to avoid any odor capable of attracting predators, but also unwanted insects and flies. These are, indeed, true flying hazards. They carry

hundreds of bacteria from carcasses and excrements on their wings and legs which will contaminate the litter, food, equipment and the hutch itself. According to the fly species, they lay their eggs among the fecal



Figure 1: Female rabbit feeding her kits. Photo: Hadar Orkibi

droppings of rabbits and other rotting material, but also in skin wounds.

Before giving birth, a doe will prepare a nest made of straw, hay and fur plucked from her abdomen. Odorless so as not to attract flies and other unwanted biting or blood sucking bugs, in addition to predators. After kindling, she licks her newborn kits to dry them and ingests the placenta remnants to remove any smell of blood, before feeding them their first colostrum milk. By these measures, she protects her kits, but also herself. Indeed, pathogens use all entry doors to infiltrate an organism. Hutch hygiene is, therefore, essential to limit the presence of bacteria, but not only...

Attractive molecule for breastfeeding

Rabbit kits are born blind and naked, and must drink their first milk so as not to die of

hunger and cold. The nursing doe provides them with her milk for 3 to 4 minutes per feed once a day only. Speed is, therefore, essential. Removing fur from her abdomen to make the nest exposes her teats (Figure 2). However, this is not enough for the newborn to quickly find the nourishing teats. Since nature never does things by half, the teats of the lactating rabbit release a volatile compound contained in the milk – 2-methylbut-2-enal, which acts like a pheromone (Figure 3). When rabbit kits detect this molecule, it triggers a reaction which incites them to rush towards the source of milk, seek and grab a teat and drink.

Its release by the doe and its reception by her kits represents a coevolution that ensures the successful reproduction and survival of the offspring in this species.

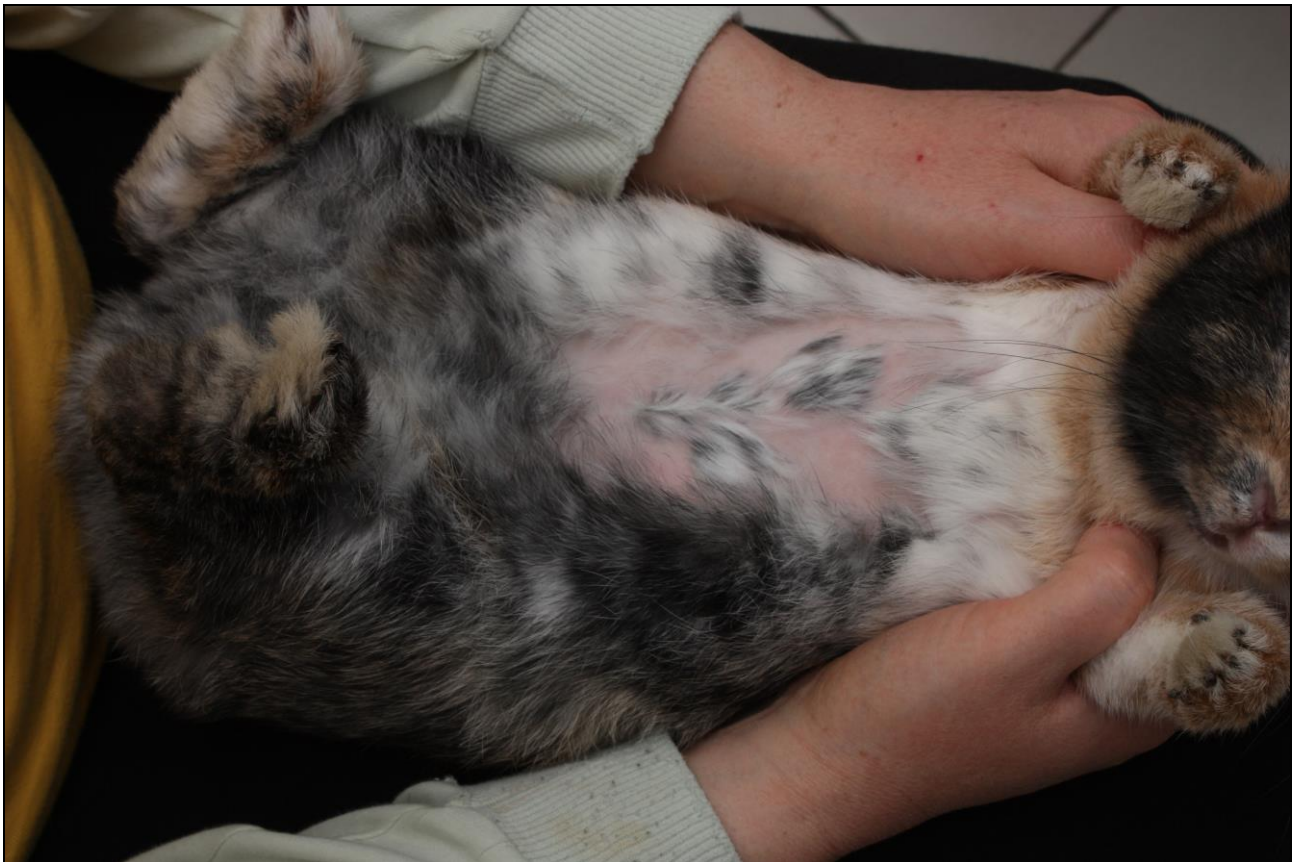


Figure 2: When building its nest, the female rabbit removes hair from its abdomen, at the same time exposing the teats. Photo: Arie van Praag

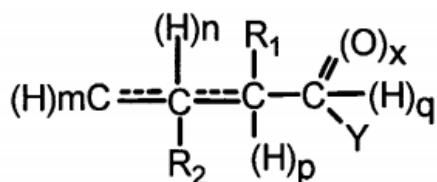


Figure 3: A volatile compound, 2-methylbut-2-enal, contained in the milk of the rabbit encourages its young to drink.

The teats located on the belly are most accessible to kits; those located between the thighs and between the front limbs are less so. If the litter is prolific, the kits in search of milk will feed on all the teats. Weak newborn will not have the strength to drink enough and may starve to death. When the litter is small, the more difficult to reach teats may remain full and engorged with milk.

Inflammation of the teat

A female rabbit may become infected

with bacteria such as streptococcus or, more often, staphylococci such as *Staphylococcus aureus*. Mastitis caused by *Escherichia coli* has been observed, but is uncommon. Often, these pathogens remain unnoticed during gestation. They exploit nursing to enter the doe's body, when her immune system has already been affected by gestation and kindling and renders her vulnerable to infection. Healthy nursing does that receive proper care and live in clean, well ventilated and odorless environments are not spared by these pathogens. Nursing rabbits with a particularly high milk production are particularly susceptible to mastitis (Figure 4).

Pathogen bacteria use mucocutaneous tissues (e.g., teat) or airways (e.g., respiratory tract) to infiltrate the body of the doe and endanger her life as well as that of her kits. A similar danger exists when there is insufficient drainage of the doe's milk. The



Figure 4: Female rabbits with a high milk production are predisposed to mastitis. Photo: Arie van Praag

udder may remain engorged with milk due to a small litter, an early weaning or a deformation of the teat. The weight and volume of udders engorged with milk will lead to the appearance of skin cracks or crevices on the teat. In a female rabbit that is weakened by gestation and kindling, this will favor the infiltration of bacteria into the teat. Bacteria proliferate in this environment that is favorable for them, and spread along the ducts, contaminating milk (Figures 5, 6). When an antibiotic treatment is started rapidly, the infection remains limited to one or two teats. If untreated, bacteria will start to invade the lymphatic and blood systems, allowing their spread throughout the body and cause sepsis, which is often fatal.

Clinical signs

Diagnosis is based on clinical signs and behavior of the doe. It is, therefore,

important to examine the teats a few days after parturition in order to detect a blockage of milk inside a milk canal. In this case, a painful lump is present in the teat. Any sign indicative of a trauma to the teat, a teat injury or mastitis should also be taken seriously. A doe is, indeed, particularly sensitive to mastitis during the second week after giving birth. It is often preceded by milk stasis in one or more teats.

In case of an infection, the teat is hard to the touch, is swollen, reddish, and feels warm to the touch (Figure 5). There is no pus. The female instinctively prevents touching her infected teats and shows a pain reaction when palpated. A congestive infection is treated with broad-spectrum antibiotics (enrofloxacin or cefalexins) for 5 days with a daily application of an astringent solution on the teat, e.g., vinegar. Non-steroidal anti-inflammatory pain relievers



Figure 5: Autopsy of a rabbit with an abscess in the hard swollen udder, with the presence of pus. Photo: Michel Gruaz

may be given if the doe shows signs of pain.

Without treatment, bacteria that are more or less adapted to this biotope, e.g., *Staphylococcus aureus*, spread within the breast tissue and contaminate milk present in the milk ducts (Figure 5). *Staphylococcus aureus* infections are particularly destructive as this pathogen releases a staphylococcal alpha-toxin which leads to necrosis of blood vessels (Figure 6). Infected tissues take on a purple or bluish color. The extent of the infection can range from one teat to the entire mammary gland. The female rabbit becomes feverish, listless and drinks a lot more in the early phase of infection. Without medical support, she will stop eating or drinking. Her hind-limbs may become paralyzed, leading her to take a characteristic position. At this stage, the risk of mortality is high.

In severe or chronic cases, the infection spreads throughout the reproductive system, especially in the uterus. Mastectomy accompanied by ovariectomy can save the rabbit, but anesthesia and surgical intervention are risky because of the weakened general condition of the animal.

Mastitis is painful, and milk sucking by her young kits further increases this pain. As a result, the female rabbit feeds her kits less, or rejects them. The milk produced has a lower quality and is contaminated. The young rabbits will in turn be contaminated and may become sick, even die, or transmit the bacteria to a nurse rabbit.

Diagnosis

Diagnosis is based on behavior and examination of the teats, their appearance,

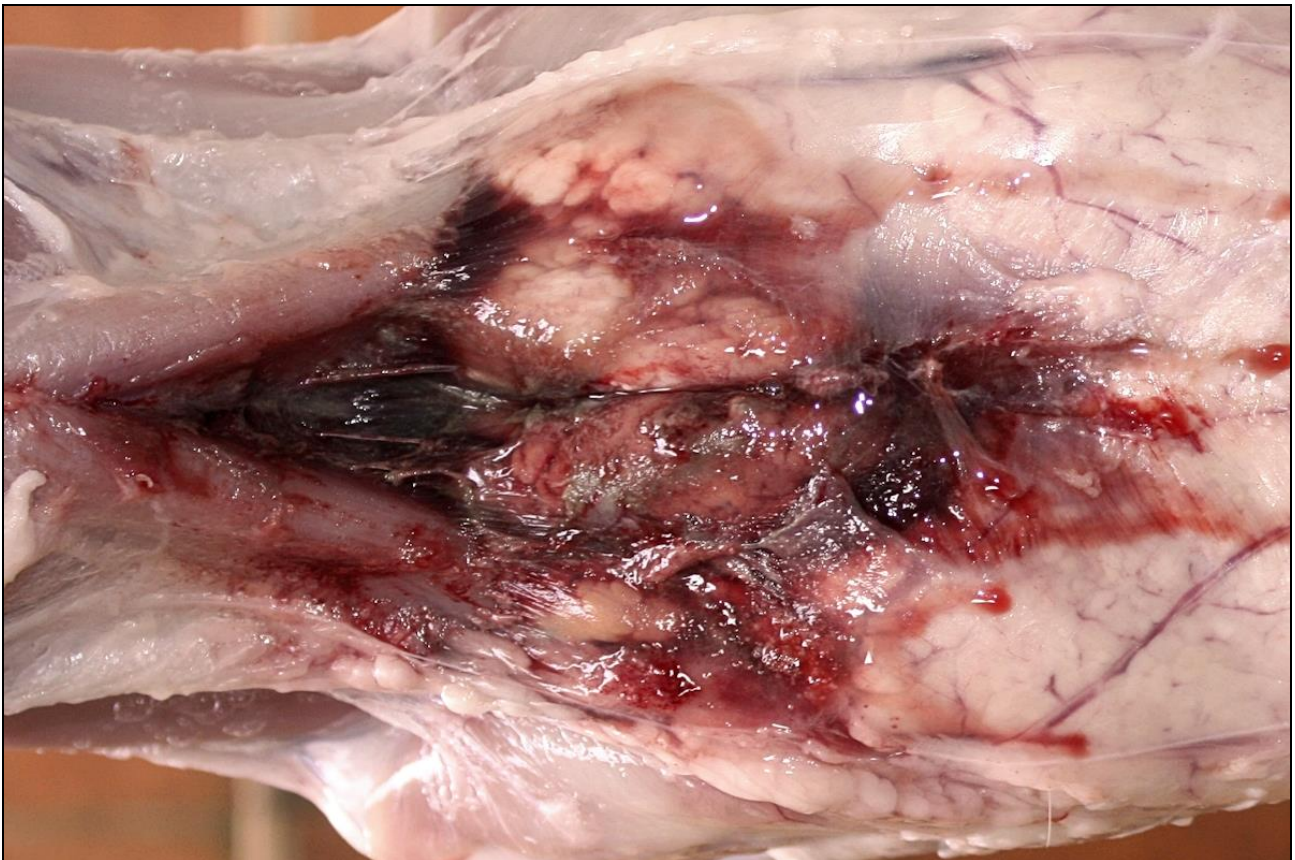


Figure 6: Autopsy of a rabbit with blue discoloration of breast tissue caused by necrosis of blood vessels by a staphylococcal alpha-toxin. Photo: Michel Gruaz

their reddish or blue color, their volume, or the presence of pus, etc.

A blood test and urine analysis help confirm a systemic infection and determine the therapeutic strategy to be undertaken: antibiotic therapy or surgical intervention.

Transmission to kits

Newborn rabbit kits are very vulnerable in the nest. If their mother is carrying pathogen bacteria, even without showing signs of disease, kits aged 0 to 15 days old may in turn become infected via contaminated milk. Bacteria present in infected teats can indeed be transmitted via milk. They may develop yellow diarrhea, which is dangerous for their survival. Other bacterial germs include streptococci.

The multiplication of *Staphylococcus aureus* bacteria in young kits may lead to generalized dermatitis, accompanied by skin wounds and small abscesses. The severity of the infection depends on the virulence of the pathogen strain, the virulent strains being linked to high mortality (Figure 7).

The presence of staphylococci and streptococci is also linked to the appearance of pustules all over the body of rabbits (Figure 8). These pus filled pimples could be the result of infected hair follicles. When they rupture, they release a small amount of pus and a bloody serosity. An orange-yellow crust covers the wound before healing. A disinfectant solution can be applied on the affected areas of kits, such as Betadine. This skin infection is rarely fatal in rabbit kits. In a litter of rabbits with skin pustules, the only kit without pustules developed a joint swelling instead, characteristic of an infection in the ankle joint (Figure 9). These infections lead to joint destruction, with lysis of cartilage and bone structures.

Other bacteria can infect young rabbits. *Pasteurella multocida* causes problems in the respiratory tract, but also abscesses in the neck, throat, legs, back and reproductive system. *Escherichia coli* can lead to severe digestive issues.

The control of bacteria in the rabbit's environment includes preventive methods of disinfection, monitoring or even isolation of



Figure 7: Kits suffering from dermatitis and skin abscesses caused by *Staphylococcus aureus*. Photo: MediRabbit



Figure 8: 9 day old rabbit with white pustules over all its body. Photo: Michel Gruaz



Figure 9: In a litter of 6, one of the youngsters developed swelling in the right hind paw joint at the age of 5 days. Such swelling has been diagnosed as septic arthritis in adult rabbits. In the absence of clinical analysis, an abscess cannot be excluded either. The other kits of the litter all developed a slight attack of pustules a few days later. Photo: Michel Gruaz

examination and bacteriological investigations. Treatment consists of appropriate antibiotic therapy.

Acknowledgements

A big thank you to Hadar Orkibi (Israel) for providing the picture of her rabbit for this article.

References

- Adlam C, Thorley CM, Ward PD, Collins M, Lucken RN, Knight PA. Natural and experimental staphylococcal mastitis in rabbits. *J Comp Pathol*. 1976 Oct;86(4):581-93.
- Adlam C, Ward PD, McCartney AC, Arbuthnott JP, Thorley CM. Effect immunization with highly purified alpha- and beta-toxins on staphylococcal mastitis in rabbits. *Infect Immun*. 1977 Aug;17(2):250-6.
- Charra R, Datiche F, Casthano A, Gigot V, Schaal B, Coureaud G. Brain processing of the mammary pheromone in newborn rabbits. *Behav Brain Res*. 2012 Jan 1;226(1):179-88.
- Guerrero I, Ferrian S, Penadés M, García-Quirós A, Pascual JJ, Selva L, Viana D, Corpa JM. Host responses associated with chronic staphylococcal mastitis in rabbits. *Vet J*. 2015 Jun;204(3):338-44.
- Goñi P, Vergara Y, Ruiz J, Albizu I, Vila J, Gómez-Lus R. Antibiotic resistance and epidemiological typing of *Staphylococcus aureus* strains from ovine and rabbit mastitis. *Int J Antimicrob Agents*. 2004 Mar;23(3):268-72.
- Hanser HI, Faure P, Robert-Hazotte A, Artur Y, Duchamp-Viret P, Coureaud G, Heydel JM. Odorant-odorant metabolic interaction, a novel actor in olfactory perception and behavioral responsiveness. *Sci Rep*. 2017 Aug 31;7(1):10219.
- Hermans K, Devriese LA, Haesebrouck F. Rabbit staphylococcosis: difficult solutions for serious problems. *Vet Microbiol*. 2003 Jan 2;91(1):57-64.
- Hughes K, Watson CJ. The Mammary Microenvironment in Mastitis in Humans, Dairy Ruminants, Rabbits and Rodents: A One Health Focus. *J Mammary Gland Biol Neoplasia*. 2018 Jun;23(1-2):27-41.
- Hughes K, Watson CJ. Sinus-like dilatations of the mammary milk ducts, Ki67 expression, and CD3-positive T lymphocyte infiltration, in the mammary gland of wild European rabbits during pregnancy and lactation. *J Anat*. 2018 Aug;233(2):266-273.
- Kullander S. Studies on the hormonal control of the milk-ejection activity in lactating rabbits. *Acta Endocrinol (Copenh)*. 1963 Oct;44:313-24.
- Legendre A, Faure P, Tiesset H, Potin C, Jakob I, Sicard G, Schaal B, Artur Y, Coureaud G, Heydel JM. When the nose must remain responsive: glutathione conjugation of the mammary pheromone in the newborn rabbit. *Chem Senses*. 2014 Jun;39(5):425-37.
- Luo M. Got milk? A pheromonal message for newborn rabbits. *Bioessays*. 2004 Jan;26(1):6-9.
- Montúfar-Chaveznava R, Trejo-Muñoz L, Hernández-Campos O, Navarrete E, Caldelas I. Maternal olfactory cues synchronize the circadian system of artificially raised newborn rabbits. *PLoS One*. 2013 Sep 5;8(9):e74048.
- Opdebeeck JP. Mammary gland immunity. *J Am Vet Med Assoc*. 1982 Nov 15;181(10):1061-5.
- Orwin PM, Fitzgerald JR, Leung DY, Gutierrez JA, Bohach GA, Schlievert PM. Characterization of *Staphylococcus aureus* enterotoxin L. *Infect Immun*. 2003 May;71(5):2916-9.
- Norcross NL. Immune response in the mammary gland. *J Dairy Sci*. 1971 Dec;54(12):1880-5.
- Rajeshwari, Y.B. & Satyanarayan, K. & Kailas, M.M.. (2000). Mastitis in a rabbit - A case report. 77.
- Said AH. Experimental coliform mastitis in rabbits. A biochemical and histopathological study. *Zentralbl Veterinarmed B*. 1969 Jul;16(5):387-403.
- Trejo-Muñoz L, Navarrete E, Montúfar-Chaveznava R, Caldelas I. Temporal modulation of the canonical clockwork in the suprachiasmatic nucleus and olfactory bulb by the mammary pheromone 2MB2 in pre-visual rabbits. *Neuroscience*. 2014 Sep 5;275:170-83.
- Vancraeynest D, Hermans K, Haesebrouck F. Prevalence of genes encoding exfoliative toxins, leucotoxins and superantigens among high and low virulence rabbit *Staphylococcus aureus* strains. *Vet Microbiol*. 2006 Oct 31;117(2-4):211-8.
- Vancraeynest D, Haesebrouck F, Deplano A, Denis O, Godard C, Wildemaue C, Hermans K. International dissemination of a high virulence rabbit *Staphylococcus aureus* clone. *J Vet Med B Infect Dis Vet Public Health*. 2006 Nov;53(9):418-22.
- Viana D, Selva L, Callanan JJ, Guerrero I, Ferrian S, Corpa JM. Strains of *Staphylococcus aureus* and pathology associated with chronic suppurative mastitis in rabbits. *Vet J*. 2011 Dec;190(3):403-7.
- Wang LU, He CL, He BK, Guo Q, Xiao CG, Yi Q. Effects of Jin-Ying-Tang on *Staphylococcus aureus*-induced mastitis in rabbit. *Immunopharmacol Immunotoxicol*. 2012 Oct;34(5):786-93.