

A Hare-Raising Adventure: *Encephalitozoon cuniculi* in Rabbits

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Introduction

The production of meat from rabbits has been utilized as a food source for more than 3,000 years.¹ There have been no major religious conflicts with the use of rabbit meat and, therefore, can be a great protein source of humans worldwide.^{1,5} In addition to their meat, rabbits are raised and produced for wool, scientific studies, 4-H education and companionship. Recently, rabbit meat has been reintroduced into the American cuisine due to the interests of chefs in major city hubs. In the 2012 Agriculture census, there were more than 5,000 rabbit farms that produced approximately 853,000 rabbits in the United States for the sale and distribution of meat products.⁵ According to Penn State Extension services, it is estimated that Pennsylvania, alone, contributed to the production and sale of 112,000 rabbits in 2002.¹

The two most common breeds of rabbit used for meat production are the medium-sized New Zealand whites and Californians.¹ A typical litter size is between 5 to 6 rabbits. However, a single breeding female, called a doe, can produce upwards of 25 to 50 offspring in a year, which is distributed over 5 litters.⁶ One breeding male, known as a buck, is used to breed 8 to 10 does. The infant rabbits, known as kits, are weaned around 30 days of age. Each litter can grow to produce 125 to 250 pounds of meat per year and online sale prices ranged from \$6 to \$18 per pound of meat in 2012.^{5,6} In 2019, the range of meat prices have ranged from \$7.50 to \$13 per pound of meat. The size of operation dictates the profitability of rabbit farms as it relates to the overhead feed cost to produce 4 pound rabbits.⁶ Factors that disrupt the production value of meat rabbits include malnutrition, poor housing and disease.

Disease conditions are common issues within the meat rabbit production system. The main attributions to disease are associated with husbandry. Proper housing and nutrition are paramount for healthy rabbit stock. The most common diseases and physiologic conditions

include, but are not limited to: conjunctivitis, pasteurellosis, coccidiosis, enteritis complex, mammary gland edema, mastitis and ulcerative pododermatitis. ⁶

Another major disease associated with rabbits is caused by infection with *Encephalitozoon cuniculi* and results in encephalitozoonosis. This organism is a microsporidial, obligate, intracellular and potentially zoonotic parasite. *E. cuniculi* commonly infects rabbits and was first described in laboratory rabbits in 1922. ³ Humans can be susceptible to *E. cuniculi* infection when they are immunosuppressed. *E. cuniculi* has a worldwide distribution and infection has been reported within rabbit populations in Europe, Asia, Africa and North America. ³ The diagnostic tests used to determine seroprevalence includes ELISA, PCR, IFAT and CIA. One retrospective study demonstrated that rabbit populations within the United States had an *E. cuniculi* seroprevalence of 62%.⁴ Chronicity and clinical signs vary, but often include ataxia, head tilt, seizures, cortical blindness and acute death.

There are three major stages of the *E. cuniculi* life cycle: the meront, sporont and sporoblast. The meront is the proliferative stage that undergoes differentiation through the asexual process of merogony. Sporonts multiply within the host cell and develop polar tubules, vacuoles and plasma membranes to become sporoblasts. Sporoblasts are the final and infective stage that will rupture out of the host cell and be spread throughout the host. ^{3,4} The mature spores are shed in the urine of an infected rabbit and infection occurs when the host ingests or inhales these spores. The spores can persist, in some cases, for more than four weeks in a humid environment.

The most common sites associated with lesions include the brain, heart, liver, lungs and kidneys. However, lesional formation within the brain does not consistently appear for approximately 3 months after the initial infection. ³ Granuloma formation within the brain and

kidneys are common post-mortem findings, but the degree of inflammation is an inconsistent factor in the severity of clinical signs.

Treatment options are limited due to the complexity of the organism; however, there are studies that suggest a susceptibility to albendazole and itraconazole.² Adequate housing and clean cages are essential for the reduction of disease prevalence. Use of 0.1% bleach solutions in conjunction with detergent with an addition of lime in the soil and utilization of UV radiation aid in disinfection and are common industrial practices. Additionally, management systems that include proper staged housing for groups of rabbits based on their litter, sex and age are important to preventing the spread of disease.³

History

During December of 2018, a producer of a meat rabbit farm in the coastal region of Mississippi noticed that a large portion of their meat rabbit stock showed signs of illness that consisted of going off feed, severe weight loss and scours. The operation consisted of 200 head of California white meat rabbits. The rabbits were fed a commercial rabbit diet. Bucks, pregnant does, nursing does, and weaned kits were housed separately, however, these groups could be found within the same barn space. The kits were weaned at approximately 3 weeks of age before they were moved and placed in groups of 7 individuals based on sex. Rabbits of different litters were comingled during this time. Healthy rabbits were raised until they weighed approximately 5 pounds before they were sold at market. Approximately 50 to 60 rabbits became acutely ill and died with no neurologic signs observed at the time of death over a period of 3 to 4 months. The most severely affected group were 40-day old, weaned rabbits. The producer consulted with his referring veterinarian who recommended that the deceased rabbits be submitted for necropsy.

Diagnostics

The producer submitted two rabbits for necropsy to the Mississippi Research and Diagnostic Laboratory in Pearl, MS on March 4, 2019. A single male and a single female juvenile rabbit were frozen and shipped to the laboratory for necropsy. The selected rabbits acutely died and demonstrated clinical signs typical of other affected rabbits in the herd. The gross necropsy report from the Mississippi Research and Diagnostic Laboratory indicated that both rabbits had a mildly thin body condition score and normal ingesta and fluid within the stomach and small intestine. Both rabbits had a dilated cecum with abundant and dry material within the lumen. Fecal staining around the anus was observed in both rabbits. The female rabbit had mild ocular discharge, dilation of the small and large bowel with copious, mucoid, intraluminal material.

Fecal flotation demonstrated numerous (>400) coccidial organisms of the genus *Eimeria*. Anaerobic culture was consistent with *Clostridium perfringens*. Non-suppurative encephalitis, nephritis and myocarditis were reported on necropsy examination. Gram stain of brain tissue revealed a gram-positive, variably sized, round to oval spore, suggestive of *Encephalitozoon cuniculi*. Histologic findings of the brain included moderate lymphocytic perivascular meningoencephalitis with multifocal gliosis, malacia and intralumenal microsporidia. The pathological diagnosis was *E. cuniculi* in both rabbits.

Outbreak investigation

The Mississippi State University College of Veterinary Medicine's Population Medicine Rotation consulted with the producer on April 7, 2019. At the time of the visit, it was noted that many juvenile rabbits were thin to emaciated and some rabbits were found laterally recumbent,

demonstrated tremors and torticollis. After inspection of the facility and operation, the Population Medicine rotation promoted new guidelines to improve the conditions. Three main areas were addressed in a letter to the producer that included: housing management, disinfection and biosecurity.

The housing management style was not contiguous with market standards. It was recommended that an “all-in-all-out” operation be implemented to prevent comingling of rabbits from different litters, age or sex. One barn should be used primarily for nursing does and pre-weaned kits. The other barn should be used for growing the kits to market weight.

Recommendations of disinfectants and sanitation procedures expressed the importance of these materials in minimizing the spread of *E. cuniculi* between rabbits as they moved from one part of the operation to the next. The producer had a system of burning the hair that accumulated on the cages between each batch. The following recommendations were made to improve disinfection:

1. Detergent may be used to remove soil, residual burned hair, urine and feces from the cages and walls.
2. Use of a 0.1% bleach solution to soak cages for 10 minutes before rinsing thoroughly.
3. Quaternary ammonia solutions may be used to disinfect cages, walls and materials.
4. Utilize the sunlight to aid in disinfection of cages.
5. Remove excess feces and urine from beneath the cages and apply an agricultural lime solution.
6. The soil may be treated with liberal application of a 2.8% formalin solution.

Biosecurity measures were recommended to reduce the accidental spread of *E. cuniculi* and included proper clothing, animal handling and isolation protocols. Clothing designated to a specific barn would minimize transmission between buildings. Coveralls and rubber boots, as an example, are easily cleaned and stored in one location. The team recommended that animals be handled in a specific order, from the most susceptible to healthy to sick. Additionally, a designated area of isolation far away from healthy stock for both sick and recently purchased individuals was emphasized.

Case Outcome

After the new strategy was implemented by the producer, the first batch of rabbits to reach market weight showed a significant reduction in clinical signs associated with *E. cuniculi* and the death rate was near zero percent. Since our visit, the producer increased the number of rabbits and has 65 rabbits at market weight. Additionally, the producer has 90 kits near weaning weight and will be the largest number produced thus far. The producer has expressed satisfaction with the housing, disinfection and biosecurity recommendations.

References

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