

Rabbit reproduction

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Introduction

Rabbit production (also referred to as cuniculture) is the agricultural practice of breeding and raising domestic rabbits, usually for meat, fur, research, show and as pets. The domestication of and rearing of rabbits for meat and fur production began in the 16th century, and has evolved from a simple backyard production of hutch raised rabbits to extensive operations capable of producing thousands of animals. The European Union continues to be the world's largest producer of rabbit meat accounting for about 55% of the global production, followed closely by China. In the United States the rabbit industry is relatively small and no reliable statistics exist describing the meat industry in the terms of number of producers and tonnage of meat produced. In fact in the US, rabbits are not recognized as an agricultural commodity by the Department of Agriculture and are instead regulated by the Food and Drug Administration. Hence they are not regarded as a separate species in the agricultural census. The American Rabbit Breeders Association Inc. (www.arba.net) is the single largest and oldest organization in the US dedicated to the development, promotion and improvement of the rabbit industry. Rabbit meat has started gaining popularity due to several advantages over red meat. It is low in fat, cholesterol and sodium, high in protein and has a pleasant taste similar to chicken meat. Owing to their small body size, short generation interval and high reproductive capacity, ability to grow rapidly on feeds not directly consumed by humans (grain free) and the potential for genetic improvement, rabbit meat is an attractive primary source of meat in many regions of Europe and Africa. The two most popular breeds of rabbits raised for meat production are the New Zealand White and the Californian owing to their high meat to bone ratio characteristics and white fur. Fur producers prefer the Rex and the American Chinchilla breeds.

Rabbits are a valuable animal model for biomedical research, including studies in cardiovascular medicine, neurophysiology, ophthalmology, immunology, asthma research, arthritis and toxicology.

With respect to embryological research, the rabbit has several advantages over other animal models as its embryonic morphology is archetypical for mammals during many phases of uterine development (e.g., gastrulation, neurulation, gonad development) and its late implantation makes it relatively accessible at these early stages of development.¹ Due to the phenomenon of induced ovulation in rabbits after coitus (or artificially by hormonal treatments), it is easier to time pregnancies with an accuracy unsurpassed in other common laboratory animals. This greatly facilitates the analysis of the highly dynamic developmental processes over a broad interval of developmental stages, from blastocyst formation to neurulation at four to nine days after coitus. Moreover, the high cell numbers and yield in rabbit blastocysts (the largest spherical blastocyst in mammals), relatively late implantation at a time when gastrulation is already proceeding, detailed morphologic and molecular knowledge on gastrulation stages, and a hemochorial placenta structure similar to the human placenta make the rabbit an ideal reproductive animal model for studying human health.² In the research industry New Zealand Whites are the preferred breed as they are less aggressive in nature and have fewer health problems compared to other breeds.

Keywords: Rabbit, reproductive management, reproductive disease

Reproductive anatomy and physiology

Male

The reproductive system of the male rabbit or buck is comprised of the external genitalia (penis, prepuce and scrotal sac), internal genitalia (testis and spermatic cords) and a full set of accessory sex glands (vesicular, prostate and bulbourethral glands). The testes descend at about 12 weeks after birth

and lie in two separate hemiscrotal sacs cranial to the penis. The inguinal canal does not close in rabbits and hence they are termed “functional cryptorchids” as the position of the testes depends on many factors including body position, body temperature, breeding activity, gastrointestinal tract filling, and the amount of abdominal fat. They are also able to voluntarily pull up the testes when they are frightened or during fighting. The short back-slanted penis lies caudal to the testes and points forward when erect. The glans penis is not well developed, is tapered, and covered by the prepuce. These anatomical peculiarities hold special consideration when attempting to perform orchiectomies in bucks. It is highly recommended to perform surgical closure of the open inguinal canal to prevent postsurgical hemiscrotal herniation of the abdominal viscera. Likewise due to the caudal position of the penis, it is possible to adopt a pre-scrotal approach with a single incision on the midline during orchiectomies³ as an alternative to a scrotal approach. Depending on the breed and level of nutrition bucks can reach sexual maturity between four and eight months of age. New Zealand White bucks have been known to have an increased daily sperm output from 20 weeks of age to a mature level at 31 weeks of age. Ejaculate volume for bucks can range between 0.5 to 1.5 milliliters per ejaculate with a concentration ranging from 10 to 300 million spermatozoa per milliliter. This varies among bucks and depends on the breed, frequency of collection and level of stimulation. Rabbits can experience testicular recrudescence in the wild with a reduction in the testicular size in autumn and a peak increase in late spring.

Female

In the female rabbit or doe, the ovaries, oviducts and the uterus are paired organs similar to other species of mammals. The ovaries are not enclosed in an ovarian bursa as is found in carnivores and rodents but instead are surrounded by fat which also envelopes the mesovarium and mesosalpinx. Female rabbits have a bicornuate duplex uterus lacking a uterine body and having two separate cervixes that open directly and separately into an elongated vaginal canal which is about six to ten cm long. The urethra opens midway along the ventral aspect of the vaginal body at the vaginal vestibule. The external genitalia of the doe include a urogenital sinus, which is continuous with the vagina and whose external lips form the vulva. The color and moistness of the vulva can be used as an indicator of sexual receptivity. A doe with a moist red or pink vulva is more likely to be receptive to the buck than a one with a pale and dry one.

Puberty in does is dependent on the breed and plane of nutrition with some does showing receptivity as early as three and one-half months of age and capable of conception at four to four and one-half months. It is however advisable to delay mating in does until they have achieved at least 80 percent of their mature body weight.

Rabbits do not have a defined estrous cycle, but are induced ovulators like cats and ferrets. Ovulation occurs about ten to 11 hours after coitus or can be induced by injecting luteinizing hormone (LH). Though rabbits do not have an estrous cycle, they are not in constant heat as sometimes thought. Follicular development occurs in waves as in other species and these follicles persist for around 12 to 14 days coincident with the doe's receptivity. In absence of coitus the follicles become atretic and a new wave starts after about four days. Does are less receptive to the male during these four days. Thus a doe has a cycle of about 16 to 18 days, with about 12 to 14 days of receptivity and four days of quiescence.

Determining the sex of a newborn (kit) may be done accurately a day or two after birth. At this age the external genitalia of both sexes may be similar in appearance and hence needs to be carefully examined. The newborn may be restrained on their back in the palm of the hand with the head extended towards the heel of the hand. After pressing the tail back and down, gentle pressure may be applied to the external genitalia to expose the reddish mucous membrane. In the case of a doe a slit is visible with slight depression next to the anus, while in the case of a buck a small circular opening might be visible. As bucks get older it is possible to extrude and expose the penis. Bucks will also have a greater anogenital distance than does. Alternatively, young rabbits may also be sexed at weaning or by around three weeks of age when the external genitalia will have a more defined appearance.

Breeding management

As mentioned above, the ideal age for breeding is primarily breed dependent along with a proper plane of nutrition. Smaller breeds (Polish) can be bred as early as four months of age, medium sized breeds (New Zealand Whites and Californians) at six months, while it is best to wait until at least nine to 12 months to breed the larger breeds (Flemish giants) of rabbits. Bucks should be put to service typically a month later than does, as they take a longer time to mature sexually. Does that are sexually receptive regardless of age usually have a moist, swollen and reddened vulva, whereas the vulva may be small and whitish in instances where the female is not receptive. Although this is a reliable indicator of 'when to breed', it is advisable to maintain age, breeding records and dates before deciding to include a doe in the breeding program. Receptive does are usually restless and rub their chins on the cage, water and feed troughs. Does can be aggressive towards other individuals placed in their cage, hence they should always be taken to the buck's cage for mating. This also reduces the chances of territorial fights in case where the buck is presented to the doe in her cage. If the doe is truly receptive mating occurs immediately and when it is complete the buck usually falls to his side. Sometimes male rabbits emit a cry towards the end of mating before falling and this often coincides with ejaculation. Does can be bred two or three times to the buck after they are placed in the cage as this increases the chances of conception. Sometimes breeders may rebreed the doe to a different buck. If mating does not take place the doe can be presented to another buck. However, if she is not receptive even then, she should be put away and tried again after a few days. Bucks and does should not be left unattended for longer than a few minutes as there is a risk of the buck getting injured. If mating does not occur in a few minutes, it is advisable to remove the doe to another buck's cage. Occasionally, it may be necessary to physically restrain a female for mating, especially in case of shy does.

Pregnancy and gestation

The gestation period in rabbits ranges from 29 to 32 days. Since rabbits are induced ovulators, a short mating bout including ejaculation is sufficient to induce a rapid release of LH from the anterior pituitary. Plasma levels of LH have been shown to rise within three minutes after copulation and ejaculation and reach a plateau within 15 minutes.^{4,5} Rabbits ovulate ten to 11 hours after coitus and only one ejaculation is sufficient to induce ovulation in a majority of cases unlike cats which require multiple intromissions and ejaculations in order to ovulate.⁵⁻⁷ Fertilization occurs at around ten hours after mating and the rabbit blastocyst attaches to uterine epithelium late in embryogenesis as compared to other mammals.² Implantation starts at day 6 plus 18 h; while definitive mesometrial chorioallantoic placentation occurs at day 8.⁸ The rabbit placenta is discoid and hemodichorial (two cellular layers of chorion between the maternal and the fetal blood) in structure and similar to primate placentas in terms of growth and fetomaternal exchanges during pregnancy.⁹ Gestation length may sometimes be prolonged especially if the doe is carrying small litters and has been observed to extend up to 35 days.

Pregnancy diagnosis

Pregnancy status in does may be determined by test-mating does by returning them to the buck's cage. This is not a reliable method as some pregnant does may accept service, while some non-pregnant ones may decline. Also, noting an increased abdominal girth or gain in flesh, though indicative, is not always reliable. Palpation of the caudal abdomen to feel the developing fetuses is a faster and more reliable method of pregnancy diagnosis in rabbits. Most breeders prefer palpating at about two weeks after mating to feel the marble shaped fetuses developing in the uterus. However with experience and care it is possible to feel the growing embryos as early as ten days without causing them injury. If no developing embryos are felt by ten to 12 days, the doe can be returned to the buck's cage for mating. However many does may not breed at ten to 12 days due to pseudopregnancy and these animals should be checked again at 18 days to determine receptivity. Palpating earlier than day ten is generally not recommended due to the fear of injuring the developing embryos and also because it is easy to confuse them with fecal pellets in the caudal abdomen. With practice it is also possible to become proficient in identifying retained fetuses or abnormalities of the reproductive tract such as abscesses, cysts or tumors.

Does may sometimes experience fetal loss prior to day 19 of gestation and may resorb the fetuses. Hence breeders prefer re-palpating by 28 to 29 days before putting the doe into a nest box, to ascertain that she is indeed pregnant. Real-time abdominal ultrasonography, though not widely used as the preferred method, may also be useful to detect presence of embryonic vesicles in the uterine lumen reliably as early as the ninth day of gestation. Again with experience some practitioners are able to diagnose pregnancy as early as the seventh or eighth day when the diameter of the embryonic vesicle is in the range of 8 to 9.5 mm.¹⁰

Parturition and maternal care

Parturition or kindling in rabbits usually occurs by day 30 to 32 after breeding. A few days before the anticipated date, a nest box containing bedding material such as straw or shavings should be provided to the doe. Does will also pull fur from their dewlap and mammary gland area to complete the nest. Parturition usually occurs in the early morning and lasts for about 30 minutes, with the kits born every one to five minutes. Kits are hairless, blind and deaf at birth. Occasionally in cases of large offspring kindling can be delayed for a day or two. It is important to check the doe to make sure that there is no dystocia. The number of kits in the litter varies among breeds and can range from fewer than four (small breeds) to eight to ten in larger breeds like the New Zealand Whites and Flemish Giant. Does usually eat the placenta upon completion of parturition and may occasionally resort to cannibalism if they are disturbed or nervous. Those that have not kindled by day 32 to 34 of gestation may be induced by injecting oxytocin (1 to 3 units per animal). Does usually nurse the newborn immediately after birth and later only once a day for a short period of time. Colostrum is produced for the first two to three days and thereafter regular lactation begins. Does bearing large litters are often in a negative energy balance owing to the greater demands placed on lactation and also have reduced appetite prior to kindling. It is desirable to gradually increase the amount of feed in the first week after kindling to meet these demands until full feed intake is reached. In intensive breeding systems does may be re-bred within 24 hours after kindling. However, this type of breeding management also increases the percentage of culled does per year. Several breed-back schedules (e.g., at 7, 14, 21, 28, 35 and 42 days) are followed by breeders based on their level of experience and facilities available. However, an ideal re-breeding schedule usually depends on the condition of the doe after the previous parturition. Does with large litters and lactating heavily should not be bred until the young are weaned. Litters are usually weaned by 28 days of age, as milk production is declining and the young have started consuming solid feed.

Common reproductive disorders

Pseudopregnancy

Pseudopregnancy can occur in does due to a sterile mating, in does mounting each other, or sometimes when does mount the young in their own litter. It may also be seen in pet rabbit does housed singly. The condition can last for 15-17 days and does may not be receptive to the buck during this period. Matings occurring during pseudopregnancy usually are not fertile. Towards the end of pseudopregnancy does may display nesting behavior and pull out fur. Mammary development is most pronounced in the first ten days of false pregnancy, after which involution typically follows. Pseudopregnancy resolves spontaneously but may recur or may result in hydrometra or pyometra.¹¹ Ovariectomy is the treatment of choice and may be performed after the mammary glands undergo involution.

Pregnancy toxemia

Pregnancy toxemia is an often fatal metabolic disorder which occurs in rabbits during the last week of gestation. Though the underlying mechanism is unknown, it is more common in obese does and in cases of inadequate caloric intake. In addition environmental changes and stress can predispose a pregnant doe to this condition. Reduced feed intake may also be caused due to hairball formation occurring when does pull their fur for nest building. Clinical signs include weakness, depression, incoordination, anorexia, abortion, convulsions, and coma and can progress over one to five days, or death may occur acutely. Supportive therapy with fluids to correct metabolic derangements, combined

with calcium gluconate and corticosteroids are the mainstay of the treatment plan. Pregnancy toxemia carries a very grave prognosis, and treatment is usually unrewarding. The best approach is prevention by avoiding fasting or undernutrition during late pregnancy and by preventing obesity and sudden stress at all times.

Dystocia and retained fetuses

Dystocia is not common in rabbits since normal delivery is usually complete within 30 minutes and rarely are the kits delivered several hours apart. The normal presentations in does are anterior and breech and it may be essential to palpate does 24 hours after delivery to determine if any fetuses have been retained. Does may be predisposed to dystocia if they are obese, have a narrow pelvic canal, are carrying large fetuses or experiencing uterine inertia. Does may have persistent contractions and may continue straining. Occasionally a greenish-brown vaginal discharge may be observed. Radiographs may provide a definitive diagnosis and reveal abnormalities of the fetus or a narrow pelvic canal. Oxytocin (1-3 units IM per animal) may aid uterine contractions, while in cases of uterine inertia 5 to 10 mL of 10% calcium gluconate orally 30 minutes before administering the oxytocin may prove useful. Does are kept in a quiet dark room after administration. If the medical therapy does not work, a cesarean section is indicated although prognosis can be guarded.

Abortion and fetal resorption

Abortion can occur in does after day 19 of gestation, whereas resorption usually occurs in the event of embryonic or fetal death before day 19. As with other species, obtaining a thorough clinical and breeding history of the individual and the herd is of utmost importance. Aborting animals should always be checked for presence of retained fetuses. All aborted material should be submitted for bacterial culture and histopathology. There are numerous causes for abortion and fetal resorption in rabbits including infections, stress, trauma, neoplasia, inappropriate drug use and dietary imbalances such as deficiencies of vitamins A and E and protein. Listeriosis should be considered in does experiencing late term abortions.¹²

Uterine adenocarcinoma

Uterine adenocarcinomas are the most common tumors of the genital tract in rabbits. Their occurrence is independent of breeding history but is largely affected by age. Certain breeds such as Tan, French silver, Havana, and Dutch, older than four years of age have an incidence of 50 to 80 percent.^{13,14} Uterine adenocarcinomas are slow growing tumors, with local invasion to adjacent peritoneal structures and sometimes hematogenous spread to the lungs, liver and brain.¹³ Early clinical signs, such as decreased fertility, small litter size, and an increased incidence of fetal retention or resorption and stillbirths may be recognized in a breeding doe. Cystic mammary glands can develop concurrently with uterine hyperplasia or adenocarcinoma. In late stages, clinical signs may range from depression, anorexia and ascites to dyspnea if pulmonary metastases are present. Diagnosis can be made based on clinical signs, abdominal palpation, radiology and abdominal ultrasound. Ascites may be present. Palpation of the caudal abdomen may reveal an enlarged uterus or nodular masses (1 to 5 cm in diameter), or both. Chemotherapy is not often attempted; but ovariectomy may be curative if the tumor is confined to the reproductive tract. Animals should be reexamined every few months for several of years to monitor for any signs related to metastasis. Uterine adenocarcinomas can be best prevented with an ovariectomy in pet rabbits before they reach two years of age. Pet owners may be advised to conduct an annual or semi-annual examination of intact animals three years of age or older.

Cannibalism

Though cannibalism is more of behavioral issue and not a primary reproductive disorder, it is nevertheless an important concern to breeders as it can significantly affect the production efficiency of a breeding unit. It is common for does to eat their placenta and dead kits after kindling. They may also devour the entire litter in some instances. Various theories to explain this behavior have been proposed including the doe's level of feeding and low energy status, environmental stress such as loud noises,

handling by strangers and mixing with strange animals. Certain lines or families of rabbits are more prone to cannibalize their young than others and this could be attributed to their nervous nature. Breeders usually prefer culling does that cannibalize two litters in a row in absence of management errors.

Venereal spirochetosis or rabbit syphilis

Rabbit syphilis or vent disease is caused by a spirochete *Treponema paraluis-cuniculi* and can be spread by direct contact as well as by the venereal route. It is a disease of major concern in rabbitries as it can result in a decreased rate of conception and increased incidence of metritis, placenta retention, and neonatal deaths.¹⁵ Lesions first appear on the skin of the perineum and genitalia and begin as areas of redness that progress to edema, vesicle formation, ulcerations, and scabs in both does and bucks. The lesions are painful and can impair breeding activity. Syphilis is easily treatable with long-acting penicillin and tetracyclines in water. The disease can be introduced into the herd after introducing a new animal (buck or doe) or after loaning a buck to service someone else's does. Infected animals may be identified by serologic surveys with a microhemagglutination test or the rapid plasma reagin (RPR) card test which are very specific. Risk of *T. paraluis-cuniculi* infection increases with parity and does that have had six or more litters are often found seropositive as are bucks that have been in a breeding program for more than six to 12 months.¹⁶

Metritis, pyometra and orchitis

Does may occasionally suffer from metritis and pyometra, with venereal transmission being the most common route of infection. The most common organisms isolated are *Pasteurella multocida* and *Staphylococcus aureus*. Clinical signs include anorexia, lethargy, weakness, enlarged abdomen and vaginal discharge. History of the doe may indicate a recent parturition, pseudopregnancy or an inability to rebreed. In mild cases, it may be possible for the doe to kindle successfully or she may suffer from abortions and fetal resorption. Nulliparous does are at an equal risk of developing metritis and pyometra. Diagnosis may be reached based on clinical signs, abdominal palpation, ultrasonography and radiography. Though antibiotic, fluid and supportive therapy may be attempted, it is extremely difficult to achieve effective drainage of the tenacious uterine exudate in affected does. Ovariohysterectomy remains the treatment of choice mainly due to the high incidence of *P. multocida* infections.

Bucks on rare occasions may suffer from orchitis and epididymitis due to venereal transmission or due to bite injuries on the scrotum caused during fighting. Clinical signs may include swelling of the testes, micro or macro abscesses, fever, anorexia, weight loss and low conception rates. *P. multocida* is the organism most often isolated from clinical cases. Treatment of choice is castration and antibiotic therapy. Bucks should be housed separately to prevent fighting and subsequent injuries. Similarly, they should not be left unsupervised with a female in a cage during mating as females can be very aggressive.

Reduced fertility

Fertility issues are usually multifactorial in rabbits and may include malnutrition (e.g., excess vitamin A, deficiencies of vitamins A, D, or E), heat stress, systemic illness, nitrate contamination of food or water, environmental disturbances, a decrease in daylight, endometrial carcinoma, metritis, or pyometra. Old age and reproductive senescence or breeding at too young an age are additional causes of infertility. Vitamin E deficiencies are known cause myodystrophy leading to abortions, stillbirths and neonatal mortality. Hyper- and hypo-vitaminosis A are also major nutritional causes of reproductive failure and infertility. Breeders and owners should be advised regarding proper nutrition of their animals using the National Research Council dietary guidelines.

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