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Review Article

Studies on Breeding Failures in Dogs: A Review

Oziegbe Stanley David[1*], Kuzayed Grace Imaben[1], Abonyi Festus Otaka[2], Ezema Chuka[2]

[1]Department of Theriogenology and Production, Faculty of Veterinary Medicine, University of Jos, Bauchi Rd, Jos 930105, Plateau, Nigeria
[2]Department of Animal Health and Production, Faculty of Veterinary Medicine, University of Nigeria, Nsukka, Obukpa Rd, Nsukka 410105, Enugu, Nigeria

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***Corresponding Author:** Oziegbe Stanley David
Department of Theriogenology and Production, Faculty of Veterinary Medicine, University of Jos, Bauchi Rd, Jos 930105, Plateau, Nigeria

Abstract

The domestic dog is a non-seasonal breeder. The female is monestrus and has a reproductive cycle that is marked by extended periods of proestrus and estrus. The estrous period is characterized by an estrogen peak that coincides with rising circulating progesterone concentration prior to ovulation. After estrus is diestrus and then anestrus, with the ovarian cycle regulated by the hypothalamic-pituitary-gonadal axis. In the male spermatogenesis is controlled by the hypothalamic-pituitary-gonadal axis with testosterone playing a vital role. The reproductive cycle of most wild canids is similar to that of domestic dogs. Diestrus is followed by an extended period of ovarian inactivity. The causes of breeding failure in dogs are numerous and require thorough investigations for accurate diagnosis. Breeding failures can be infectious or non-infectious. Among the infectious causes in the bitch, bacterial endometritis was found to be responsible for the majority of reported cases. Non-infectious causes include primary and secondary anoestrus, cystic conditions of the uterus, and degenerative diseases of the endometrium. In the male, the causes can also be infectious and non-infectious. Non-infectious causes like bilateral cryptorchidism and acquired anatomical abnormalities can also cause male infertility. Spermatocele or sperm granulomas, obstruction of the genital ducts or inguinal or scrotal hernia, and prostatitis lead to infertility. Infections can lead to orchitis/epididymitis, with alteration of the quality of the semen. Nutrition also has important implications for reproductive performance. Undernutrition can result in loss of body condition, delay the onset of puberty, and ultimately lead to infertility.

Keywords: Breeding, Dog, Domestic, Failures, Infertility, Nutrition.

INTRODUCTION

The domestic dog is a non-seasonal breeder, while its wild cousins, the grey wolf, coyote and dingo are seasonal breeders [1]. Female dogs are monestrus and have a reproductive cycle that is marked by an extended period of proestrus and estrus (approximately 9 days each). There is an estrogen peak during estrus that coincides with rising circulating progesterone concentration, before ovulation [2]. After estrus is diestrus, a luteal phase that lasts for 2 months with or without pregnancy. Diestrus is followed by anestrus, a period of 2-10 months characterized by ovarian inactivity or quiescence [3].

In female dogs (bitches) the ovarian cycle is regulated by the hypothalamic-pituitary-gonadal axis [4]. There is an increase in gonadotropin-releasing hormone pulses before proestrus from the hypothalamus which stimulates the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary [3]. The increase in pituitary hormone pulses leads to follicular growth that stimulates gonadal steroidogenesis and the rise in estrogen during proestrus triggers an LH surge that is followed by ovulation 60 hours later in female dogs [5].

The female gamete of dogs exhibits some unique characteristics; the oocytes contain a large amount of cytoplasmic lipids in comparison to other mammalian species [6]. Lipid yolk bodies appear first in the cytoplasm of the primary oocyte and increase throughout the entire process of oogenesis, giving it a dark appearance distinct from that of other mammalian species [7].

The distribution of lipid bodies varies among oocytes obtained from different reproductive stages. Those obtained during the follicular phase showed a diffuse pattern of lipid bodies compared to those retrieved during the anestrus or luteal period which showed peripheral or perinuclear distribution [8].

In dogs, oocytes are released at an immature stage and could take 48-72 hours to complete nuclear maturation within the oviduct [9]. In domestic dogs, the oocyte remains fertile 4-5 days after nuclear maturation and 6-7 days post ovulation [10].

Fertilization occurs at the middle or distal part of the oviduct in the bitch, two-pronuclei zygotes can be observed 92 hours post ovulation and between 29- and 73 hours post-mating in the raccoon dog [11].

The male dog is a non-seasonal breeder and spermatogenesis occurs year-round but takes place only during breeding season in canids that are strict seasonal breeders [12]. Spermatogenesis is controlled by the hypothalamic-pituitary-gonadal axis with testosterone playing an important role [13].

Sperm can be recovered from dogs when they reach sexual maturation at around 6-8 months of age [14]. Sperm maturation takes place in the epididymis and gametes acquire fertilizing ability when they reach the cauda region [15].

Studies in domestic dogs showed that the entire process of spermatogenesis takes 62 days and after ejaculation, spermatozoa can survive in the female reproductive tract for up to 7 days [10].

In vitro, studies revealed that sperm from dogs can penetrate immature oocytes [16], but in vivo fertilization does not occur until 83 hours post-ovulation, despite the presence of spermatozoa. In vitro studies showed that dog metaphase II oocytes may require an additional period of 12 to 24 hours to fully acquire developmental competence, or 5-6 days after the LH surge [17].

2.0 Breeding failure in dogs

Breeding failure occurs in dogs and the causes are numerous. Both male and female dogs (bitches) can be affected. It requires thorough investigations such as history taking [18], physical examination, and laboratory investigation for proper diagnosis [19]. The laboratory investigation includes vaginal swabs for microbial culture, cytological examination, semen quality and food analysis.

Breeding failure can be infectious or non-infectious. Among the infectious causes is, bacterial endometritis found to be responsible for the majority of cases reported in the bitch. Non-infectious causes include primary and secondary anoestrus, cystic conditions of the uterus, and degenerative diseases of the endometrium [20, 21].

In the male, breeding failure can also be infectious and non-infectious. Non- infectious causes like bilateral cryptorchidism, acquired anatomical abnormalities, spermatocele or sperm granulomas, inguinal or scrotal hernia, and prostatitis lead to infertility [22]. Infections can lead to orchitis/epididymitis, leading to alteration in the quality of the semen [22]. Nutrition also has important implications for reproductive performance, under nutrition can result in the loss of body condition, delay the onset of puberty, and ultimately lead to infertility in dogs [23].

2.1 Infertility in the Bitch

Infertility is the inability of the bitch to produce offspring due to different reasons, such as systemic diseases, organ dysfunctions, infectious diseases, and hormonal imbalances, a thorough case history is needed, which should comprise of signalment, general health, previous disease treatments and the breeding history of the male dog used to mate the bitch [18]. A successful diagnosis requires a systematic diagnostic pathway [19].

2.1.1 Infectious causes

Infertility in bitches can be caused by different types of pathogens. Bacterial endometritis was found to be responsible for the majority of infertility cases in the bitches. The following bacteria, *Pasteurella multocida*, Groupe G *Streptococcus*, *Staphylococcus intermedius*, *Escherichia coli*, and *Proteus mirabilis* were isolated from the uterus of bitches with infertility problems [24] and the bacteria were likely from the cranial vagina. *Brucella canis* is a species-specific agent that causes infertility in bitches, with resorption, late abortion, and weak puppies or normal puppies that may spread the bacteria [25].

2.1.2 Non-infectious causes

2.1.2.1 Primary and secondary anoestrus

Primary anoestrus or lack of oestrus at 24 months of age can be caused by organ dysfunctions and certain treatments [19]. The diagnosis is made thorough case history, exclusion of silent heat, genetic disorders of sexual development, hypothyroidism, and systemic diseases [18]. A case of primary anoestrus due to diet-induced hyperthyroidism was reported [26]. Secondary anoestrus coincides with the prolongation of the inter-estrus interval [27].

2.1.2.2 Cystic conditions of the uterus

Cyclic bitches can develop proliferative and cystic degenerative diseases of the endometrium; the most frequent is cystic endometrial hyperplasia [20, 21]. This disease is mainly caused by the periodic priming effect of estrogen and progesterone on the endometrium, being aggravated by delayed downregulation of estrogen receptors. It is accompanied by decreased uterine

perfusion, accumulation of fluids, inflammation, and delayed uterine clearance after mating [21]. Local irritations by bacteria may cause the same histological findings [28, 29].

Infertility may occur despite regular cycles and the inability to conceive may be due to the effect of progressive cystic degeneration [21, 23]. Degenerative diseases of the endometrium such as fibrosis with degeneration of the endometrial glands, pseudoplacentational endometrial hyperplasia, and endometritis were most frequently found in bitches with infertility [30].

2.1.2.3 Congenital abnormalities

Abnormalities of the vulva, vestibule, and vagina, such as circumferential vaginal strictures in the bitch may lead to infertility due to the inability to mate normally [31]. The incidence of infertility in these cases is quite low. Thorough examination prior to first breeding is very important and vaginal septa can then be removed surgically [32].

2.1.2.4 Hormonal imbalances

Prolonged oestrus in bitches can be due to hypoestrogenism, marked by non-receptive behavior and vaginal mucous below average [33].

Hypoluteoidism is luteal deficiency during pregnancy when serum progesterone concentration drops below 5ng/ml at week 4-5 of gestation causing resorption or abortion [34]. Primary and secondary hypoluteoidism can be differentiated, the first without obvious cause, the second caused by any infectious or non-infectious disturbance during pregnancy causing fetal distress [35].

Primary luteal deficiency diagnosis is performed by excluding causes of secondary luteal deficiency. It has been questioned whether primary luteal deficiency due to abnormal corpora luteal function exists [18]. Case history is important, repeated pregnancy failure may indicate luteal deficiency and hypothyroidism.

The impact of hypothyroidism on fertility can be a subject of debate. Negative effects on conception rate, peri-parturient mortality and puppy birth weight have been observed in one study [36]. Other studies did not find increased incidence of reproductive disorders in hypothyroxinemic dogs compared to normal dogs [37].

The measurement of thyroxin and thyroid stimulating hormone should be performed in case of repeated fetal resorption or abortion and must be emphasized that disturbances of the thyroid gland function can be caused by other organ or systemic diseases. Most of the cases are acquired; cases of congenital hypothyroidism have been described [38].

2.2 Infertility in the Male Dog

Much is not known about infertility in the male dog and causes remains unknown in 70% - 74 % of cases [18]. In human, when semen quality is poor, assisted reproduction techniques are utilized such as *in vitro* Fertilization (IVF) or Intra-Cytoplasmic Sperm Injection (ICSI). These techniques are not readily available for dogs [39]. The prognosis of infertility remains very poor. The complete clinical examination of dog is vital; some diseases may begin by causing infertility before resulting in general health problem.

2.2.1 Anatomical abnormalities

Bilateral cryptorchidism causes azoospermia, while unilateral monorchidism does not create any fertility problems [40]. Dimorphism in large breeds may lead to mating problems when the female cannot support the weight of the male during mating.

Acquired anatomical abnormalities may also cause male infertility, Spermatocele or sperm granulomas, stenosis or obstruction of the genital ducts or inguinal or scrotal hernia, and may lead to azoospermia or aspermia [41].

2.2.3 Prostatic problems

Prostatitis is a major cause of infertility in the male dog; it decreases the volume of ejaculate and alters sperm motility. The pH of prostatic fluid is often changed [22] and this impedes the capacity of spermatozoa to move freely. Infectious agents causing prostatitis may act directly on sperm cells, killing sperm in situ, or making it unable to progress in the female genital tract due to pyospermia or hematospermia [22].

2.2.4 Epididymal, testicular and urinary problems

The testicles produce spermatozoa and they acquire motility as well as fertilizing ability during epididymal transit, any disorder affecting these organs leads to infertility [22]. Cystitis or uretritis may interfere with sperm motility as they can modify the acidity of the urethra and food-induced alkalinization of urine may produce the same effect [42].

2.2.5 Retrograde ejaculation

Retrograde ejaculation is the backflow of semen into the bladder during ejaculation. This can lead to either aspermia or oligospermia. The hypogastric nerve is responsible for the closure of the bladder during ejaculation, but a small amount of sperm always flows back into the bladder [43] and fertility may be affected when this amount becomes too high. It may be influenced by the state of repletion of the bladder and the identified causes of the problem in dogs are urethral calculus, cystitis, and post-surgery strictures [44].

2.2.6 Hormonal problems

Disorders in the hypothalamus-pituitary axis may have an effect on spermatogenesis and fertility, which can be transient, or severe [45]. Semen quality will

drop in a period of a few weeks to a few months and bitches mated during this period will not be pregnant [18]. If nothing is done, the decrease in the semen may continue until complete azoospermia is observed, at this stage infertility becomes irreversible.

Hypopituitarism can lead to azoospermia, and hypothalamic or pituitary tumors may lead to infertility [46]. Prolactine adenomas may play a negative role in fertility. Idiopathic insufficiency with a lack of production of gonadotropins, follicle stimulation hormone (FSH) or luteinizing hormone (LH) may alter spermatogenesis [18].

Testicular tumors responsible for excessive hormonal secretion (Sertoli cells tumors, Leydig cells tumors) may cause a decrease in spermatogenesis, even when these tumors are located in one testicle and small in size. The negative impact on fertility is due to direct destruction of testicular tissue, induction of inflammation, elevation of intra-scrotal temperature, and production of estrogen or androgens that may exert negative feedback on the hypothalamus and pituitary [18]. Hypothyroidism and adrenal dysfunction are potential causes of infertility.

2.2.7 Infectious diseases

These represent a major cause of infertility in male dogs in breeding kennels. Infections can lead to orchitis/epididymitis, with alteration in the quality of semen. There is no evidence that viral diseases contribute directly to male infertility [22], infectious agents can be present in seminal fluid and infect bitches after mating, leading to infertility.

Canine brucellosis is responsible for a rapid decrease in the quality of semen, causing acute and chronic orchi-epididymitis [47]. *Mycoplasma* and *Ureaplasma* have been isolated from the prepuce and urethra of infertile dogs [22].

Fungi infections have been suspected to cause genital problems in males. *Blastomyces dermatidis* was identified in one case of orchitis and in several cases of balanoposthitis [48].

2.2.8 Drugs and Infertility

Steroid hormones such as (corticosteroids, androgenic or anti-androgenic compounds, estrogens) and other drugs like antineoplastic agents, cimetidine, and tricyclic antidepressant amitriptyline may inhibit the central regulation of spermatogenesis or epididymal maturation of sperm and therefore accelerate a decrease in fertility [18].

2.2.9 Genetic problems

Chromosomal abnormalities in some phenotypically normal male dogs may lead to infertility. Kartagener's syndrome in dogs is characterized by respiratory tract disease, male sterility, and hydrocephalus [49, 50].

2.2.10 Abnormal sexual behavior

In male dogs lacking libido, it may be difficult to know if the underlying cause is organic or psychological. The same disorder, like bad quality semen causing infertility with normal libido may also in some cases affect Leydig cells and create a loss of libido [49].

2.2.11 Miscellaneous causes

Males that mate too often may show a decline in libido and prolonged sexual abstinence may cause a decrease in semen quality, especially in giant breeds [51]. The first ejaculate from a dog after a prolonged period of sexual rest contains a high percentage of old and dead sperm that have been stored in the epididymis [49], obesity due to peri-scrotal fat, may produce a similar effect.

Trauma, such as dog bites, lacerations, kicks, and blows of testes may destroy the barrier between the blood flow and the seminiferous tubes and generate an autoimmune spermatogenic arrest due to anti-sperm antibodies [50]. This disruption of the immunological barrier occurs also in the case of Brucellosis, resulting in sperm agglutination [22]. Fucosidosis is a lysosomal storage congenital disease affecting the function of epididymal epithelial cells, which causes the retention of cytoplasmic droplets and has been described in dogs [18]. Idiopathic testicular degeneration is also a common cause of infertility, due to azoospermia, in dogs [49].

2.3 Effects of nutrition on reproduction

The interaction between nutrition and reproduction has important implications for reproductive performance [52]. Undernutrition results in the loss of body weight and body condition, delays the onset of puberty, increases the post-partum interval to conception, interferes with normal ovarian cyclicity by decreasing gonadotropin secretion, and increases infertility [53].

Insufficient intake of energy, protein, fats, vitamins, micro- and macro-minerals are associated with sub-optimal reproductive performance. Energy balance is the single most important nutritional factor related to poor reproductive function in animals [54].

The effect of dietary protein on reproduction is complex (55). Prolonged inadequate protein intake has been reported to reduce reproductive performance. It has also been found that reproductive performance may be impaired if protein is fed in amounts that greatly exceed requirements in the cow [56, 57].

Fatty acids and cholesterol are substrates for hormone synthesis, increasing fat in the diet may increase levels of reproductive hormones (progesterone, prostaglandins) and fats can act directly on the

reproductive axis. The effects of fat may be independent of or additive to those of increased energy availability. Higher progesterone levels during the luteal phase generally result in improved fertility and increasing dietary fat leads to increased follicular growth [58]. These changes in follicular growth and hormone production may enhance reproduction [59].

Vitamins are important for a lot of functions including reproductive function in animals and one of such is vitamin E. It functions as an intra-cellular antioxidant scavenging for free reactive oxygen and lipid hydroperoxidases, converting them to non-reactive forms and thus maintaining the integrity of membrane phospholipids against oxidative damage and peroxidation [60].

In vitamin E and selenium deficiency condition, these free radicals accumulate and not only damage cell membranes, but also disrupt several processes linked to the synthesis of steroids [61], prostaglandins [62], sperm motility and the development of the embryo [63]. It is not surprising therefore that negative impacts of vitamin E and selenium deficiencies have been observed on various components of the reproductive events, including ovulation rate [64], uterine motility, sperm motility and transport [65], conception rate and post-partum activities, fetal membrane expulsion [66], embryo survival, milk production, post-natal growth [67].

Minerals are important for all physiological processes in animals including reproduction [57]. Mineral deficiencies and imbalances are often cited as causes of poor reproduction. It is clear that adequate amounts of minerals must be provided, but little is known about the effects of marginal deficiencies and imbalances. The same is true of excessive intakes of minerals which may be harmful [68].

3.0 CONCLUSION

Breeding failure is common in dogs and the causes are numerous, they can be infectious or non-infectious and require thorough investigations through proper history taking, physical examination, and laboratory investigation for successful diagnosis.

It has been established that the interaction between nutrition and reproduction has important implications for reproductive performance. Undernutrition results in the loss of body weight and body condition, delays the onset of puberty, increases the post-partum interval to conception, interferes with normal ovarian cyclicity by decreasing gonadotropin secretion, and increases infertility. Insufficient intake of energy, protein, fats, vitamins, micro- and macro-minerals are all associated with sub-optimal reproductive performance. It is important that dogs are fed the right amount and quality of nutrients for proper reproductive performance to prevent breeding failures.

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