DOI: 10.21451/1809-3000.RBRA2022.031

Anais do Congresso Internacional da Associação Latinoamericana de Reprodução em Pequenos Animais.
Punta del Este, Uruguay, 29 a 30 de novembro de 2022.

Fertility disorders in male dogs

Wojciech Niżański

Department of Reproduction, Wrocław University of Environmental and Life Sciences, Poland

Abstract

Male dog fertility disorders are usually troublesome and challenging for a practicing veterinarian. It may be generally assumed, that reproductive potential in this species is lower than in farm animals and it is still decreasing. This situation starts to be similar to human medicine, where we observe dramatic drop of reproductive capacity, which resulted in the need of implementation of Assisted Reproductive Technologies (ART). Situation in dogs is more complicated owing the fact, that the use of ART meets many obstacles. Low fertility potential in dogs appears to be the result of variable factors such as: specific criteria of selection for reproduction in which fertility performance in not a priority, lack of periodical obligatory fertility check, species specific predisposition for many reproductive diseases and no age limit for reproductive use of males. Dogs are kept in human environment and exposition for civilizational by-products influences negatively not only on our health, but also on health our 'minor brothers'. It should be bear in mind, that reproductive organs are very sensitive for environmental factors disrupting homeostatic balance. The decline in male dog fertility over the past decades was proved, with potential link to environmental contaminants (4). They were found in pet foods and were also detected in the sperm and testes of adult dogs causing a detrimental effects on sperm function. Over the 26 years of the study of Lea et al. (4), authors found a decrease in the percentage of normal motile sperm. Between 1988 and 1998, sperm motility declined by 2.5 per cent per year. Then from 2002 to 2014 sperm motility continued to decline at a rate of 1.2% per year. In addition, the male pups had an increased incidence of cryptorchidism. Basics of physiology of reproduction of male dogs. Normally the puberty in males is associated with presence of normal sperm cells in genital organs. It is reached in male dogs at age around 5-6 months. Such a young dog obviously cannot be used for reproduction. Reproductive maturity is associated later, with development of normal sexual behavior and production of sufficient number of normal, fertilizing competent spermatozoa. It corresponds with 12-18 months of animal age. Testicular descent is completed usually before weaning period, but sometimes testicles may reach scrotum later, but never after the end of 6 month of age. That time inguinal canals start to be so narrow, that caudal passing of gonads is unlikely. Male dogs have only one accessory sexual gland - prostate, which produces vast portion of seminal plasma.

Keywords: dog, andrology, infertility, semen, sperm cell.

Content

Congenital reproductive disorders. Disorders of Sex Development (DSD). Exact incidence of congenital abnormalities of the genital tract in dogs is difficult to evaluate. Some of them occur within **internal structures** of the reproductive system. Thus, many congenital malformations of internal parts of the genital tract in dogs not intended for breeding remain unnoticed. They are more likely diagnosed on an occasion of detailed examination performed in genetically valuable breeding dogs. On the other hand, congenital malformations of **external genitalia** result in obvious clinical signs that are usually noticed by the owner and are easily diagnosed by veterinarians. Morphological anomalies of reproductive system are called DSD, which are classified into three major categories: 1) DSD caused by sex chromosome abnormalities; 2) XY DSD – disorders in animals with a normal set of XY chromosomes; 3) XX DSD – disorders observed in animals with a normal female chromosome set - XX (5,7,8,910). **Sex chromosome DSD.** A normal constitution of male dog chromosomes is 78,XY. Different sex chromosome abnormalities causing DSD were described, including aneuploidies, structural rearrangements and lymphocyte XX/XY chimerism. ***XXY trisomy*** in humans is called Klinefelter syndrome. Such individuals present phenotype party resembling female and male. ***Leukocyte chimerism XX/XY*** occurs in heterosexual siblings, which developed placental anastomoses. Transfer of factos responsible for male development produced by embryonic gonads, through anastomoses, leads to abnormal sex development. We observed such abnormalities in males presenting residual penis, a prepuce located in a position typical for males and no

E.mail: wojciech.nizanski@upwr.edu.pl
Recebido: 6 de novembro de 2022
Aceito: 08 de novembro de 2022

palpable testicles or scrotum, but with a prostate. XY DSD. This includes also multifactorial cryptorchidism and hypospadias. Until now, a normal SRY gene was observed in such dogs and cats. The function of testicles is usually impaired and their structure is abnormal, while external genitalia are often ambiguous. Until now only a single causative mutation responsible for **Persistent Müllerian Duct Syndrome (PMDS)** was identified in dogs. The mutation of Müllerian inhibiting substance type II receptor (MISRII) gene occurred in Miniature Schnauzers and was reported in different populations of this breed. Recently we described two PMDS Miniature Schnauzer Dogs which developed Sertoli cell tumour or uterine leiomyoma. A well-known ***Androgen Insensitivity Syndrome (AIS)*** is caused by mutations of androgen receptor (*AR*) gene. In such animals, binding of testosterone (T) and dihydrotestosterone (DHT) to the receptor is impaired. Testicles are usually located caudally to kidneys, structures originating from Müllerian ducts fail to regress, but male external genitalia are present. Until now no causative mutation in dogs or cats was found. The cytogenetic analysis revealed in such individuals a normal male chromosome complement (78,XY) and endocrionological analysis showed a low level of testosterone (0.75 ng/mL). ***Cryptorchidism*** is the most common DSD in dogs, while ***hypospadias*** was concerned as a rare disorder. However, recent studies showed that most probably it is not true. Knowledge on genetic background of these disorders in domestic animals, including dogs, is very scarce. There are several reports on searching for DNA polymorphism associated with these multifactorial disorders, but until now no conclusive results were obtained. In hypospadias the external urethral orifice is not located on the tip of the penis, but on the side of the glans, corpus of penis or in the perineum. There is no reliable information on the level of heritability of this condition in animals. There are discrepancies regarding data on its incidence. It was assumed that the incidence of hypospadias is very low (approx. 0.005%) in dog population and most frequently diagnosed in Boston Terriers. However, we revealed that incidence of this disorder can be underestimated. In a retrospective search for hypospadias in 19,950 medical records of male dogs from a single veterinary clinic in Poland (2006-2017), 10 cases of penile hypospadias were found (0.05%). The majority of the reports concerned German Shepherd Dogs (8 cases among 1,511 male dogs of this breed), and thus, the estimated incidence of hypospadias in this breed was 0.5%. Dogs with hypospadias had a normal XY chromosome complement and presence of normal testicle, often in bifid scrotum. The external urethral orifice was usually located below the anus in the perineal region (perineal hypospadias). All these males had a normal XY chromosome complement. Testicles, rudimentary penis and an urethral orfice, localized dorsally to penis, were reported. In cryptorchid animals one (unilateral c.) or both (bilateral c.) testicles are retained in the abdomen (abdominal c.), within the inguinal canal (inguinal c.) or in the prescrotal region (ectopic c.). This is a hereditary condition. The incidence of cryptorchidism in dog population was estimated for 1.2% to >5.0%. In this species unilateral cryptorchodism is predominantly diagnosed (79%), more likely right-sided (65.7%). The predisposition for this condition was reported in miniture breeds (<9.1 kg), including in Toy poodle, Pomeranian, Yorkshire terrier, Miniture dachshund, Cairn terier, Chihuahua, Maltese, Boxer, Pekignese, English buldog, Miniture schnauzer, Sheltie, Siberian husky. Temperature stimulation of undescended testicle/s results in testicular degeneration, impaired spermatogenesis, atrophy of seminiferous tubules, neoplasia (9-13x higher risk) and clinical implications of these changes. The risk of testicular torsion is also severly increased. Diagnosis is based on history, clinical and ultrasound examination, LH, steroid hormone and AMH measurements and gonadal stimulation test. The therapy of choice is gonadectomy or hemigonadectomy with vasectomy. The exclusion from breeding program is obligatory. **XX DSD.** The most common type of this DSD category, observed in dogs, is characterized by the presence of testicles or ovotesticles, uterus, oviducts and virilized external genitalia - usually it is enlarged clitoris (9). Until now this hereditary DSD was diagnosed in almost 40 dog breeds. Pathomechanism of this condition, including molecular background, is still not fully understood (7,8,10). Using different molecular and cytogenetic techniques a polymorphic site (copy number variation – CNV) upstream *SOX9* gene, showed association with DSD phenotype. **Congenital strictures of prepuce** result in phimosis/paraphimosis. These conditions influence negatively reproductive performance and may result in secondary pathologies as urinary incontinence and balanopothitis. They may be considered as a part of complex symptoms of DSD. **Diagnosis of DSD** is based on clinical examination, imaging (ultrasound, computerized tomography, contrast X-ray), histological assessment, hormone measurements, as well as cytogenetic and molecular genetic analysis. In cases of suspicion of DSD the first step of genetic testing is analysis of sex chromosomes, which routinely is carried on *in vitro* cultured leukocytes. The most difficult step of the examination is searching for causative mutations or associated DNA polymorphisms. In majority of DSD cases of inheritance model is not well elaborated and understood. However these defects have a genetic background. **Veterinary care of DSD patients.** In all cases of DSD gonadectomy and removal of remnants of tubular organs is advisable. Postponement of surgical intervention may diminish the comfort

of life and walfare of animal and may contribute to increased risk of development of pathological changes within atypical genital organs.

Aquired fertility disorders in male dogs may affect different element of genital organs: testicle, epididymis, scrotum, deferent duct, urogenital canal, prepuce, penis and prostate. Pathologies of genital organs include septic and aseptic **inflammation, infection and its consequences, degeneration, fibrosis, atrophy, neoplasia.**

Orchitis/Degeneration/atrophy/fibrosis of testicular tissue. Testicular degeneration and atrophy results in decrease in size and softening of consistency of testicles. Degeneration may be caused by orchitis, autoimmune orchitis, chronic infection of testicles, testicular neoplasia, fever, inflammation of the scrotum. Degeneration due to chronic orchitis may be not noticed by the owners and may result in **terato-, oligo- and astehnozoospermia (OAT).** Sometimes the chronic inflammation may result in fibrosis of testicles. Orchitis more commonly is observed in younger dogs, but inflammation of testicular tissue may accelerate senile changes, especially if the condition is subclinical or mild and chronic i.e. poorly detectable and thus not treated for a long time. Orchitis may be septic and many bacteria were isolated from these cases. Autoimmune destruction of testes occurs when trauma or inflammation exposes testicular tissue to immune system. Secondary formation of antisperm antibodies may destruct testes and sperm cells produced in them. This condition may be result of infection, may be idiopathic or may accompany lymphoid thyroiditis. Typical for inflammation is the presence of leukocytes in semen and pathology of sperm cell morphology and motility. In degeneration usually the number of sperm cells of improper morphology are observed in spermiogram. The impairment of spermatogonial function may then results in atrophy of seminiferous tubules and oligospermia. At the end azoospermia is observed. FNA is performed to confirm the diagnosis. It was revealed for subfertility cases caused by testicular degeneration, the decrease of all CASA sperm parameters (1,3), especially cell velocity which is directly linked to ability to penetrate *zona pellucida*. **Tumors of testicles.** Testicular neoplasia is second most common tumor type in male dogs after skin tumors. Incidence is 0.91%. Mean age of diagnosis is 9.0 years-11 years. There are three main types of tumors: SCT Sertoli Cell Tumor, SEM Seminoma and ICT Interstitial Cell Tumor. Incidence of SCT is 44%, for SEM 31% and for ICT 25%. Cryptorchid dogs are prone to development of tumors. SCT tumors cause usually symptoms of estrogenization including skin changes, attractiveness, hair loss and decrease in semen quality. ICT results usually in hyperandrogenism with aggressiveness, hyperlibidosis, prostatomegaly, perianal adenoma, tail gland hyperplasia. SEM may result in alopecia, hiperpigmentation of flank, prostate disease, non-insulin dependent diabetes mellitus. All neoplastic changes decrease the quality of semen, change libido and may influence fertilizing ability of sperm cells. The relationship between neoplastic testicles and the risk of fetal embryonal malformations is not assessed. **Scrotal and penial acquired disorders.** Scrotal inflammation is common condition in dogs. Inguinal location of scrotum facilitates its contact with floor/ground, which predisposes male dogs to its lesions. They may result in expansion of infection/inflammation onto the testicular capsule and gonads and may cause orchitis and gonadal degeneration. Balanoposthitis is common in dogs. The mucoid or serous preputial discharge is cause by viral infections (e.g. herpes) or may be a part of systemic atopy. Yellow or greenish discharge may suggest bacterial complication. **Prostate diseases.** Pathological conditions of the prostate are common in dogs. The increase in their incidence is mostly observed in older age and could be related to the physiological androgen-dependent hyper-development (6). Bening Prostatic Hyperplasia (BPH) develops as the result of constant influence of the active metabolite of testosterone – dihydrotestosterone (DHT) on prostatic glandular tissue. Impairment of the function and distorsion of the structure of the gland are the obvious reasons for frequent simultaneous development of prostatitis and BPH. BPH is one of the most important geriatric problem in intact male dogs. Prostatitis is the second most common prostatic pathological condition in dogs and is observed in males independently of the age but frequently as result of BPH in older dogs. **General reproductive problems in aged dogs.** There is no legal time limit for reproductive use of old male dogs**.** Aged dogs may fail to achieve normal copulation due to lack of libido and a decrease in blood testosterone level. It was noticed that males that mate too frequent may show a earlier decline in libido. Paradoxally sexual abstinence may cause a decrease of fertility outcome (2). Any hormonal trouble in aged dogs may suppress the hypothalamus-pituitary axis and therefore have an influence on libido, spermatogenesis and fertility. Hypopituitarism, adrenal dysfunction, hypothalamic or pituitary tumors and prolactin adenomas may lead to infertility and azoospermia. The link between hypothyroidism and low libido and semen quality is still unclear. Orthopedic problems, pain and neuropathies like spinal cord injuries may enhance a decrease in libido. **Changes of semen quality in aged dogs.** It is generally assumed that age influences negatively the semen quality. However, decrease in semen quality is different in normal healthy dogs which undergo senile changes and in dogs presenting different forms of fertility disorders specific for older age. A relationship was confirmed between the age of the

dog and characteristics of the ejaculate. Dogs of 2–3 years of age had the largest volume of sperm and highest sperm concentration. It was proved that with increasing age seminal markers decrease, as the volume of the ejaculate, motility, percentage of morphologically normal sperm cells, total sperm count and others.

Conclusion

There are variety of causes of infertility in males dogs. Many of them are unclear and difficult to elucidate and studies on them are demanded. The diagnosis of reproductive disorders in male dogs necessitates specialized knowledge, equipment, experience and intuition. Methods of their treatment are commonly based on protocols used in human medicine and in many cases the extrapolation of results obtained in medicine is the only one wise solution. Usually traditional pharmacological treatment or application of simple reproductive biotechniques is implemented. Advanced assisted reproductive technologies are not available in dogs.

References

Domosławska A, Zduńczyk S, Niżański W, Janowski T. Assessment of semen quality in infertile dogs using computer-assisted sperm analysis by the Hamilton-Thorne Semen Analyser. Bull Vet Inst Pulawy 2013; 57, 429-432.
Fontbonne A. Infertility in male dogs: recent advances. Rev Bras Reprod Anim, Belo Horizonte 2011; 35, 266-273.
Fréour T, Jean M, Mirallie S, Barriere P. Computer-assisted sperm analysis parameters in young fertile sperm donors and relationship with age, Syst Biol Rep Med 2012;58:102-106.
Lea RG, Byers AS, Sumner RN, Rhind SM, Zhang Z, Freeman SL, Moxon R, Richardson HM, Green M, Craigon J & England GCM. Environmental chemicals impact dog semen quality in vitro and may be associated with a temporal decline in sperm motility and increased cryptorchidism. Sci Rep. 2016; 16: 33267.
Meyers-Wallen V. Sex Dev 2012 ;6, 46-60.
Niżański W, Levy X, Ochota M, Pasikowska J. Pharmacological treatment for common prostatic conditions in dogs - benign prostatic hyperplasia and prostatitis: an update. Reprod Domest Anim. Suppl 2014; 49, 8-15.
Nowacka-Woszuk et al. Anim Reprod Sci 2007; 98, 371-376.
Świtonski et al. Sex Dev 2011; 5, 141-6.
Świtoński M. Reprod Biol 2014; 14, 44-50.
Szczerbal et al. Sex Dev 2016; 10, 74-8.