

Cryptorchidism in the Dog How it happens, How to diagnose, Whether to Treat

In order to understand how cryptorchidism develops, one must have a clear understanding of sexual differentiation and development. Normal sexual development in the dog is dependent upon 3 factors: 1) the sex chromosomes; 2) normal development of the ovaries or testicles; 3) normal development of the external genitalia (vulva, prepuce) and the effects of the sex steroid hormones on physical appearance (i.e. large jowls and increased size and muscling in males and finer facial features and smaller stature in females). There is a sex-determining gene, called SRY, which is present only on the Y chromosome. In its presence, testicles will develop and the fetus will be male, while in its absence, ovaries will develop and the fetus will be female. Since spermatozoa carry either one X (female) or one Y (male) chromosome, the sex of the embryo is determined at the time of fertilization by the spermatozoa that fertilizes each egg. All eggs carry one X chromosome. The sex of the embryo is not distinguishable until after day 30 of gestation when the ovaries and testes can first be differentiated from each other.

Initially, sex cords develop in the area of the kidneys and will eventually differentiate into either ovaries or testes. Furthermore, there are 2 sets of tubules that develop in each embryo initially. If the fetus develops into a male, the tubules that persist are the mesonephric or Wolffian ducts; and if the fetus develops into a female, the tubules that persist are the paramesonephric or Müllerian ducts. The ductular system that does not develop eventually regresses. Until sexual differentiation begins each embryo is uncommitted sexually and has sexual bipotentiality.

The substance that determines the progression toward either male or female development is called testis determining factor (TDF) and is controlled only by the Y chromosome. Testicular differentiation occurs by 36 days of gestation. The first hormone produced by the embryonic testis is Müllerian inhibiting substance (MIS) (or antiMüllerian hormone or Müllerian regression factor) and is produced by the cells that line the testicular tubules. In a male fetus, MIS causes regression of the female tubular system between days 36 and 46 of gestation. The second hormone produced by the embryonic testis is testosterone (T). Testosterone is converted to an active metabolite (di-hydro testosterone or DHT) which then promotes development of the remaining male tubular tract, the prostate gland, penis, and the external genitalia.

Normal testicular descent in the dog occurs in three steps: 1) movement through the abdominal cavity into the internal inguinal ring; 2) movement through and out of the inguinal canal; and 3) movement from the inguinal canal to the scrotum. Descent may fail at any point in any one of these 3 stages. Initially the testes lie near the kidneys in the abdominal cavity. There is a ligamentous cord called the gubernaculum which attaches to the end of the testis and then runs through the inguinal canal and attaches at the far end to the scrotum. The gubernaculum enlarges under stimulation of certain protein hormones to anchor the testis in place during testicular descent. Testosterone stimulates development of the genitofemoral nerve which is required for normal testicular descent to begin. An outpouching of the abdominal lining (the peritoneum) called the vaginal process, grows into the gubernaculum in dogs at about 36 days of gestation. The gubernaculum continues to grow both in length and



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width which causes expansion of the inguinal canal and pulls the testis and epididymis toward the scrotum as it grows. Once the testicle has moved through the inguinal canal, the gubernaculum begins to shrink, thereby pulling the testicles into their final scrotal position. Testosterone is particularly important in the descent of the testes from the external inguinal ring to the scrotum. The testes pass through the inguinal canal three to four days after birth and reach their final scrotal position by 14 - 35 days of age.

Neither lack nor excess of hormones (testosterone, luteinizing hormone, follicle stimulating hormone or estrogen) are likely to contribute to cryptorchidism. This is proven by the fact that cryptorchid animals do not have different levels of these hormones compared to normal males, and that treatment with stimulating medications (GnRH, gonadotropin releasing hormone or hCG, human chorionic gonadotropin) does not successfully resolve the condition regardless of the age administered.

Cryptorchidism is considered to be hereditary and an autosomal recessive trait. This means it is carried by both dam and sire lines. It is difficult to determine if a bitch is a carrier of the cryptorchid gene due to the high numbers of male puppies required to all have 2 scrotal testes by 6 months of age (at least 40 normal male puppies).

There are a number of breeds at risk for cryptorchidism including the Boxer, English Bulldog, Cairn terrier, Chihuahua, Miniature Dachshund, Maltese, Pekingese, Pomeranian, Toy, Miniature and Standard Poodle, Miniature Schnauzer, Old English Sheepdog, Shetland Sheepdog, Siberian Husky, and Yorkshire Terrier. Other inherited conditions associated with cryptorchidism include inguinal and umbilical hernia, hip dysplasia, patellar luxation, and penile and/or preputial defects.

If the testicle begins to enlarge prior to its entry into the internal inguinal ring or if its descent is slowed, it may be retained abdominally. If it begins to enlarge after entering the internal ring but before leaving the external ring or if normal testicular descent through the inguinal canal is altered or stopped, the animal may become an inguinal cryptorchid. The right testicle is retained more commonly than the left due to its more forward starting position in the abdomen.

Retained testicles are smaller than scrotal testes, and the location of retention is positively correlated with size. Abdominally retained testes are smaller than inguinally retained testes, which are in turn smaller than testes outside the external inguinal ring but not yet in the scrotum. The reduction in sperm production (spermatogenesis) in retained testicles also worsens with the degree of retention. Even though spermatogenesis does not progress normally in retained testes, steroidogenesis does, so libido is unaffected by this condition. Thus, while cryptorchid dogs may show interest in and breed bitches, unless they have one descended testicle, they will most likely be sterile or at a minimum, infertile. In cases of inguinal retention, dogs may have lower than normal numbers of spermatozoa/ejaculate and increased abnormal forms. Retained testicles are predisposed to neoplasia (9 – 14x higher than normal) and testicular torsion.

Lack of 2 testicles in the scrotum by 8 weeks of age is considered to be suspicious for cryptorchidism. Classically, it has been accepted by the time an animal reaches 6 months of age, if it does not have 2 scrotal testicles, it is considered a cryptorchid. But realistically, with the vast differences in age at puberty between breeds this is probably not a reasonable expectation. Based on the average age at puberty for any given breed, one would expect to



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have both testes in the scrotum within 2 months of attaining puberty to be considered normal. This means that for large and giant breed dogs, testicular descent may not be complete until well over a year of age. Small and medium breed dogs should still be considered cryptorchid if 2 testes are not in the scrotum by 6 - 8 months of age.

When trying to determine the location of a retained testicle, careful palpation of the inguinal region and the area just lateral to the penis and prepuce should be performed. Lymph nodes and fat are commonly mistaken for testes, as is the gubernacular outgrowth within the scrotum. Testicles should be freely movable and have an attached epididymis. Ultrasonography may be attempted to locate a cryptorchid testicle and is more successful in locating inguinal rather than abdominal testes. This is due to the smaller size of the abdominal testes and the fact that they may be located anywhere in the abdominal cavity (although they tend to lie along a line drawn from the end of the kidney to the opening of the external inguinal ring). Abdominal testes appear to have the same structure as scrotal testes on ultrasound examination. However, if an abdominal testis is neoplastic, it may be larger and have an abnormal appearance.

In cases where there is no history of neutering but there are no testicles palpable, an hCG or GnRH stimulation test can be performed to determine if testicular tissue is still present. A baseline testosterone is obtained. A stimulating hormone is administered and testosterone concentrations are obtained at 1 and 4 hours post injection. The baseline concentration should more than double if testicular tissue is present. Cryptorchid males do tend to have less marked response to GnRH stimulation testing than their intact counterparts. Use of serum LH testing is not accurate for diagnosis of castrated males due to overlap of resting ranges of cryptorchid and neutered males.

Typically, no treatment is recommended for cryptorchidism beyond castration. If an animal does not have 2 scrotal testes by the time 2 months beyond puberty, the individual should be neutered and not used in any breeding program due to the hereditary nature of the disease and the other associated heritable conditions. There are a number of published and anecdotal protocols involving multiple injections of either hCG or GnRH to stimulate precocious puberty and encourage testicular growth and descent, but there is no strong scientific evidence that any of them is consistently effective. Various degrees of success are associated with these treatments proving the multifactorial and polygenetic nature of the disease.

Further anecdotal reports of massaging the inguinally retained testes towards the scrotum to hasten its descent are unlikely to be the case except in the shy individual who is retracting the testes towards the body when touched. Daily manipulation of the scrotum and perineal area, may make these individuals more relaxed when the scrotum is palpated, thus allowing the testes to remain in their scrotal position.

In humans, where the basis for medical treatment was derived, treatment is actually both medical and surgical. Because of the increased risk of testicular cancer in cryptorchid men at middle age, doctors treat cryptorchids aggressively. Young boys (pre-pubertal) who are found to be cryptorchids first have surgery to locate the testicle and then the testicle is sutured to the scrotum with a heavy suture. The goal of the suture is to put tension on the testicle to pull it towards the scrotum as the gubernaculum should have. Once the testicle is in the scrotum, the suture material hopefully creates scar tissue causing the testicle to adhere



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there. After surgery the boys are treated with stimulating hormones to induce precocious puberty and thus stimulate testicular and gubernacular enlargement. Therapeutically, the combination of hormone therapy and surgery result in testicular descent in about $\frac{2}{3}$ of the patients who have inguinal or lower cryptorchidism. Success with abdominal cryptorchids is very low. Of those that descend a large proportion (about 30 - 50%) will relapse once the suture breaks down and hormone therapy has been stopped.

In humans, doctors are not concerned about male fertility when considering medical and surgical therapy for cryptorchidism. There are so many advanced techniques available for subfertile men nowadays, that this problem can be overcome using in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI) or other advanced reproductive techniques. Nor are doctors concerned about a patient passing on this potentially heritable condition to their male offspring. Because most families have only 1 – 3 children, the chance of a male offspring having the condition is low. Human doctors are mainly concerned about decreasing the risk of testicular neoplasia in middle age. So while in animals reducing the risk of neoplasia is also a concern, we are also very concerned with passing heritable defects through lines and the ability of the male to be fertile without expensive reproductive interventions. Since most dogs only live to be between 10 and 14 years of age, the numbers of testicular tumors found in intact males who are cryptorchid is much lower than the incidence in humans because the human lifespan is so much longer.

Furthermore, successful medical treatment of cryptorchids may increase the fertility in an affected dog, thereby perpetuating the trait in his offspring. Additionally, the increased risk of neoplasia remains whether the testes descend or not, so in a successfully treated animal, failure to neuter at a young age increases his risk for neoplasia later in life. Since cryptorchidism is associated with other heritable defects, (hip dysplasia, patellar luxation, inguinal hernia etc.) which can affect quality of life for our pets, breeding these individuals is strongly discouraged.

Removal of all affected males, their offspring and their parents from the breeding program is the recommended course. Waiting until puberty is fully attained is recommended before deeming any individual a cryptorchid