Genetic parameters of cryptorchidism and testis size in Friesian colts

Anouk Schurink [a,*], Adrianne de Jong [a], Hans R. de Nooij [b], Ids Hellinga [c], Bart J. Ducro [a]

[a] Animal Breeding and Genomics Centre, Wageningen University, PO Box 338, 6700 AH Wageningen, the Netherlands
[b] Dierenartsencombinatie Gorredijk, De Klok 22, 8401 CM Gorredijk, the Netherlands
[c] Koninklijke Vereniging "Het Friesch Paarden-Stamboek", PO Box 624, 9200 AP Drachten, the Netherlands

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ABSTRACT

In males with cryptorchidism, one or both testes do not descend into the scrotum thereby affecting among other things fertility. Testis size has been suggested to contribute to cryptorchidism. Therefore, the aim of our study was to estimate genetic parameters of cryptorchidism and testis size in Friesian colts. Data on cryptorchidism (0/1, n=1327) and testis size (cm, n=868 with size of both testes estimated) in Friesian colts of 1–7 months-of-age were gathered by a veterinarian during inspections from 2009 to 2012. Heritabilities, phenotypic and genetic correlations were estimated using ASReml4 including age of the colt (in months), location, year and month of inspection as fixed effects. Prevalence of cryptorchidism was 14.2%. Most affected colts (88.3%) were unilateral, while 11.7% were bilateral cases. Of the unilateral cases, significantly fewer colts had a left retained testis (35.5%) compared to a right retained testis (64.5%). Heritability of cryptorchidism was 0.13 (SE=0.06) and increased slightly when only cases of 4 months and older were considered. Based on literature and our findings we advise not to inspect colts at a very young age. Mean testis size significantly differed between left (3.47 cm) and right testis (3.19 cm). Heritability of left testis size (0.12 ± 0.07) was lower compared to heritability of right testis size (0.31 ± 0.10), where genetic correlation between left and right testis size was 0.87 (SE=0.12). The genetic correlation between left testis size and cryptorchidism was −0.94 (SE=0.15) and between right testis size and cryptorchidism was −0.64 (SE=0.23). At the age of the investigated Friesian colts, cryptorchidism genetically coincides with smaller testis size. The development of the left and right testis might differ, which could be hereditary in nature. More precise phenotyping, like recording position and size (and side) of the retained testis and age of the stallion, might contribute additionally to disentangling the genetic background of equine cryptorchidism and identifying the gene(s) affecting this disorder. For now, the continuation of the data recording as described in our study will enable the studbook to estimate breeding values and thereby select against cryptorchidism.

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1. Introduction

Cryptorchidism is observed in many species such as dogs, pigs, horses and humans (Amann and Veeramachaneni, 2007). Recently, Eriksson et al. (2015) showed that 9.4% of the investigated yearling Swedish-born Icelandic stallions had cryptorchidism. In males with cryptorchidism, one (unilateral) or both (bilateral) testes do not descend into the scrotum. Testis descent consists of several stages and therefore a non-scrotal testis can be located in the abdominal cavity, the inguinal canal or outside the abdominal wall (Amann and Veeramachaneni, 2007). Amann and Veeramachaneni (2007) and Stout (2013) discussed that abdominal and inguinal cryptorchidism could be (genetically) different disorders. Testis size might contribute to abdominal cryptorchidism, as a too large

size of the testis might hamper passage through the inguinal canal (Amann and Veeramachaneni, 2007). Coomer et al. (2016) noted that size of testes within the inguinal canal was variable. A common remark made at castration of 39 cryptorchid stallions reported by Eriksson et al. (2015) was a larger than normal size difference between the testes. Differences in size of the left and right testis have been observed (Johnson et al., 1991; Gregory et al., 2013) and variation in testicular development between testes within a stallion is present (Collingsworth (1996) (in Cox, 1999); Johnson et al., 1991). Regarding these observations, it is worthwhile to incorporate testis size when investigating cryptorchidism.

Unilateral cases of cryptorchidism are usually fertile, while bilateral cases are sterile (Mueller and Parks, 1999). Due to an elevated temperature of the retained testis, unilateral cases often have a lower sperm count (Morel, 2015). Cryptorchidism not only influences fertility of affected stallions, but has also been suggested to be a high risk factor for testicular malignant tumours (Stick, 1980; Hayes, 1986). Moreover, the cryptorchid stallion could

display undesirable behaviour, as Leydig cells of the retained testis keep producing testosterone due to the elevated temperature (Mueller and Parks, 1999). In order to eliminate these potential negative effects of cryptorchidism, stallions are castrated. However, surgery with general anaesthesia is often applied to castrate an affected stallion, which is technically more demanding, costly and risky compared to the castration of an unaffected stallion (Coomer et al., 2016; Searle et al., 1999).

Genetic research on cryptorchidism in horses is very limited. A genetic background is suggested, as breed and family differences in prevalence have been observed (Hayes, 1986; Leipold et al., 1986). Heritability of equine cryptorchidism was estimated only by Eriksson et al. (2015) based on 595 Icelandic stallions of 12 months-of-age. Heritability on the observed scale was 0.12 (SE=0.08) and on the underlying continuous scale 0.35 (SE=0.24). De Nooij (2012) showed that about 15% of the investigated Friesian colts had cryptorchidism. However, no genetic research on neither cryptorchidism nor testis size has been performed in this breed. Therefore, the aim of our study was to estimate genetic parameters of cryptorchidism and testis size in Friesian colts. Using these estimated genetic parameters, a breeding strategy could be developed that aims at reducing cryptorchidism in stallions.

2. Materials and methods

2.1. Data collection and description

Data were gathered by one veterinarian during inspections from 2009 to 2012, as an inventory study aimed at estimating the prevalence and heritability of cryptorchidism in Friesian colts. Inspections with many participating colts in the north of the Netherlands were visited to enable an efficient data collection. In principal all colts were scored, unless the owner refused to participate (which happened only very rarely during the 4 years of data collection). Inspections took place on 15 locations from June until October (Table 1). About 300 observations were made each year. Most inspections were visited during July, August and September, where only two locations had fewer than 30 observations (Table 1). Data included 1328 Friesian colts of which one was excluded from the analyses due to missing pedigree. The available 1327 Friesian colts descended from 80 sires and 1095 dams. Birth month of the colts ranged from January until August. Average age at inspection was 4 months-of-age and ranged from 1 (n=39) to 7 months-of-age (n=1). Inbreeding coefficient was calculated using full pedigree in CFC 1.0 (Sargolzaei et al., 2006), where average number of discrete generation equivalents was 12.3. Average inbreeding coefficient was 0.17 (SD=0.01) and ranged from 0.08 to 0.28.

2.2. Trait definitions and analyses

For each testis separately it was recorded whether it was retained or not. Colts were scored as unaffected (CRYPT=0) when both testes descended and as affected (CRYPT=1) when at least one of its testis was retained. The variable CRYPT contained 1327 observations (Table 2). There were too few bilateral cases (n=22) to analyse as a separate category or even trait. We performed an analysis where bilateral cases were removed (UNI=0 for unaffected stallions, UNI=1 for unilateral cases). The variable UNI contained 1305 observations (Table 2). We also considered whether unilateral cases (bilateral cases were removed) had a left (CRYPT_LEFT) or right retained testis (CYRPT_RIGHT). The variable CRYPT_LEFT contained 1198 observations and the variable CRYPT_RIGHT 1246 (Table 2). Normal testes descend before the colt is 2 weeks-of-age according to Bergin et al. (1970). However,

Table 1
Data description including the number of colts (n) and percentage per variable for 1327 Friesian colts.

Variable	n	Percentage
Year		
2009	316	23.8
2010	361	27.2
2011	361	27.2
2012	289	21.8
Month		
June	84	6.3
July	309	23.3
August	447	33.7
September	416	31.3
October	71	5.4
Location		
AS	19	1.4
BB	33	2.5
BH	68	5.1
DT	114	8.6
ER	38	2.9
GR	80	6.0
KZ	31	2.3
NG	38	2.9
OB	108	8.1
OM	45	3.4
OD	13	1.0
SN	249	18.8
WG	306	23.1
WM	48	3.6
WV	137	10.3

the phenomena of late testicular descent is not uncommon (Amann and Veeramachaneni, 2007). As age of examination might affect the status of the colt, we also performed an analysis during which only affected stallions of ≥ 4 months-of-age were considered (CRYPT ≥ 4). The variable CRYPT ≥ 4 contained 1207 observations (Table 2). As the dependent variables considered binary data, a binomial distribution with a logit link function was applied.

Location, year and month of inspection, age (in months), birth month and inbreeding coefficient of the colt were considered as fixed effects. Significance of these effects was tested using the GLIMMIX procedure in SAS 9.3 (SAS Inst. Inc., Cary, NC). Birth month and inbreeding coefficient did not have a significant effect on any of the dependent variables and were therefore not included in the model. Because different fixed effects significantly affected different dependent variables, we decided to use a consistent model for all dependent variables that were investigated (despite potential non-significance):

$$\eta_{ijklm} = \mu + location_i + year_j + month_k + age_l + animal_m$$

where η_{ijklm}=the linear predictor, μ=the population mean, $location_i$=the fixed class effect of location of inspection (i=1, 2, 3, …, 15), $year_j$=fixed class effect of year of inspection (j=2009, 2010, 2011, 2012), $month_k$=fixed class effect of month of inspection (k=June, July, August, September, October), age_l=fixed class effect of age in months at inspection (l=1, 2, 3, …, ≥ 6) and $animal_m$=random additive genetic effect of the mth colt (m=1, 2, 3, …, 1327) with $\sim N(0, \mathbf{A}\sigma_a^2)$. $\mathbf{A}$=matrix of additive genetic relationships among Friesian colts in our data, σ_a^2=additive genetic variance. Residual variance (σ_e^2) was fixed to $\pi^2/3$, related to the inverse logit link function.

From 2010 onwards, size (in cm) of descended testes was estimated applying the GD Animal Health method to investigate testes of stallions during stallion inspection. In short, the length of the testis is estimated using the fingers' width of the veterinarian's