Birth Defects: High Time for Active Management

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Breeding with Friesian horses means looking forward with anticipation to the day that the birth is impending and intensely enjoying a healthy foal that playfully dances around its dam. In almost all cases that is what happens and we want to keep it that way. Fact is, however, that breeding with Friesians in a small number of cases will turn into a very big disappointment. That the stallion of choice does not always bring the expected improvements is part of the calculated risks of breeding. It is hard to understand when a healthy mare and a studbook stallion, that successfully completed an extensive inspection, produce a foal with serious birth defects - and even harder to accept.

How do horses pass on hereditary defects?

The most plausible means is that a single recessive hereditary factor (d) is responsible for the development of a dwarf foal, and another recessive hereditary factor (w) for the development of a foal with water on the brain. For a chance to get a foal with a defect both the stallion and the mare need to be a carrier of the hereditary defect (genotype Dd for dwarf and Ww for water on the brain).

Index 1: Sire and dam are carriers of water on the brain.

		Sire Ww	
		W	**w**
Dam	**W**	WW (not a carrier)	Ww (carrier)
Ww	**w**	Ww (carrier)	ww (water on the brain)

Conclusion: In the event of the birth of a foal with the defect, both the sire and the dam are always carriers of the defect. The combination of two carriers of the same defect gives 25% chance of a foal with a defect (index 1). A carrier makes half of his or her offspring a carrier. The other half is with genotype DD or WW, just as free and clear from the defect as a foal from two non carriers (index 2).

Index 2: Sire carrier of dwarfism and dam not a carrier.

		Sire Dd	
		D	**d**
Dam	**D**	DD (not a carrier)	Dd (carrier)
DD	**D**	DD (not a carrier)	Dd (carrier)

In the breeding of Friesian horses dwarfism and water on the brain occurs. Both defects can be traced back to a disturbance in the development of the foal's embryo. This disturbance stems from a deficiency in the gene package of the unborn foal. To make a start in reducing the number of foals born with birth defects these defects need to be reported and registered with their lineage to get an overview of the carriers in the population. With this data we can try to prevent suspected carriers being matched for breeding (risk-bearing breedings) and through selection we can reduce the number of carriers in the population, by seeking out the carriers.

Reporting

The big problem the studbook is now facing is the fact that only part of the defects are reported. The result is that no usable information can be given to breeders yet, because the overview of carriers is too incomplete at this time. The importance of reporting was brought to the attention of breeders last year and that already has resulted in improvement. Another problem is recognizing the defect. Water on the brain leads to a large number of the cases of premature births. Depending on the stage of the pregnancy, the defect will not always be recognizable. In the case of an aborted fetus it is recommended to have the veterinarian determine if there are any detectable defects. In case of detectable defects, the veterinarian can take a DNA sample and in all cases a birth announcement needs to be made.

Distribution of Carriers

When breeding within a closed population the chance that carriers are matched for breeding is mainly determined by the influence that stallion carriers have had in the past. The first

dwarf foals were registered by the stallion Us Heit (1917) and his son Cremer (1932). The development of this hereditary defect stems, therefore, from well before that time. From the data that has been recorded so far it is increasingly becoming clear that the recessive allele that causes the dwarfism deviation has come into the stallion Jarich (1962) via the dam line. Jarich passed it along to his son Wessel and he in turn passed it along to his son Oege. There will no doubt be a small number of mares within the current breeding population that are carriers through the dam line, or possibly through undetected carrier stallions from before Jarich. Still, in almost all dwarf foals that have been reported, Jarich, Wessel or Oege appear in the lineage, both on the sire's and the dam's side. For water on the brain the same applies as with dwarfism - Jarich was the carrier and passed it along to half of his daughters and to his son Wessel. Wessel in turn passed along the recessive allele to his sons Oege and Djurre. These four stallions together with half of their daughters (and that's quite a few mares) form almost the whole basis of the carriers that are currently present in the breeding population. Because of the big influence that the double carriers Wessel and Oege have had, it is now estimated that one in five Friesian horses is a carrier of one of the two birth defects. The graph below shows the relationship between the number of carriers in the population and the number of foals with a birth defect to be expected. If no action is taken to prevent risk-bearing breedings then it is expected that, per year, 60 of the 6000 foals born will be born with a birth defect. Depending on the use of carrier stallions the number of carriers in the population can increase higher and that will cause an exponential increase in the number of foals with birth defects.

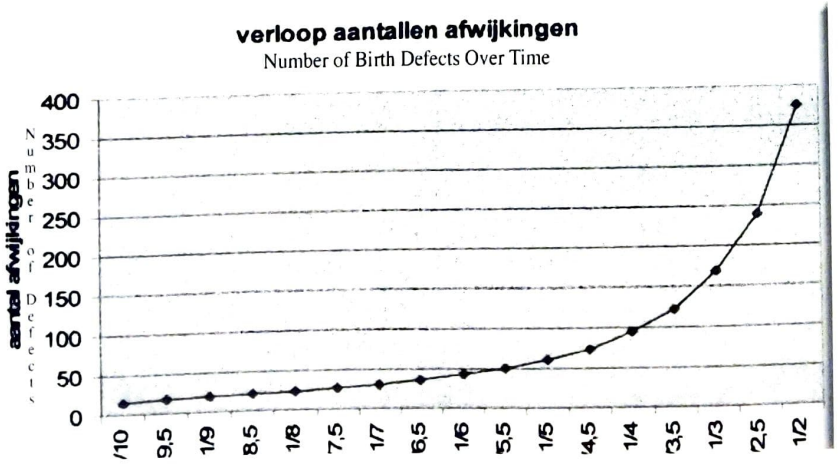
Risk-Bearing Breedings

If it is not known which horses are the carriers within a population then avoiding inbreeding is the only way to lower the chance of birth defects. For this purpose the inbreeding coefficient is used as the indicator. A few generations ago this was an effective way to avoid risk-bearing breedings. If Wessel or Jarich was present in both the lineage of the selected sire and the dam's, this would, after all, result in an inbreeding coefficient that would be too high and based on that the combination would not be used. Wessel, meanwhile, has great-great-grandsons and daughters that are producing carriers themselves. You will therefore not encounter Wessel until you go further back in the lineage. The inbreeding percentage therefore says little in 2006 about the chance of having a dwarf foal or a foal with water on the brain. To say something useful about the risks of a certain desired breeding more information about the carriers in the current day population is indispensable.

If all defects are properly reported the stallions that are carriers will sooner or later be exposed, because one or more foals with defects will be produced by them. For the mares that is different. A mare produces too few foals to determine her to be a carrier or not. Only if a mare has had a foal with a birth defect can she be positively identified as a carrier. To evaluate the risks one therefore needs to especially look at the sires in the lineage of the dam and sire of the future foal. The chance of having a dwarf foal or one with water on the brain can be limited to a minimum by not combining a mare with a known carrier stallion in her lineage with a stallion that is a carrier himself or also has a known carrier stallion in his lineage. Table 3 shows the chances of a foal with birth defects if the carriers on the sire and dam sides are known.

Identifying Carriers

Preventing risk-bearing breedings is one method of dealing with birth defects. Identifying carriers is a second method. Carrier stallions with a lot of offspring create further distribution of the recessive factor in the population. Half of the offspring will become a carrier from the stallion in question. But stallions are used a lot because they have usable characteristics and with that positively contribute to breeding. Being a carrier therefore does not necessarily have to be a reason to no longer use them. If the first method is successful, then good carrier stallions can continue to positively contribute to breeding without any problems. The other half of their offspring is after all as free from defects as offspring from a non-carrier stallion. Being a carrier should therefore be part of the selection on qualities of a breeding stallion. How heavy it should weigh in the evaluation is in turn dependent on the efficacy of method one. The efficacy of method one is in turn dependent on the number of defects that are reported on the birth announcements.



DNA Research

A stallion can only then be recognized as a carrier when the first foal with a birth defect is reported. This means that the risks for young stallions, that have few or no offspring, can only be evaluated on the grounds of their lineage. To track down carriers sooner, a marker test is necessary which can tell if a stallion is a carrier or not through DNA analysis. As

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soon as these tests are available, the incompleteness of the registration of birth announcements will no longer play a role and it can be determined with certainty if a horse is a carrier. Young stallions can then be screened just like it is done with the red factor. Mare owners can then also have their brood mares tested. As of that moment all risk-bearing breedings can be prevented and then the dwarf Friesians and Friesians with water on the brain will be a thing of the past. To further the development of these marker tests, DNA material of foals with birth defects is necessary. The more defects are reported, the more DNA material will be available, and the faster the tests will be available. The faster these tests are available the faster we can start with combating a further increase in the number of carriers.

Tabel 3

Kans op een afwijkend veulen (Chance of a Foal with Birth Defect)		Carrier in the Lineage of the Foal's Sire: **Drager in de stamboom van de vader van het veulen**						
Drager in de stamboom van de moeder van het veulen (Carrier in the Lineage of the Foal's Dam)		V	VV	VM	VVV	VVM	VMV	VMM
	M	1/4	1/8	1/8	1/16	1/16	1/16	1/16
	MV	1/8	1/16	1/16	1/32	1/32	1/32	1/32
	MM	1/8	1/16	1/16	1/32	1/32	1/32	1/32
	MMV	1/16	1/32	1/32	1/64	1/64	1/64	1/64
	MVM	1/16	1/32	1/32	1/64	1/64	1/64	1/64
	MMV	1/16	1/32	1/32	1/64	1/64	1/64	1/64
	MMM	1/16	1/32	1/32	1/64	1/64	1/64	1/64

How Does a Hereditary Defect Come About?

Cellular division is a complicated biochemical process and, because of a multitude of circumstances or coincidences, something can occasionally go wrong. If something goes wrong in the production of ovums or sperm cells then that will almost always lead to unusable ovums or sperm cells. Every once in a while such a mishap will not immediately have dramatic consequences and a normally functioning cell cluster with a small defect will develop.

Suppose that, with the nuclear fission which precedes the production of ovums with Hilda Q in 1880, such a mishap occurred. One of the ovums of Hilda Q lacks a very tiny bit of chromosome 9 that is necessary for the making of a vitamin-like substance that plays an essential role in the development of the central nervous system. Coincidence has it that this ovum is fertilized by a sperm cell of the stallion Apollo and develops into a filly. There is nothing wrong with chromosome 9 of Apollo's sperm cell and the embryo that is produced from the joining of ovum and sperm cell can simply make the necessary substance, resulting in a normal foal without any birth defects. If this mare starts to produce ovums herself, then half will have chromosome 9 with the mistake of Hilda Q and the other half will be Apollo's good chromosomes 9. If one of the ovums with Hilda Q's chromosomes 9 is then fertilized with a sperm cell of another stallion then another carrier of the defect is created.

Suppose that this time it's a stallion that will be used for breeding and has some 40 offspring. In this case, 20 sons and daughters of this stallion are carriers. In this manner the distribution of the defect will continue for several generations without any signs of the defect. Not until someone decides to match a stallion with Hilda Q in his lineage with a mare who also has Hilda Q in her lineage, does the chance exist that both horses are carriers of the defect. If that is the case then in 25% of the births, the unborn foal will get chromosome 9, with the defect, from both the dam and the sire. Result: the embryo cannot make the necessary substance, a deviating development of the central nervous system comes about and the foal is stillborn with water on the brain. The development of a hereditary defect has therefore nothing to do with inbreeding. The chance that a defect will manifest itself in the form of a foal with a birth defect, however, has everything to do with inbreeding.

The author wrote this article on behalf of the work group, Birth Defects and Inbreeding.

Mares and foal in Weiland. Photo by Drs. Ben Horsman © www.horsmans.com