A review of reproductive and congenital diseases with treatment options in Friesian horses

Platts, Jessica Rose

THE UNIVERSITY OF ZAGREB
FACULTY OF VETERINARY MEDICINE

INTEGRATED UNDER-GRADUATE AND GRADUATE
UNIVERSITY STUDIES IN
VETERINARY MEDICINE

MASTER'S THESIS

Jessica Rose Platts

A review of reproductive and congenital diseases with treatment options in Friesian horses

Zagreb, 2024

Jessica Rose Platts

Department of Obstetrics and Reproduction

Head of the Department: prof. Dr. sc. Tugomir Karadjole

Mentor: prof. Dr. sc. Nikica Prvanović Babić

Members of the Committee for Defence of the Master's Thesis:

1. Assoc. Prof. Ivan Folnožić DVM, PhD
2. Full Prof. Nikica Prvanović Babić DVM, PhD
3. Assoc. Prof. Iva Getz DVM, PhD
4. Full Prof. Silvijo Vince DVM, PhD

This thesis contains 31 pages, 4 figures, and 46 literature citations

ACKNOWLEDGEMENTS

I would like to thank Professor Prvanović Babić for your support and guidance with this thesis and for being such a positive and motivating role model.

Also, to the many other professors at the faculty and the other inspiring vets I have met along the way, thank you for the part you have played in my education and for starting my veterinary career.

My colleagues, the class of 2018/2019, thank you for making these 6 years such a memorable experience. It was wonderful getting to know you all and I wish all of you the very best in your careers.

Jess, it would have been a lot harder without you. Thank you so much for all your help, comic relief and friendship over these 6 years, and I hope for many more.

Thank you, Val, for your infectious confidence and motivational words. And of course, for being my partner in our equine struggle.

It would be impossible to mention everyone else individually, however I hope the people closest to me recognise my appreciation for them and that my vet school experience would not have been the same without you all.

Finally, thank you to my family, Lucy and especially my parents, without whom this dream would not have become reality. Words cannot express the gratitude I have for your continuous love and support; I am very lucky.

ABBREVIATIONS

KFPS = *Koninklijke Vereniging Het Friesch Paarden-Stamboek* - Royal Association, The Friesian Horse Studbook

CSF = cerebrospinal fluid

B3GALNT2 = beta-1,3-N-acetylgalactosaminyltransferase 2

SHOX = short-stature homeobox gene

B4GALT7 = beta-1,4-galactosyltransferase 7

RFM = retained foetal membranes

TNB = total number of living normally structured sperm cells

Table of contents

1. INTRODUCTION

Equine reproduction in a specific breed studbook aims to selectively breed horses for predetermined characteristics and traits. One breed for which this is particularly obvious is the Friesian.

Friesian horses are desired for their distinctive black coats and calm, intelligent demeanour. It is the native breed of The Netherlands and so there in particular, the Friesian has a strong cultural significance. Historically, they were used as war horses, with references to the breed being used as far back as Roman times, within Nero's army, and it is supposed William the Conqueror rode into battle on a Friesian in 1066 at the Battle of Hastings (SAVELKOULS, 2015).

Initially, the breed was quite small, around 140cm but robust and with the strength to carry soldiers and armour of up to 250kg. Around the 1600's, as warfare and needs changed, the Friesian breed did too. Heavy and strong were no longer characteristics of priority, instead a lighter, more nimble horse was sought after. This led to the creation of the baroque Friesian, influenced by Andalusian horse blood, which is now like the modern Friesian horse that we see today (Figure 1), (GEURTS, 1970). Majestic and eye-catching, the breed then became incredibly popular with the rich for carriage driving and the sport of dressage. However, as technology advanced and the need for horses in agriculture and the battlefield dwindled, the Friesian population began to decline.

In 1879, in attempts to revive the breed, the KFPS was established by native Friesian farmers and landowners. A program to rescue the breed was initiated, however, to preserve the integrity of the Friesian and its distinctive look, no cross breeding with outside blood was permitted. Despite their work, in 1913, only 3 purebred Friesian stallions were alive and approximately 300 broodmares. The horses were bred to be less refined and more robust, reverting to the initial workhorse stamp, whilst still maintaining the classic black coats and docile nature. Although this worked temporarily, industrialisation continued to thrive and the work of the horses in the field just could not compare (SAVELKOULS, 2015).

Figure 1. A modern-day Friesian mare. Authors image

Again, to try keep the breed alive, the Friesian was marketed as a leisure and sports horse, particularly for four-in-hand carriage driving. Popularity also increased significantly as the breed began to appear in the media and films. Advances in reproductive technologies in the 1970s meant breeding could occur at much faster rates. In 2005, the population of registered Friesians worldwide was 70,000, a significantly healthier number than the 3000 just 25 years before (SAVELKOULS, 2015).

Although the breed was no longer at risk of extinction, because the initial genetic pool was so small and due to the desire to protect the uniqueness of the Friesian horse, a high amount of inbreeding occurred (SEVINGA et al., 2004b). This was not without repercussions and the Friesian horse is now predisposed to certain ailments, both related to reproduction and otherwise as a consequence of this unavoidable inbreeding (BYARS, 2007, BOERMA et al., 2015).

This thesis aims to highlight some of the reproductive issues and congenital disorders that occur in Friesian horses because of this inbreeding and discuss this in relation to the wider horse population. Additionally, it will discuss current therapeutic options available to treat some of those disorders.

2. REVIEW OF THE RESULTS OF PREVIOUS RESEARCH

2.1 Hydrocephalus

Hydrocephalus occurs when, within the ventricles of the brain, there is an accumulation of cerebrospinal fluid (SIPMA et al., 2013). It is understood that there are 3 underlying mechanisms that create this pathology: 1) an obstruction of flow of CSF within the ventricular system, 2) a change in absorption of CSF or 3) increased production of CSF (REKATE, 2008). Depending on the underlying process, hydrocephalus can further be classified into internal or external/communicating.

Internal hydrocephalus usually occurs when there is a blockage of flow of CSF between the ventricles, whereas in communicating hydrocephalus, CSF is still able to flow within the ventricular system and this type commonly occurs when there is an increased production of CSF, or, if there is an issue with the absorption of it (SCHURR et al., 1953). Additionally, hydrocephalus can be a congenital disorder when development of the ventricular system is altered. If a tumour is causing the obstruction or some form of inflammatory process, the hydrocephalus is acquired. In animals, congenital hydrocephalus is the most frequently seen, often due to obstruction of CSF flow (SCHURR et al., 1953) and currently there are no acquired cases of hydrocephalus in horses that have been scientifically reported or proven.

In Friesian horses, hydrocephalus occurs at a higher incidence than in other breeds (BOERMA et al., 2012), potentially due to the higher likelihood of genetic diseases due to the breed having an inbreeding coefficient of 15% (SEVINGA et al., 2004b). Foals affected are usually stillborn or die very soon after birth and often cause dystocia in the mares due to the enlarged cranium (Figure 2) being unable to pass through the birth canal (OJALA and ALA-HUIKKU, 1992; KOLB and KLEIN, 2019).

Figure 2. A Friesian foal with hydrocephalus (SIPMA et al., 2013)

Foals of the Friesian breed affected by hydrocephalus typically have an enlarged cranium and the ossification of the skull bones are incomplete. The petrosal bone is commonly malformed. Widths of affected foal skulls are 3 times wider than non-hydrocephalic skulls and are doubled in height. The cerebral cortices are significantly thinner than expected due to dilation of the ventricular cavities. On microscopic evaluation, the amount of grey and white matter is decreased and the ratio of white to grey matter is also reduced compared to normal, unaffected foals (SIMPA et al., 2013).

Stenosis of the jugular foramen has been established as the most likely aetiology causing hydrocephalus in Friesian foals (SIMPA et al., 2013). This uncommon anatomical fault is due to a genetic mutation that in other horse breeds, due to the rarity of the condition, is likely a dominant mutation and not X-linked (OJALA and ALA-HUIKKU, 1992). In Friesian horses, congenital hydrocephalus is inherited autosomal recessively with a nonsense mutation in B3GALNT2 gene found to be responsible (DUCRO et al., 2015). With regards to prevalence, in Mexico, almost 10% of Friesian stallions are carriers of the mutated B3GALNT2 gene (AYALA-VALDOVINOS et al., 2017) which is like results found in the Netherlands in which 13% of stallions and 17% of mares are heterozygous for the mutation (DUCRO et al., 2015).

As the prevalence of this mutation is relatively high within the Friesian population, care should be taken when matching mares and stallions, as a foal from two heterozygous carriers will have a 25% chance of being affected by hydrocephalus and 50% of their foals will also be carriers. This is already quite challenging given the level of inbreeding within the breed (SEVINGA et al., 2004b). Ironically, it is also likely this hydrocephalus causing mutation is a consequence of the high level of inbreeding in Friesian horses.

Due to the high incidence of congenital diseases in the Friesian breed, recently registered stallions are tested to establish heterozygosity or homozygosity for the B3GALNT2 mutation, and this information is made public knowledge for potential breeders. It is advisable to avoid the mating of two heterozygous individuals and therefore owners are also encouraged to genetically screen their mares too. The mutation of B3GALNT2 has been found in other breeds such as Belgian horses (KOLB and KLEIN, 2019), which further reiterates the importance of genetic screening for carriers within other breeds as well to prevent hydrocephalus occurring. Additional methods to prevent hydrocephalus include preimplantation genetic testing. This could prove useful in the Friesian breed when the number of individual breeding animals is already reduced and the removal of all carriers from the breeding population is not really feasible.

2.2 Dwarfism

Dwarfism is a congenital disease that is relatively uncommon in the wider horse population. Horses with the condition do not reach their full adult size and can suffer additional health problems associated with abnormal development. It is estimated that dwarfism will occur in the Friesian horse population once in every 400 foals born (OSINGA, 2000) and occurs due to genetic mutations that arose from the Friesian breed's small genetic pool.

The mechanism of dwarfism stems from impaired bone growth at a young age (BOEGHEIM et al., 2017). This can result in either proportional or disproportional dwarfism. Proportional dwarfism, in which the animal appears relatively normal, just with an overall decrease in size is common in dogs (KOOISTRA et al., 2000). This has been described in the German shepherd breed, often due to pituitary gland malfunction and the dogs remain 'puppy-like' due to the lack of growth hormone (BOEGHEIM et al., 2017). Disproportionate dwarfism, as is the case in Friesian horses, results in the head and body size being almost normal, but a reduction in limb length causes these horses to be smaller than their non dwarf counterparts (Figure 3). Friesians with dwarfism only reach around 50% of their expected adult body weight and their legs are 25% shorter than a fully grown adult (BACK et al., 2008).

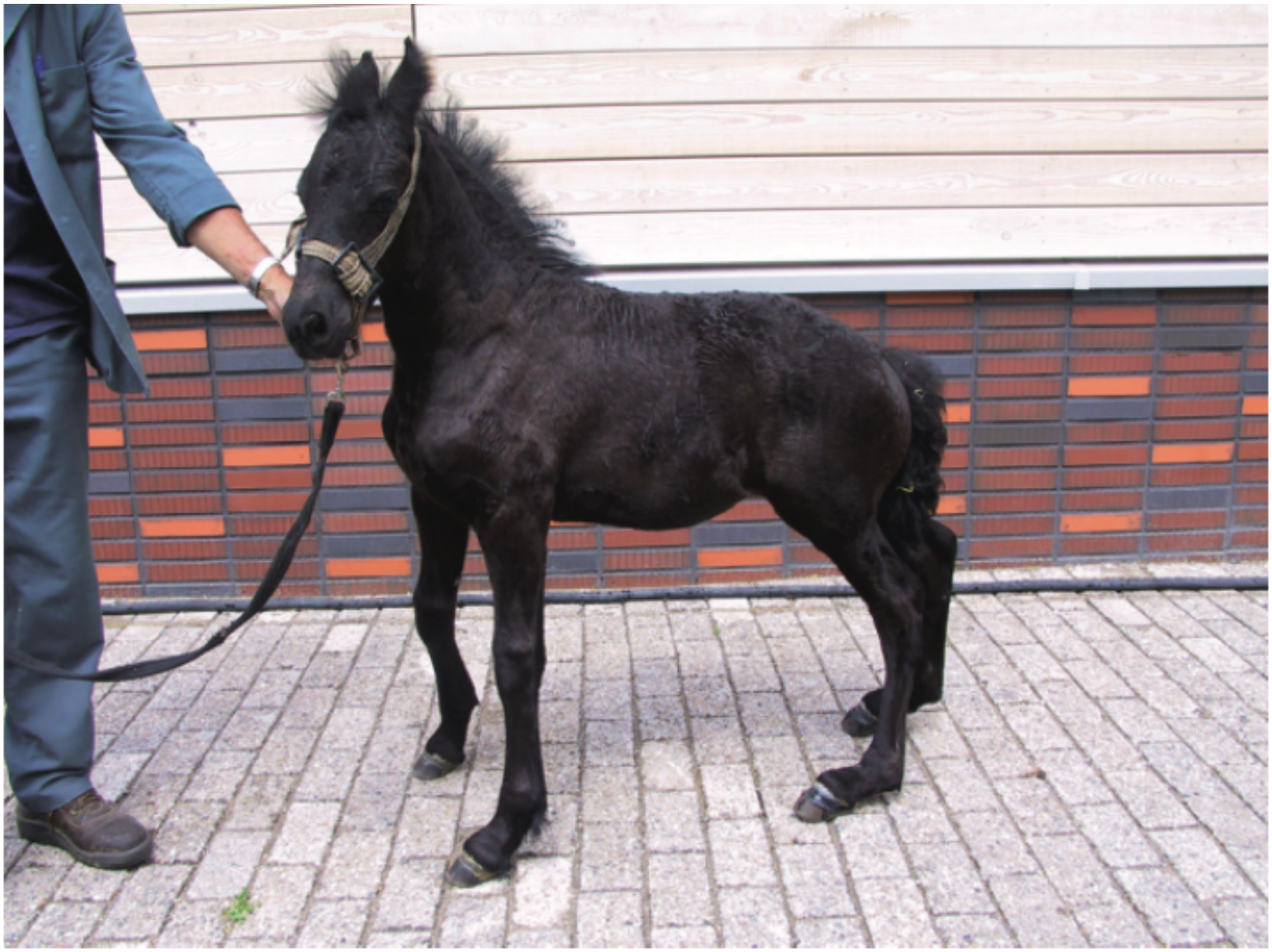

Figure 3. A Friesian foal with dwarfism, note the hyperextended fetlocks (BOERMA et al., 2012)

In miniature horses and Shetland ponies, dwarfism has been attributed to mutations in the aggrecan gene (DE ANDRADE et al., 2020) and SHOX gene (RAFATI et al., 2016) respectively. Contrastingly, a mutation in the B4GALT7 gene has been proven to cause the typical dwarf phenotype in Friesian horses (ORR et al., 2010; LEEGWATER et al., 2016). Phenotypically, as foals, Friesian dwarfs are smaller than would be expected for their age with an associated reduction in body weight. The foals also suffer from extreme laxity in the flexor tendons, resulting in hyperextension of the fetlocks, although this surprisingly does not limit the ability of the foals to gallop and jump around out in the field. Muscles over the whole body tend to be poorly developed, weaker and there is a 'dip' at the level of the 10th-16th thoracic vertebrae. Despite their smaller size, the foal's appetites tend to be normal (BACK et al., 2008). Friesian dwarf foals' heads are also normal, and they do not possess mandibular prognathism, a domed forehead or enlarged eye sockets which are common and defining characteristics in miniature horse dwarf foals (METZER et al., 2017; DE ANDRADE et al., 2020).

There doesn't seem to be a reason why adult Friesian dwarfs wouldn't be able to reproduce as examination of mares has shown a fully mature reproductive tract and ovaries cycling as one would expect. Colts also produce normal semen (BACK et al., 2008). This also seems to be the case in other breeds as dwarf miniature horses, mistaken for just small adults, have been used as breeding animals and produced offspring. It should be noted that foals born from dwarf horses also have dwarfism and are afflicted with additional developmental abnormalities (DE ANDRADE et al., 2020).

Unlike in dogs where dwarfism results due to a lack of growth hormone (VOORBIJ and KOOISTRA, 2009), dwarfism in Friesians cannot be treated by hormone therapy. As the cause is on the molecular level and causes problems in the physeal growth (ORR et al., 2010), the dwarfism cannot be reversed. However, as the genetic causative mutation has been identified, it is possible to screen and exclude carriers from the breeding program. This may cause issues in an already small gene pool though if more individuals are discounted. Therefore, it is recommended that breeders know the carrier states of the mare and potential stallions to avoid mating two heterozygous individuals.

Other considerations may be the possibility of a pony breed or toy variety of the Friesian horse, however given the health problems associated with the Friesian breed anyway, plus the additional joint laxity experienced by the dwarfs, this may not ethically be in the best interests of the breed as healthy animals cannot be guaranteed. The issues that have arisen in the small animal world, when dogs and cats have been bred for aesthetic reasons should also be considered and whether this will cause more issues than benefits in an already troubled breed. Although some Friesian dwarfs live well despite their deformities (BACK et al., 2008), long term health must be considered and the stress their skeletal system will undergo due to abnormal loading must not be discounted. Since the breed has suffered the consequences of inbreeding to maintain specific breed standards, it must also be considered whether breeding for a 'pony type' undermines the breed criteria. The foals born with dwarfism will also never reach full athletic working potential.

2.3 Retained foetal membranes

Passing of the foetal membranes is the third and final stage of parturition and in normal, healthy mares, will occur within 90 minutes postpartum (ROSSDALE and MAHAFFEY, 1958). Although there is some debate over when the placenta is considered retained, the consensus is that if the membranes have not been passed within 3 hours of birth (SEVINGA et al., 2004a), intervention and treatment should commence.

Exact aetiology of retained foetal membranes is unknown and currently there is no way to predict if it will occur, however mares that had retained placentas before are more likely to be at risk of retained placenta again (PROVENCHER et al., 1988). Uterine atony and associated disturbance of normal uterine contractions post parturition is understood to be the most likely cause, although some studies have shown that in draft mares, histologic abnormalities of the placenta that cause adhesions of the allantochorion to the endometrium is at fault for retention of the foetal membranes (RAPACZ et al., 2012).

Risk factors associated with RFM include dystocia, abortion, twins, c-section, prolonged gestation, and draft breeds. Conditions such as dystocia and c-section that require manhandling of the uterus seem to predispose to RFM as the manipulation can interrupt the normal loosening process of the membranes, leading to higher incidence of retention. Whether the foetus is alive or dead at the start of C-section also has bearing on foetal membrane retention. One study showed that if the foetus was alive at the beginning of the procedure, 70% of mares had RFM whereas 35% had RFM if the foetus was dead, suggesting that the autolytic process affecting the foetus may help in loosening the membranes, preventing retention (VANDEPLASSCHE et al., 1971). Studies have shown that Friesian mares with RFM have lower serum calcium levels than mares that do not have RFM (SEVINGA et al., 2002b) which shares similarity in dairy cows in which hypocalcaemia can cause a reduction in contractions of the myometrium and predispose to RFM (IWERSEN and DRILLICH, 2015).

The incidence of retained placenta in Friesians is 54% (SEVINGA et al., 2004a) which is noticeably higher than the 2-10% in the general horse population (PROVENCHER et al., 1988). In the Friesian breed, inbreeding has been shown to be partly at fault for the higher occurrence of RFM, and that to prevent further increases in RFM incidence, the breeding population should be enlarged to prevent breeding of closely related individuals (SEVINGA et al., 2004b).

Consequences of retained foetal membranes can include laminitis which occurs due to delayed involution of the uterus and increased necrosis of the remaining foetal membranes in utero, which can lead to bacterial proliferation and subsequent septicaemia and toxaemia which can damage the sensitive laminae of the hoof (VANDEPLASSCHE et al., 1971). Mares are also at risk of metritis and becoming systemically ill in up to 47% of cases (WARNAKULASOORIYA et al., 2018).

An intact placenta when laid out will appear as an ‘F’ shape, with the velvet like chorionic surface and the silvery, shiny allantois inverted as the foal has been pushed through the birth canal (Figure 4). Diagnosis of RFM is done by visual examination of any expelled placenta to check for tears or holes that may indicate missing portions. RFM should also be a primary differential in any mare that has recently foaled and is becoming restless or showing signs of laminitis or colic.

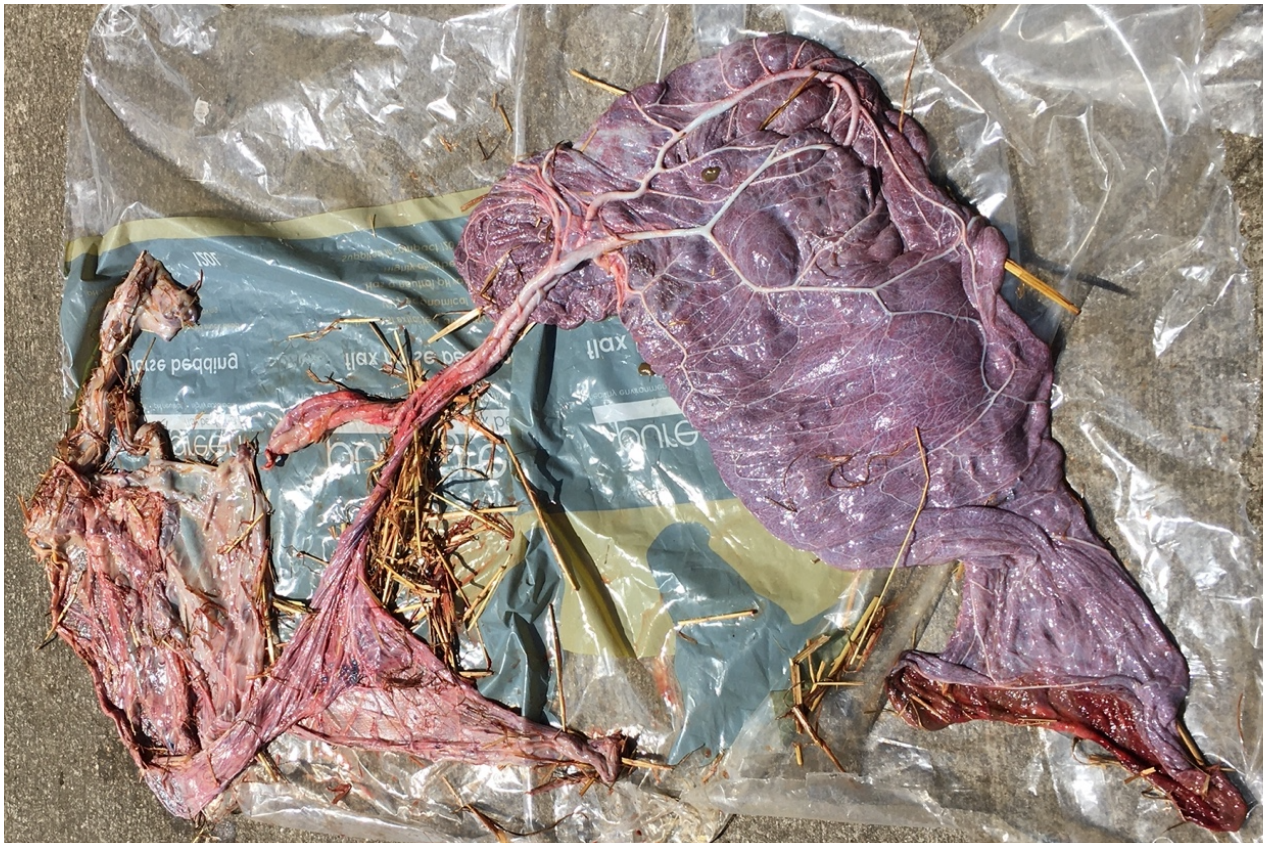

Figure 4. An intact placenta. Authors image

Treatment of RFM usually involves a combination of manual removal, oxytocin, uterine lavages, and antibiotics (WARNAKULASOORIYA et al., 2018).

If the placenta is partially detached and hanging from the mare, gentle traction may be attempted. This may be complicated if the mare is nervous and uncooperative, although this does not tend to be the case in Friesians as the breed tends to be more docile and calmer and allow for vaginal exams and manipulation (MAASKANT et al., 2010). Manual extraction in some cases is not possible or does not work (VANDEPLASSCHE et al., 1971) and currently is not recommended as initial treatment due to the haemorrhage risk it carries (WARNAKULASOORIYA et al., 2018).

Pulmonary embolism has also been observed as an extremely rare complication of manual removal of the placenta (VANDEPLASSCHE et al., 1971). Despite the possible complications, studies have shown that in Friesian mares, there is no difference in the reproductive performance of the mares that were treated with manual removal of the membranes and those that were treated medically (SEVINGA et al., 2002a).

Oxytocin, in conjunction with uterine lavage, is one of the most useful and widely recommended drugs for treating retained foetal membranes as it stimulates uterine contractions. Dosage and route of administration varies between practitioners, but high doses given intramuscularly up to every 2 hours seems to be the most common protocol (WARNAKULASOORIYA et al., 2018).

It can also be given intravenously or in an infusion slowly over 60 minutes (VANDEPLASSCHE et al., 1971). Care must be taken with higher doses as there is the potential to cause uterine spasm, rather than contraction and subsequent signs of colic (CANISSO et al., 2013). The addition of calcium to the infusion with oxytocin may also be beneficial if the mare has hypocalcaemia (SEVINGA et al., 2002b).

Large volume uterine lavage with sterile isotonic saline may also help loosen the retained membranes and additionally help to remove bacteria and toxins that may be accumulating. Often this is repeated until the membranes have been expelled, although some practitioners recommend continuing lavages for 1-2 weeks after (WARNAKULASOORIYA et al., 2018). These treatments are often combined with broad spectrum antibiotics and non-steroidal anti-inflammatory drugs to alleviate the systemic effects the mare may be experiencing.

Although a potentially life-threatening complication of foaling, once treated, RFM does not have an impact on the reproductive performance in Friesian mares, provided there are no other pathologies such as uterine tears or bleeding (SEVINGA et al., 2002a). These results are compatible with findings in other breeds (PROVENCHER et al., 1988). Sending mares that have had RFM to be bred on their foal heat is thought to be inadvisable (PROVENCHER et al., 1988), however in Friesian mares RFM does not mean foal heat breeding has to be avoided (SEVINGA et al., 2002a). Breeders with Friesian broodmares should make every effort to create a clean environment for foaling and should complications arise, act promptly to protect the reproductive performance and health of the mare.

2.4 Stallions

The Friesian stallion population fell to just 3 registered stallions at one point in time (SAVELKOULS, 2015), meaning a lot of the modern-day population of Friesians are inbred. Fortunately, today, the number of approved stallions has risen to approximately 95 (www.kfps.nl, 2024) but there is a concern that this has negatively impacted the fertility of these stallions, due to them all having common ancestors.

As some semen traits have been shown to be heritable in warmblood stallions, (GOTTSCHALK et al., 2016), it is important to know the quality of semen the Friesian stallions to ensure they are adequately fertile as the breed needs as much genetic variety as possible. Surprisingly, a study done on 1146 Friesian stallions found that the higher level of inbreeding within the breed does not negatively impact semen quality of the stallions (BOER, 2007). This is in stark contrast to other studies done in Shetland ponies and Creole horses in which it has been concluded that inbreeding does influence semen quality (VAN ELDIK et al., 2006, DINI et al., 2020, BETANCUR et al., 2023).

In order to be eligible to be registered in the studbook, Friesian stallions must undergo vigorous testing procedures that involve temperament evaluations, riding analysis and their potential for success in sport is also assessed. Part of this testing includes a breeding soundness examination. During said test, the stallions' external genitalia are examined and any deviations from normal anatomy will automatically exclude them from further investigation. The average size of testicles in a 3-year-old Friesian stallion is 5-6 cm wide and 8-10cm long (HORSMANS, 2006). The scrotum of the stallions should contain two testicles of similar size which, according to the studbook by volume, cannot be more than 50% different from each other (www.kfps.nl, 2024). Following a physical exam, semen is then collected in an artificial vagina and assessed according to 5 criteria: 1) colour, 2) volume, 3) concentration of sperm cells, 4) morphology of sperm cells and 5) motility (HORSMANS, 2006).

The KPFS as of 2024 will accept stallions that have, in an average of two ejaculates, a minimum of 50% motile, and therefore alive sperm, and 50% of the viable sperm must have normal, physiological morphology. The TNB of each stallion is then calculated using the following equation:

TNB in millions = % of motile sperm x % of normally structured sperm x volume x concentration

In 3-year-old stallions, a TNB of 600 million is accepted as a minimum and stallions that are 4 years or older should have a TNB of 1000 million (www.kfps.nl, 2024). Friesian stallions older than 3.5 years old have been shown to have higher quality semen than stallions that are 2.5 years old (BOER, 2007) which is concordant with the fact younger stallions may not be fully mature yet. The Friesian, as a draft breed, is recognised to matures more slowly, hence the decreased criteria for the younger stallions. It is understood the testicles of Friesians may not be at the maximum capacity for sperm production until 6-8 years of age (HORSMANS, 2006).

It was noticed only ejaculate quantity increased with the level of inbreeding in Friesian stallions (BOER, 2007), however quantity of ejaculate is not an indicator of quality, as the sperm cells can be non-motile or not morphologically normal (HORSMANS, 2006). Anomalies of the acrosome were also found to be relatively common in Friesian stallions and the percentage increased with age (BOER, 2007), which perhaps accounts for the high number of stallions being rejected from the studbook. This contrasts with studies done in other breeds where semen quality was found to be highest in stallions over 20 years old (WILSON et al., 2019), although this was in comparison to 5–9-year-old stallions that were regularly competing alongside stud duties.
These mixed conclusions across the breeds reiterate the need for continued research within these fields.

Unfortunately, 50% of the prospective Friesian stallions presented for registration fail the breeding soundness exams due to poor quality of semen (BOER, 2007). This is concerning considering the breed would benefit from as much genetic diversity as possible.

2.5 Genetic Testing Panels

Since it is such common knowledge that Friesian horses suffer from so many genetic diseases, laboratories across the globe offer a multitude of genetic testing panels, many specific to the Friesian horse. This allows owners and breeders to know the genetic profile of their horse and therefore make ethical and responsible decisions regarding pairing horses for mating. For example, the risk of hydrocephalus occurring in foals can be reduced if a mare known to be heterozygous for the mutated B3GALNT2 gene, the causative agent of hydrocephalus in Friesians, is sent to a stallion who is homozygous for not carrying the mutated gene.

As well as screening for diseases, some panels also offer coat colour screening. Friesians are predominantly black, however as the red gene is still present, all be it in low frequency, the possibility of a chestnut foal can occur. Breeders will want to avoid this occurrence to preserve the characteristic black colour of the Friesian.

Practical horse genetics in Australia, offers a "Friesian health and colour panel" which includes testing for the red/black gene, plus the hydrocephalus and dwarfism genes (www.practicalhorsegenetics.com.au, 2024). Similarly, UC Davis in America has a "Friesian health panel" which screens for dwarfism, hydrocephalus and distichiasis, another disease Friesians are predisposed to. Horses affected with this have eyelashes that grow abnormally and can have impaired vision if the eyelashes are in contact with and irritate the cornea. This test is performed from a hair sample (www. vgl.ucdavis.edu, 2024). All Friesian mares and stallions in the US must have been DNA tested and checked for carrier status of these disorders in order to be registered to the Friesian Sporthorse Association (www.friesiansporthorseassociation.com, 2024).

In the U.K, Laboklin screens for the B4GALT7 gene causing dwarfism. This test can be performed using a hair sample, buccal swab or whole blood. These multiple sample options make testing relatively easy and accessible, even to owners with needle shy horses, where obtaining a blood sample can be difficult (www.laboklin.co.uk, 2024).

Efforts are also being made to identify genetic markers for other ailments Friesian horses suffer from in a higher incidence such as megaoesophagus and aortic fistulation and rupture (SONNEVELD, 2014)

With so many laboratories globally offering these panels, breeders all over can determine the genetic status of their horses and make choices that will hopefully help to eradicate, if not definitely reduce the incidence of these disorders and help to build a healthier breed.

3. CONCLUSIONS

The breeding goal of the KFPS is: ‘A functionally built utility horse with the Friesian breed characteristics, which is healthy and vital, has a talent for performing in sports, has a reliable character and is workable.’ (www.kfps.nl, 2024).

It is clear that this has not always been possible, and the Friesian horse has suffered the effects of a narrow genetic pool throughout its tumultuous history. Congenital diseases such as hydrocephalus and dwarfism are still potential problems, although since 2014 and the availability of genetic tests, awareness is much more prevalent, allowing breeders to make informed and ethical decisions. Friesian genetic testing panels mean the carrier status of individuals can be found out, allowing the best matches to be made and eliminates part of the guessing game that comes with breeding.

With the studbook making kinship values of stallions available to the public and DNA testing becoming more accessible and widespread, the defining characteristics of the Friesian horse can be maintained whilst decreasing further inbreeding as much as possible, thus minimising congenital diseases and creating a healthier breed that will thrive over future generations.

4. REFERENCES

1. DE ANDRADE, D.G.A., R. M. BASSO, A. J. MAGRO, R. LAUFER-AMORIM, A. M. BORGES, J. P. DE OLIVEIRA-FILHO (2020): Evaluation of a new variant in the aggrecan gene potentially associated with chondrodysplastic dwarfism in Miniature horses. Sci. Rep. doi:10.1038/s41598-020-72192-3
2. AYALA-VALDOVINOS, M.A, J. GALINDO-GARCIA, D. SÁNCHEZ-CHIPRÉS, T. DUIFHUIS-RIVERA (2017): Genotyping of friesian horses to detect a hydrocephalus-associated c.1423C>T mutation in B3GALNT2 using PCR-RFLP and PCR-PIRA methods: Frequency in stallion horses in México. Mol Cell Probes. 32:69-71, doi: 10.1016/j.mcp.2016.12.005
3. BACK, W., J.J VAN DER LUGT, P.G NIKKELS, A.J VAN DEN BELT, J.H VAN DER KOLK, T.A STOUT (2008): Phenotypic diagnosis of dwarfism in six Friesian horses. Equine. Vet. J. 40:282-7. doi: 10.2746/042516408X278201
4. BETANCUR, G.R., K.B. RODAS, A.U SUAREZ (2023): Relationship of semen quality to inbreeding and gait of Colombian Creole horses. *Ciência Rural*, *53*(3), doi: 10.1590/0103-8478cr20210703
5. BOEGHEIM, I.J.M, P.A.J. LEEGWATER, H.A VAN LITH, W. BACK (2017): Current insights into the molecular genetic basis of dwarfism in livestock. Vet J. doi: 10.1016/j.tvjl.2017.05.014
6. BOER, M (2007): Effects of inbreeding on semen quality of Friesian stallions. Masters thesis, Wageningen University.
7. BOERMA, S., W. BACK, M.M. SLOET VAN OLDRUITENBORGH-OOSTERBAAN (2012): The Friesian horse breed: A clinical challenge to the equine veterinarian? Equine Vet. Educ. 24: 66-71.
8. BYARS, T.D (2007), “It's always something!” Clinical complications in a Friesian mare. Equine Vet. Edu. 19: 251-252. doi: 10.2746/095777307X191941
9. CANNISSO, I.F., J.S. RODRIGUEZ, M.G. SANZ, M.A.C. DA SILVA (2013): A clinical approach to the diagnosis and treatment of retained foetal membranes with an emphasis placed on the critically ill mare. JEVS. 33:570–9. doi: 10.1016/j.jevs.2012.08.006
10. DINI, P., T. BARTELS, I. REVAH, A.N. CLAES, T.A.E STOUT, P. DAELS (2020): A retrospective study on semen quality parameters from four different Dutch horse breeds with different levels of inbreeding. Theriogenology. 157:18-23. doi: 10.1016/j.theriogenology.2020.07.017.
11. DUCRO, B.J., A. SCHURINK, J.W.M. BASTIAANSEN (2015): A nonsense mutation in B3GALNT2 is concordant with hydrocephalus in Friesian horses. BMC Genomics. 16, 761. doi: 10.1186/s12864-015-1936-z
12. GEURTS, R. (1970). The breed structure of the Friesian horse. *Tijdschrift Voor Diergeneeskunde, 95*, 536-540.
13. GOTTSCHALK, M., H. SIEME, G. MARTINSSON, O. DISTL (2016): Heritability of semen traits in German Warmblood stallions. Anim Reprod Sci. 170:10-4. doi: 10.1016/j.anireprosci.2016.03.004.
14. HORSMANS, B. (2006): The sperm inspection in Freisian stallions. ‘The Friesian’ July 2006 pg 32-36 https://fhana.com/app/uploads/2020/07/The-Sperm-Inspection-of-Friesian-Stallions-July-August-2006.pdf

15. IWERSEN, M., M. DRILLICH (2015): Retained foetal membranes in dairy cows Livestock 2015 20:3, 142-146
16. KOLB, D.S., C. KLEIN (2019): Congenital hydrocephalus in a Belgian draft horse associated with a nonsense mutation in B3GALNT2. Can Vet J. 60:197-198.
17. KOOISTRA, H.S., G. VOORHOUT, J.A, MOL, A. RIJNBERK (2000): Combined pituitary hormone deficiency in german shepherd dogs with dwarfism. Domest Anim Endocrinol. 19:177-90. doi: 10.1016/s0739-7240(00)00074-6.
18. LEEGWATER, P.A., M. VOS-LOOHUIS, B.J. DUCRO, I.J. BOEGHEIM, F.G. VAN STEENBEEK, I.J. NIJMAN, G.R. MONROE, J.W. BASTIAANSEN, B.W. DIBBITS, L.H. VAN DE GOOR, I. HELLINGA, W. BACK, A. SCHURINK (2016): Dwarfism with joint laxity in Friesian horses is associated with a splice site mutation in B4GALT7. BMC Genomics. 17:839. doi: 10.1186/s12864-016-3186-0.
19. MAASKANT, A., C.M. DE BRUIJN, A.H. SCHUTRUPS, T.A.E. STOUT (2010): Dystocia in Friesian mares: Prevalence, causes and outcome following caesarean section. Equine Vet. Educ., 22: 190-195.
20. METZGER, J., A.C, GAST, R. SCHRIMPF, J. RAU, D. EIKELBERG, A. BEINEKE, M. HELLIGE, O. DISTL (2017): Whole-genome sequencing reveals a potential causal mutation for dwarfism in the Miniature Shetland pony. Mamm Genome. 28:143-151. doi: 10.1007/s00335-016-9673-4.
21. OJALA, M., J. ALA-HUIKKU (1992): Inheritance of hydrocephalus in horses. EVJ. 24:140-3. doi: 10.1111/j.2042-3306.1992.tb02799.x.
22. ORR, N., W. BACK, J. GU, P. LEEGWATER, P. GOVINDARAJAN, J. CONROY, B. DUCRO, J.A. ARENDONK, D.E. MACHUGH, S. ENNIS, E.W. HILL, P.A. BRAMA (2010): Genome-wide SNP association-based localization of a dwarfism gene in Friesian dwarf horses. Anim Genet. doi: 10.1111/j.1365-2052.2010.02091.x.
23. OSINGA, A. (2000): "Het fokken van het Friese paard." Scaafsma & Brouwer Grafishe Bedrijven, Dokkum 43-90
24. PROVENCHER, R., W.R. THRELFALL, P.W. MURDICK, W.K. WEARLY (1988): Retained foetal membranes in the mare: A retrospective study. Can Vet J. 29:903-10.
25. RAFATI, N., L.S. ANDERSSON, S. MIKKO, C. FENG, T. RAUDSEPP, J. PETTERSSON, J. JANECKA, O. WATTLE, A. AMEUR, G. THYREEN, J. EBERTH, J. HUDDLESTON, M. MALIG, E. BAILEY, E.E. EICHLER, G. DALIN, B. CHOWDRAY, L. ANDERSSON, G. LINDGREN, C.J. RUBIN (2016): Large Deletions at the SHOX Locus in the Pseudoautosomal Region Are Associated with Skeletal Atavism in Shetland Ponies. G3 (Bethesda) 7;6:2213-23. doi: 10.1534/g3.116.029645
26. RAPACZ, A., K. PAŹDZIOR, A. RAŚ, T. ROTKIEWICZ, T.E. JANOWSKI (2012): Retained Foetal Membranes in Heavy Draft Mares Associated with Histological Abnormalities. JEVS, Vol 32, Issue 1, Pg38-44, doi: 10.1016/j.jevs.2011.06.015.
27. REKATE, H.L (2008): The definition and classification of hydrocephalus: a personal recommendation to stimulate debate. Cerebrospinal Fluid Res. 22;5:2. doi: 10.1186/1743-8454-5-2.
28. ROSSDALE, P.D, L.W. MAHAFFEY (1958): Parturition in the thoroughbred mare with particular reference to blood deprivation in the newborn. Vet. Rec 70, 142
29. SAVELKOULS, J. (2015): The Friesian horse and the Frisian horse. The (re)invention and the historicity of an iconic breed. *De Vrije Fries*, *95*, 9-42.

30. SCHURR, P.H, R.L. MCLAURIN, F.D. INGRAHAM (1953): Experimental studies on the circulation of the cerebrospinal fluid and methods of producing communicating hydrocephalus in the dog. J Neurosurg. 10:515-25. doi: 10.3171/jns.1953.10.5.0515.
31. SEVINGA, M., J.W. HESSELINK, H.W. BARKEMA (2002): Reproductive performance of Friesian mares after retained placenta and manual removal of the placenta. Theriogenology. 15;57:923-30. doi: 10.1016/s0093-691x(01)00691-4.
32. SEVINGA, M., H.W. BARKEMA, J.W. HESSELINK (2002): Serum calcium and magnesium concentrations and the use of a calcium-magnesium-borogluconate solution in the treatment of Friesian mares with retained placenta. Theriogenology. 15;57:941-7. doi: 10.1016/s0093-691x(01)00716-6.
33. SEVINGA, M., H.W. BARKEMA, H. STRYHN, J.W. HESSELINK (2004): Retained placenta in Friesian mares: incidence, and potential risk factors with special emphasis on gestational length. Theriogenology. 1;61:851-9. doi: 10.1016/s0093-691x(03)00260-7.
34. SEVINGA, M., T. VRIJENHOEK, J.W. HESSELINK, H.W. BARKEMA, A.F. GROEN (2004): Effect of inbreeding on the incidence of retained placenta in Friesian horses. J Anim Sci.82:982-6. doi: 10.2527/2004.824982x.
35. SIMPA, K.D., P. CORNILLIE, M.N. SAULEZ, T.A. STOUT, G. VOORHOUT, W. BACK (2013): Phenotypic characteristics of hydrocephalus in stillborn Friesian foals. Vet Pathol. 50:1037-42. doi: 10.1177/0300985813488955
36. SONNEVELD, M. (2014): Aortic rupture in the Friesian horse. A search for a genetic background. Master's thesis, Utrecht university
37. VOORBIJ, A.M.W.Y., H.S. KOOISTRA (2009): Pituitary dwarfism in German shepherd dogs. J Vet Clin Sci. 2 4-11.
38. VANDEPLASSCHE, M., J. SPINCEMAILLE, R. BOUTERS (1971): Aetiology, pathogenesis and treatment of retained placenta in the mare. EVJ. 3:144-7. Doi: 10.1111/j.2042-3306.1971.tb04459.x.
39. VAN ELDIK, P., E.H. VAN DER WAAIJ, B. DUCRO, A.W. KOOPER, T.A. STOUT, B. COLENBRANDER (2006): Possible negative effects of inbreeding on semen quality in Shetland pony stallions. Theriogenology. 1;65:1159-70. doi: 10.1016/j.theriogenology.2005.08.001.
40. WARNAKULASOORIYA, D.N., C.D. MARTH, J.A MCLEOD, D.W. HANLON, N. KREKELER (2018): Treatment of Retained Foetal Membranes in the Mare-A Practitioner Survey. Front Vet Sci. 19;5:128. doi: 10.3389/fvets.2018.00128
41. WILSON, M., J. WILLIAMS, V.T, MONTROSE, J. WILLIAMS (2019): Variance in Stallion Semen Quality among Equestrian Sporting Disciplines and Competition Levels. Animals (Basel).25;9:485. doi: 10.3390/ani9080485
42. www.kfps.nl - last accessed at 9:26am GMT on 15/05/2024
43. https://practicalhorsegenetics.com.au/index.php?test=frs#:~:text=Breeders%20of%20both%20pure%2D%20and,%2C%20hydrocephalus%2C%20and%20Friesian%20dwarfism – last accessed at 3:58pm GMT on 09/06/2024
44. https://www.laboklin.co.uk/laboklin/showGeneticTest.jsp?testID=8553 – last accessed at 4:06pm GMT on 09/06/2024

45. https://vgl.ucdavis.edu/panel/friesian-health-panel#:~:text=This%20health%20panel%20bundles%20together,can%20be%20purchased%20on%20MyVGL. – last accessed at 4:12pm GMT on 09/06/2024
46. http://www.friesiansporthorseassociation.com/FriesianSporthorseDNA.html - last accessed at 4:17pm GMT on 09/06/2024

5. SAŽETAK

Jessica Rose Platts

Proučavanje reproduktivnih i urođenih bolesti s mogućnostima liječenja kod frizijskih konja

Populacija frizijskih konja ima višu razinu parenja u srodstvu od one općeprihvaćene. Urođeni poremećaji poput hidrocefalusa i patuljastog rasta javljaju se u većoj prevalenciji nego kod drugih pasmina konja, a široko je prihvaćeno da su posljedica navedenog parenja u srodstvu. Najčešći uzrok hidrocefalusa kod frizijskih konja je stenoza jugularnog otvora zbog mutacije na genu B3GALNT2. Ovu mutaciju nosi otprilike 10% pastuha i 17% kobila. Patuljasti rast kod frizijskih konja ima prevalenciju od 0,25% i uzrokovan je mutacijom na genu B4GALT7. Ždrebad koja je rođena s ovom bolešću manja je od nezaraženih konja i imaju vrlo slabe tetive fleksora. Ova mutacija dovodi do mogućnosti stvaranja frizijske pasmine u „tipu ponija“, međutim potrebno je uzeti u obzir etiku i dobrobit uzgoja za takve karakteristike. Frizijske kobile su u 54% slučajeva izložene riziku od zadržavanja plodnih ovoja. Vlasnici i veterinari moraju brzo djelovati i pravilno liječiti ovu komplikaciju kako bi spriječili daljnje komplikacije i zaštitili zdravlje kobile. Trenutno preporučena terapija uključuje ispiranje maternice i oksitocin.

Frizijski pastusi podvrgavaju se rigoroznom testiranju kako bi bili primljeni u matičnu knjigu pastuha i 50% njih biva odbijeno. Mlađi pastusi imaju lošiju kvalitetu sjemena od starijih i srodstvo ne utječe na kvalitetu sjemena frizijskog konja. Postoje kontradiktorni podaci iz studija na drugim pasminama u vezi s učincima parenja u srodstvu na kvalitetu sjemena, pa su potrebna daljnja istraživanja.

Ključne riječi: parenje u srodstvu, urođene bolesti, genetika, frizijski konj

6. ABSTRACT

Jessica Rose Platts

A review of reproductive and congenital diseases with treatment options in Friesian horses

The Friesian horse population has a higher than generally accepted level of inbreeding. Congenital disorders such as hydrocephalus and dwarfism occur in a higher prevalence than other breeds of horses, widely accepted to be a consequence of this inbreeding. The most common cause of hydrocephalus in Friesian horses is stenosis of the jugular foramen due to a mutation in the B3GALNT2 gene. This mutation is carried by approximately 10% of stallions and 17% of mares. Dwarfism in Friesian horses has a prevalence of 0.25% and is caused by a mutation on the B4GALT7 gene. Foals born affected by this disease are smaller than unaffected horses and have very lax flexor tendons. This mutation gives rise to the possibility of a 'pony type' Friesian, however ethics and welfare of breeding for such characteristics need to be considered. Friesian mares are at risk of retained foetal membranes 54% of the time. Owners and vets must be quick to act and treat this complication correctly to prevent further complications and protect the health of the mare. Current recommended therapy includes uterine lavages and oxytocin.

Friesian stallions undergo rigorous testing to be accepted into the studbook and 50% of them are rejected. Younger stallions have poorer quality semen than older ones and inbreeding does not influence semen quality in Friesian horses. There is contradicting data from studies in other breeds regarding inbreeding effects on semen quality, so more research is required.

Key words: inbreeding, congenital diseases, genetic, Friesian horse

7. CURRICULUM VITAE

I was born in Leicestershire, U.K on 05/10/1999 and attended the local school: Thornton Primary, for 6 years. I obtained 10 GCSEs from South Charnwood High School and 3 A-Levels from Wyggeston and Queen Elizabeth I college, graduating in 2018. During my school years, I played field hockey, netball and tennis and worked at Altar Stones Lane Cattery - a job I thoroughly enjoyed. I have ridden horses for most of my life and volunteered at the local riding school for 2 years.

I enrolled at the Faculty of Veterinary Medicine, University of Zagreb, Croatia in September 2018. I volunteered in the Equine Clinic at the faculty for 18 months, in addition to spending time in the small animal reproduction and surgery departments. Throughout my studies I completed several externships encompassing small animal, farm, and equine medicine. I am fortunate that this allowed me to travel to many places including Scotland, Cornwall and London, around Croatia, and further afield to Kentucky, USA.