**Equine uveitis in the UK: a retrospective study (2008-2018)**

Fernando Malalana\*1, Joanne Lesley Ireland1, Gina Louise Pinchbeck2, Cathy Marie McGowan3

1 Institute of Veterinary Science, University of Liverpool, Leahurst campus, Neston, UK

2 Institute of Infection and Global Health, Institute of Veterinary Science, University of Liverpool, Leahurst campus, Neston, UK

3 Institute of Ageing and Chronic Disease, Institute of Veterinary Science, University of Liverpool, Leahurst campus, Neston, UK

**\* Corresponding author email:** [f.malalana@liverpool.ac.uk](mailto:f.malalana@liverpool.ac.uk)

**\* Corresponding author telephone:** 01517946041

**Keywords:** horse, eye, intraocular inflammation, enucleation

**Word count:** 3238

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**Abstract:** Uveitis appears to be less prevalent in the UK compared to other parts of the world and studies characterising the disease in the UK are lacking. The objectives of this retrospective study were to describe acute and recurrent cases presenting for management of uveitis in a referral hospital on the North West of England and compare the signalment of horses presenting with uveitis with the equine hospital population during the same period. Medical records of horses presented to the referral Equine Hospital, University of Liverpool with signs of uveitis between 2008 and 2018 were reviewed and clinical details extracted. Seventy horses presented with uveitis; 33 were classified as acute and 37 as recurrent cases. Sixteen of the horses were affected bilaterally. More bilateral cases were classified as recurrent than acute (p=0.04). No differences in age or sex were noted between acute and recurrent cases, or between cases and the general hospital population. Warmbloods and Appaloosas were overrepresented when compared to the general hospital population (p<0.001). Twenty one horses (30%, CI 20.5-41.4) underwent surgery for the control of the uveitis. Fourteen of the 70 horses (20.0%, CI 12.3-30.8) underwent enucleation.

**Introduction**

Uveitis refers to inflammation of the uveal tract (iris, ciliary body and choroid) of the eye 1. This inflammation can be acute in onset, chronic (unresolved) or recurrent (equine recurrent uveitis; ERU). Further, ERU can be active (during an ongoing inflammatory episode) or quiescent (no active inflammation). Uveitis can be further classified as primary (endogenous) or secondary to injury, insult or abnormality; either ocular or systemic 1. The pathophysiology of uveitis in horses is complex and the inciting events of the disease are not fully understood 2. *Leptospira* spp. has been frequently associated with the disease 3-7. In addition, a number of genetic risk factors have been identified in the Appaloosa and German Warmblood 8-10.

There is limited information on uveitis in horses in the UK. A survey of horse owners in northern Britain reported a 1% prevalence of recurrent ocular disease (although this did not refer specifically to uveitis) 11. A study in geriatric horses suggested that 5 out of 83 horses had signs consistent with previous inflammatory disease of the iris 12, whereas a more recent study suggested a prevalence of uveitis of 0.3% in the UK equine population, based on an online owner survey undertaken over a seven day period 13. These prevalence estimates appear much lower compared to that of the rest of Europe (8-10%) 14 or the United States (2-25%) 15. The reasons for this difference in prevalence are not clear but probably are due to genetic differences between horse populations, with native UK horses perhaps being more resistant to the disease, and differences in *Leptospira* serovar distribution.

A number of recent retrospective studies in Germany, Canada and the United States have characterised the disease further with regards to age of presentation, affected sex or breed, treatment or outcome 16-18 but similar studies in the UK are lacking.

The aims of this study were to:

1. Characterise the signalment and disease characteristics of horses presenting with uveitis to a referral hospital in the North West of England
2. Identify differences between horses presented for a single acute episode of uveitis and horses admitted for management of recurrent uveitis
3. Compare the signalment of horses presented for uveitis with that of the equine hospital population during the same time period

**Materials and methods**

A search of the medical records of the referral Equine Hospital at the University of Liverpool was performed to identify all horses with a confirmed diagnosis of uveitis between January 2008 and December 2018. The typical geographic coverage of the Hospital includes the West Midlands and North-West of England and North Wales. Diagnosis of uveitis required a complete ophthalmological examination including direct and indirect ophthalmoscopy and slit lamp biomicroscopy. The indirect ophthalmic examinations were performed using a standard 20 dioptre hand held lens and a light source (Heine Finoff transilluminator1) or head mounted binocular indirect ophthalmoscope (Heine Omega 2001). The direct examination was performed using a standard direct ophthalmoscope (Heine Beta 2001). The slit lamp examination was performed initially with a desk mounted slit lamp (Kowa SL-52) and since 2014 with a portable slit lamp (Kowa SL-152). Sedation with an alpha-2 agonist or alpha-2 agonist/opioid combination and/or auriculopalpebral nerve blockade were performed to facilitate the ocular examination if required.

Horses were included in the study if they had signs consistent with acute or recurrent uveitis as previously described 1. Horses were classified as having acute uveitis if they were showing active, ongoing, signs of intraocular inflammation at the time of the examination but no evidence of previous uveitis could be found. Horses were classified as having recurrent uveitis if there were clear signs of previous uveitic episodes, whether they were also showing signs of ongoing inflammation at the time of the exam or not, or if there was a history of previous episodes of uveitis. Only primary uveitis cases were considered and horses were excluded from the study if the uveitis was associated with another ocular condition (for example ulcerative keratitis), injury or systemic disease.

Variables such as breed, age, sex, eye affected, time of the year, stage of disease, diagnostic details, treatment and short-term outcome were recorded. Signalment of the general hospital population for the period of the study was also obtained for comparison. Data were managed in Microsoft Excel3. The normality of continuous data was analysed with a Kolmogorov-Smirnov test. Continuous data are described as mean and standard deviation for normally distributed data and as median and interquartile range (IQR) for skewed data. Categorical data are described as proportions with 95% confidence intervals (CI). Differences in groups were analysed using Student’s t test for normally distributed continuous variables, Mann Whitney U for skewed continuous and Chi-square or Fisher’s exact test (for variables in which n≤5) for categorical variables. A p<0.05 was considered indicative of statistical significance. IBM SPSS Statistics for windows version 24.0 was used for the statistical analysis4.

**Results**

During the period of January 2008 to December 2018 a total of 15745 horses attended the referral Equine Hospital. Seventy horses met the inclusion criteria (0.44%, CI 0.35-0.56%) (tables 1 and 2). Of these, 33 horses presented for treatment of an acute episode (47.1%, CI 35.9-58.7%) whereas 37 were admitted for investigation and management of recurrent uveitis (52.9%, CI 41.3-64.1%). Within the recurrent cases, 26 were admitted during a quiescent stage (70.3%, CI 54.2-82.5) and 11 during an episode of active inflammation (29.7%, CI 17.5-45.8). Age of cases ranged from 1 to 24 years (median 10.5 years, IQR 9) similar to the age for the general hospital population (median 10 years, IQR 8). Although it would appear as if acute cases presented earlier in life, no statistically significant difference in age (p=0.23) was noted between acute (median 9 years, IQR 9) and recurrent cases (median 12.0 years, IQR 10) (Figure 1).

There were 25 mares (35.7%, CI 25.5-47.4), 43 geldings (61.4%, CI 49.7-72.0) and 2 stallions (2.9%, CI 0.8-9.8) in total. No statistically significant difference between this distribution of sexes and that of the general hospital population in the same period (mares 38.2%, CI 36.9-39.6; geldings 58.8%, CI 57.3-60.2; stallions 3%, CI 2.5-3.5) was noted (p=0.90). There was no difference in sex distribution between acute (11 mares, 21 geldings and 1 stallion) and recurrent (14 mares, 22 geldings and 1 stallion) cases (p=0.93).

Thirty two horses were affected only in the right eye (45.7%, CI 34.6-57.3), 22 only in the left (31.4%, CI 21.8-43.0) and 16 were affected bilaterally (22.9%, CI 14.6-34.0). There was no statistical difference between right and left eye (p=0.08). There were more bilateral cases classified as recurrent than acute (p=0.04) (Figure 2).

The most common breeds affected were Warmbloods and Warmblood crosses (30.0%, CI 20.5-41.5), Cobs and Cob crosses (17.1%, CI 10.1-27.6), Welsh and Welsh crosses (12.9%, CI 6.9-22.7), Thoroughbreds and Thoroughbred crosses (11.4%, CI 5.9-21.0) and Appaloosas and Appaloosa crosses (5.7%, CI 2.2-13.8%). When compared to the general hospital population Warmblood and Warmblood crosses (16.9% of hospital admissions, CI 15.9-18.0) and Appaloosa and Appaloosa crosses (0.7% of hospital admissions, CI 0.5-1) were overrepresented (p<0.001). The percentage of bilateral vs unilateral cases was highest in Appaloosas and Appaloosa crosses (75%, CI 30.1-95.4) and Warmbloods and Warmblood crosses (33.3%, CI 17.2-54.6) compared to Welsh and Welsh crosses (22.2%, CI 6.3-54.7), Thoroughbreds and Thoroughbred crosses (11.1%, CI 20-43.5) or Cobs and Cob crosses (8.3%, CI 1.5-35.4) although differences between breeds did not reach statistical difference (p=0.07) (Figure 2).

The month of presentation was also recorded. Horses were admitted to the hospital throughout the year (Figure 3), with December (10 cases), April (9 cases) and September (8 cases) being the months when most cases were admitted. There was, however, no statistical difference in the distribution of cases per month when compared with the admissions of the general hospital population (p=0.16).

Six horses were tested for *Leptospira* spp. involvement. This involved measurement of antibody levels to a number of *Leptospira* serovars by microagglutination test (MAT) in both aqueous humour and serum. Two cases were considered positive (aqueous humour titre ≥4 times the serum titre): one to *L. hardjo* (aqueous titre 1/1600 vs serum titre 1/400) and another one to *L. hebdomanis* (aqueous titre 1/800 vs serum titre 1/200).

Medical therapy of active uveitis involved in most cases combinations of a topical corticosteroid (prednisolone acetate or dexamethasone), topical atropine and systemic anti-inflammatory drugs (flunixin meglumine or phenylbutazone). In one case, a horse also received low-dose intravitreal preservative-free gentamicin.

Twenty one horses (30.0%, CI 20.5-41.4) underwent surgery for the control of the uveitis. Surgical options for the management of recurrent cases included placement of suprachoroidal cyclosporine A implants in 18 cases, five of them bilaterally. One of the cases that had bilateral cyclosporine A implants placed required a second surgery for placement of two new implants 36 months after the original procedure. Another horse underwent bilateral placement of cyclosporine A implants in 2010 which controlled the ocular inflammation until 2016 when the right eye was enucleated due to recurrence of the uveitis. Long term follow up of the other cases was not available but there were no short term complications with either of these procedures. In addition, three horses were referred to other facilities for pars plana vitrectomy (one of them bilaterally). The reasons for choosing this treatment option were marked vitreal involvement (2 cases) and a positive *Leptospira* result (1 case). Of these three horses, one of them suffered a detached retina and another a posterior lens capsule rupture as a consequence of the surgical procedure.

Fourteen out of the 70 horses (20.0%, CI 12.3-30.8) underwent enucleation of an affected eye. One of these horses had both eyes enucleated due to chronic pain and bilaterally detached retinas. No major complications were encountered after any of these procedures.

**Discussion**

This is the first retrospective survey of uveitis (both acute and recurrent) cases presenting to an equine referral hospital in the UK. It is important to note that when comparing this to other similar studies in other parts of the world they often focus specifically on equine recurrent uveitis cases whereas the current study included all types of primary uveitis cases examined, whether it was a single acute episode or a chronic or recurrent case. A number of similarities, however, are observed between studies. Median age at presentation in this study (10.5 years) is similar to mean age of presentation in studies in the USA (11.7 years) 17 and Canada (12.13 years) 18. In the current study the most common age of presentation was between 5 and 7 years of age and despite the wide range of ages almost a third of all cases were recorded in horses 7 years old or younger, indicating that uveitis can affect horses early on life with potentially significant welfare implications throughout the rest of their life.

The sex distribution is remarkably similar between this study (61.4% geldings, 35.7% mares and 2.9% stallions) and the North American studies 17,18 and was consistent with the general hospital population. Gerding and Gilger 17 however found that geldings were overrepresented when compared to their general hospital admissions and Szemes and Gerhards 19 also reported geldings to be significantly more affected by ERU than mares and stallions.

With regards to breed, we found an overrepresentation of Warmblood and Warmblood crosses and Appaloosa and Appaloosa crosses, in agreement with previous studies 17,19. Studies have found a number of genetic factors associated with an increased risk of development of ERU in German Warmbloods which may explain the increased frequency of uveitis in this breed 8,9. Appaloosa horses contributed the largest proportion of horses with ERU in both North American studies (24.1% in the USA and 62.5% in Canada) 17,18. Whilst the proportion of Appaloosas was not as high in our study, probably because this breed is not as common in the UK as it is in North America, they were also overrepresented when compared to our general hospital population. Genetic factors contributing to an increased risk of development of ERU in this breed have also been investigated 10.

In addition, we found Appaloosa horses to have the largest proportion of bilateral cases, a finding already noticed in previous studies 17,20. It is important to note that this finding, however, was not statistically significant in our study, potentially as a result of the low total number of Appaloosa horses in our population. Our total percentage of bilateral cases (22.9%) was nevertheless much lower than the North American studies, with figures between 67.5 and 93.6% 17,18 but similar to the German studies (between 32 and 36.4%) 16,19. This is, once again, probably as a result of the smaller number of Appaloosa horses in the European studies compared to the American ones. Another explanation for this low number of bilateral cases in our study is the fact that we included acute uveitis cases, as well as ERU cases, which are less likely to be bilateral. Interestingly whilst all other studies found similar frequencies of disease in the right and left eye, we seemed to have a higher number of affected right eyes (45.7%) compared to left (31.45), although this was not statistically significant. There is no clear explanation for this finding and probably is just as a result of the low number of cases in the study. A cross sectional study of working horses in Ethiopia also found a significantly higher prevalence of ocular disease in the right eye compared to the left 21. The authors of this study hypothesized that this could be explained by the use of whips by predominantly right-handed drivers, something that it is unlikely to play a role in our population.

In this study, bilateral cases were more likely to be classified as recurrent than as acute. If during an ocular examination signs suggest chronic inflammation in one eye it is therefore advisable to examine the contralateral eye carefully, even if no pain or inflammation is reported, since low grade insidious disease could potentially go unnoticed.

Despite sun exposure being frequently cited as a risk factor for the development of uveitis 1 we did not find any seasonal effect and horses were presented to the hospital throughout the year. It is of course possible that a delay occurred between the horse developing the signs and presentation to the hospital for examination and therefore this result should be interpreted with caution.

Twenty one horses underwent a surgical procedure aimed at controlling the ocular inflammation. Of these, 18 had a suprachoroidal cyclosporine A implant placed. Cyclosporine A is not anti-inflammatory but rather an immunosuppressive drug used for the control of uveitis in human patients. Cost makes the use of this drug systemically financially non-viable for most owners and therefore a suprachoroidal slow-release implant was developed and tested in horses 22. Long term studies have shown these devices to be effective at reducing the number and severity of episodes of uveitis but it is suggested that because of depletion of the drug from the implant a repeat surgery may be needed at or before 48 months after the original procedure 23. In this study only one horse required placement of new implants. This horse had implants placed bilaterally and showed good control of the inflammation for 36 months at which point signs of ocular inflammation recurred. This was once again controlled after placement of new implants.

Pars plana vitrectomy was considered the most appropriate treatment option in three cases. The aim of this procedure is the clearance of the ocular media from the posterior segment and it has been shown particularly effective in the management of *Leptospira* associated cases 24-25. Of the three horses selected for this option, two had extensive vitreal involvement and the third one had tested positive for *Leptospira* spp. Two of these horses, however, suffered serious complications. One of them suffered a detached retina and subsequent blindness, although the inflammation was successfully controlled following the surgery. In the other case the posterior lens capsule ruptured and the intraocular inflammation persisted, probably as a result of phacoclastic uveitis. Therefore, if contemplating performing or referring a case for this procedure, good case selection and previous owner counselling need to be considered. However, due to the low number of horses receiving pars plana vitrectomy it is difficult to draw any conclusions on this data.

Only 6 horses in this study were tested for *Leptospira* involvement. This low number is likely due to the fact that traditionally *Leptospira* has been considered to only be involved in a very small number of cases of uveitis in the UK 26. A recent study suggested that only 6.7% of ERU cases in the UK where associated with *Leptospira* 27, a much lower figure than in other parts of the world.

Enucleation was the final outcome in fourteen patients. Removal of the affected eye, either under general anaesthesia or standing sedation, should be considered in cases refractory to treatment and provides immediate and definitive control of the ocular pain. Owners of horses that have an eye enucleated should be encouraged by a recent study reporting good prognosis in general for return to work and good client satisfaction for unilateral cases 28. Bilateral cases that do not respond to treatment may require euthanasia, however bilateral enucleation can be considered on a case by case basis 29. One horse in this study had both eyes enucleated. This horse presented with bilateral painful eyes and detached retinas. Since he was already blind and managing well at home it was considered that bilateral enucleation would not have any further effect on vision whilst removing the source of pain would greatly improve his quality of life.

This study had some limitations. First of all, the retrospective nature of the study means it is possible that some data are missing or may have been misinterpreted. For example, the classification of acute or recurrent was not made at the time of the examination but it was based on analysis of the clinical records so there is the possibility that some cases have been incorrectly classified. This study involves a referred population so a selection bias exists. It is very likely that relatively simple, acute cases that responded favourably to treatment are mostly seen and dealt with in a first opinion setting. Likewise, since enucleation is a surgical procedure performed with relative frequency in first opinion practice, it is probable that a number of recurrent or unresponsive cases where the owner did not want to pursue any other treatment options were not referred for management at the hospital. Another limitation is the relative low number of cases. Despite the search of clinical records extending ten years only 70 cases could be recruited to the study. This is probably a representation of the lower prevalence of ERU in the UK compared to other parts of the world. Finally, no follow up of the cases was attempted. Therefore it is possible that some acute cases did actually progress to recurrent, or that some recurrent unresponsive cases underwent further therapy at other centres or were eventually enucleated without our knowledge.

In summary, whilst relatively uncommon in the UK, uveitis can affect horses from a relatively young age and become a chronic source of ocular pain and inflammation. The disease appears to have a relatively higher frequency than expected in Warmbloods and Appaloosas. It is more likely that a recurrent case will have both eyes affected so regular monitoring of both eyes in those horses with signs of chronic or recurrent uveitis in one eye is strongly recommended.

Table 1: Details of acute uveitis cases.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Case | Age | Sex | Breed | Eye affected |
|  |  | | | |
| 1 | 23 | Gelding | Cob cross | Right |
| 2 | 17 | Mare | Cob | Right |
| 3 | 1 | Mare | Unrecorded | Left |
| 4 | 9 | Mare | Thoroughbred | Right |
| 5 | 18 | Stallion | Lusitano | Right |
| 6 | 17 | Gelding | Thoroughbred cross | Right |
| 7 | 7 | Gelding | Warmblood | Bilateral |
| 8 | 6 | Gelding | Warmblood | Left |
| 9 | 11 | Gelding | Sports Horse | Left |
| 10 | 11 | Gelding | Connemara | Right |
| 11 | 5 | Mare | Warmblood | Bilateral |
| 12 | 6 | Gelding | Irish draught | Right |
| 13 | 7 | Mare | Cob cross | Left |
| 14 | 7 | Gelding | Warmblood | Left |
| 15 | 15 | Mare | Thoroughbred | Left |
| 16 | 7 | Gelding | Welsh | Right |
| 17 | 14 | Gelding | Thoroughbred cross | Left |
| 18 | 6 | Gelding | Lusitano | Right |
| 19 | 17 | Gelding | Irish draught | Left |
| 20 | 19 | Gelding | Donkey | Right |
| 21 | 2 | Mare | Sorts Horse | Bilateral |
| 22 | 13 | Gelding | Warmblood | Bilateral |
| 23 | 3 | Gelding | Warmblood | Right |
| 24 | 6 | Mare | Cob | Right |
| 25 | 12 | Gelding | Thoroughbred cross | Left |
| 26 | 9 | Mare | Warmblood | Left |
| 27 | 7 | Gelding | Warmblood | Left |
| 28 | 5 | Gelding | Warmblood | Right |
| 29 | 9 | Gelding | Welsh cross | Right |
| 30 | 10 | Mare | Warmblood | Right |
| 31 | 6 | Mare | Cob | Left |
| 32 | 18 | Gelding | Warmblood | Right |
| 33 | 8 | Gelding | Cob | Right |

Table 2: Details of recurrent uveitis cases.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Case | Age | Sex | Breed | Eye affected |
|  |  | | | |
| 1 | 14 | Mare | Cob | Bilateral |
| 2 | 13 | Gelding | Appaloosa | Left |
| 3 | 7 | Gelding | Cob | Left |
| 4 | 6 | Gelding | Welsh | Right |
| 5 | 13 | Mare | Appaloosa | Bilateral |
| 6 | 12 | Mare | Pony | Left |
| 7 | 5 | Gelding | Welsh cross | Bilateral |
| 8 | 12 | Gelding | Sports Horse | Left |
| 9 | 3 | Gelding | Welsh | Left |
| 10 | 24 | Mare | Welsh cross | Left |
| 11 | 12 | Gelding | Irish draught | Bilateral |
| 12 | 4 | Mare | Connemara | Left |
| 13 | 9 | Mare | Welsh | Bilateral |
| 14 | 16 | Gelding | Appaloosa | Bilateral |
| 15 | 15 | Gelding | Warmblood | Bilateral |
| 16 | 6 | Gelding | Cob | Right |
| 17 | 5 | Gelding | Welsh | Right |
| 18 | 11 | Gelding | Warmblood | Right |
| 19 | 19 | Mare | Thoroughbred cross | Left |
| 20 | 5 | Mare | Cob | Right |
| 21 | 16 | Gelding | Warmblood | Bilateral |
| 22 | 13 | Stallion | Warmblood | Left |
| 23 | 13 | Mare | Appaloosa | Bilateral |
| 24 | 7 | Gelding | Warmblood | Right |
| 25 | 15 | Mare | Warmblood | Right |
| 26 | 8 | Gelding | Warmblood | Right |
| 27 | 19 | Mare | Cob | Right |
| 28 | 6 | Gelding | Warmblood cross | Bilateral |
| 29 | 24 | Mare | Cob | Right |
| 30 | 19 | Mare | Thoroughbred | Right |
| 31 | 5 | Gelding | Andalusian | Right |
| 32 | 22 | Mare | Welsh | Right |
| 33 | 9 | Gelding | Warmblood | Right |
| 34 | 23 | Gelding | Warmblood | Bilateral |
| 35 | 14 | Gelding | Sports Horse | Right |
| 36 | 2 | Gelding | Connemara | Left |
| 37 | 23 | Gelding | Thoroughbred cross | Bilateral |

Figure 1: Distribution histogram of age of all horses presenting with uveitis to an equine hospital (n=70; total) and divided into recurrent (n= 37) and acute (n=33) cases.

Figure 2: Number of unilateral and bilateral cases of uveitis divided by breed.

Figure 3: number of cases of uveitis according to month of presentation for acute, recurrent and all cases combined.

**Manufacturers’ addresses**

1Heine Optotechnik, Kientalstrasse 7, D-82211 Herrsching, Germany.

2Kowa Optimed Deutschland GmbH, Bendemannstrasse 9, 40210 Dusseldorf, Germany.

3Microsoft Corporation, Redmond, Washington, USA

4IBM Corporation, Armonk, New York, USA

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