Assessment of subclinical venous catheter-related diseases in horses and associated risk factors

T. E. Geraghty, S. Love, D. J. Taylor, J. Heller, D. J. Mellor, K. J. Hughes

A total of 102 horses that had a catheter introduced intravenously to facilitate treatment had the catheterised jugular vein and contralateral vein examined by ultrasound every 48 hours. Subclinical complications were defined by thrombus formation or thickening of the venous wall, and the data were analysed to establish risk factors for the development of these complications. The horses with a rectal temperature above 38.5°C when the catheter was introduced were four times more likely to develop complications, than the horses with a lower temperature. The administration of a NSAID while the catheter was in place reduced the risk of complications developing.

INTRAVENOUS catheters are commonly introduced into horses to provide sustained and secure access to the vein to facilitate the administration of therapeutic or anaesthetic drugs and the performance of diagnostic procedures. Complications that may develop include thrombus formation, thrombophlebitis, bacteraeemia and intravascular or intracardiac foreign bodies; they can greatly increase morbidity and recovery time in affected animals (Bayly and Vale 1982, Hoskinson and others 1991) and are often considered to have a multifactorial aetiology (Spurlock and Spurlock 1990). Thrombophlebitis is the most frequently reported complication and occurs most often in animals with systemic disease, including endotoxaemia, salmonellosis and diarrhoea (Lankveld and others 2001, Dolente and others 2005). Bacterial colonisation of a catheter may increase the rate of occurrence and duration of the complications and the associated morbidity (Spurlock and Spurlock 1990).

Clinical signs of thrombophlebitis can develop within 24 hours of catheterisation, including local increase in temperature, thickening of the venous wall and subcutaneous pethervenous tissues and signs of pain on palpation (Hipp and others 1991). Clinical thrombophlebitis is characterised ultrasonographically by an irregularly shaped hypoechoic luminal mass with homogenous echogenicity or pockets of hyper- and hypoechochogenicity (Gardner and others 1991, Pusterla and Braun 1995). In addition, affected veins often resist compression. Treatment may involve the administration of antibiotics, systemic and/or topical NSAIDs and hot packing to encourage drainage from the affected area. Surgical intervention is rarely required. The administration of anticoagulant drugs, such as heparin or aspirin may reduce the rate of growth of the thrombus, but no licensed thrombolytic agents are available for use in horses and thrombophlebitis often has a protracted course.

It is desirable to detect thrombophlebitis early so that treatment can be commenced to reduce the risk of morbidity. The removal of an affected catheter may prevent or reduce the severity of vascular disease or complications, but early detection is hampered by the limited sensitivity of the clinical signs alone. The ultrasonographic appearance of clinical thrombophlebitis is well known, but the appearance of subclinical disease is not so well known. Hipp and others (1991) reported that thrombophlebitis in horses can be detected by ultrasonography 24 hours earlier than by conventional diagnosis, but their description was limited. Regular ultrasonographic investigation of all catheterised veins may be impractical but it could be valuable for veins at high risk of developing disease.

This paper describes the results of a study designed to assess the value of ultrasonographic and microbiological examinations for the detection of subclinical venous disease and to determine the risk factors associated with its development.

Materials and methods
Between October 24, 2005 and June 31, 2006, 102 horses into which one or more intravenous catheters were introduced to facilitate diagnostic procedures, anaesthesia or treatment were studied.

Catheters
When the catheter was expected to remain in place for longer than 24 hours, a 14-G, 13 cm polyurethane catheter (Milacath Extended Use; Mila International) was used, but for shorter periods a 14-G, 8 cm polytetrafluoroethylene (PTFE) catheter (Intraflon 2; Intraflon) was used. The catheters were introduced into either the right or left external jugular vein, using a sterile technique; the hair coat at the insertion site was clipped, the site was scrubbed with 2 per cent chlorhexidine gluconate solution for five minutes and wiped with surgical spirit, and the catheter was introduced by an operator wearing sterile gloves. The catheters were flushed with 10 ml of sterile saline solution containing 10 μg/ml heparin every four hours, and before and after the administration of medications.
Microbiological investigation
Four samples were taken when each catheter was removed for semi-quantitative direct culture (Maki and others 1977) and indirect culture: a skin swab from the catheter insertion site, fluid aspirated from the catheter, a two-inch section of catheter adjacent to the hub, and a two-inch section of the tip. The sections of catheter were rolled across a 5 per cent sheep blood agar plate for direct culture and were then transferred to sterile bijous containing 2 ml of nutrient broth for indirect culture. The sheep blood agar plates were incubated at 37°C for 24 hours and then inspected. A positive culture was recorded if there were more than 15 colony-forming units (cfu). The catheter sections in the nutrient broth were incubated at 37°C for 48 hours, agitated for 30 seconds and a loop-full of broth was streaked on to a 5 per cent sheep blood agar plate and incubated for a further 24 hours. The skin swab and a loop-full of fluid aspirated from the catheter lumen was streaked on to 5 per cent sheep blood and MacConkey’s agar plates and incubated aerobically at 37°C for 24 hours. Any bacterial isolates were identified by standard laboratory techniques.

Ultrasound examination
The catheterised jugular veins were examined by ultrasound immediately after the catheters were introduced and then every 48 hours while they were in place. A 12·5 MHz linear transducer was used to make a cross-sectional ‘brightness mode’ (B mode) scan of the length of the catheterised region. To facilitate ultrasonographic imaging in the lumen and walls, the vein was distended by partially occluding it at a point adjacent to the thoracic inlet. During the ultrasonographic procedure, digital callipers were used to measure the thickness of the medial and lateral walls of the vein at both the insertion site and the catheter tip, and the measurements (in mm) were recorded. Areas of venous wall thickening, thrombosis or abnormal perivascular tissue were recorded. The contralateral vein was examined in the same way to serve as a control. Catheter-associated vascular disease was defined by thrombus formation and/or a more than 50 per cent increase in the thickness of the wall of the vein compared with a previous or control vein measurement. Hypoechoic thickening of subcutaneous tissue between the skin and wall of the vein was interpreted as periphlebitis/perivascular swelling. When the left and right jugular veins were both catheterised they were both examined and no control vein was available.

Data recorded
When it was admitted, each horse’s age, breed, sex, weight, current use, admission date and clinical signs were recorded. When the catheter was introduced the horse’s rectal temperature, heart rate, respiratory rate, mental state, body condition, capillary refill time, skin turgor and total plasma protein concentration and packed cell volume were recorded. The contralateral vein was examined in the same way for 12 hours to 20 days (mean [sd] 3·6 [3·89] days). Fifty-seven of the horses were examined because of musculoskeletal conditions, 26 had signs of abdominal pain (18 with large intestinal disease and eight with small intestinal disease), and 19 had other conditions including respiratory, neurological and ophthalmic disease. Sixty-one of the horses were 41 thoroughbreds and thoroughbred crosses, 19 ponies, 16 cobs, six draft horses, three Arabs and Arab crosses and 17 horses of other breeds. Seventy-two of them were used for general purposes, 12 for racing, four for show jumping, four for police work and eight were retired.

Eighty-two of the catheters were long-stay polyurethane, and 37 were short-stay PTFE. Eighty-nine of the horses had one catheter introduced, but 10 had two catheters, two had three catheters and one had four catheters introduced sequentially. The catheters remained in place for 12 hours to 20 days (mean [sd] 3·6 [3·89] days). Fifty-seven of the horses were examined because of musculoskeletal conditions, 26 had signs of abdominal pain (18 with large intestinal disease and eight with small intestinal disease), and 19 had other conditions including respiratory, neurological and ophthalmic disease. Sixty-one of the horses were considered to be independent. Continuous variables (including the horse’s rectal temperature and heart rate when it was catheterised and the period for which the catheter remained in place) were transformed to biologically appropriate categorical variables (heart rate: <40 bpm, 40 to 60 bpm, 61 to 80 bpm, >80 bpm; respiratory rate: <20 breaths per minute [brpm], 20 to 40 brpm, >40 brpm; rectal temperature: <37°C, 37 to 38·5°C, >38·5°C; skin turgor: tenting <2 seconds, tenting >2 seconds). Thirty-six risk factors were evaluated. A univariate analysis was applied initially, using logistic regression to generate odds ratios (OR) and 95 per cent confidence intervals (CI) to define the preliminary relationships in the data. Variables with P<0·05 were considered for inclusion in a multivariable analysis which was performed by forward stepwise inclusion of variables into the model, variables with P<0·05 being retained. Biologically plausible interaction terms were considered and retained if P<0·05. The performance of the final multivariable model was evaluated with the Hosmer-Lemeshow goodness-to-fit test. A separate univariate analysis was performed by logistic regression to define the relationship between catheters that were colonised by bacteria when they were removed and any associated vascular disease, with P<0·05 being considered significant.

Results
Data were recorded from 119 catheters introduced into 102 horses (seven stallions, 57 geldings and 35 mares). They ranged in age from two months to 28 years, with a mean (sd) of 9·5 (6·04) years. There were 41 thoroughbreds and thoroughbred crosses, 19 ponies, 16 cobs, six draft horses, three Arabs and Arab crosses and 17 horses of other breeds. Seventy-two of them were used for general purposes, 12 for racing, four for show jumping, four for police work and eight were retired.

Eighty-two of the catheters were long-stay polyurethane, and 37 were short-stay PTFE. Eighty-nine of the horses had one catheter introduced, but 10 had two catheters, two had three catheters and one had four catheters introduced sequentially. The catheters remained in place for 12 hours to 20 days (mean [sd] 3·6 [3·89] days). Fifty-seven of the horses were examined because of musculoskeletal conditions, 26 had signs of abdominal pain (18 with large intestinal disease and eight with small intestinal disease), and 19 had other conditions including respiratory, neurological and ophthalmic disease. Sixty-one of the horses were
admitted to the medical service, and 41 to the surgical service. Ninety-three of the horses survived and were discharged, but the other nine were euthanased owing to the severity of their condition. Only one case of clinically evident catheter-related thrombophlebitis was recorded.

**Ultrasonographic examination**

Ninety-eight catheterised veins were examined ultrasonographically in 89 of the horses. The other 13 were unable to walk to the ultrasonography room without compromising their clinical condition. When the catheters were inserted the mean (sd) thicknesses of the medial and lateral walls of the veins at the insertion site were 0·91 (0·55) mm and 0·99 (0·68) mm respectively, and at the level of the tip they were 0·76 (0·34) mm and 0·83 (0·47) mm respectively. The mean comparable measurements from the control veins at the same time were 0·95 (0·52) mm and 0·87 (0·44) mm respectively.

No changes were observed in 57 of the 98 veins while the catheters were in place (Fig 1); the mean (sd) thicknesses of the medial and lateral walls of the vein at the insertion site were 0·75 (0·14) mm and 0·8 (1·7) mm respectively, and at the tip, 0·72 (0·12) mm and 0·74 (0·12) mm respectively. Thickening of the walls of the vein (Fig 2) was associated with 27 of the catheters in 23 of the 89 horses; the mean (sd) thicknesses of the medial and lateral walls of the vein at the insertion site were 1·56 (0·84) mm and 1·82 (0·94) mm respectively, and at the tip 2·03 (0·95) mm and 1·83 (1·2) mm respectively. Catheter-associated thrombosis, typically described as hyperechogenic or mixed echogenic material with irregular borders located within the lumen (Fig 3), was observed in 16 of the veins in 15 horses. Thirteen of the thrombi were at the insertion site of the catheter and three were at the tip. There was thickening of the wall of the vein and thrombosis in seven catheterised veins in seven horses. Periphlebitis/perivascular swelling (Fig 4) was observed in association with 17 catheters in 15 of the horses. In one horse a homogenous hyperechogenic mass, identified as a haematoma due to damage to the carotid artery, was detected (Fig 5).

**Microbiological investigation**

Ninety-two catheters were examined microbiologically. Microbial cultures from seven catheters (Table 1) were positive by direct culture and a further five catheters were positive by indirect culture. In one horse Acinetobacter baumannii was isolated from both the catheter tip and a swab taken from the skin adjacent to the insertion site before the catheter was removed. No bacteria were grown from the fluid aspirated from any of the catheters. Two of the horses from which direct culture of the catheter was positive were not examined by ultrasound for welfare reasons. Three of the catheters that were positive by direct culture were associated with thrombosis and venous wall thickening detected ultrasonographically. There was no significant relationship between the bacterial colonisation of the catheters and vascular disease.

**Risk factors for development of catheter-related venous changes**

Data from the first catheter inserted into 86 horses were included in the statistical analysis, of which 27 (31·4 per cent) had subclinical catheter-related disease. Of the 36 variables incorporated into the univariable analysis, seven satisfied the inclusion criteria for the multivariable model (Table 2). Packed cell volume and total plasma protein concentration were included in the univariable analysis, but all the other haematological and blood biochemical variables (including specific tests of haemostasis and fibrinolysis) were not included owing to a lack of data.

As a result of the forward stepwise logistic regression analysis, only ‘NSAID administered via the catheter’ and ‘rectal temperature more than 38·5°C at time of catheterisation’ met the criteria to remain in the multivariable model (Table 3). Biologically plausible interactions were not significant. The Hosmer-Lemeshow goodness-of-fit test chi-squared value for the final model value was 0·28 (P=0·870) indicating a good fit of the data.

The horses with a rectal temperature above 38·5°C when the catheter was inserted were more than four times more likely to show signs of catheter-related vascular disease than horses with a temperature between 37·0 and 38·5°C.

Horses that had had NSAIDs administered through the catheter were only one-third as likely to develop evidence of catheter-related vascular disease as the horses that had not.

Two intravenous NSAID preparations were used during the study; a 200 mg/ml solution of phenylbutazone (Equipalazone Injection; Arnolds), and a 50 mg/ml solution of flunixin meglumine (Finadyne Solution; Schering-Plough Animal Health). There were no significant differences between the groups results observed in the horses treated with these two NSAIDs; however, the numbers in each category were small and the lack of a significant difference may be due to the lack of power of the model.
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Discussion

The repeated ultrasonographic examinations of the catheterised veins showed that 59 per cent of the catheters caused no detectable changes in the vascular and perivascular tissues. Thickening of the walls of the vein and/or thrombosis were detected in 27 per cent of the veins and were the most common abnormal findings. Thickening could be easily differentiated from thrombosis by the ultrasound examination; thickening appeared as a diffuse hypoechoic thickening of the venous wall and a smooth luminal surface, whereas thrombosis appeared as a hyperechoic or mixed echogenic irregularly shaped mass protruding into the lumen of the vessel, often with only a small point of contact with the vessel wall. Thickening of the wall of the vein was often observed within minutes of the introduction of the catheter, whereas the earliest thrombus was observed 24 hours later. The thickening was observed to resolve before the catheter was removed. The pathological processes that lead to thickening of the venous wall are uncertain, but may include inflammation, oedema and/or haemorrhage during the initial stages of the disease process. The protective effect of both NSAIDs on the development of thrombosis is uncertain. However, phenylbutazone can irritate the endothelium when administered intravenously (Bayly and Vale 1982) and may cause sufficient damage to release subendothelial Aα, platelets, or platelet-endothelial interactions, respectively. The protective effect of both NSAIDs on the development of subclinical vascular changes may have been due to a reduction in the production of thromboxane A2 by platelets and in their function, and the administration of NSAIDs may have maintained them free of bacteria.

The administration of NSAIDs through the catheters protected them against subclinical vascular changes. The horses given NSAIDs were three times less likely (OR=0–36) to develop vascular changes than the horses that were not given NSAIDs. However, phenylbutazone can irritate the endothelium when administered intravenously (Bayly and Vale 1982) and may cause sufficient damage to release subendothelial Aα, platelets, or platelet-endothelial interactions, respectively. The protective effect of both NSAIDs on the development of vascular changes may have been due to a reduction in the production of thromboxane A2 by platelets and in their function, and the amelioration of some of the cardiovascular effects of endotoxaemia (Lohmann and Barton 2004). Significant associations between the development of catheter-related complica-

**TABLE 1: Semi-quantitative microbiological results of the direct culture of sections of catheter obtained from the tip and adjacent to the hub after the removal of seven catheters from the jugular veins of horses**

<table>
<thead>
<tr>
<th>Catheter</th>
<th>Hub</th>
<th>Tip</th>
<th>Same organism isolated from skin swab</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td>No</td>
</tr>
</tbody>
</table>

**TABLE 2: Results of a univariate analysis of the risk factors for the development of subclinical changes in the jugular veins of horses after the insertion of a catheter**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Number of cases</th>
<th>Number of controls</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt;20 years</td>
<td>26</td>
<td>52</td>
<td>1</td>
<td>0·29</td>
<td>0·03-2·45</td>
</tr>
<tr>
<td></td>
<td>≥20 years</td>
<td>1</td>
<td>7</td>
<td>0·29</td>
<td>0·03</td>
<td>0·01-1·15</td>
</tr>
<tr>
<td>Breed</td>
<td>TB/TB x</td>
<td>11</td>
<td>23</td>
<td>1</td>
<td>0·19</td>
<td>0·02-1·66</td>
</tr>
<tr>
<td></td>
<td>COb</td>
<td>1</td>
<td>11</td>
<td>0·19</td>
<td>0·02-1·66</td>
<td>0·13</td>
</tr>
<tr>
<td></td>
<td>Pony</td>
<td>7</td>
<td>11</td>
<td>0·13</td>
<td>0·04-4·37</td>
<td>0·64</td>
</tr>
<tr>
<td></td>
<td>Arab/Arab</td>
<td>1</td>
<td>1</td>
<td>0·20</td>
<td>0·12-3·66</td>
<td>0·61</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>7</td>
<td>13</td>
<td>0·13</td>
<td>0·03-3·61</td>
<td>0·84</td>
</tr>
<tr>
<td>Season of admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Summer</td>
<td>2</td>
<td>8</td>
<td>0·89</td>
<td>0·16</td>
<td>0·25</td>
</tr>
<tr>
<td></td>
<td>Winter</td>
<td>19</td>
<td>32</td>
<td>0·86</td>
<td>0·76-5·30</td>
<td>0·16*</td>
</tr>
<tr>
<td>Admitted as medical/surgical case</td>
<td>Medical</td>
<td>19</td>
<td>33</td>
<td>1</td>
<td>0·76</td>
<td>0·58-1·14</td>
</tr>
<tr>
<td>Rectal temperature at catheterisation (°C)</td>
<td>&lt;37</td>
<td>2</td>
<td>1</td>
<td>0·03</td>
<td>0·10</td>
<td>0·92</td>
</tr>
<tr>
<td></td>
<td>37.85</td>
<td>20</td>
<td>54</td>
<td>1</td>
<td>0·46</td>
<td>0·46-0·54</td>
</tr>
<tr>
<td>Heart rate at catheterisation (bpm)</td>
<td>&lt;40</td>
<td>10</td>
<td>13</td>
<td>1</td>
<td>0·45</td>
<td>0·46-0·56</td>
</tr>
<tr>
<td></td>
<td>40-59</td>
<td>14</td>
<td>35</td>
<td>1</td>
<td>0·72</td>
<td>0·71-0·74</td>
</tr>
<tr>
<td>NSAID administered via catheter</td>
<td>No</td>
<td>16</td>
<td>23</td>
<td>1</td>
<td>0·63</td>
<td>0·06-0·69</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>11</td>
<td>36</td>
<td>0·44</td>
<td>0·71-1·11</td>
<td>0·08</td>
</tr>
</tbody>
</table>

* Variables with P<0·25 were included in the multivariable analysis
CI Confidence interval, OR Odds ratio, TB Thoroughbred
tions in horses and high heart rates, endotoxaemia, salmonellosis, and fever have been reported by Lankveld and others (2001) and Dolente and others (2005). Endotoxaemia can predispose to thrombus formation by damaging endothelial cells, stimulating the release of TF, activating the coagulation cascade and platelets and stimulating the release of platelet-activating factor from granulocytes (Morris 1989, Lohmann and Barton 2004). In this study there was a significant association between fever when the catheter was introduced and subclinical complications; the horses with a rectal temperature above 38-5°C were more than four times likely to develop a complication (OR=4.4). Fever and signs of cardiovascular compromise, for example, a rapid heart rate, cold extremities and congested mucous membranes, are often observed in horses with systemic inflammatory disorders, including endotoxaemia (Lohmann and Barton 2004). Gastrointestinal disease is the most common cause of endotoxaemia in horses (Lohmann and Barton 2004) and they frequently require an intravenous catheter to facilitate their treatment. The association between fever and subclinical catheter complications suggests that the horses may have been systemically compromised and had disturbances to their cardiovascular function and haemostatic mechanisms. The fact that there were no significant associations between the horses’ heart rates, capillary refill times or disease categories and the vascular complications may have been due to the small numbers in each category.

The ultrasound examinations made it possible to detect catheter-related changes that were not clinically evident. The thickening of the walls of the vein and the thrombus formation detected sonographically were not associated with the development of clinical thrombophlebitis, and did not interfere with the normal function of the catheters. The clinical staff were aware of the results of ultrasound examinations and the catheters were frequently removed in an effort to reduce the likelihood of clinical thrombophlebitis developing. The subclinical changes indicated that the delicate haemostatic and fibrinolytic balance had been disturbed and clinical changes were more likely. In several cases there was some evidence that a thrombus was increasing in size, increasing the risk of thrombophlebitis developing if the catheter had been kept in place.

The regular ultrasound investigations were easy and inexpensive. Introducing a catheter into a healthy horse for a short period carries a very low risk of complications and ultrasound monitoring of the vein is unnecessary. However, the coagulation status of a sick horse may be adversely affected and regular ultrasonographic examinations could detect the early signs of catheter-related changes and allow the catheter to be removed before clinical thrombophlebitis develops; it may be possible to introduce another catheter into a different vein. The results of the present study indicate that while a catheter remains in situ, a thrombus will not dissolve and it may grow. However, no ultrasound examinations were made after a catheter had been removed and it is unknown how rapidly a thrombus might dissolve.

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References


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**TABLE 3: Results of the multivariable analysis of the risk factors for the development of subclinical changes in the jugular veins of horses after the insertion of a catheter**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Change in the level of risk</th>
<th>OR</th>
<th>se</th>
<th>Z</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAID administered via catheter</td>
<td>Decrease</td>
<td>0·36</td>
<td>0·51</td>
<td>−2·04</td>
<td>0·13</td>
<td>0·056</td>
</tr>
<tr>
<td>Rectal temperature &lt;38·5°C at catheterisation</td>
<td>Increase</td>
<td>4·40</td>
<td>0·76</td>
<td>5·95</td>
<td>1·1-22·7</td>
<td>0·04</td>
</tr>
</tbody>
</table>

CI: Confidence interval, OR: Odds ratio.
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