Causes of pleural effusions in horses resident in the United Kingdom

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Summary

Pleural effusions (PE) reportedly occur most commonly secondary to bacterial pneumonia with neoplastic effusions contributing a minority of cases. The majority of reports originate from America and Australia, where long distance transport of horses, a recognised risk factor, may occur more frequently than in the United Kingdom (UK). Anecdotally, a greater proportion of horses with PE are diagnosed with neoplasia in the UK than has been reported. The aim of this retrospective study was to describe the causes of PE in horses in the UK, and to identify markers that can help differentiate between septic and neoplastic causes of PE. Medical records from 4 equine hospitals in the UK were searched for horses diagnosed with PE. Information recorded included signalment, admission physical examination and biochemical findings, and characteristics of the effusion (volume, cell count, total protein (TP) concentration). A total of 69 horses were identified, with 26 (38%) diagnosed with a neoplastic effusion. The remainder were categorized as septic, including 14/43 (32.5%) that had a history of international transport. Horses with septic effusions were significantly younger (8 vs 13 years; P=0.001) and had significantly smaller volumes of pleural fluid drained at admission (9.8l vs 32.2l; P<0.001). Horses with septic PE had a significantly higher rectal temperature (38.6 vs 38.2°C; P=0.03), fibrinogen concentration (7.8g/l vs 5.3g/l; P=0.01) and serum amyloid A concentration (230mg/l vs 59mg/l; P=0.02) than those with neoplastic effusions. A significantly higher pleural fluid cell count and TP concentration was identified in horses with septic PE ($63.9x10^9$/l vs $8.6x10^9$/l; P<0.001; 57.5g/l vs 35.9g/l; P=0.04). These results suggest that in the UK neoplastic effusions account for a greater proportion of PE than previously reported. A large volume of PE in an older horse with a low cell count and relatively low TP concentration should increase the index of suspicion of neoplasia.

Introduction

The majority of cases of pleural effusion reported in the scientific literature describe horses with septic pleuropneumonia, resulting from extension of bacterial infection of the lungs in to the pleural cavity, and most of these studies originate from the United States or Australia. (Smith 1977; Raphel and Beech 1982; Sweeney 1992; Collins *et al* 1994; Austin *et al* 1995; Racklyeft *et al* 2000; Arroyo *et al* 2015) In the United Kingdom, however, a greater proportion of pleural effusion cases seem to be caused by neoplasia, although the evidence to support this is scarce. (Mair *et al* 2004; Mair 2012) Early determination of the cause of a pleural effusion is paramount, so that prompt and appropriate treatment can be instigated in cases amenable to treatment, or euthanasia be performed in cases with a hopeless prognosis. The aim of this study was thus to determine whether horses identified with pleural effusion and which are resident in the UK are more frequently diagnosed with neoplasia than has been reported in previous studies, and to determine whether factors present at admission could be used to increase the index of suspicion for a neoplastic pleural effusion.

Methods

Records of horses presented to four equine referral hospitals in the United Kingdom between 2000 and 2014 were searched for horses in which a pleural effusion had been diagnosed. The cause of the effusion was then categorised as either neoplastic, septic or 'other' based on information in the medical records including history, analysis of pleural fluid and tracheal wash characteristics, ultrasonographic and radiographic findings, and post mortem results as applicable. A history of travel prior to the development of clinical signs was recorded, as was admission clinical and clinicopathological data, and outcome. Outcome was recorded as survival to discharge. Clinical data recorded included signalment, admission heart rate, respiratory rate and rectal temperature, clinical signs and duration of those signs prior to admission, and volume of pleural fluid drained at

admission. Clinicopathological data included admission packed cell volume, total plasma protein concentration, serum amyloid A and fibrinogen concentrations, pleural fluid nucleated cell count (NCC) and total protein concentration, results of cytological examination of pleural fluid, and bacterial culture results of tracheal wash samples, pleural fluid or both. When a sample was obtained from both sides of the thorax, the mean protein and nucleated cell count was used for statistical comparisons. Normality of continuous data was assessed utilising the Kolmogorov-Smirnov statistic, and differences between categories compared as appropriate. No cases of pleural effusion due to 'other' reasons were identified and thus differences between septic and neoplastic pleural effusions were compared using either the independent t test or the Mann Whitney U test. For all tests, the null hypothesis was rejected when $P<0.05$.

Results

A total of 69 horses with pleural effusions were identified. Not all data was available for all horses. The horses ranged in age from 1-28 years (n=56; median 10.5 years, interquartile range (IQR) 10 years) and included a variety of breeds, with the largest single group being Thoroughbreds or Thoroughbred crosses. (24/65; 38%) There were 33 geldings, 23 mares and 5 intact males.. Clinical signs present at admission were recorded for the majority of horses, and were similar for horses with either neoplasia or septic causes of effusion. The most common signs included increased respiratory rate (greater than 15/minute) and/or effort (59/64), tachycardia (heart rate greater than 44 beats per minute; 56/64), depressed mentation (42/59), nasal discharge (27/59), lethargy (21/59), pyrexia greater than 38.5°C (31/62), cough (15/59) and weight loss (15/59). Peripheral masses or lymphadenopathy were only identified in 2 horses. The duration of clinical signs was recorded in 40 horses, and ranged from 1 day to 6 months. (median 7 days)

A diagnosis of neoplasia was made in 26/69 (38%) of horses. A definitive diagnosis was made in 23 of these; the diagnosis was made in 12 horses at post mortem examination and in 11 via cytological analysis of pleural fluid. In an additional 3 horses a presumptive diagnosis of neoplasia was made. In

one of these three horses, thoracic radiographs revealed multifocal rounded radiodense lesions throughout the lungs and the mediastinum, although cytological or histological confirmation was not pursued. In the second, a mediastinal mass was identified via ultrasonography, and in the third, masses within the kidney and pelvic cavity were identified via ultrasonography, in addition to 2 masses within the lungs evident on thoracic radiographs. Lymphoma was diagnosed in 11 horses, unspecified carcinoma in 3, mesothelioma in 3, melanoma in 2 and for 7 horses a specific type of neoplasia was not confirmed.

Forty three horses were diagnosed with pleural effusions caused by septic causes. Within this category, 17/43 (39.5%) had a history of international travel; 5 horses had travelled from Ireland to the UK, 5 from mainland Europe to the UK, 3 from Argentina to the UK, 1 from New Zealand to the UK. In an additional 3 horses a history of travel was documented but no details provided as to the duration or distance. For horses with no history of travel, other risk factors identified included general anaesthesia (n=1) and oesophageal disorders (intra-luminal obstruction n=2; extra-luminal compressive mass n=1; oesophageal rupture n=2).

Table 1 shows admission clinical and clinicopathologic findings. Horses with neoplastic effusions were significantly older (median 13 years vs 8 years; P=0.001), had a significantly lower rectal temperature (mean 38.2°C vs 38.6°C; P=0.04), and lower acute phase protein concentrations (serum amyloid A: median 59mg/l vs 230mg/l, P=0.02; fibrinogen mean: 5.3g/l vs 7.8g/l, P=0.01) versus horses with septic pleural effusions. No significant differences in heart rate, respiratory rate, packed cell volume or total plasma protein concentration were identified between horses with neoplastic vs septic effusions.

Pleural fluid analysis was performed in 48 horses. The NCC and total protein concentration of the pleural fluid were both significantly lower in horses with neoplastic effusions compared to septic effusions (median NCC 8.6 +/-15.3x10^9/l vs 63.9 +/- 68x10^9/l; P<0.001; median total protein concentration 35.9 +/-16.9g/l vs 57.5 +/- 43g/l; P=0.04). The mean volume of pleural fluid drained at

admission was significantly greater in horses with neoplasia (32.2 +/-17.9l) than those with septic effusions (9.8 +/-7.6l; P<0.001).

Bacterial culture of either tracheal wash samples, pleural fluid aspirates or both was performed in 34 cases with a final diagnosis of septic pleural effusion. No growth was obtained in 6/34 (17.6%), a single isolate was obtained in 10/34 cases (29%) and a mixed bacterial population in 18/34 (52.9%). The most common isolates were *Streptococcus* spp. (16 isolates), *Escherichia coli* (12), *Enterococcus faecalis* (6) and anaerobes (6; including *Bacteroides* spp (3), *Fusobacterium necrophorum (2)* and *Clostridium perfringens (1)).* Other isolates included *Actinobacillus* spp, *Corynebacterium* spp and *Klebsiella* spp (all single isolates).

Details of diagnostic imaging results, including radiographic and ultrasonographic findings, were not recorded in sufficient detail in most cases to allow for meaningful analysis. For example, the presence or absence of pleural fluid on ultrasonographic examination was noted, but characterisation of pulmonary parenchymal changes, fibrin accumulation or presence of gas bubbles within pleural fluid was not consistently reported.

Outcome was recorded as survival to discharge. Overall, there were 43 non-survivors, 24 survivors and 2 horses in which outcome was not recorded. For horses with septic pleural effusions, survival rate was 47.6% (20/42). All horses with septic pleural effusions secondary to an oesophageal disorder died or were euthanased. Six horses with neoplastic effusions were discharged from the hospital, presumably for either palliative treatment or euthanasia at home, although this was not recorded.

Discussion

The findings of this study support the clinical impression that in the UK, pleural effusions secondary to neoplasia occur relatively more frequently than has been previously described in reports from

other countries. Although direct comparisons are difficult due to differing study designs, one similar study from the United States of America reported neoplasia as a cause of pleural effusion in only 11% of 37 horses. (Smith 1977) A second study, also from the USA, identified 32/122 (26%) of horses with effusion caused by 'non-infectious' causes, although these were not further categorised. (Raphel and Beech 1982) Long distance transport is a recognised risk factor for the development of pleuropneumonia and septic pleural effusion. (Raphel and Beech 1982; Austin *et al* 1995) Head elevation during transportation minimizes a horse's ability to clear lower respiratory tract (LRT) secretions and inhaled bacteria. (Norton *et al* 2013) Combined with the physiologic stress associated with travelling, the defence mechanisms of the LRT such as mucociliary transport, pulmonary alveolar macrophages and neutrophils can become overwhelmed. (Smith 1996; Oikawa *et al* 1995; Norton *et al* 2013) Establishment of infection within the lungs results in increased capillary permeability of the inflamed lung and visceral pleura, resulting in the accumulation of a sterile transudate within the pleural cavity. Bacteria from the infected lung rapidly invade the pleural space, resulting in the accumulation of a large volume of fluid packed with inflammatory cells, cellular debris and bacteria. (Oikawa *et al* 1995; Reuss and Giguère 2015) Most studies define long distance transport as over 500 miles, and as such, it is possible that the relatively short distances that horses travel within the UK, as compared to countries like the USA and Australia, may contribute to the lower proportion of septic pleural effusions. Interestingly, in the current study, 40.5% of horses with septic pleural effusions had a history of long distance travel (in 14/17, known international transport) in comparison to 24.4% reported by Raphel and Beech (1982). Thus, long distance transport is a consistent risk factor for the development of pleuropneumonia, regardless of geographic location.

In this study, horses with neoplasia were significantly older than those with septic pleural effusions. Horses with pleuropneumonia are typically young, with mean ages of 3.6 years and 2.5 years in 2 studies. (Collins *et al* 1994; Arroyo *et al* 2015) Presumably, this is associated with an increased likelihood for younger horses to be transported long distances for competitive reasons, or to

undertake high intensity exercise. In the current study, horses with septic pleural effusions were older than in other reports with a median age of 8 years, suggesting that age in itself may not be a specific risk factor, more that factors which increase the risk of developing septic pleural effusions are more likely to occur in younger horses. Whilst horses with neoplasia were older than those with septic pleural effusions in the current study, neoplasia can affect any age of horse. (Taintor and Schleis 2011) Lymphoma is typically identified in horses aged 4-10 years, with a mean age of 7 years in one study (Mair *et al* 1985; Taintor and Schleis 2011) As such, although there was a statistically significant difference between the age of both groups, young age in itself should not be relied on to rule out neoplasia as a cause of pleural effusion.

Consistent with previous reports, neoplasia in this study was associated with large volume accumulation of pleural fluid, with up to 55l drained in several horses. (Figure 1) (Mair *et al* 1985; Mair *et al* 2004) The development of such large volume effusions is presumed to occur due to decreased lymphatic drainage, especially when mediastinal masses are present, and/or to increased fluid production, when the neoplasm affects the pleural surfaces. (De Heer *et al* 2002; Mair *et al* 2004) In most horses with neoplasia in the current report, the pleural fluid was described as a modified transudate, with a relatively low NCC and moderately increased total protein concentration. As would be expected, both the NCC and the total protein concentration were significantly higher in horses with septic causes of pleural effusion.

A definitive diagnosis of neoplasia can be made if cytologic evaluation of the fluid identifies neoplastic cells or if masses are accessible for biopsy. (Figures 2 and 3) (Sweeney and Gillette 1989; Mair *et al* 2004) Lymphoma is believed commonly to result in exfoliation of neoplastic cells into the pleural fluid and in two reports up to 40% of cases were diagnosed ante-mortem via cytologic analysis of pleural fluid. (Mair *et al* 2004; Lee *et al* 2013) Similarly, in the current study, a diagnosis of neoplasia was made in 38% of horses via cytologic examination of pleural fluid. As has been

previously described, most cases in the current series did not present with a peripheral lymphadenopathy or visible mass that would be amenable to biopsy for histological analysis. (Mair *et al* 2004) A recent report described biopsy of intrathoracic masses in 2 horses via thoracoscopy, allowing the authors to confirm a diagnosis of neoplasia in each case, suggesting that in selected cases, this may be an appropriate and effective diagnostic tool. (Lee *et al* 2013)

The prognosis for horses with septic pleural effusion in the current series was relatively poor, with only 47% of horses surviving to discharge. From the records available, it was not possible to determine whether horses were euthanased due to poor prognosis and failure to respond to treatment, or whether euthanasia was elected for financial reasons. Previous reports have similarly identified overall survival rates of approximately 50% (Racklyeft *et al* 2000) although more recent reports suggest that with early identification and treatment, outcomes can be much improved. (Arroyo *et al* 2015; Tomlinson *et al* 2015) Factors associated with failure to survive in previous studies have included infection caused by anaerobic bacteria, a larger volume of pleural fluid and the presence of fibrinous effusions. (Figures 4 and 5) (Sweeney *et al* 1991; Racklyeft and Love 2000; Tomlinson *et al* 2015) Anaerobic bacteria were only identified in 6 horses in the current study, making correlations between their presence and survival difficult to interpret. Consistency in reporting fibrinous effusions precluded analysis of this characteristic. Pleural fluid drainage (as compared to thoracocentesis for sampling) was only performed in 13 horses with septic PE; although not recorded, it may be that, in the remaining horses, the volume of effusion did not warrant drainage, although this is a presumption as accurate measurements of ultrasonographic dimensions of visible pleural fluid were not recorded in most cases. In the current report, all cases with septic effusions secondary to oesophageal disorders did not survive. Two horses developed aspiration pneumonia secondary to oesophageal obstruction, two developed oesophageal rupture of unknown cause, and one had an extra-luminal mass compressing the oesophagus, resulting in aspiration. Five cases of intrathoracic oesophageal perforations with resultant septic pleural effusions have recently been reported, all with a similarly grave outcome. (Hepworth-Warren *et al* 2015) Aspiration of feed

material and subsequent pneumonia following oesophageal obstruction was not reported in 60 horses treated in a primary care setting. (Duncanson 2006) In comparison, 8/34 horses presented to a referral hospital developed pneumonia, which was significantly associated with duration of clinical signs. (Feige *et al* 2000) Interestingly, the degree of feed material contamination of the trachea (assessed endoscopically) was not associated with the development of pneumonia, suggesting that this may not be a sensitive tool in the assessment of whether aspiration has occurred or not. Considering the poor outcome in horses with oesophageal disorders, close monitoring of animals with oesophageal obstruction, and prompt evaluation and treatment of those suspected of having aspiration is warranted. (Feige *et al* 2000)

This study is limited by its retrospective nature; not all data was available for all horses. A definitive diagnosis of the type of neoplasia was not obtained in all horses, making a more detailed assessment of characteristics of individual tumour types impossible. Survival was based solely on survival to hospital discharge, which is likely to have skewed the data as several horses with neoplasia were classified as survivors due to the fact that they went home, presumably for euthanasia or palliative therapy. Although successful treatment of thoracic neoplasia has been reported, the prognosis is still considered hopeless. (Mair *et al* 2004; Saulez *et al* 2004)

Pleural effusions can develop for a number of reasons, the two most common being pleuropneumonia (septic) and neoplasia. In this study, horses with septic pleural effusions were younger than those with neoplasia, had significantly higher acute phase protein concentrations at admission, and had a smaller volume of pleural effusion with a higher NCC and total protein concentration. Of the 26 horses with confirmed or suspected neoplasia, the diagnosis was confirmed at post mortem in 12 horses, although in some cases a high index of suspicion existed without confirmation via cytological analysis of pleural fluid or lymph node aspirate. In 11 horses, a diagnosis was made ante-mortem using cytological analysis of pleural fluid, and in 3 horses, masses evident on ultrasound or radiography were consistent with neoplasia but cytological confirmation was not

pursued. This information may be helpful in making a prompt diagnosis when the clinician is presented with a horse with pleural effusion.

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References:

Arroyo, M., Slovis, N. and Moore, G. (2015) Septic pleuropneumonia in 97 horses. Proceedings of the American College of Veterinary Internal Medicine Annual Forum, Indianapolis.

Austin, S.M., Foreman, J.H. and Hungerford, L.L. (1995) Case-control study of risk factors for the development of pleuropneumonia in horses. *J. Am. Vet. Med. Assoc*. **207** 325-328.

Collins, M.B., Hodgson, D.R. and Hutchins, D.R. (1994) Pleural effusion associated with acute and chronic pleuropneumonia and pleuritis secondary to thoracic wounds in horses: 43 cases (1982-1992) *J. Am. Vet. Med. Assoc.* **205** 1753-1758.

DeGeer, H.L., Parry, B.W. and Grindem, C.B. (2002) Pleural Fluid. In: *Diagnostic cytology and hematology of the horse,* Eds: R.L. Cowell and R.D. Tyler, Mosby Inc., Missouri, pp 107-126.

265 Duncanson, G.R. (2006) Equine oesophageal obstruction: a long term study of 60 cases. *Equine Vet.*
266 *Educ.* **18** 262-265

267 Feige, K., Schwarzwald, C., Fürst, A. and Kaser-Hotz, B. (2000) Esophageal obstruction in horses: a
268 retrospective study of 34 cases. *Can. Vet. J.* **41** 207-210

269 ~~Groover, E.S. and Woolridge, A.A. (2013) Equine haemothorax. *Equine Vet. J.* **25** 536-541.~~

270 Hepworth-Warren K.L., Wilgenbusch, C.M., Wong, D.M., Fales-William, A.J., Wiechert, S.A. and
271 Sponseller, B.A. (2015) Intrathoracic oesophageal perforation and secondary pleuropneumonia: Five
272 cases. *Equine Vet. Educ.* **27**, 283-290.

273 Lee, W.L., Tennent-Brown, B.S., Barton, M.H., Almy, F.S., Uhl, E.W., Howerth, E.W., Reis, J.L.,
274 Linnenkohl, W.L. and Peroni, J.F. (2013) Two horses with thoracic lymphoma diagnosed using
275 thoracoscopic biopsy. *Equine Vet. Educ.* **25** 79-83.

276 Mair, T.S., Lane, J.G., and Lucke, V.M. (1985) Clinicopathological features of lymphosarcoma
277 involving the thoracic cavity in the horse. *Equine Vet. J.* **17** 428-433.

278 Mair, T.S. and Brown, P.J. (1993) Clinical and pathological features of thoracic neoplasia in the horse.
279 *Equine Vet. J.* **25** 220-223.

280 Mair, T.S., Rush, B.R. and Tucker, R.L. (2004) Clinical and diagnostic features of thoracic neoplasia in
281 the horse. *Equine Vet. Educ.* **16** 30-36.

282 Mair, T. Pleural effusions and pleuropneumonia. (2012) In: 51st British Equine Veterinary Association
283 Congress, Birmingham, England.

284 Norton, J.L., Jackson, K., Chen, J.W., Boston, R., Nolen-Walston, R.D. (2013) Effect of clenbuteral on
285 tracheal mucociliary transport in horses undergoing simulated long-distance transportation. *J. Vet.*
286 *Intern. Med.* **27** 1523-7.

287 Oikawa, M., Takagi, S., Anzai, R., Yoshikawa, H. and Yoshikawa, T. (1995) Pathology of equine
288 respiratory disease occurring in association with transport. *J. Comp. Pathol.* **113** 29-43.

289 Racklyeft, D.J., and Love, D.N. (2000) Bacterial infection of the lower respiratory tract in 34 horses.
290 *Aust. Vet. J.* **78** 549-559.

291 Racklyeft, D.J., Raidal, S. and Love, D. (2000) Towards an understanding of equine pleuropneumonia;
292 factors relevant for control. *Aust. Vet. J.* **78** 334-8.

293 Raphel, C.F., and Beech, J. (1982) Pleuritis secondary to pneumonia or lung abscessation in 90
294 horses. *J. Am. Vet. Med. Assoc.* **181** 808-810.

295 Reuss, S.M. and Giguère, S. (2015) Update on bacterial pneumonia and pleuropneumonia in the
296 adult horse. *Vet. Clin. N. Am. Equine Pract*. **31** 105-120.

297 Saulez, M.N., Schlipf, J.W., Cebra, C.K., McDonough, S.P. and Bird, K.E. (2004) Use of chemotherapy
298 for treatment of a mixed-cell thoracic lymphoma in a horse. *J. Am. Vet. Med. Assoc.* **224** 733-738

299 Smith, B.L., Jones, J.H., Hornof, W.J., Miles, J.A., Longworth, K.E. and Willits, N.H. (1996) Effects of
300 road transport on indices of stress in horses. *Equine Vet. J.* **28** 446-54.

301 Smith, B.P. (1977) Pleuritis and pleural effusion in the horse: a study of 37 cases. *J. Am. Vet. Med.*
302 *Assoc.* **170** 208-211.

303 Sweeney, C.R. and Gillette, D.M. (1989) Thoracic neoplasia in equids: 35 cases (1967-1987). *J. Am.*
304 *Vet. Med. Assoc.* **195** 374-377.

305 Sweeney, C.R. Holcombe, S.J., Barnigham, S.C. and Beech J. (1991) Aerobic and anaerobic bacterial
306 isolates from horses with pneumonia or pleuropneumonia and antimicrobial susceptibility patterns
307 of the aerobes. *J. Am. Vet. Med. Assoc.* **198** 839-42.

308 Sweeney, C.R. (1992) Causes of pleural effusion in the horse. *Equine. Vet. Educ.* **4** 75-77.

309 Taintor, J. and Schleis, S. (2011) Equine lymphoma *Equine Vet. Educ.* **23** 205-213.

310 Tomlinson, J.E., Reef, V.B., Boston, R.C. and Johnson A.J. (2015) The association of fibrinous pleural
311 effusion with survival and complications in horses with pleuropneumonia (2002-2012): 74 cases*. J.*
312 *Vet. Intern. Med*. epub ahead of print DOI: 10.1111/jvim.13591

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Table 1: Clinical and clinicopathologic findings in horses with septic and neoplastic pleural effusion. [a]median (Interquartile range (IQR)); [b]mean (standard deviation) [*]Significant difference between septic and neoplastic groups

PARAMETER	SEPTIC GROUP	NEOPLASTIC GROUP	P
Age[a] (years; n=55)	**8 (9)**	**13 (12)**	**0.001***
Heart Rate[a] (bpm; n=64)	**56 (15)**	**60 (16)**	**0.8**
Respiratory rate[a] (/min; n=65)	**29 (21)**	**36 (21)**	**0.9**
Temperature[b] (°C; n=63)	**38.6 (0.89)**	**38.2 (0.74)**	**0.04***
Packed cell volume[b] (%; n=67)	**36.5 (11.8)**	**36.9 (12.2)**	**0.9**
Total plasma protein concentration[b] (g/l; 62)	**66.8 (11.95)**	**63.71 (17.99)**	**0.4**
Fibrinogen concentration[b] (g/l; n=56)	**7.8 (3.3)**	**5.3 (2.9)**	**0.01***
Serum amyloid A concentration[b] (mg/l; n=49)	**230 (200)**	**59 (238)**	**0.02***
Total volume of pleural fluid[b] (l; n=28)	**9.8 (7.6)**	**32.2 (17.9)**	**<0.001***
Pleural fluid nucleated cell count[a] ($x10^9$/l; n=48)	**63.9 (68.0)**	**8.6 (15.3)**	**<0.001***
Pleural fluid total protein concentration[a] (g/l; n=47)	**57.5 (43.0)**	**35.9 (16.9)**	**0.04***

Figure 1: Large volume effusion drained from the pleural cavity of a horse with lymphoma.

Figure 2: Histopathology from a lymph node obtained at post mortem examination in a horse with lymphoma. Sheets of immature and mitotically active lymphomatous cells are noted throughout the section.

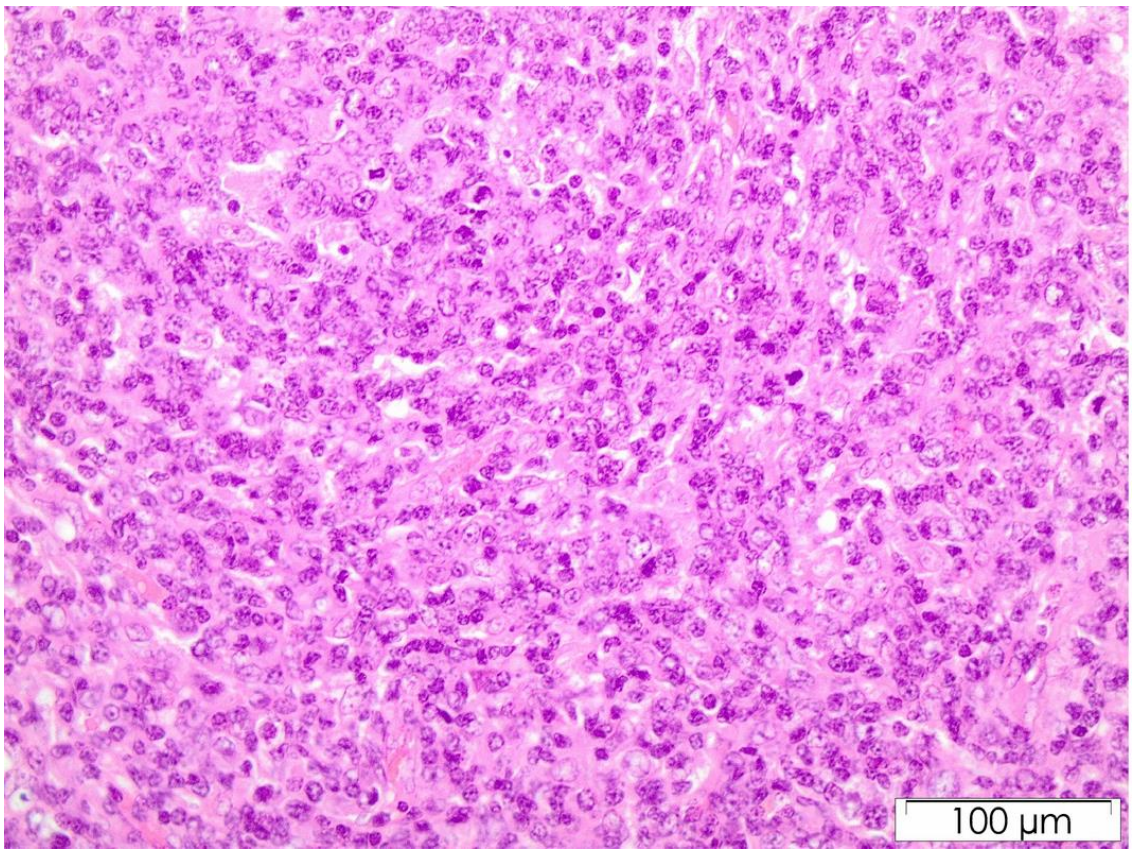

Figure 3: Pleural effusion from a horse with neoplasia, identifying large round cells with eccentric nucleus.

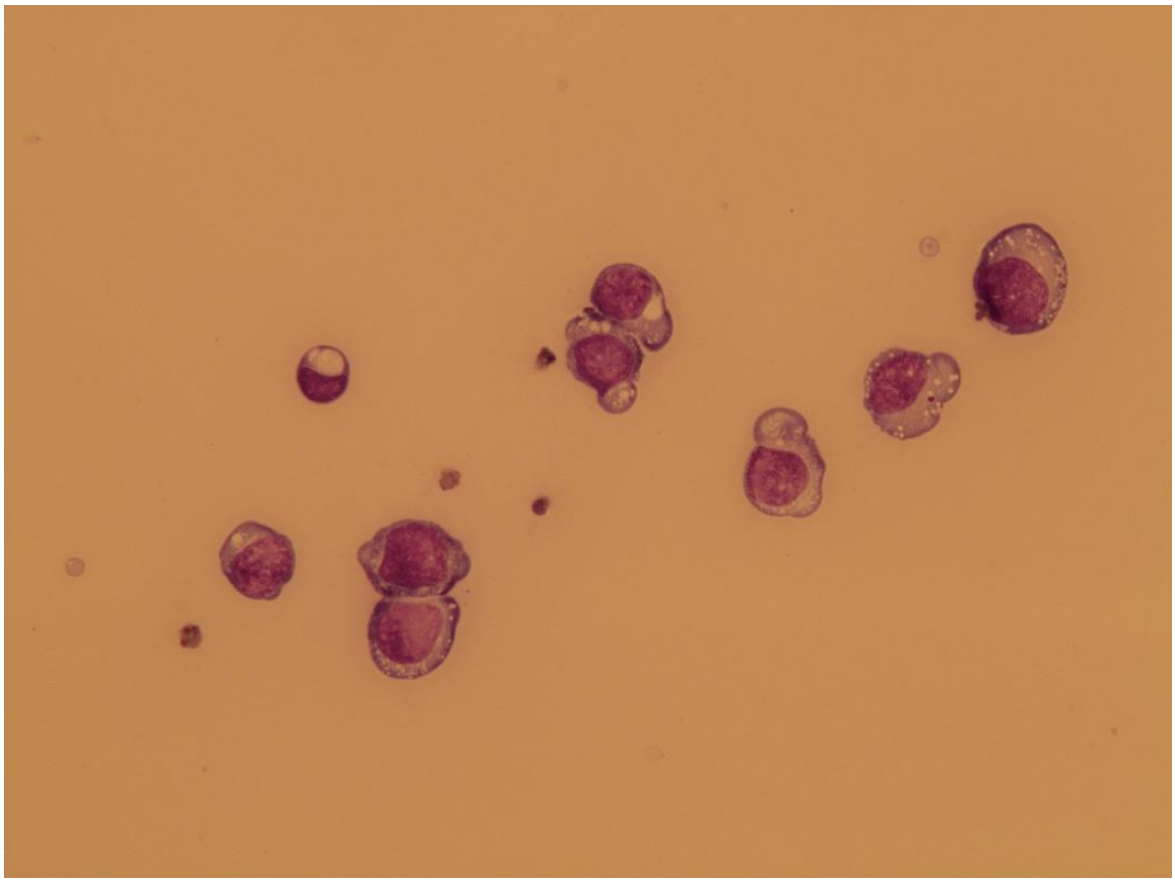

Figure 4: Ultrasonographic image of a horse with fibrinous pleuropneumonia.

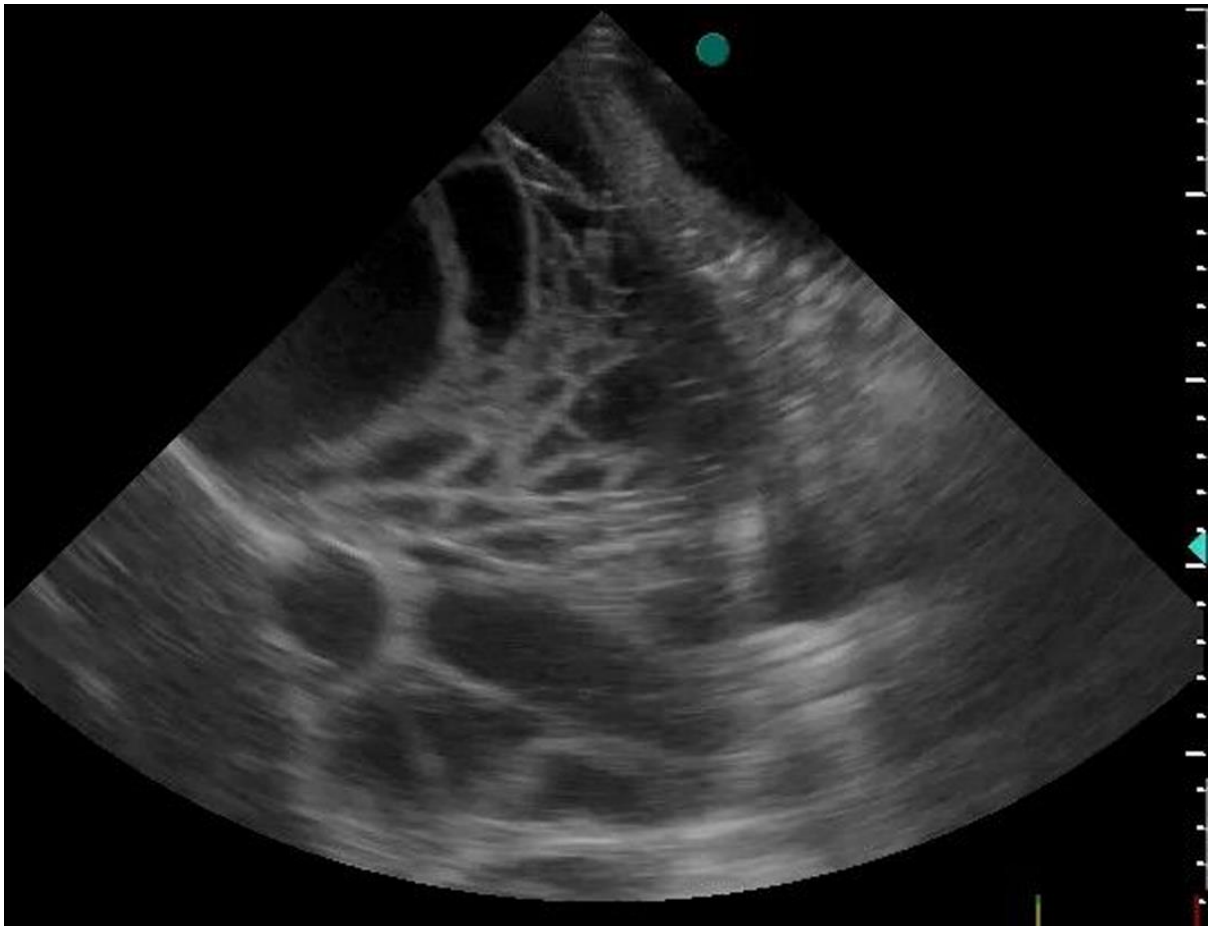

Figure 5: Post mortem image of horse with severe fibrinous pleuropneumonia, markedly worse on the left.