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Retrospective study on clinical findings of 84 horses with peritonitis

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1. Introduction and objective

Peritonitis is defined as inflammation of the peritoneum, the serous membrane which lines the abdominal cavity and abdominal organs. The peritoneum is sensitive to insults of different aetiology and the inflammatory response is expressed by an increase in white blood cells and protein of the peritoneal fluid. Clinical signs include tenderness on abdominal palpation, pyrexia, depression. The condition can potentially become fatal. Peritonitis is a common complication to gastrointestinal disease, injury and surgery. I have looked at 84 patient records of horses admitted to Evidensia Strömsholm Equine Referral Hospital in Sweden with the diagnosis of peritonitis between the years of 2004 and 2015. The objective of the thesis is to compare clinical parameters and culture result of peritoneal fluid between survival and non-survival groups.

2. Literature review

2.1. The peritoneum and peritonitis

2.1.1. Anatomy and physiology

The peritoneum is the serous membrane which lines the abdominal cavity, the abdominal organs and the male scrotum. In males it is a closed sac; in females there is a communication with the external environment by means of the two fallopian tubes (Reed *et al*., 2004; Smith B.P., 2015; White *et al*., 2008). The peritoneum is anatomically divided into two sections. The portion of the peritoneum which lines the abdominal wall, diaphragm and pelvis is regarded as the parietal peritoneum whilst the portion which reflects over the organs is the visceral peritoneum (Smith B.P., 2015; Zachary and Donald McGavin, 2012). The omentum, ligaments and mesenteries are doubled layers of peritoneum with a suspensory function as well as providing a medium for nervous innervation and blood supply to organs. The ligaments connect organs to each other, or to the abdominal wall; and mesenteries strictly suspend the intestines and female reproductive tract to the abdominal wall. The omentum runs between the stomach and the abdominal wall. (Zachary and Donald McGavin, 2012). Certain structures in the abdominal cavity are excluded from the peritoneal cavity, e.g. the kidneys. These structures are referred to as retroperitoneal in their position and includes most of the structures within the pelvic cavity (Reed *et al*., 2004). The peritoneum provides an important site for fat deposition and is subject to serous atrophy in situations of starvation. Healthy peritoneum should be smooth and shiny (Zachary and Donald McGavin, 2012).

The visceral and parietal peritoneum receives vascular supply from different origin. The visceral peritoneum is supplied by

splanchnic vessels whilst the parietal peritoneum receives nutrients from lower intercostal, lumbar and iliac arteries and empties the venous blood into the caudal vena cava (Smith B.P., 2015). The omentum is important for revascularisation of structures e.g. after surgery and provides also vascular supply for metastatic tumours (Zachary and Donald McGavin, 2012). Residing peritoneal macrophages and mast cells, mesothelial cells and activated T-cells provide a local cellular defence. The diaphragmatic lymphatics collect fluid, debris and foreign material into the thoracic duct (Smith B.P., 2015) by means of the thoracic stomata or sub-endothelial pores (Reed *et al*., 2004).

The visceral peritoneum is innervated by the visceral autonomic nervous system. Small type C sensory fibres respond to ischaemia, pressure, distention, spasm and traction by a dull pain sensation (Reed *et al*., 2004; Smith B.P., 2015). The parietal peritoneum receives innervation of somatic and visceral afferent nerves by means of the phrenic and intercostal nerves. Stimuli of the parietal peritoneum is perceived as a sharp somatic pain response, elicited by external palpation and with a clinical presentation of splinted abdomen and a reluctance to move (Reed *et al*., 2004; Smith B.P., 2015; Zachary and Donald McGavin, 2012).

The histological structure of the peritoneal membrane is three layers. At the base there is a loose connective tissue layer which is covered by a basal lamina on top of which one layer of mesothelial cells rest, coated in a thin film of peritoneal fluid. The loose connective tissue with the fluid allow movement and lubrication for gliding movement of organs (Eggleston and Mueller, 2003; Smith B.P., 2015; Zachary and Donald McGavin, 2012). The mesothelial cells are of mesodermal origin (White *et al*., 2008) and have the ability to rapidly regenerate which is thought to be originating from

stem cells in deeper tissues. It gives the regeneration the ability to take place all across the affected area rather than from the edges of the lesion (Zachary and Donald McGavin, 2012). The mesothelial cells play a central role in initiating and resolving inflammation, by having both pro-coagulation and fibrinolytic properties (Delgado *et al*., 2009; Reed *et al*., 2004).

Peritoneal fluid provides anti-friction for abdominal organs (Reed *et al*., 2004; Smith B.P., 2015), prevents adhesions and possess some antimicrobial protection by means of fibrinolytic mediators, macrophages, chemotactic agents and complement factors (Reed *et al*., 2004). The fluid is constantly excreted and reabsorbed by passive diffusion across the semi-permeable peritoneum. When visualising the abdomen using ultrasonography there should only be a very small volume of fluid visible in the cranial portion of the ventral abdomen (Smith B.P., 2015). Healthy equine peritoneal fluid does not contain free fibrinogen thus it should not clot when exposed to air (Zachary and Donald McGavin, 2012). Fluid movement direction is cranial-ventrally by means of diaphragmatic movement and gravity (Reed *et al*., 2004; White *et al*., 2008)

2.1.2. Pathophysiology of peritonitis

Inflammation of the peritoneal membrane is termed peritonitis (Davis, 2003; Kahn, 2010; Smith B.P., 2015; Zachary and Donald McGavin, 2012). The initiating insult can be of mechanical, chemical or of infectious origin (Dart and Bischofberger, 2011; Reed *et al*., 2004). Peritonitis is classified as acute or chronic; localised or diffuse; septic or aseptic; primary, secondary or tertiary (Dart and Bischofberger, 2011; Davis, 2003; Kahn, 2010; Smith B.P.,

2015). The most commonly encountered form of peritonitis is acute, diffuse, septic peritonitis (Reed *et al*., 2004).

The pathogenesis is similar in all cases regardless of inciting cause (Davis, 2003; Lores *et al.*, 2011). It is characterised by activation of mesothelial cells, depression of fibrinolysis and fibrin precipitation accompanied by an influx of neutrophil granulocytes in response to release of chemoattractant molecules and inflammatory mediators (Reed *et al*., 2004). When describing the pathogenesis, it is subdivided into phases of a timeline. The contamination phase refers to the initial three to six hours of acute inflammatory response and if the peritonitis is unresolved, it is continued to the acute diffuse phase, lasting for up to five days. The next, transitional phase is dominated by fibrinolysis or maturation of adhesions and can go on for four to 10 days. Phase of chronic abscessation will follow if the cause could not be eliminated (Reed *et al*., 2004).

Resident macrophages and mast cells respond to peritoneal insult by the release of histamine and serotonin that dilate the vessels and increase the vascular permeability. This results in a transudation of fluid and proteins from the vascular space into the peritoneal cavity (Davis, 2003; Smith B.P., 2015). There is also an influx of complement factors (White *et al*., 2008) and neutralising antibodies (Reed *et al*., 2004). Considering the size of the equine abdomen it should be realised that the large surface area is able to accommodate a severe influx of fluids and haemodynamic disturbances (Mair *et al*., 1990). Loss of proteins results in hypoproteinaemia and facilitation of bacterial growth in the peritoneal cavity. Vasodilation accompanied by massive fluid losses into the peritoneal cavity can cause severe hypotension and shock (Kahn, 2010). Tumour necrosis factor (TNF-α) and interleukin-1 (IL-1) are chemotactic agents, attracting

peripheral neutrophils' migration and degranulation. (Davis, 2003; Smith B.P., 2015). Mesothelial cells express adhesion molecules that promote chemotaxis (White *et al*., 2008) will also transform into macrophages themselves (Reed *et al*., 2004). Prostaglandin, leukotrienes and platelet activating factor (PAF) are other substances released from mast cells and macrophages that promote and sustain the inflammatory response (Davis, 2003; Smith B.P., 2015). Damage of mesothelial cells inhibits fibrinolytic activity by the exposure of tissue thromboplastin and decreasing level of plasminogen activators which promote the precipitation of fibrin, originating from plasma-originating fibrinogen. The fibrin adhesion fence off the local insult, e.g. bacteria, and aid in healing of damaged peritoneum (Davis, 2003; Smith B.P., 2015). Depending on the cause of inflammation, fibrin will precipitate locally or disperse diffusively in the peritoneal cavity (White and Edwards, 2001). As the inflammation resolves, the fibrin is lysed. However, if the inflammation reaction persists and the inciting cause is not eliminated the fibrin adhesion mature into fibrous structures and abscesses form around persisting foreign material (Davis, 2003; Smith B.P., 2015).

Although peritonitis serves to protect the peritoneal cavity, it can be damaging if diffusely dispersed across the abdominal cavity and accompanied by reflex ileus and severe hypovolaemia and hypoproteinaemia (White and Edwards, 2001). Death of neutrophils releases degrading enzymes such as superoxide and myeloperoxidase (Davis, 2003; Smith B.P., 2015) which damage healthy mesothelial cells and further aggravate the inflammation (White and Edwards, 2001). Ileus with associated distention of the bowel compromises the mucosal integrity and there is transmural leakage of bacteria. Presence of bacteria can cause a

generalised response to bacterial metabolic products and toxins (Reed *et al*., 2004). Shock is usually the cause of death (White and Edwards, 2001).

Primary peritonitis is of either infectious or idiopathic origin. The pathogen arrives via the haematogenous route (Kahn, 2010). It most commonly occurs in septic neonates (Smith B. P., 2015). In older foals and young horses primary peritonitis is usually caused by Streptococcus species or *Rhodococcus equi* (Elce, 2006). It is rarely encountered in adult horses and is mainly affecting immunocompromised individuals (Kahn, 2010; Smith B. P., 2015; Tenneth-Brown *et al*., 2010). In a study of 65 horses, those with idiopathic peritonitis were of significantly younger age (Henderson *et al*., 2008). It should be kept in mind that a primary peritonitis could be secondary but the underlying cause has not yet been identified (Mair *et al*., 1990). Progression of primary peritonitis is often chronic. Secondary peritonitis more common in adult horses and is usually acute, of bacterial origin and often progress to generalised disease (Kahn, 2010). Tertiary peritonitis is described in humans where peritonitis recur or when a secondary peritonitis persists beyond treatment (Dart and Bischofberger, 2011; White *et al*., 2008).

The causative agent in septic peritonitis is characteristic of the origin. A mixed flora is often detected in the case of transmural leakage from the intestines (Kahn, 2010). Regardless of origin; once the pathogen has arrived it is able to disseminate throughout the peritoneal cavity within 3-6 hours. The rapid spread is facilitated by the movement of the intestinal peristalsis and diaphragmatic movement (Lores *et al.*, 2011) and the small omentum which is very small in the horse and less able to localise infection and inflammation, compared to other species (Lores *et al.*, 2011; Ramirez *et al*., 1997; Zachary and Donald McGavin, 2012). Aseptic

peritonitis lacks pathogens, i.e. it's caused by sterile irritants such as free blood (Kinsley *et al*., 2010), bile, urine or chemicals. Aseptic peritonitis can progress to septic peritonitis (Kahn, 2010; Reed *et al*., 2004) when the inflammation weakens the integrity of the gastrointestinal walls.

2.2. Aetiology of peritonitis

In the gastrointestinal tract, the highest concentration of bacteria is present in the caecum and colon where each ml of fluid contains$1x10^9$ and $1x10^5$ anaerobic and aerobic bacteria, respectively. The potential for serious peritoneal contamination explains the high mortality of bowel penetration and secondary bacterial contamination (Reed *et al*., 2004). The umbilicus in neonatal foals is a potential ingress for pathogens (Lores *et al.*, 2011), navel infections are associated with less favourable prognosis when complicated by septic peritonitis and adhesions (Elce, 2006).

Infectious peritonitis of mixed microbial infection is most common, but single bacteria can reach the peritoneum by the haematogenous route or by means of the fallopian tubes. Common single bacteria isolated in peritonitis are *Actinobacillus equuli, Rhodococcus equi, Streptococcus equi subspecies (ssp) equi, Streptococcus equi ssp zooepidemicus* and *Corynebacterium pseudotuberculosis* (Reed *et al*., 2004). *Streptococcus equi ssp equi* is a pathogen unique to the horse. It causes strangles, a disease of the upper respiratory tract with high morbidity and low mortality. When the infection is found anywhere in the body but the pharyngeal region it is referred to as atypical, metastatic or "bastard strangles" (Kahn, 2010). It disseminates by means of blood, lymph and along cranial nerves. Atypical strangles has been reported in outbreaks on farms with a frequency of up to 20%. Among

several places in the body, *Streptococcus equi ssp equi* can form intraabdominal abscesses e.g. in the liver, spleen and mesentery (Whelchel and Chaffin, 2009).

Actinobacillus equuli is a non-motile Gram negative commensal bacterial pleomorphic rod of the healthy equine oral cavity, respiratory tract and gastrointestinal passage (Patterson-Kane *et al*., 2001; Stewart, 2006; Tenneth-Brown *et al*., 2010). It is infamous for causing neonatal septicaemia and enteritis. Although rarely reported in adults, it causes respiratory disease, abortion, haemorrhagic diathesis, pericarditis, periorchitis and enteritis. Peritonitis caused by *Actinobacillus equuli* is rare and characterised by a specific clinical presentation with an excellent response to treatment and 100% survival rate. *Actinobacillus equuli* was found with a prevalence of 12-88% in the oral cavity. There are at least 28 antigen groups discovered (Matthews *et al*., 2001) with a variation in strains between individual horses and within the same one horse over time. There is yet no useful method to identify if there are pathogenic versus apathogenic strains. The pathogenesis of *Actinobacillus equuli* peritonitis is unknown. It is suspected that it is inoculated into the peritoneal cavity by migrating Strongyle larvae (Patterson-Kane *et al*., 2001; Matthews *et al*., 2001) with reported cases having evidence of a large worm burden (Tenneth-Brown *et al*., 2010). The bacterium has been isolated from verminous aneurysms of the cranial mesenteric artery caused by *Strongylus vulgaris*. Foals are thought to be infected by Strongyle larvae that cross the placenta to prenatal foals. The migrating parasite is thought to inoculate a foreign strain of the bacterium originating from the gastrointestinal tract of a different horse into a new host. Other routes of entry are via the umbilicus of the foal, per oral or aerogenous. There is a regional difference in frequency of the disease, with the

majority of cases reported in Australia. In general, this is a disease of adult horses, the youngest case reported was 9 months old (Matthews *et al*., 2001). Recovery from *Actinobacillus equuli* is reported to be 100% with prompt and aggressive treatment (Tenneth-Brown *et al*., 2010). A fatal case has been described in an adult horse, however there was a very high dose of phenylbutazone noted in the history and the horse did not receive either antimicrobial treatment or any other supportive therapy. On necropsy, there were unusually extensive lesions in the abdominal cavity. Erosions on the large colon were detected, which were thought to be due to the non-steroidal anti-inflammatory drugs (NSAIDs) administered ante-mortem, so the bacterium was suspected to arrive to the peritoneal cavity by transmural migration (Patterson-Kane *et al*., 2001).

Clostridium septicum was cultured from a fatal peritonitis in association with a castration (Shearer *et al*., 2015). Equine diseases caused by Clostridia have often a fatal outcome but one case of survival of clostridial peritonitis was reported in a Percheron mare by Hepworth-Warren *et al*., (2016). The species identified was *Clostridium haemolyticum*, origin was thought to be from the gastrointestinal tract or parasites. Survival in this case was largely attributed to application of aggressive and early therapy. Although not a frequent equine pathogen, *Listeria monocytogenes* has been reported to cause neonatal septicaemia and associated septic peritonitis (Montiero *et al*., 2006). A subtype of common variable immunodeficiency (CVID) of humans is described in adult horses where there often is a history of recurrent and unusual bacterial infections. Chronic peritonitis was described in a two year old quarter horse which was diagnosed with CVID and the pathogens (*Actinobacillus equuli* and *Escherichia coli*) were believed to be secondary to a respiratory infection

which was allow to settle in the peritoneal cavity as the immune system was very weak (Tenneth-Brown *et al*., 2010). Viruses such as influenza (*Orthomyxoviridae*), equine viral arteritis (*Arteriviridae*) and African horse sickness (*Reoviridae*) can cause peritonitis (Reed *et al*., 2004).

Abdominal abscesses form when the immune system fail to clear an irritating agent. Among several reported causes of abdominal abscessation are foreign bodies, *Streptococcus equi ssp equi, Rhodococcus equi, Escherichia coli and Bacterioides.* (Elce, 2006) Vaginal tears can develop into abscesses (Delling *et al*., 2012) and hepatic abscesses have been associated with peritonitis (Mair *et al*., 1990). Although most perirectal abscesses have a retroperitoneal location, there may be peritoneal association and bacteria isolated are of typical faecal origin e.g. *Escherichia coli* and *Streptococcus zooepidemicus* (Elce, 2006). Perforation of the intestinal wall by parasitic migration e.g. *Anoplocephala perfoliata* or small strongyles has been associated with peritonitis as well as peritonitis consequent to ischaemia of the bowel wall caused by verminous arteritis associated with Strongylus vulgaris (Reed *et al*., 2004).

Peritonitis may be caused as a complication to a veterinary procedure such as abdominocentesis, biopsy of liver or uterus; or puncture of bowel or spleen (Reed *et al*., 2004). Manual palpation per rectum always involves the risk of causing a rectal tear and consequent peritonitis. Age and breed is a risk factor, leaving older horses and miniature breeds and Arabian horses especially predisposed (McMaster *et al*., 2015). Peritonitis as well as local abscessation developed as a complication to percutaneous caecal puncture has been described in literature (Unger *et al*., 2014). Indication for the procedure should be reserved for the severe abdominal distention refractory to analgesia and where

surgery is not permitted for e.g. financial constraints (Corley and Stephen, 2008). Some degree of peritonitis must be expected even in the successful transcutaneous caecal punctures, but they should be self-limiting and localised (Unger *et al*., 2014). Decompression per rectum has been described to cause an acute onset of septic peritonitis. However, results are controversial (Scotti *et al*., 2013).

Peritonitis is a very common complication of castration with a reported frequency of 63%. It is usually a consequence to poor surgical technique or improper use of emasculators (Schumacher *et al*., 1988). The vaginal tunic which encloses the testes has two layers with the (Kilcoyne, 2013) parietal tunic of the scrotum being a direct extension of the peritoneum (Kinsley *et al*., 2010; Schumacher *et al*., 1988). Thus there's a direct communication between the testes and the peritoneal cavity (Blanchard *et al*., 2003; Schumacher *et al*., 1988). The mesothelial cells lining the vaginal process possess phagocytic properties and prevent ascending infections (Kinsley *et al*., 2010). In addition, the funicular portion of the vaginal process is collapsed as it passes through the abdominal wall (Blanchard *et al*., 2003; Kilcoyne, 2013). Infection of the testes is not common and is usually caused by direct trauma and less often by an infectious agent arriving with the blood stream (Kinsley *et al*., 2010). Equine castrations have a complication rate recorded to be 10.2% and a mortality rate of 0.3% (Kilcoyne, 2013). Although septic peritonitis is rare, a case of septic peritonitis with fatal outcome caused by anaerobic bacteria was reported by Shearer *et al*. (2015). Subcutaneous emphysema was found and an associated heavy growth of *Clostridium septicum*. Non-septic peritonitis is more common and lasts for up to five days after castration (Blanchard *et al*., 2003; Kilcoyne, 2013; Shearer *et al*., 2015). In a study done

by Schumacher et al. (1988) looking at 24 routine castrations they concluded that although total nucleated cell count (TNCC) may be high in the peritoneal fluid post-castration it is not always clinically significant. There was a close relationship between free red blood cells in the sample and a high TNCC, suggesting that free blood trigger an inflammatory response by the peritoneum. Although no culture was done on the peritoneal fluid samples in that study, no intracellular bacteria or degenerated neutrophils were detected on cytological examination, indicating that the increase in neutrophils in the peritoneal fluid is not a response to a bacterial contamination.

Free urine in the peritoneum (uroperitoneum) is a chemical irritant to the peritoneal membrane and predisposes the peritoneal cavity to secondary bacterial infections. Rupture of the urinary bladder (cystorrhexis) is uncommon in adult horses but has been described (Peitzmeier *et al*., 2015; Snalune and Mair, 2006). It can be caused secondary to urolithiasis obstruction of the urethra or although rare, in mares the bladder may rupture during parturition (1 of 10,000 foalings). Cystorrhexis is most frequently seen in neonatal foals due to trauma (Snalune and Mair, 2006) but peritonitis is an uncommon complication (Lores *et al.*, 2011). Peritonitis in association with cystorrhexis appears to be more frequently reported in adults compared to foals. It is thought to be related to the more frequent bacterial contamination in adults e.g. when there is a bacterial cystitis in the aetiology (Snalune and Mair, 2006). Uterine tears occur usually during the second stage of parturition and most frequently at the tip of the gravid horn. Direct bacterial contamination lead to septic peritonitis (Mogg *et al*. 2006).

Trauma from dystocia, accidents or during breeding in mares, the rectum may tear and lead to septic peritonitis with fatal

outcome if not addressed promptly (McMaster *et al*., 2015). Foreign bodies in the gastrointestinal tract can penetrate the intestinal or gastric mucosa, causing septic peritonitis (Lohmann *et al.*, 2010). The clinical signs are non-specific and therefore should foreign body penetration be on the list of possible causes of peritonitis when establishing a diagnosis (Ramirez *et al*., 1997).

Diverticulum of the small intestine, especially on the mesenteric side of the ileum, can lead to perforation and septic peritonitis. Muscular hypertrophy is often concurrent and because of detected eosinophilic infiltration, it has been proposed to be caused by visceral larval migrans (Snalune and Mair, 2006). Idiopathic perforation in four horses was reported by White and Mair (2008) where all horses had peritonitis with signs of a low grade colic, and endotoxin shock. One case was suspected to be associated with *Anoplocephala perfoliata* and/or cyathostomiasis. It was highlighted that an early exploratory laparotomy could be warranted in non-responsive moderately painful peritonitis. Caecal perforation and consequent septic peritonitis can have several different aetiologies, e.g. perforation caused by *Anoplocephala perfoliata* (Mair *et al*., 1990). If the perforation is on the dorsal aspect of the caecum there may be atypical findings such as no signs of faecal contamination of abnormal peritoneal fluid collected which make diagnosis difficult (Gray *et al*., 2014). A case of septic peritonitis from a small colon perforation caused by ulceration of an inflammatory polyp was reported (Saulez *et al*., 2004).

Chemical peritonitis is caused by non-infectious matter irritating the peritoneum e.g. physiological excretions such as urine, bile or lymph; or iatrogenic introduced materials such as talc from surgical gloves, contrast agent and lavage solutions (Reed *et al*., 2004).

2.3. Diagnosis of peritonitis

It is essential to perform a full clinical examination (Smith B.P., 2015). If recently castrated or foaled, the genital tract should carefully be examined (Smith B.P., 2015). Collecting abdominal fluid confirms the diagnosis of peritonitis but not the cause (White and Edwards, 2001), the results obtained must be put in context with other clinical and laboratory findings (Reed *et al*., 2004).

2.3.1 Clinical signs

Clinical signs depend on the aetiology and duration of the inflammation but are generally non-specific (Reed *et al*., 2004; White and Edwards, 2001). Compared to other domestic species, horses are in general very pain intolerant (Zachary and Donald McGavin, 2012).

Peracute peritonitis display signs of severe endotoxaemia, circulatory failure and depression or colic. Pyrexia may or may not be present (Reed *et al*., 2004). The peracute case is often found dead. Acute, diffuse peritonitis that have had some time to develop show signs of shock and dehydration (White and Edwards, 2001). The localised, subacute or chronic peritonitis present often with normal heart rate, respiratory rate and faecal output with weight loss, intermittent fever, ventral oedema, slight dehydration and decreased borborygmi. Signs of abdominal pain are not always evident or occur intermittently. In some cases there is chronic diarrhoea (Reed *et al*., 2004; White and Edwards, 2001). Foals present with signs like in the adult horse but their condition deteriorates more rapidly and pleural effusion is detected in some cases (Reed *et al*., 2004). Concurrent ileus frequently observed in peritonitis is caused by spinal sympathetic inhibitory reflexes. It is speculated to develop as a protective feature in peritonitis to prevent spread of bacteria

with the movement of intestinal peristalsis (Hepworth-Warren *et al*., 2016). Ileus can also be caused by bacterial endotoxins (Smith B.P., 2015).

In a retrospective study performed in Australia by Matthews *et al*. (2001) horses that were diagnosed with *Actinobacillus equuli* presented a characteristic set of clinical signs. Interestingly, the horses never progressed to endotoxaemic shock. Increased respiratory sounds and pleural effusion has been reported in some cases (Matthews et al., 2001; Mogg and Dykgraaf, 2006; Stewart, 2006).

2.3.2. Rectal palpation

Palpation per rectum is a useful cost-effective diagnostic aid which can be performed by the ambulatory veterinarian in the field and give important clues about the state of the abdomen. The risk of tearing the rectum whilst performing the exam must be carefully considered when electing this diagnostic aid (McMaster *et al*., 2015).

In the acute and peracute peritonitis horse, palpation per rectum induces a pain response. There is a gritty feeling, either due to faecal contamination of the abdomen or fibrin precipitation. In chronic peritonitis, pain can sometimes be expressed if palpating adhesions. Distended bowel and secondary impaction are sometimes palpated (Reed *et al*., 2004). Palpating where there is distended bowel floating in large volumes of peritoneal fluid gives an empty impression (White and Edwards, 2001). Enlarged mesenteric lymph nodes and unidentifiable masses can also be relevant findings (Smith B.P., 2015). However, in many cases of peritonitis there are no abnormalities palpated (Smith B.P., 2015; White and Edwards, 2001). Diagnosis of parasitic arteritis by rectal palpation is a very inaccurate method (Dyson, 1983; Matthews et al., 2001) and correlate very little with findings

at necropsy (Stewart, 2006). Oedema of the large colon or caecum can be palpated in case of an infarct (White and Edwards, 2001).

2.3.3 Diagnostic imaging

Trans-abdominal or trans-rectal ultrasonography should be performed to evaluate presence of an abnormally large amount of peritoneal fluid, distended intestinal loops or abscesses. Abnormalities are detected in 50-90% of examinations (Smith B.P., 2015). It is also helpful to locate smaller pockets of fluid to collect by abdominocentesis (White *et al*., 2008). Standing radiography can be used in foals to visualise possible abnormalities (White and Edwards, 2001).

2.3.4 Abdominocentesis

Analysis of the peritoneal fluid gives indirect information about the state of the intraabdominal organs (Matthews *et al*., 2002). Abdominocentesis is a rapid, cheap and minimally invasive diagnostic tool (Matthews *et al*., 2002; Snalune and Mair, 2006) and is the main diagnostic tool in the diagnostic workup of the peritonitis case (Reed *et al*., 2004). The procedure can be performed in a field setting, has a low morbidity and results are obtained straight away or within hours (Matthews *et al*., 2002). Peritoneal fluid parameters can be used to differentiate patients that will respond well to conservative therapy from those who need abdominal surgery (Matthews *et al*., 2002). Serial samplings are recommended and fluctuations in values over time are not uncommon due to pocketing of fluid within the peritoneal cavity (Dyson, 1983). Macroscopic exam evaluating turbidity and colour has to be done accompanied by laboratory examination of total protein, total nucleated cell count (TNCC) and differential and gram staining (Reed *et al*., 2004).

2.3.4.1 Sampling procedure

It has to be stressed that abdominocentesis must be performed prior to administration of antimicrobial drugs to not kill potential bacteria for culture (Mair *et al*., 1990). However, an antibiotic removal device can be used if antimicrobial drugs were given prior to sampling (Reed *et al*., 2004). It is recommended to take several samples during the course of the disease (Mair *et al*., 1990). Using either a sharp-tipped needle or a blunt-tipped teat cannula, the method has been described in literature (Corley and Stephen, 2008; Reed *et al*., 2004). Which method is superior to the other was investigated by Duesterdieck-Zellmer et al. (2014). There were no significant differences between the two methods. However, using a blunt-tipped teat cannula increase the incident of blood contamination. To overcome the contamination risk one is advised to use a small bit of gauze placed between the abdominal wall and the hub of the cannula which collects dripping blood which otherwise would drip into the collection tube.

A blood sampling tube containing EDTA is preferred for cytology. It must be adequately filled since the EDTA otherwise will change the refractive index of the fluid and alter the laboratory results. An empty, sterile tube is used to collect fluid for macroscopic examination and culture (Reed *et al*., 2004).

2.3.4.2 Macroscopic examination: volume, turbidity and colour

Useful information can be obtained by evaluating the fluid volume and macroscopic features, making it an excellent diagnostic tool in the field (Smith B.P., 2015). Macroscopic examination of the fluid has a diagnostic importance for the decision to refer for surgery (Matthews *et al*., 2002). Normal

peritoneal fluid should be of little volume, clear and straw coloured and not coagulate (Reed *et al*., 2004). Large volume of clear fluid could be a sign of uroperitoneum or ascites. Turbidity indicates an increase in cells and proteins (Smith B.P., 2015). Serosanguinous fluid is an indication of either free erythrocytes or haemoglobin. The risk of splenic puncture or contamination of the sample with skin bleeding must always be considered. Green coloured sample is a sign of either enterocentesis, or bowel rupture. When there is tissue necrosis in the abdominal cavity the fluid sample has a brown colour (Smith B.P., 2015). Differentiation between intraabdominal haemorrhage and blood contamination of the sample is possible by assessing the presence of platelets which are few or absent in abdominal haemorrhage. Splenic puncture can be identified by a higher haematocrit compared to peripheral blood (Reed *et al*., 2004).

2.3.4.3. Total protein, total nucleated cell count and differentiated white blood cells

Evaluation of total protein in the peritoneal sample is easily performed in the field with a refractometer or by biochemical methods in a laboratory setting. It gives information about level of extravasation of proteins from the vascular space into the peritoneal cavity (Matthews *et al*., 2002). Normal peritoneal fluid has a total protein content of less than 1.5 g/dl, above 2.5 g/dl is regarded as abnormal.

TNCC in normal peritoneal fluid should be less than $5x10^9$/l (Reed *et al*., 2004). However, TNCC as a diagnostic aid is often regarded as unreliable due to cell clumping and fragmentation (Matthews *et al*., 2002). It should be complemented by differential white blood cell count (Ramirez *et al*., 1997) which also gives information about duration of the disease. In acute peritonitis, there is

abundancy in polymorphonuclear leukocytes (PMN) e.g. neutrophil granulocytes (Matthews *et al*., 2002). For example, a high TNCC on its own cannot diagnose septic peritonitis. It is more informative when a high TNCC is accompanied by intracellular bacteria visualised on cytology and toxic or degenerated neutrophils are present too (Ramirez *et al*., 1997). In the acute stage of peritonitis, there is a high TNCC with abundance of PMN. In chronic peritonitis, TNCC is lower with more mononuclear cells (lymphocytes and monocytes) and high phagocytic activity (Dyson, 1983; White and Edwards, 2001).

TNCC can be high without necessarily a life threatening peritonitis concurrently (Schumacher *et al*., 1988). This makes it a challenge to diagnose true clinical peritonitis in postoperative horses (Davis, 2003). It is well documented that post-castration causes an increase in TNCC with samples being highly blood-tinted without the presence of infectious pathogens or clinical presentation of peritonitis. It is explained by the irritation to the peritoneal membrane caused by post-castration bleeding. It's therefore questionable whether abdominocentesis is a useful in the post-castration patient (Schumacher *et al*., 1988). In horses after exploratory laparotomy, there is a documented high concentration of total protein and TNCC in the abdominal fluid for up to six days (Kinsley *et al*., 2010). The value should decline to normal soon after day six and a persistently high or increasing TNCC could indicate a pathological process (Reed *et al*., 2004). TNCC of the peritoneal fluid may be as high as $100x10^9$/l after transcutaneous caecal puncture which may give inaccurate analysis of peritoneal fluid (Unger *et al*., 2014).

2.3.4.4. Cytology

Care must be taken to not contaminate the sample when performing the abdominocentesis (Dyson, 1983), and a high amount of extracellular bacteria should be suspicious of skin contamination (Smith B.P., 2015). Cellular morphology and possible bacteria present can be evaluated using Wright-Giemsa and Gram staining on a microscopy glass slide. Degenerative signs e.g. vacuolisation or nuclear swellings indicate infection. Intraabdominal neoplasia can be diagnosed by the presence of exfoliated cells (Smith B.P., 2015) but transformed mesothelial cells in chronic peritonitis are easily mistaken for neoplastic cells so care must be applied when attempting to identifying the cells (Reed *et al*., 2004). Diagnosis of neoplasia by peritoneal fluid cytology was successful in 11 of 25 cases (Elce, 2006). Negative cytology for neoplastic cells should not rule out neoplasia on its own (Dyson, 1983). Toxic neutrophils in the presence of intracellular and extracellular bacteria suggest rupture of intraabdominal organs (Dyson, 1983). Diagnosis of peritoneal abscesses by peritoneal fluid was successful in 3 out of 15 cases. Intracellular or free bacteria could be a sign of an intraabdominal abscess (Elce, 2006).

Rupture of the stomach along the greater curvature or perforated duodenal ulcers in foals can in some cases be localised in the omental bursa and a mixed flora of extracellular bacteria, but a low TNCC and total protein is detected in the peritoneal fluid sample (Reed *et al*., 2004).

2.3.4.5. Culture and sensitivity

The frequency of obtaining a positive culture result is reported in horses as 9.5-77.8% (Lores *et al.*, 2011; Smith B.P., 2015). Enrichment broth and blood culture are recommended (Smith B.P., 2015). Bruker MALDI biotyper

can be used to identify species (Hepworth-Warren *et al*., 2016).

In 60% of positive cultures of septic peritonitis, a mixed flora is identified (White and Edwards, 2001), the origin is usually the gastrointestinal tract. Gram negative species are the most common isolates (Hepworth-Warren *et al*., 2016) and especially members of *Enterobacteriaceae*. One study found *Escherichia coli* being the most frequently cultured pathogen (Reed *et al*., 2004; Stewart, 2006). Among anaerobes *Bacillus, Clostridium* and *Bacteroides* are common isolates (Davis, 2003) among *Bacteroides fragilis* is the most commonly isolated anaerobic bacterium with a prevalence of 10-20%. It is however difficult to culture (Reed *et al*., 2004; Stewart, 2006).

Interestingly, in human and laboratory animals a relationship has been identified between pathogens (*Bacteroides fragilis* and *Escherichia coli*) in septic peritonitis where by means of selective reduction and synergism an initiating pathogen provides an optimal environment for the pathogens which will dominate the septic process. In horses, it is suspected to exist a similar synergistic relationship involving anaerobes, coliforms, *Streptococcus ssp* and *Corynebacterium pseudotuberculosis* (Reed *et al*., 2004).

2.3.4.6. Miscellaneous diagnostic methods

Septic peritonitis can be diagnosed by comparing glucose concentration in peritoneal fluid and serum. Septic peritoneal fluid has a difference in glucose concentration of more than 50 mg/dl, compared to serum. Septic peritonitis is also diagnosed when the peritoneal fluid pH is less than 7.3, glucose less than 30 mg/dl and fibrinogen more than 200 mg/dl (Smith B.P., 2015). The acidic pH is due to bacterial metabolites and lactate produced in neutrophil glycolysis

(Saulez *et al*., 2004). L- and D-lactate was highest in the peritonitis equine patient compared to other abdominal diseases. However measurement of D-lactate is not yet commercially available (Smith B.P., 2015). Lactate is a fairly labile molecule and assessing the concentration in the peritoneal fluid must be done instantly after sampling. On the other hand lactate dehydrogenase (LDH) is a lot more stable and keeps well in a refrigerated environment for several days. LDH in peritoneal fluid as a prognostic indicator for horses with colic was recently investigated. Three different methods of measurement were compared which gave very different results but showed similar trend. A very high LDH concentration was measured in patients with sepsis and intraabdominal neoplasia, however it could not differentiate between the two patient groups (Smuts *et al*., 2016).

Alkaline phosphatase (ALP) enzyme is increased in peritoneal fluid if there is intestinal damage, however, ALP is found in many tissues other than intestines. To differentiate the intestinal ALP isoenzyme I-phenylalanine is added to the sample. I-phenylalanine inhibits all ALP isoenzymes but the one of intestinal origin (Saulez *et al*., 2004). Tissue growing factor-β3 (TGF-β3) measured in peritoneal fluid of colic horses was the highest in those with peritonitis (Smith B.P., 2015). D-dimer is the product of plasmin mediated degradation of fibrin. An increased concentration in peritoneal fluid correlates significantly with exudative fluid and severe gastrointestinal disorders. In horses with peritonitis, D-dimer was measured at the highest concentration in non-surviving horses (Delgado *et al*., 2009).

Streptococcus equi ssp equi M-protein (SeM) is a virulence factor which inhibits macrophages in the pathogenesis. It can be used for diagnosis by identifying its gene by PCR (Whelchel and Chaffin, 2009).

2.3.5. Complete blood count and biochemistry

Complete blood count (CBC) accompanied by biochemistry should be performed and the results obtained vary with duration and severity of peritonitis (Reed *et al*., 2004) but are often non-specific (Davis, 2003). Increased packed cell volume (PCV) is common (Davis, 2003). Neutropenia in early stages of the peritonitis is followed by neutrophilia which reflects the influx of neutrophils from the intravascular space to the peritoneal cavity that is followed by recruitment from the bone marrow (Mair *et al*., 1990). Endotoxemia will cause neutropenia. In 40% of patients there is a more than 5% left shift. Hyperfibrinogenaemia is common (Smith B.P., 2015). Chronic disease is reflected by increased neutrophil count and monocytosis together with a high plasma protein concentration where a large portion is represented by globulins (Smith B.P., 2015). Where abscesses are present, the chronic parameters are often accompanied by anaemia (Reed *et al*., 2004). Pre-renal azotaemia is the result of fluid shift (hypovolaemia) and low glomerular pressure, with increased blood urea nitrogen and serum creatinine as result (Smith B.P., 2015; White and Edwards, 2001) and electrolyte imbalances such as hyponatraemia, hyperkalaemia and hypochloraemia (Smith B.P., 2015; White and Edwards, 2001). Metabolic acidosis with an increased anion gap is expected with a declining clinical status (Smith B.P., 2015). In the neonatal foal with azotaemia and the same electrolyte imbalances as above, must have uroperitoneum high up on the differential list (Reed *et al*., 2004). Plasma D-dimer was measured the highest concentration in horses with peritonitis and indicates a high activity of disseminated intravascular coagulation (Delgado *et al*., 2009).

2.3.6. Parasitology

When no other identifiable cause of peritonitis is present, parasites should be considered as possible causes. There is some evidence that gastrointestinal transmural migration of strongyles causes damage to the intestines and by compromising the blood supply indirectly causes peritonitis (Dyson, 1983). Verminous arteritis caused by *Strongylus vulgaris* larvae was a prominent lesion in a study by Mair *et al*. (1990). Parasite migration in healthy ponies has documented effect on the peritoneal fluid (Schneider *et al*., 1988), but the presence of eosinophils in peritoneal fluid is not a definitive diagnosis. Peripheral blood eosinophilia is suggestive of parasite infestation, but seasonal variation in eosinophil concentration must be taken into consideration (Dyson, 1983). Worm burden can be investigated by looking at parasitic faecal egg count (FEC), however it does not give any information of parasitic arteritis or visceral larva migrans (Matthews et al., 2001).

2.3.7. Exploratory laparotomy

Surgery is sometimes warranted to diagnose and address the underlying cause of peritonitis (White and Edwards, 2001), however, it must be remembered that peritonitis is an important post-operative complication (Mair *et al*., 1990).

2.3.8. Actinobacillus equuli

Horses diseased with *Actinobacillus equuli* peritonitis have a characteristic set of clinical signs and often no abnormalities detected on palpation per rectum (Mogg and Dykgraaf, 2006). Peritoneal fluid is turbid with a high TNCC and total protein concentration (Matthews et al., 2001; Matthews *et al*., 2002). Peripheral blood CBC and biochemistry results can be varied, but it is not uncommon to have normal leukocyte and neutrophil counts. In 50% of cases, there is

hyperfibrinogenaemia (Mogg and Dykgraaf, 2006). In a study *Actinobacillus equuli* peritonitis was diagnosed not only by positive culture result but also by a set of characteristic clinical signs and rapid response to treatment (Matthews et al., 2001).

2.4. Treatment of peritonitis

Establishing a therapy plan for peritonitis can be a challenge since finding the cause is often difficult (Mair *et al*., 1990). Treatment goals for the equine peritonitis patient should be 1) to eliminate the cause, if identified; 2) to restore fluid and electrolyte balance; 3) to provide adequate analgesia (Dyson, 1983) and 4) to actively prevent the development of complications (Smith B.P., 2015). Aggressive treatment as early as possible in the course of the disease is key factor for success (Reed *et al*., 2004; White and Edwards, 2001). Uncomplicated primary peritonitis often respond well to antimicrobial therapy whereas secondary peritonitis has a favourable response depending on the cause e.g. degree of bacterial contamination. Tertiary peritonitis is difficult to treat and requires long-term therapy (White *et al*., 2008). Treatment should be continued until white blood cells and plasma fibrinogen concentrations are considered normal (Stewart, 2006). CBC and biochemistry is followed up throughout the therapy of the horse. Where heparin is administrated there may be a decline in PCV which is reversed 48 hours after the end of therapy (Davis, 2003).

2.4.1. Antimicrobial therapy

As soon as the abdominocentesis has been performed, antimicrobial therapy should be administered (Smith B.P., 2015; White *et al*., 2008). Antimicrobial therapy which target the most common causative pathogens (White and Edwards, 2001) is started usually before a definite cause is identified

(Hepworth-Warren *et al*., 2016) since a culture result can take several days (Stewart, 2006). Lipophilic drugs such as fluoroquinolones or potentiated sulphonamides (TMS) have a profound penetration of the peritoneal cavity as well as the capsule of an abscess (Davis, 2003; Smith B.P., 2015; White *et al*., 2008). However, during inflammation the diseased peritoneum is penetrable for hydrophilic drugs as well (Smith B.P., 2015) but not necessarily if abscesses or adhesions are present (Davis, 2003). The standard protocol includes beta-lactam antibiotic (potassium-penicillin, 22,000-44,000 IU/kg q6 hrs IV) combined with an aminoglycoside (gentamicin, 6.6 mg/kg q24 hrs IV). The two drugs act synergistically with a broad spectrum. As soon as culture and sensitivity results are back, the antimicrobial therapy should be modified accordingly. Sodium ampicillin has a broader spectrum against gram negative bacteria than penicillin. Most anaerobes are susceptible to penicillin, but the penicillin resistant *Bacteroides fragilis* is frequently isolated, therefore a complement of metronidazole (15 mg/kg q6-8 hrs PO) can be elected (Reed *et al*., 2004). Enrofloxacin can replace gentamicin with the benefit of being more lipophilic and efficient against Staphylococci with less nephrotoxicity compared with gentamicin (Smith B.P., 2015). Enrofloxacin is contraindicated in young horses because of its damaging effect to cartilage during growth and development (Reed *et al*., 2004). In neonatal foals, amikacin is given to cover the most common bacteria of neonatal sepsis (Smith B.P., 2015). In older foals where *Rhodococcus equi* is suspected, a combination of a macrolide with rifampin is indicated. Azithromycin or clarithromycin are good choices of macrolide drugs with broader spectrum and fewer side effects than erythromycin (Davis, 2003; Smith B.P., 2015). *Streptococci* in primary peritonitis respond well to penicillin. *Actinobacillus equuli* responds well to penicillin (Reed *et al*.,

2004), although some resistance has been reported (Matthews *et al*., 2001).

Parenteral antibiotics can be replaced by per oral choices once the gastrointestinal motility is re-established and dehydration is corrected (White *et al*., 2008). The length of antimicrobial treatment depends on response and underlying cause with a minimum of 7 to 10 days. In the presence of intraabdominal abscesses, the treatment may continue for up to 8 weeks (Smith B.P., 2015). TMS has a broad spectrum of activity but is not effective against Streptococci. It is excellent for long-term per oral treatment although resistance is common. Chloramphenicol has a broad spectrum and a bacteriostatic action, therefore it must be prescribed with caution to immunocompromised or endotoxaemic horses (Davis, 2003). Due to its short half-life, it needs to be administered frequently. It is known to cause inappetence in horses and is contraindicated in immunocompromised individuals. Care must be applied when administering chloramphenicol since it causes aplastic anaemia in humans (White *et al*., 2008). Rifampin has a good penetration of abscesses when combined with macrolides. Doxycycline has a broad spectrum (Reed *et al*., 2004) and anti-inflammatory properties.

2.4.2. Anti-inflammatory and endotoxaemia therapy

Nonsteroidal anti-inflammatory drugs (NSAIDs) should be administered regardless of cause since they counteract inflammation and provide analgesia. Flunixin meglumine is the drug of choice (1 mg/kg IV q12 hrs) with sufficient analgesia, and if administered in the acute stage, it can reduce adhesions. It targets endotoxaemia when administered at a lower dose (0.25 mg/kg IV q6-10 hrs) (Reed *et al*., 2004). Flunixin meglumine can be replaced by phenylbutazone (2.2-

4.4 mg/kg IV or PO q12 hrs) or COX-2 inhibitors such as etodolac (Davis, 2003) or firocoxib (Smith B.P., 2015). A study revealed anti-inflammatory characteristics of lidocaine (Smith B.P., 2015). Dimethyl sulfoxide (DMSO) is a free radical scavenger with anti-inflammatory properties (0.1-1 g/kg IV q12-24 hrs) (Davis, 2003) Antibodies in hyperimmune plasma bind and neutralise endotoxins. Polymyxin B (2000-6000 IU/kg in 1 l 0.9% NaCl q12 hrs) successfully binds endotoxin, but the potential nephrotoxicity must be carefully monitored (Reed *et al*., 2004) and the drug is contraindicated in case of azotaemia (Davis, 2003).

2.4.3. Fluid therapy

Dehydration is a common clinical finding in the horse with peritonitis where fluid shift of large volumes into the peritoneal cavity is accompanied by pre-renal azotaemia, hypoproteinaemia and electrolyte disturbances. Absorbed bacterial endotoxins combined with an imbalance in acid-bases and electrolytes decrease the cardiac output and impair the circulation (Kahn, 2010). The horse has to be hydrated before abdominal lavage and drainage is performed (Davis, 2003). Addressing circulatory imbalances must be regarded as equally important as treating the initiating cause of peritonitis (Hepworth-Warren *et al*., 2016)

With concurrent ileus, oral fluids are contraindicated. Intravenous polyionic crystalloid fluids are generally used (Smith B.P., 2015; White *et al*., 2008) at twice the maintenance dose to correct the fluid imbalance. Severe hypovolaemic shock may require hypertonic saline (4 ml/kg) as well (Smith B.P., 2015; White *et al*., 2008). Once the horse is resuscitated it can be continued on maintenance dose until it starts to drink (White *et al*., 2008). In severe peritoneal influx of plasma proteins, fluids which can

increase the plasma oncotic pressure is indicated. Hydroxyethyl starch (HES) 6% or hyperimmune plasma can be used. Plasma is more expensive than HES but has the benefit of containing proteins as well as (Davis, 2003) the ability to counteract endotoxaemia (Smith B.P., 2015). In a case study describing peritonitis caused by *Clostridium haemolyticum*, there was an immediate marked improvement after low molecular weight tetra-starch (TES) was administered (Hepworth-Warren *et al*., 2016). Electrolytes must be closely monitored and administration of parenteral (Smith B.P., 2015) potassium (20-40 mEq/l) and/or calcium gluconate may be necessary (White *et al*., 2008). Enteral electrolytes can also be administered, but where there is concurrent ileus, oral fluids are contraindicated. Positive energy and nitrogen balance should be maintained during hospitalisation (Dyson, 1983) and parenteral nutrition should be considered (Davis, 2003).

2.4.4. Anthelmintic therapy

Anthelmintic therapy is indicated if the underlying cause of peritonitis is suspected to be of parasitic origin, especially if there is an unknown or poor history of anthelmintic management (Smith B.P., 2015).

2.4.5. Abdominal drainage and lavage

Performing abdominal lavage and placement of an abdominal drain can be done under standing sedation or during general anaesthesia. Methods have been described in literature (Corley and Stephen, 2008; Davis, 2003; Eggleston and Mueller, 2003). It is thought to serve best when applied in the acute, diffuse peritonitis phase of the pathogenesis (Reed *et al*., 2004). Drainage on its own is considered insufficient and should be combined with lavage (Davis, 2003).

Abdominal lavage removes debris and prevents a persistent inflammation (Reed *et al*., 2004) by removing inflammatory mediators, bacteria and its metabolites (Dyson, 1983; Smith B.P., 2015). By infusing large volumes of fluid, the benefit is believed to mechanically separate serosal surfaces, thus prevent adhesions to form. It was described to reduce adhesions postoperatively in a study (Eggleston and Mueller, 2003). Abdominal lavage and drainage is indicated for a surgical case when TNCC of the peritoneal fluid is more than $100x10^{9/}$l (Davis, 2003; Smith B.P., 2015). The benefits of abdominal lavage are controversial and the possibility of iatrogenic introduction of a pathogen should be carefully considered when electing the therapy (Stewart, 2006). Performing abdominal lavage in the case of primary peritonitis is thought to be of little therapeutic value (White *et al*., 2008), but in suspected cases of gastrointestinal perforation it is definitely a crucial therapy along with exploratory laparotomy (Davis, 2003). Sterile polyionic warm fluids with a neutral pH should be used. Up to 20 litres can be infused, but some abdominal discomfort is to expect due to pressure and stretching of the parietal peritoneum (White *et al*., 2008). Due to the large size of the equine abdomen, directing the fluid during lavage is difficult (Dyson, 1983). Infusion into the drain followed by a short period of walking with the drain clamped (Kinsley *et al*., 2010). The lavage can be performed up to twice daily for 5 days. The aim is to obtain clear fluid (White *et al*., 2008). Successful lavage should decrease the TNCC and total protein concentration, like a declining inflammation would present (Reed *et al*., 2004). Samples can be sent for cytology and compared, but note must be taken that there is a slight inflammation reaction towards the drain and lavage itself (White *et al*., 2008).

When inserting a drain after abdominal surgery, it is important to place it at a different location to the incisional wound. It should be placed to the right and as far cranial as possible to prevent access by the omentum which has the tendency to clog the drain (White *et al*., 2008). Open peritoneal drainage is used successfully in human patients and benefits are the removal of debris and decreased adhesion formation. In an experimental model in dogs using open peritoneal drain there was a rapid clinical improvement documented, and in rabbits the survival rate increased from 15% to 60%. Due to the practical and anatomical obstacles encountered in the horse this method of peritoneal drainage was considered impossible. However in an experimental study where a plastic mesh was sutured to the ventral aspect of the abdomen no herniation was detected but all subjects developed incisional infection (Chase *et al*., 1996).

Complications of abdominal drainage and lavage include ascending infection, enterocentesis, herniation and cutaneous oedema. In a study, 47% developed minor complications and the incidence of incisional infection was 32%, compared to 23.5% in the control group. (Smith B.P., 2015).

The use of isotonic lavage fluids prevents creating an osmotic gradients and further fluid loss (White *et al*., 2008). Lavage should be performed after fluid resuscitation is complete (Reed *et al*., 2004) and hydration as well as electrolyte status and protein concentrations must be monitored throughout the lavage (Smith B.P., 2015). Heparin can be added with a concentration of 30,000-50,000 IU/l lactated Ringers solution (Eggleston and Mueller, 2003). Intraabdominal antimicrobials have not been proven to be of superior benefit (Stewart, 2006). There is little information on antimicrobial concentrations in the peritoneal cavity (Dyson, 1983). The effect of different lavage solutions on a clinically healthy

peritoneum was investigated by Schneider *et al*. (1988). Four groups of ponies received peritoneal lavages of a volume of 10 litre each. Infusion using normal saline (0.9% NaCl) as well as normal saline with addition of potassium penicillin ($5x10^6$ U) and neomycin sulphate (3 g) showed no significant findings on necropsy. Povidone-iodine of 3% and 10% had an irritating and direct toxic effect to the peritoneal membrane with a less severe to severe diffuse, fibrinous peritonitis on necropsy. Throughout the lavage therapy total protein, PCV and electrolytes must be closely assessed (Davis, 2003).

2.4.6. Surgery

Performing exploratory laparotomy gives a good visual examination of the peritoneal cavity and the possibility to directly correct any identified causes of peritonitis. During surgery, it is also possible to perform a thorough abdominal lavage and placement of a drain through which fluid and debris can evacuate post-operatively. A retrospective study found that of those cases of peritonitis with no clinical abnormalities survived to discharge without surgery whilst those with more severe signs of abdominal pain and absent borborygmi were less likely to survive to discharge without surgical intervention (Southwood and Russel, 2007). Using peritoneal fluid colour characteristics can be useful when deciding whether the equine patient needs surgery. Colour and total protein was more predictable than TNCC in a study. Interestingly, medical cases were identified with a higher accuracy compared to identifying those horses that needed surgery, with the exception of when the colour was serosanguinous (Matthews et al., 2002). To treat or find out the cause of peritonitis surgery may be an option. Under general anaesthesia intraabdominal abscesses can be located and drained (Smith B.P., 2015).

2.4.7. Prevention of complications

Complications are commonly encountered and their prevention can have an impact on outcome (Smith B.P., 2015).

2.4.7.1 Adhesions

Adhesions are a frequent cause of repeat laparotomy and a source of pain and intestinal obstruction (Delgado *et al*., 2009). The mesothelial cells of the peritoneum initiate and resolve peritonitis by excreting pro-coagulant and fibrinolytic molecules (Delgado *et al*., 2009). Under physiological conditions fibrinous adhesions start form within 1 hour after onset of peritonitis and should be resolved after 48-72 hours. However, in the absence of adequate fibrinolytic activity the fibrinous adhesions mature to tough and permanent fibrous structures by the deposition of collagen (Delgado *et al*., 2009; Eggleston and Mueller, 2003). There is a speculated genetic predisposition to adhesion formation in humans (Delling *et al*., 2012). The frequency of which adhesions occur is not easy to estimate since many cases are subclinical and few necropsies are performed. Disease involving the small intestine is highly associated with adhesions because the serosa seems to be more sensitive to insult as well as being attached to the abdominal wall by the long mesentery, giving it the length and mobility to adhere to awkward abdominal locations (Southwood and Baxter, 1997). To assess the risk for adhesion development, peritoneal D-dimer concentration can be useful (Delgado *et al*., 2009). The fibrinolytic system regulates adhesion formation and involves several components working in a cascade-like system. Tissue plasminogen activator (tPA) and urokinase or urinary plasminogen activator (uPA) activate plasminogen to become the active plasmin (Eggleston and Mueller, 2003) which

breaks down fibrin to fibrin degradation products (FDP) and D-dimer. Plasmin also breaks down fibrinogen to FDP (Delgado *et al*., 2009). This chain of reaction is regulated by plasmin activator inhibitors 1 and 2 (PAI-1, PAI-2) which are activated by e.g. endotoxins or trauma. Plasmin is regulated negatively by α2-antiplasmin, α2-macroglobulin and α2-antitrypsin. A decreased activity of plasmin is either because of a low concentration of tPA and uPA or a high concentration of inhibitors (Eggleston and Mueller, 2003).

Prophylactic treatment of adhesion formation is one of several goals of the treatment plan for the horse with peritonitis. Prevention rather than treating already formed adhesions is regarded a superior approach (Southwood and Baxter, 1997). There is no gold standard treatment but the general goals are to reduce inflammation, increase the activity of the fibrinolytic system, stimulate gastrointestinal motility and provide mechanical separation of serosal surfaces (Eggleston and Mueller, 2003).

Systemic antimicrobial treatment and anti-inflammatory drugs such as dimethyl sulfoxide (DMSO) and flunixin meglumine have been advocated to reduce adhesion formation indirectly by target inflammation and infection (Smith B.P., 2015). Abdominal lavage, previously described in detail, reduce adhesion formation. There are several possible additives to the lavage solution. 1% sodium carboxymethylcellulose used intraoperatively in a study was highly effective in increasing survival rate (Smith B.P., 2015). Addition of heparin (20-40 U/kg) is administered in the lavage fluid or by subcutaneous injection. PCV must be monitored throughout the heparin administration since it causes reversible precipitous drops by rouleaux formation of the red blood cells (Davis, 2003). Recombinant tPA added to 0.4% sodium hyaluronate is, although expensive, efficient in

preventing adhesions (Smith B.P., 2015). Frequent rectal manipulation has been described to prevent ad novo adhesions to develop. Once adhesions have been formed, standing hand-assisted laparoscopic adhesiolysis has been done in horses. In experimental human surgery, laparoscopic adhesiolysis has shown to be superior when compared to open surgery. Not all adhesions are subject to adhesiolysis, the level of maturation and associated vasculature must be taken into consideration (Delling *et al*., 2012). Omentectomy, although controversial, has been described to decrease clinically relevant adhesions by providing vascularisation to damaged tissue. A significant side effect seen was abdominal pain brought on by traction and tension as well as creating potential spaces for entrapment and strangulations (Eggleston and Mueller, 2003). Different protective tissue-coating solutions can be used. Bioresorbable hyaluronate-carboxymethylcellulose membrane (Seprafilm®) has proved effective and is applied intraoperatively over damaged serosa, providing protection for a week before cleared by macrophages (Eggleston and Mueller, 2003). There are materials and methods used in human surgery and medicine which have potential application for the equine patient. A polyethylene glycol ester spray has successfully been used in humans intraoperatively by application to serosa, giving 7 days protection before adsorbed by hydrolysis (Delling *et al*., 2012).

Systemic heparin for up to 72 hours has been reported to reduce adhesion formation (Smith B.P., 2015). Heparin is contraindicated in cases of peritonitis in association with intraabdominal haemorrhage e.g. post-partum for the risk of re-bleeding (Mogg *et al*. 2006). It does not seem to be necessary in peritonitis caused by Actinobacillus equuli (Stewart, 2006). There are a range of dosages described

(Mogg and Dykgraaf, 2006; Reed *et al*., 2004). It causes red blood cell aggregation which can have an effect on capillary perfusion (Reed *et al*., 2004).

2.4.7.2. Other complications

In the presence of ileus, gastric decompression must be performed. Efforts should be made to restore gastrointestinal motility by administering prokinetics. Lidocaine (1.3 mg/kg) bolus and continued thereafter (0.05 mg/kg/min) until borborygmi returns. Erythromycin lactobionate given as bolus (0.5-2 mg/kg) every 12 hours or metoclopramide (0.25 mg/kg/h) given over an hour's time can also be used for the same goal (Davis, 2003).

Caution should be taken when NSAIDs and aminoglycosides are administered since they can have nephrotoxic side effects (Stewart, 2006). Amikacin has lower nephrotoxicity compared to gentamicin and could be an adequate replacement (Smith B.P., 2015).

Prophylactic measures for laminitis are hoof support and NSAID therapy accompanied by aggressive restoration of fluids and an effort to combat endotoxaemia (White *et al*., 2008). Although the risk of laminitis is strongly associated with peritonitis, a study of 55 cases with peritonitis had no case of laminitis recorded in complications (Nógrádi *et al*., 2011).

2.4.8. Treatment of Actinobacillus equuli

Peritonitis caused by *Actinobacillus equuli* has an excellent response to treatment (Matthews *et al.,* 2001). Although being a Gram negative bacterium it has got a sensitivity pattern similar to Gram positive bacteria (Stewart, 2006). Therapy using penicillin has been documented to have a 90-100% response (Matthews *et al*., 2001; Mogg and Dykgraaf,

2006), with some resistance reported (Matthews *et al*., 2001). In the case of resistance or other factors preventing using the standard treatment there is also good response to ampicillin, gentamicin, tetracycline and TMS (Stewart, 2006). Larvacidal anthelmintic treatment is advocated because of the suspicion of *Strongylus vulgaris* playing a central role in the aetiology (Matthews et al., 2001). With appropriate treatment, clinical signs should cease within 48 hours (Matthews et al., 2001; Mogg and Dykgraaf, 2006), but treatment is required for between 5 days to 4 weeks (Matthews et al., 2001).

2.5. Prognosis and outcome

2.5.1. Prognosis

The prognosis depend on eliciting the cause and response to therapy (Lores *et al.*, 2011; Smith B.P., 2015); complications, hydration and surgery (Nógrádi *et al*., 2011). Prompt and early treatment of acute septic peritonitis has a fair to good prognosis (Smith B.P., 2015). Diarrhoea has been suggested to indicate a poor prognosis (Dyson, 1983). Presence of bacteria in the peritoneal fluid suggests damage to the gastrointestinal organs and a guarded to poor prognosis although there are controversial results in some studies (Nógrádi *et al*., 2011). Transmural leakage of bacteria must be differentiated from peritonitis caused by *Actinobacillus equuli* which may appear similar but has a different prognosis and response to therapy (Matthews *et al*., 2001).

Fibrinogen concentration in peripheral blood is a good tool to monitor response to therapy (Mair *et al*., 1990) and abdominal ultrasound and CBC are useful to monitor progress (Smith B.P., 2015). In human medicine, prognosis and response to treatment is assessed by activated C protein and pro-calcitonin levels in blood. It is possible to use

commercially available assays and dip sticks, making it a promising future diagnostic tool in equine medicine (Elce, 2006). It has been suggested that monitoring peritoneal cytokines e.g. TNFα and IL-6 to determine normal versus abnormal levels could be a potential future aid in determining the prognosis of peritonitis (Elce, 2006).

2.5.2. Outcome

The outcome of peritonitis depends heavily on the cause (Hepworth-Warren *et al*., 2016). The short-term survival rate varies among different studies, from 53% to 86% (Henderson *et al*., 2008). Peritonitis of idiopathic origin was highly associated with good short-term survival (94%) as well as long-term survival (84%) (Henderson *et al*., 2008). However, several retrospective studies have excluded cases with peritonitis where there is a history of abdominal surgery or castration (Dyson, 1983; Henderson *et al*., 2008; Southwood and Russel, 2007); cases of peritonitis where surgery was indicated (Dyson, 1983; Mair *et al*., 1990), gastrointestinal rupture (Dyson, 1983; Mair *et al*., 1990; Southwood and Russel, 2007), foals (Mair *et al*., 1990; Nógrádi *et al*., 2011), iatrogenic causes or neoplasia (Mair *et al*., 1990) and this must be taken into consideration when interpreting survival rates in literature. Peritonitis caused by perforation or rupture of the bowel is usually fatal (Lores *et al.*, 2011). Peritonitis caused by *Actinobacillus equuli* has a documented survival rate of 100% (Hepworth-Warren *et al*., 2016). However two documented cases in the United States of America died, a considered atypical outcome (Mogg and Dykgraaf, 2006). Peritonitis caused by urinary tract infections has a documented poor outcome (Lores *et al.*, 2011). Presence of complications may reduce survival (Lores *et al.*, 2011). In one retrospective study by Nógrádi *et al*., (2011)

complications were more frequent in non-survivals compared to survivals.

Using clinical variables to predict outcome has been investigated in several studies. In one study variables associated with the function of the circulatory system seem to be closely associated with outcome (Matthews *et al*., 2002). No gastric reflux was associated with a significantly increased survival in one retrospective study (Southwood and Russel, 2007). Horses with signs of abdominal pain on presentation had a reduced survival rate to less than 50% (Elce, 2006). Plasma D-dimer can be useful in predicting the outcome (Delgado *et al*., 2009). However, in another study of outcome in 65 horses with peritonitis, using clinical variables to predict outcome had no statistical significance (Henderson *et al*., 2008).

Peritonitis caused by *Actinobacillus equuli* has excellent long-term prognosis (Matthews et al., 2001; Mogg and Dykgraaf, 2006; Smith B.P., 2015).

3. Materials and methods

3.1. Selection criteria

There were 102 patient records collected at Evidensia Strömsholm Equine Referral Hospital. The selection was based on the official diagnosis in the database, which was either stated as peritonitis or acute purulent peritonitis. Foals were excluded because of the difference in clinical parameters, to make data analysis easier. Patient records were excluded if the reason for previous admission was unclear i.e. there was a lack of previous medical history. There were overall 18 patient files excluded which left 84 cases in total.

3.2. Data collection

The collected identification data included age, breed and gender. Number of days admitted and number of referral cases were recorded.

Included in the anamnesis was duration of clinical signs, reproductive history, history of any previous condition, recent change of environment, feeding or other; symptoms and findings prior to referral, treatments given prior to referral and response to therapy.

Status praesens at admission was recorded as follows: rectal temperature in degrees Celsius (˚C) and grouped as normal (37.5-38.5 ˚C), mild pyrexia (38.6-39.1˚C), moderate pyrexia (39.2-39.7˚C) and severe pyrexia (>39.8˚C). Heart rate was recorded as beats per minute (bpm) and grouped as normal (28-40 bpm), mild tachycardia (41-59 bpm), moderate tachycardia (60-70 bpm) and severe tachycardia (>70 bpm). Intestinal borborygmi was recorded as normal, decreased or absent. The colour of the mucous membranes was recorded as normal or abnormal and moisture as dry, tacky or moist. Capillary refill time (seconds, sec) was recorded as normal

(<2 sec) or abnormal (>2 sec). Any other relevant clinical findings and comments were recorded as well. The changes of rectal temperature (normal, improving, worsened, fluctuating, persistent pyrexia), heart rate (normal, improving, tachycardia) and intestinal borborygmi (normal, improving, decreasing, persistently decreased compared to normal) during the time of hospitalisation was recorded.

For the haematology the first or initial values were recorded. The parameters recorded were packed cell volume (PCV; %), leucocytes ($x10^9$/l) and fibrinogen (g/l). PCV was classified as normal (29-46%), high (>46%) or low (<29%); leucocytes were classified as normal (5.4-14.3$x10^9$/l), leukopenia (<5.4$x10^9$/l) or leucocytosis (>14.3$x10^9$/l). Fibrinogen was recorded as normal (1.3-2.4g/l), high (>2.4g/l) or low (<1.3g/l).

The initial or first abdominocentesis was recorded for its colour, turbidity, Total nucleated cell count (TNCC; $x10^9$/l) and total protein value (g/l) using refractometer. Taken the total number of abdominocentesis in regard, the culture result (positive or negative) was recorded.

Additional examinations included examination per rectum, nasogastric decompression and abdominal ultrasonography. Treatment recorded included abdominal lavage, antimicrobial therapy, nonsteroidal anti-inflammatory drugs (NSAIDs) and fluid therapy.

Moreover data of surgical exploration, complications, post mortem findings and outcome were collected. The outcome as recorded as survival or non-survival. Survival was defined as survival until discharge. Non-survival was defined as destruction by euthanasia or spontaneous death.

3.3 Data analysis

Statistical analysis was performed by using commercially available software (Microsoft Excel 2013 and SPSS 16.0). The analysis comprised descriptive statistics, tests for normality, two-sample t-tests, Mann-Whitney U tests, Chi-square tests and Fisher's exact tests. The mean ± standard deviation or standard error of the mean was used to describe normally distributed data, and the median ± interquartile range was calculated for not normally distributed variables. Normality was assessed using the Shapiro-Wilk statistic. Two-sample t-test was used when data were normally distributed (age, rectal temperature at admission and total protein concentration of peritoneal fluid), and Mann-Whitney U test was used when data were not normally distributed (duration of clinical signs before admission, rectal temperature before admission, heart rate at admission, PCV at admission, white blood cell count at admission, fibrinogen concentration in blood at admission, TNCC in peritoneal fluid at admission, and length of hospitalisation). Chi-square test or Fisher's exact test were used for categorical variables such as sex, breed, surgery (yes or no), abdominal ultrasonography (normal or abnormal findings), peritoneal fluid culture (negative or positive), presence of intracellular bacteria in cytological smear (yes or no), and occurrence of complications (yes or no). A significance level of $P<0.05$ was assumed. The above parameters were compared between survivor and non-survivor groups.

4. Results and discussion

4.1. Results

4.1.1. Identification

The age varied from one to 30 years, the mean age was 11.44 years. There was no statistically significant difference between survivors and non-survivors (P=0,426).

The gender distribution was 41 (48.81%) mares, five (5.95%) stallions and 38 (45.24%) geldings. There was no statistically significant association between gender and survival (P=0,065).

There were 19 breeds recorded. 20 (23.81%) Icelandic ponies, 10 (11.90%) Swedish warmbloods, 13 (15.48%) Warmbloods, seven (8.33%) Standardbreds, three (3.57%) New Forest ponies, three (3.57%) Northern Swedish horses, three (3.57%) Fjords, two (2.38%) Arabian horses, one (1.19%) Welsh mountain pony, one (1.19%) Welsh pony, one (1.19%) Welsh cob, one (1.19%) Irish cob, one (1.19%) Morgan horse, one (1.19%) Quarter horse, one (1.19%) Connemara pony, one (1.19%) Shetland pony and one (1.19%) Mini Shetland pony. 10 (11.90%) horses were of undefined breed. There was no statistically significant association between breed and survival (P=0,126).

4.1.2. Hospitalisation

The number of days admitted to the hospital varied between one and 22 days. Non-survivors were admitted for a significantly shorter period of time when compared to survivors (P<0,001), see Table 2.

4.1.3. Referral

Of the 84 horses, 57 (67.86%) were referred to Evidensia Strömsholm Equine Referral Hospital by an external

veterinarian. The non-survivors were more frequently referred (17/23; 73.91%) compared to the survivors (40/61; 65.57%).

4.1.4. Anamnesis

Duration of clinical signs prior to admission varied between 0.5 to 30 days with a mean of 3.65 days overall. There was no statistically significant difference between the survivors and non-survivors (P=0,063).

Of the mares, five (12.20%) of them had history of parturition within the last three months of which two had experienced dystocia and one had retained foetal membranes. 16 (19.05%) horses had history of previous colic, four (4.76%) horses had history of surgery and nine (10.71%) horses had history of other conditions. Five (5.95%) horses had a recent change in their environment, three (3.57%) horses had recent change in feed and one (1.19%) had recent change of other nature.

Symptoms had appeared in one mare after mating. In one horse the symptoms appeared after the girth had been pulled and in another horse the symptoms appeared three hours after administration of anthelmintic treatment. One horse had suffered a recent traumatic injury to the abdomen by a hay fork. One gelding had a history of scrotal effusion.

The symptoms claimed by the owner are summarised in Table 1. Pyrexia (71.43%) was the most common clinical sign observed with the mean of 39.59 ˚C. Non-survivors had a significantly higher rectal temperature (P<0,001). The second most common clinical sign was colic (60.71%) followed by reduced appetite (58.33%) and depression (51.19%). 18 (21.43%) horses were tachycardic with a heart rate ranging from 42 to 100 beats per minute (bpm), the mean was 67.41 bpm. Rectal palpation was performed by the

referring veterinarian in 36 (42.86%) cases and abnormal findings were recorded in 23 (63.88%) of them.

Prior to referral, 11 (13.10%) horses received spasmolytic drugs, 54 (64.29%) horses received nonsteroidal anti-inflammatory drugs (NSAIDs) and two (2.38%) horses received corticosteroid drugs. Five (5.95%) horses received alpha-2 agonist drugs, four (4.76%) received opioid drugs and four (4.76%) received non-specific analgesic drugs. 21 (25%) horses received antimicrobial treatment. 10 (11.90%) horses received per oral fluids and 10 (11.90%) horses received parenteral fluid therapy. 15 horses had information on response to treatment, seven of them (46.66%) were noted to respond to the therapy administrated whereas the remaining eight (53.33%) horses were noted to have poor or no response to therapy.

4.1.5. Physical examination

Rectal temperature, heart rate, intestinal borborygmi, mucous membrane characteristics and capillary refill time recorded at admission are summarised in Table 3. Other clinical signs recorded on admission are found in Table 4. Changes in heart rate, rectal temperature and intestinal borborygmi over the time of hospitalisation are summarised in Table 5. A statistically significant higher rectal temperature (P=0,016) was seen in non-survivors (mean 38,8062; SD 0,89701) when compared to survivors (mean 38,169; SD 0,62606) Heart rate was significantly (P<0,001) higher in non-survivors, see Table 2.

4.1.6. Additional examinations

In 73 (86.90%) of the cases, examination per rectum was performed. No abnormalities were detected (NAD) in 33 (45.21%) cases. In 40 (54.79%) cases an abnormal finding was recorded. In 15 (20.55%) horses pain was elicited when

palpating. A nasogastric tube was passed in 33 (39.29%) horses, of which six (18.18%) were reflux positive. Abdominal ultrasonography was used in 34 (40.48%) horses and there were NAD in 15 (44.12%) cases and in 19 (55.88%) cases some form of abnormal finding was recorded. Findings on abdominal ultrasound was not statistically significant for survival (P=0,075).

4.1.7. Haematology

The initial packed cell volume (PCV) was measured in 72 (85.71%) cases and 50 (70.42%) were classified as normal, eight (11.27%) were considered high and 14 (19.72%) were considered low. The mean PCV was 34.7%. There was no statistically significant difference in PCV value between survival and non-survival groups (P=0,072). Overall, blood leucocyte values were recorded in 56 cases with a mean value of $7.94x10^9$/l. 28 of these horses (50%) were classified as normal, 21 (37.5%) had leukopenia and seven (12.5%) had leukocytosis. There was a statistically significant difference between survivors and non-survivors (P=0,011) where non-survivors had a lower leucocyte count. Non-survivors had a significantly higher fibrinogen level compared to survivors (P=0,032). All haematological data as well as the distribution in the survival and non-survival groups are presented in Table 6.

4.1.8. Abdominocentesis

Abdominocentesis was performed on 80 (95.24%) horses on admission or within the first day of hospitalisation. 65 (81.25%) of the fluid samples were turbid before centrifugation. The colour of the fluid was yellow (37/72; 51.38%), orange (28/72; 38.88%), bloody (10/72; 13.88%) or brown (3/72; 4.16%). The mean total protein value was 42.60 g/l. When classified into categories according to values,

12.33% (9/73) had total protein of less than 25 g/l; 65.75% (48/73) had values between 25 and 50 g/l; 24.66% (18/73) had values between 50 and 100 g/l. There was no statistically significant difference in total protein between survivors and non-survivors (P=0,14). Overall, 94.37% (67/71) of the samples had a total nucleated cell count (TNCC) of higher than $10x10^9$/l. The mean value of TNCC was $179.53x10^9$/l and when classified into categories according to values 5.63% (4/71) were less than $10x10^9$/l; 29.58% (21/71) were between 10 and $100x10^9$/l; 23.94% (17/71) were between 101 and $200x10^9$/l; 22.54% (16/71) were between 201 and $300x10^9$/l and 18.31% (13/71) were more than $300x10^9$/l. Non-survivors had a significantly higher TNCC compared to survivors (P=0,019).

Overall abdominocentesis was performed 159 times, 1.89 times per horse. Extracellular and intracellular bacteria were visualised on cytology in two (1.26%) and 14 (8.81%) of samples, respectively. There was a statistically significant association between bacteria seen in smear and survival (P=<0,001). Culture was done on 85 (53.46%) samples. There were 30 (35.29%) positive and 55 (64.71%) negative cultures. There was no statistically significant association between culture result and survival (P=0,667). Where intracellularly located bacteria were detected on cytology 14.29% (2/14) cultures were negative. The cultured bacteria were *Actinobacillus equuli* (7/30; 23.33%), *Staphylococcus* (1/30, 3.33%), *Staphylococcus albus* (4/30, 13.33%), *Staphylococcus saphrophyticus* (2/30; 6.66%), *Staphylococcus aureus* (1/30; 3.33%), alpha-haemolytic *Streptococcus* (1/30; 3.33%), beta-haemolytic *Streptococcus* (1/30; 3.33%), beta-haemolytic *Streptococcus* group C (4/30; 13.33%), beta-haemolytic *Streptococcus equi ssp zooepidemicus* (1/30; 3.33%), *Escherichia coli* (6/30; 20%),

Enterobacter (2/30; 6.66%), *Enterococcus* (2/30; 6.66%), gram negative rod (2/30; 6.66%) and mixed flora (1/30; 3.33%). The distribution in the survival and non-survival groups is presented in Table 7.

In 16 (20%) horses where abdominocentesis was performed on admission or within the first day of hospitalisation, antimicrobial drugs had been administered by referring veterinarians prior to abdominocentesis and culture. Three (18.75%) samples had intracellular bacteria visualised on cytology; 8 (50%) horses had a negative culture result and eight (50%) horses had a positive culture result.

4.1.9. Complications

Complications were most common in the non-survival group (5/23; 21.74%) compared to the survival group (11/61; 18.03%). Swelling at or thrombophlebitis of the jugular vein, at the site of the intravenous catheter, was the most common complication (12/84; 14.29%). Other complications included hyperglycaemia (1/84; 1.19%), penicillin anaphylaxis (2/84; 2.38%) and reaction at the site of abdominocentesis (1/84; 1.19%). No horse developed laminitis. There was no statistically significant association between complications and survival (P=0,758).

4.1.10. Treatment

Abdominal lavage was performed in two (2.38%) horses. One was performed under standing sedation and the other under general anaesthesia. Indwelling abdominal drain was placed in both cases. Lavage was performed between two and three days, mean 2.5 days.

Antimicrobial therapy was administered as follows: penicillin (77/84; 91.66%), gentamicin (75/84; 89.29%), metronidazole

(18/84; 21.43%), trimethoprim and sulfadiazine combination (35/84; 41.66%) and polymyxin B (12/84; 14.29%).

Of the NSAID's administered, flunixin meglumine (75/84; 89.29%) was most frequently used followed by metamizole (10/84; 11.90%) and meloxicam (1/84; 1.19%).

Regarding fluid therapy, 12 (14,.9%) horses received per oral fluids and 56 (66.66%) received parenteral fluid therapy. Ringer acetate was the most common fluid used (53/56; 94.64%). Hypertonic saline (2/84; 2.38%), colloids (4/84; 4.76%) and hyperimmune plasma (3/84; 3.57%) was used less frequently. Potassium was supplemented in two (2.38%) horses and calcium was supplemented in one (1.19%) horse.

Enteral nutrition was administered to two (2.38%) horses.

4.1.11. Surgical exploration

A total of eight (9.52%) horses had exploratory laparotomy performed. The findings were abnormality of the reproductive organs (4/8; 50%), free pathological fluid (2/8; 25%), peritonitis (3/8; 37.5%), suspected hepatic neoplasia (1/8; 12.5%) and a mass (1/8; 12.5%). Four (50%) of the horses were euthanized on the table due to poor prognosis and four (50%) survived to recovery. Two (25%) horses died after recovery but before discharge and two (25%) survived in total. There was statistically significant association between surgical intervention and survival (P=0,005).

4.1.12. Post mortem findings

Post mortem examination was performed on three (13.04%) of the non-survivors. The findings are summarised in Table 8.

4.1.13. Outcome

There were 61 (72.62%) horses in the survival group. In the non-survival group there were 23 (27.38%) individuals. 22 of the non-survivors were euthanized for reasons ranging from poor prognosis to financial restraints; one horse died spontaneously.

The horses that underwent surgery had mortality of 75% (6/8) and survival rate of 25% (2/8) whereas those that did not have surgery had a mortality of 22.37% (17/76) and a survival rate of 77.63% (59/76).

4.2. Discussion

Peritonitis is not a very common condition of horses, being reported as the cause of 9% of colic overall; 16% of chronic colic cases and 0.7% of exploratory laparotomies (Southwood and Russel, 2007). The frequency of which peritonitis occurred as a diagnosis overall at this particular equine hospital is not recorded, but could have been of interest. Because of the method of case selection, there is a possibility that surgical cases with peritonitis as complication were rejected by the computer system. Another method of data search in the record selection could have been a useful complement and would probably have increased the number of cases included in the study.

Survivors were observed to be admitted for more days compared to the non-survivors. A reason for shorter time of hospitalisation for the non-survivors were in a couple of cases lack of financial resources, hence euthanasia was elected. The poorer clinical state of the non-survivors at time of admission, coupled with longer duration of clinical signs prior to admission also could explain the shorter time of hospitalisation in the non-survival group.

According to the anamnesis, no horse had peritonitis recorded as a previous condition. Less than a fifth of the horses had history of colic and less than 5% had history of previous surgery. As mentioned previously, the latter could be due to selection error in the computer system. Events involving parturition and breeding accidents have been described to cause peritonitis (McMaster *et al*., 2015) and such events were noted in the history of over 10% of mares in this study. One peculiar case was reported of a horse being impaled through the external abdominal wall by a hay fork, causing peritonitis. Although rare, penetration of external foreign bodies causing peritonitis has been described in literature (Lohmann *et al.,* 2010).

In a retrospective study of 21 horses by Mair et al. (1990), colic was the most frequent reason for referral which agrees with the results in this study. Pyrexia, reduced appetite and depression were also very common symptoms reported in the anamnesis in this study.

Pyrexia and ileus are frequent clinical signs with peritonitis (Dyson, 1983). In this study on admission horses in both survival and non-survival groups presented frequently with decreased borborygmi and mild to severe tachycardia. However, there was a significantly higher heart rate and rectal temperature among the non-surviving horses. Interestingly, most horses in this study had received NSAIDs prior to admission by an external veterinarian. The antipyretic properties of NSAIDs could mask underlying pyrexia in some horses.

In a retrospective study performed in Australia by Matthews *et al*. (2001) horses that were diagnosed with *Actinobacillus equuli* presented a characteristic set of clinical signs. Depression with mild to moderate increase in heart and

respiratory rate accompanied by abdominal pain (splinted, or "guarded", abdomen) was typical. In this study 85.71% (6/7) horses were mild to moderately tachycardic but only 14.29% (1/7) showed splinting of the abdomen.

According to the literature, in many cases of peritonitis there are no abnormalities palpated per rectum (Smith B.P., 2015; White and Edwards, 2001). In this study rectal palpation revealed abnormalities in most of the cases. In the acute and peracute peritonitis case, palpation per rectum induces a pain response. This clinical observation was also recorded in this study, although not in every case. Abnormalities detected by using transabdominal ultrasonography were recorded in the majority of cases, which correlates with the reported frequency of abnormalities detected of 50-90% (Smith B.P., 2015). However, there was no statistical relationship between findings on abdominal ultrasound and survival.

Dehydration commonly accompanies peritonitis so there is often an increased packed cell volume (PCV) on haematology (Davis, 2003). In this study there was no statistically significant difference in PCV between survivors and non-survivors. There was a significant difference in leucocyte count between the two groups. In the non-survival group leukopenia was most common; correlating with the deterioration of the clinical condition of those horses.

Hyperfibrinogenaemia is a common clinicopathological finding in horses with peritonitis (Smith B.P., 2015). In this study hyperfibrinogenaemia was recorded in all samples tested for fibrinogen, in both the survival and non-survival group. However, there was a significantly higher fibrinogen value in the non-surviving horses which reflects the more severe inflammation process in these cases.

Faecal egg count and tapeworm enzyme-linked immunosorbent assay (ELISA) were excluded from the data collection. Considering the suggested relationship between heavy parasitic burden and some peritonitis in literature, it could have been interesting to include.

Abdominocentesis was a frequent diagnostic aid in this study. It was not defined in the clinical records whether the abdominocentesis was performed with a needle or a teat cannula. However, according to a study by Duesterdieck-Zellmer *et al*. (2014) the total protein and total nucleated cell count (TNCC) should not be different, whichever technique is being used. Macroscopic examination of the peritoneal fluid was very thorough, although the definition of colour could interpreted as be somewhat subjective. Healthy peritoneal fluid should be clear and in most of the fluid samples in this study were turbid, suggesting a pathological cell and protein content. The majority of samples had an increased total protein value but there was no statistical significance of this finding. Peritonitis has been defined in literature as when the TNCC is more than $10x10^9$/l. In this study almost 95% of the samples had TNCC of more than $10x10^9$/l. There was a significantly higher value in the non-surviving group when compared to the surviving group. The trend in serial samplings was not determined. Thereby it is not possible to know whether there was a persistent decrease in total protein and TNCC according with clinical improvement, or if there was a fluctuation in values, as reported by Dyson (1983). Differentiated nucleated cell count was not recorded in results, which would have been more informative of duration of peritonitis (acute vs chronic).

Culture of the peritoneal fluid sample was frequently performed. The rate of positive results obtained (35,29%) correlates with the literature, were positive cultures have been

reported with 9.5% to 77.8% frequency (Lores *et al.*, 2011; Smith B.P., 2015). In this study culture results had no statistically significant association with survival. Studies have shown that although bacteria may be visualised on cytology, a negative culture result is obtained (Dyson, 1983). This was also observed in this study suggesting that there could have been a higher than recorded infectious involvement. Bacteria visualised on cytology had negative association with survival. In literature, 60% of positive cultures were identified as mixed flora (White and Edwards, 2001), in this study a single bacterium species were identified as cause of septic peritonitis more often than mixed flora. Gram negative species are the most common isolated bacteria, a finding which correlated with the literature (Hepworth-Warren *et al*., 2016). Although a common isolate, the anaerobic *Bacteroides fragilis* was not detected and could be due to its fastidious nature. There is a well-known regional difference in frequency of *Actinobacillus equuli* peritonitis, with the majority of cases reported in Australia and some cases reported in New Zealand and North America. The abundance of the disease in Australia is unexplained (Stewart, 2006; Matthews *et al*., 2001; Mogg and Dykgraaf, 2006). There was a relatively high number of positive *Actinobacillus equuli* cultures in this study and considering that the population studied was situated in Northern Europe. However, international movement (competitions, import etc.) was not recorded in the anamnesis. In a study by Matthews *et al*. (2001) on peritonitis caused by *Actinobacillus equuli*, there was 84% positive cultures of the diagnoses. Where intracellular bacteria are seen on cytology, 72% of cultures were positive. In the cases where culture was negative, *Actinobacillus equuli* peritonitis was diagnosed by characteristic clinical signs and rapid response to treatment. If the same method of diagnosis was applied in this study,

there would probably be a higher rate of *Actinobacillus equuli* peritonitis diagnoses.

Abdominal lavage was an infrequent therapeutic method in this study, so it is impossible to compare our results to literature data.

Although very few post mortem examinations were performed, each of them represent an interesting aetiology of peritonitis. In one case there was a purulent peritonitis accompanied by severe enteritis localised to the jejunum. Transmural migration of bacteria is common during inflammation of the intestinal wall and secondary peritonitis is a frequent complication. A metal foreign body was found to penetrate the small intestine in one horse. Perforation of the small intestine is not very common, it is described in adults mainly as caused by foreign bodies and sometimes with a neoplastic aetiology such as lymphomas (White and Mair, 2008). Foreign bodies are often reported to be of metal like e.g. wires like in this case; but porcupine quills have also been described as well as iatrogenic objects such as acupuncture needles. Although horses should be very selective eaters (Lohmann *et al.,* 2010), a case report describing peritonitis caused by horses ingesting hard wood foreign bodies and subsequently penetration the intestinal tract suggests that there are some individuals less selective with what they ingest (Ramirez *et al*., 1997). A suspected hepatic neoplasia was described in the post mortem findings of one horse in this study. Neoplasia can cause peritonitis with abscess formation and septic progression, as described by Stewart (2006). One horse had peritonitis following a ruptured abdominal abscess, thought to originate from an injury to the colon and uterus.

Mortality of peritonitis has been reported to be between 30% and 67% with a significant difference between those who underwent abdominal surgery (56%) and those who did not (43%) (White and Edwards, 2001). In this study the mortality rate was 75% for those that underwent surgery, which was considerably higher compared to the non-surgery group (27.38%). Surgery was a negative factor for survival in this study. The finding correlated with findings in a recent retrospective study by Nógrádi *et al*., (2011) where the decreased survival was hypothesised to be due to the risks of hypotension and decreased perfusion by general anaesthesia and the possibility to aggravate lesions or create more damage by surgical manipulation. It is also possible that surgery is more often performed in severe cases which do not respond well to medical therapy, and the decision on euthanasia is made during surgery, decreasing the survival rate of these horses. Increased heart rate and pyrexia were negative factors for survival in this study. The overall survival rate was 72.62%, (61/84) which lies within the range of 53% to 86% reported in different studies (Henderson *et al*., 2008). In the non-survival group there were 23 (27.38%) individuals. 22 of the non-survivors were euthanized for reasons ranging from poor prognosis to financial restraints; one horse died spontaneously. Financial constraint as reason for euthanasia in some horses suggests that the survival rate was not absolutely accurate, as some horses could possibly have survived with a more generous budget for further treatment. There was little information about the long-term survival, a limitation in this study. Peritonitis caused by *Actinobacillus equuli* has a documented survival rate of 100% in literature, which agreed with the results in this study (7/7).

Swelling around the jugular vein at the site of intravenous catheter insertion was by far the most common complication. Although the risk for laminitis in association with peritonitis is mentioned in literature, this study there was no complication by laminitis. Presence of complications may reduce survival according to the literature (Lores *et al.*, 2011). In one retrospective study of 55 equine peritonitis cases by Nógrádi *et al.*, (2011) complications were more frequent in non-survivals compared to survivals. In this study there was no statistically significant association between complications and survival.

The retrospective nature of this study is a limitation as the data collected e.g. the physical examination findings (excluding quantitative data such as heart rate) are very subjective to each practicing veterinarian. The study also lacks long-term follow up for a more accurate survival rate. It was not possible to contact the horse owners due the contact details being erased from the records prior to conducting the project. The low number of horses with peritonitis secondary to surgical intervention is thought to be due to an erroneous exclusion when selecting the patient records to be reviewed. It would have been interesting to observe if the overall survival rate and surgical mortality changed with higher number of cases included where peritonitis was secondary to surgery.

5. Summary

The records of 84 horses with peritonitis, admitted to Evidensia Strömsholm Equine Referral Hospital over a period of 11 years were examined. Foals were excluded as well as horses with an incomplete medical history. The objective of this study was to compare clinical parameters and culture result of abdominal fluid between survivors and non-survivors.

The overall survival rate was 72,62%. Neither breed nor gender was associated with survival. There was no significant difference in age between the two groups. The most common presenting complaint was pyrexia followed by colic, reduced appetite and depressed demeanour. Surgical intervention and bacteria seen on smear of peritoneal fluid were negative factors for survival. The heart rate and rectal temperature on admission and fibrinogen in blood were significantly higher in the non-survival group compared to the survival group.

There was no significant difference in total protein of the abdominal fluid between the two groups but total nucleated cell count was significantly higher in non-survivors. Gram negative bacterial species were most frequently isolated. There was no statistically significant association between culture result and survival. Abdominal lavage was an infrequent therapeutic method in this study. Survivors were hospitalised for a longer period of time compared to non-survivors. Thrombophlebitis was the most common complication observed. Complications had no significant association with survival. Laminitis was never observed.

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8. Appendices

Clinical sign	Total	Survivors	Non-survivors
Reduced appetite	49	33	16
Depression	43	32	11
Colic	51	45	6
Rolling	5	5	0
Pawing	14	11	3
Recumbence	17	14	3
Sweating	1	0	1
“in pain”	4	4	0
Decreased borborygmi	5	5	0
Pain on palpation of abdomen	1	1	0
Distended abdomen	1	1	0
Splinted abdomen	8	4	4
Tachycardia	18	14	4
Pyrexia	60	41	19
Shaking	7	5	2
Unsteady gait	4	1	3
Reluctance to move	5	4	1
Weight loss	5	3	2
Reduced/no faecal output	18	14	4
Diarrhoea/loose/soft faeces	14	11	3
Bloody faeces	1	1	0
Black faeces	1	1	0
Dry faeces	1	1	0
Tenesmus	1	1	0
Normal mucous membranes	3	3	0
Abnormal mucus membranes	3	2	1
Poor drinking	2	2	0
Polyuria	2	2	0
Poor lactation	1	1	0
Nasal discharge	1	1	0
Ocular discharge	1	0	1
Vaginal discharge	1	1	0
Swollen scrotum	1	1	0
Swollen head	2	2	0
Swollen distal extremities	2	1	1
Puncture wound to the abdomen	1	1	0
Findings on rectal palpation	23	19	4
Abnormalities on abdominocentesis	1	1	0
Reflux	1	1	0

Table 1. Presenting complaint

Variable	Survivors					Non-survivors					P-value
	n	Mean	SEM	Median	IQR	n	Mean	SEM	Median	IQR	
Duration of signs before admission (days)	61	3,25	0,80241	1	1,75	20	4,2375	1,19283	2	6	0,063
History temperature (˚C)	41	39,4125	0,06731	39,3	0,65	19	39,95	0,1354	39,95	0,92	<0,001
Heart rate (/min)	57	49,4211	1,52197	44	18	22	72,5455	4,57583	71	32,5	<0,001
Hospitalisation (days)	61	6,8197	0,46017	6	3	23	2,913	0,47429	2	3	<0,001
Packed cell volume (%)	52	33,175	0,84214	32	5,15	20	38,65	2,53323	35,5	17,25	0,072
Fibrinogen (g/l)	11	4,1	0,44004	3,7	0,6	6	6,9667	1,66366	6,1	5,55	0,032
Leucocytes in blood (10^9/l)	40	8,255	0,77438	7	4,65	16	7,1562	1,99075	4	4,92	0,011
Total nucleated cell count of peritoneal fluid (10^9/l)	53	1,6044	17,83146	1,425	186,55	18	2,3576	34,96687	2,49	249,5	0,019

Table 2. Comparison of numerical variables between survivors and non-survivors

Clinical sign	Total	Survivors	Non-survivors
Rectal temperature			
Mean, ˚C	38,34	38,17	38,81
Normal	39	31	8
Mild pyrexia	9	8	1
Moderate pyrexia	8	3	5
Severe pyrexia	2	0	2
Heart rate			
Mean, bpm	55,86	49,42	72,54
Normal	21	18	3
Mild tachycardia	26	25	1
Moderate tachycardia	14	9	5
Severe tachycardia	18	5	13
Intestinal borborygmi			
Normal	7	5	2
Decreased	58	42	16
Absent	4	3	1
Mucous membranes, colour			
Normal	47	40	7
Abnormal	7	14	14
Mucous membranes, moisture			
Moist	7	6	1
Dry	6	2	4
Tacky	7	7	0
Capillary refill time			
Normal	17	14	3
Abnormal	43	25	18

Table 3. Status praesens on admission

Clinical signs	Total	Survivor	Non-survivor
Rolling	1	1	0
Sweating	1	1	0
Weight shifting	1	0	1
Distended abdomen	1	1	0
Splinted abdomen	8	6	2
Reluctance to move	2	0	2
Cold extremities	4	1	3
Warm extremities	2	2	0
Shaking	2	0	2
Ventral oedema	4	1	3
Skin turgor increased	4	2	2
Thrombophlebitis	2	0	2

Table 4. Other clinical signs on admission

Clinical sign	Total	Survivors	Non-survivors
Rectal temperature			
Normal, 37,5-38,5 ˚C	52	46	6
Improving	6	5	1
Worsened	6	2	4
Fluctuating	15	8	7
Persistently pyrexia	1	0	1
Heart rate			
Normal, 28-40 bpm	12	12	0
Improving	26	24	2
Tachycardia, >40 bpm	24	7	17
Intestinal borborygmi			
Normal	9	8	1
Improving	20	18	2
Decreasing	2	1	1
Persistently decreased compared to normal	25	12	13

Table 5. Rectal temperature, heart rate and intestinal borborygmi trend over hospitalisation

Parameter (n)	Total	Survival	Non-survival
Packed cell volume (72)			
Mean, %	34,70	33,17	38,65
Normal	50	40	10
High	8	9	5
Low	14	3	5
Leucocytes (56)			
Mean, $x10^9$/l	7,94	8,25	7,20
Normal	28	26	2
Leukopenia	21	10	11
Leucocytosis	7	4	3
Fibrinogen (17)			
Mean, g/l	5,11	4,1	7
Normal	0	0	0
High	17	11	6

Table 6. Haematology

Species (n)	Survival (n)	Non-survival (n)
Actinobacillus equuli (7)	7	0
Staphylococcus (1)	0	1
Staphylococcus albus (4)	2	1
Staphylococcus saphrophyticus (2)	1	1
Staphylococcus aureus (1)	0	1
α-Streptococci (1)	1	0
B-haemolysing Streptococcus (1)	0	1
B-haemolysing Streptococcus group C (4)	2	2
B-haemolysing Streptococcus equi ssp zooepidemicus (1)	1	0
Escherichia coli (6)	3	3
Enterobacter (2)	1	1
Enterococcus (2)	1	0
Gram negative rod (2)	2	0
Mixed flora (1)	1	0

Table 7. Bacterial species in peritoneal fluid and comparison between survival and non-survival groups

Patient identification	Findings
50	*Injury to small colon/uterus which developed to an abscess which burst with associated severe peritonitis*
78	*Severe peritonitis with a foreign body (metal wire) perforating the small intestines*
96	*Severe purulent peritonitis with severe enteritis (jejunum) with multifocal hyperaemic areas along intestinal wall.*

Table 8. Post mortem examination and findings

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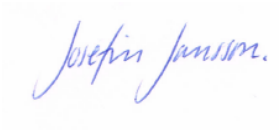

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