

Jugular thrombophlebitis in horses: A review of fibrinolysis, thrombus formation, and clinical management

Deborah Penteado Martins Dias, José Corrêa de Lacerda Neto

Abstract — Thrombophlebitis of the jugular vein is commonly observed in horses, particularly during intensive care, and leads to local and systemic inflammatory responses as well as head and neck circulatory impairment. Thrombolytic therapy is widely used in human practice with the aim of thrombus dissolution and recanalization of the injured vessels. There are similarities between human and horse coagulation and fibrinolytic processes. This review examines the fibrinolytic system, thrombus formation, and the clinical management of jugular thrombophlebitis, including thrombolytic therapy. There is evidence that early regional thrombolytic therapy for jugular thrombophlebitis in horses may be effective to achieve sustained recanalization.

Résumé — **Thrombophlébite jugulaire chez les chevaux : revue de la fibrinolyse, de la formation de thrombus et de la gestion clinique.** La thrombophlébite de la veine jugulaire est communément observée chez les chevaux, particulièrement durant les soins intensifs, et cause des réactions inflammatoires locales et systémiques ainsi que des altérations de la circulation dans la tête et le cou. La thérapie thrombolytique est couramment utilisée en pratique humaine dans le but de dissoudre les thrombus et de recanaliser les vaisseaux blessés. Il y a similitudes entre les processus coagulant et fibrinolytique des humains et des chevaux. Cette revue examine le système fibrinolytique, la formation de thrombus et la gestion clinique de la thrombophlébite jugulaire, incluant la thérapie thrombolytique. Il y a des preuves que la thérapie thrombolytique régionale précoce pour la thrombophlébite jugulaire chez les chevaux peut être efficace pour la réalisation d'une recanalisation durable.

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Introduction

Thrombophlebitis of the jugular vein in horses is a commonly observed, undesirable iatrogenic complication, particularly during intensive care. Several drugs are widely used for acute thrombolytic therapy in human practice but there are few reports on the use of thrombolytic agents to treat thrombosis in horses (1–4). This review examines the fibrinolytic system, thrombus formation, and the clinical management of jugular thrombophlebitis, including thrombolytic therapy in horses. The review also highlights the evidence supporting the use of streptokinase (SK) as a regional treatment for clinical thrombosis in horses.

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The fibrinolytic system

In 1958, Astrup (5) proposed the concept of dynamic equilibrium for coagulation and fibrinolytic systems. In this delicate balance, the fibrinolytic process breaks down fibrin which is continuously deposited throughout the cardiovascular system as a result of limited physiological activation of the coagulation. The coagulation and fibrinolytic systems interact through feedback mechanisms that are not fully understood (6). Fibrinolysis is regulated such that unwanted fibrin thrombi are removed from circulation, whereas fibrin in wounds persists to prevent blood loss and maintain hemostasis (7–9). The vascular endothelium, a highly specialized multifunctional organ, is intimately involved with regulation of hemostasis, supporting anticoagulant mechanisms, including fibrinolysis and inhibition of platelets and serine proteases, to maintain blood fluidity (10). The cascade of reactions leading to thrombus dissolution is schematically illustrated in Figure 1.

The key enzyme in the fibrinolytic system is the glycoprotein plasminogen which is produced in the liver (6). The inactive proenzyme plasminogen is converted to the active enzyme plasmin by 2 specific serine proteases: the tissue-type plasminogen activator (tPA), released from endothelial cells in response to stasis or vessel wall injury, and the urokinase type plasminogen activator (uPA), also called urokinase. The tPA-mediated

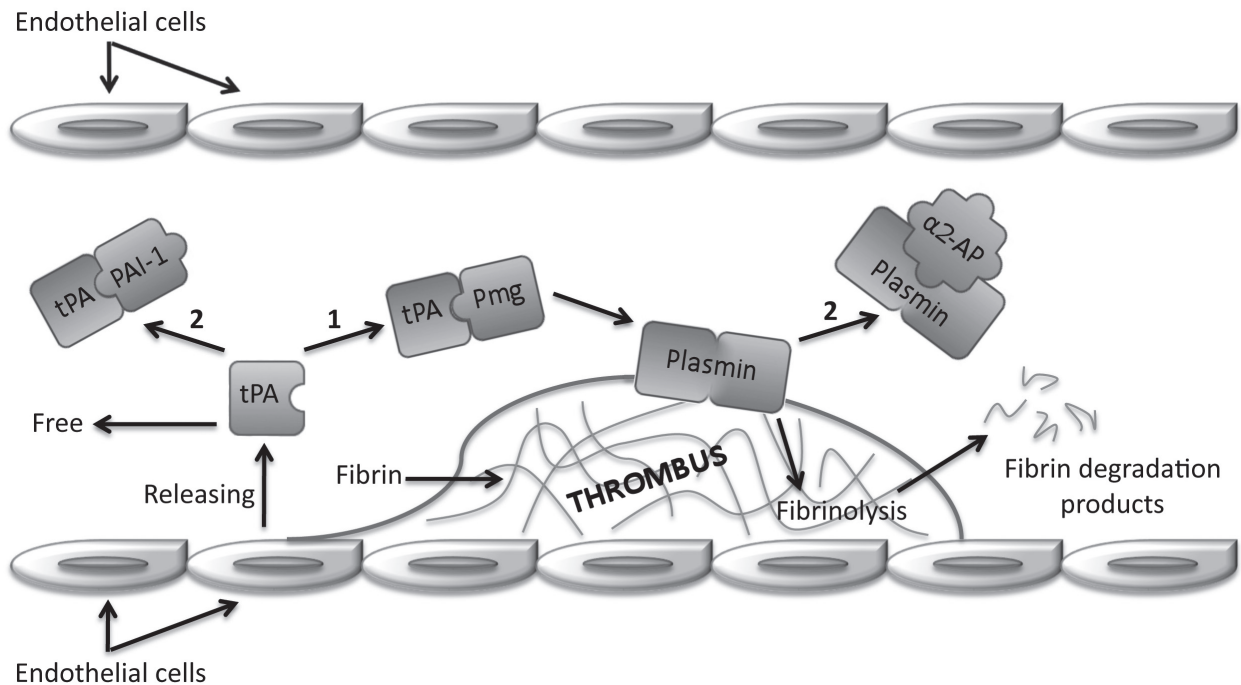


Figure 1. Schematic representation of fibrinolysis showing tissue plasminogen activator (tPA) pathway. Tags: plasminogen (Pmg); plasminogen activator inhibitor-1 (PAI-1); alpha₂-antiplasmin (α₂-AP); activation (1); inhibition (2).

pathway is primarily involved in fibrin homeostasis, and the uPA-mediated pathway is involved in cell migration and tissue remodeling (11). Activation of plasminogen to plasmin occurs by the cleavage of an arginine-valine bond, which produces changes in conformation, leading to an increased affinity for both degradation substrates and activators (6). Plasmin, a relatively nonspecific protease, has the capacity to hydrolyze fibrin and various plasma proteins, including fibrinogen and coagulation factors (6,7,12). Plasmin also activates matrix metalloproteinases that, in turn, degrade the extracellular matrix (11).

Fibrinolytic activity is modulated by plasminogen activators and inhibitors (8,10,12). The plasminogen activator inhibitor 1 (PAI-1) is a fast-acting inhibitor of tPA and uPA; PAI-2 is secreted in small amounts under normal conditions, but may be released in high concentration from damaged endothelium (10). The most important inhibitors that act at the plasmin level are alpha₂-antiplasmin and alpha₂-macroglobulin (8,12). Alpha₂-antiplasmin, a single-chain glycoprotein protease inhibitor, is the main physiologic inhibitor of plasmin (6). Plasma concentrations of alpha₂-antiplasmin are sufficient to inhibit about 50% of potential plasmin (7). The half-life of alpha₂-antiplasmin and plasmin complex is approximately 12 h (6). When massive activation of plasminogen occurs, such as during thrombolytic therapy, alpha₂-antiplasmin is depleted, and the high free plasmin levels lead to a “systemic lytic state,” increasing the risk of bleeding from wounds (7). The thrombin activatable fibrinolysis inhibitor (TAFI) is a plasma protein that attenuates the conversion of plasminogen to plasmin. During inflammatory processes, the anti-coagulant effects of protein C are impaired and activation of TAFI is retained. Therefore, fibrinolysis is decreased, adding to the prothrombotic coagulopathy associated with sepsis (9).

Tests for the assessment of fibrinolysis in horses include tests for fibrinogen concentration, fibrin degradation products (FDPs), D-dimer (DD) levels, and thromboelastography (TEG). Fibrinogen concentrations may be difficult to interpret in critically ill horses as the levels change with both inflammation and coagulopathies, although low levels may support increased fibrinolysis. Both FDPs and DD result from fibrinolysis, but FDPs result from the degradation of both fibrin and fibrinogen (13), while DDs (formed only by the plasmin digestion of cross-linked fibrin) are considered specific for fibrin (13,14). Fibrin monomers (FM), the initial products of fibrin formation, form high molecular weight complexes with fibrinogen and FDPs and is an accurate indicator of an activated state of coagulation. Fibrin monomers may be deposited locally, in cases of thrombosis, or diffusely, in cases of disseminated intravascular coagulation (DIC) in humans (15,16). In horses, FM also indicates the coagulation state. Clinical studies evaluating horses after colic surgery reported high levels of FM before the occurrence of jugular vein thrombosis (17) and DIC (18). Antithrombin (AT) inactivates thrombin and some coagulation factors, and is considered the main inhibitor of coagulation (19). In horses undergoing colic surgery, reductions in AT corresponded to the severity of intestinal lesions (20). Evaluating coagulation and fibrinolysis indicators, Feige et al (20) showed that activation of coagulation and fibrinolysis increased after the colic surgical procedure, marked by a prolonged activated partial thromboplastin time, and by increased concentrations of DD and FM. The authors also reported that surgical trauma *per se* did not influence coagulation, and changes were due to the primary disease. The study concluded that high FM and DD concentrations represent an increased risk for the development of a coagulopathy after colic surgery.

Thromboelastography measures global hemostatic function of whole blood *in vitro*, documenting the interaction between platelets and coagulation cascade proteins (21) and provides information on clot kinetics and mechanical properties from formation through maturation and fibrinolysis. The use of whole blood allows the analysis of cellular and plasma components, providing a global assessment of hemostatic potential (22,23). Validation of TEG in horses and establishment of the first reference values were performed by Paltrinieri et al (24). Thromboelastography may be a clinically useful tool in horses. For example, in horses presenting with gastrointestinal diseases, TEG was an effective method to determine coagulation and fibrinolysis changes, as well as to distinguish hypocoagulation and hypercoagulation states (22,25).

Thrombus formation

The equilibrium proposed by Astrup (5) is easily overwhelmed during pathologic coagulation states. In such states, the fibrinolytic system fails to maintain fluidity of the blood in the affected vessels, resulting in thrombosis (6). Equine diseases commonly associated with coagulation abnormalities include gastrointestinal diseases and sepsis, often associated with endotoxemia or the systemic inflammatory response syndrome (SIRS) (13,26). Other conditions in horses associated with coagulopathies include genetic coagulation defects, neoplasia, protein-losing enteropathy, and protein-losing nephropathy (26).

Horses with gastrointestinal disorders and sepsis may develop coagulopathies characterized by excessive activation of coagulation, and impairment of the fibrinolysis and anti-coagulation pathways (9,13,27,28). The degree of abnormal coagulation with gastrointestinal diseases may be mild to marked, depending upon the severity of the disorder. Simple obstructions and displacements usually produce a mild to moderate activation of the coagulation system, usually compensated by the fibrinolytic system. More severe problems such as intestinal strangulation or enteritis may produce a marked prothrombotic state, which can lead to disseminated intravascular coagulation (9,28). Medical treatment of acute abdomen, or postoperative care of horses undergoing surgery for gastrointestinal lesions is often intensive and frequently necessitates long-term maintenance of a jugular catheter for administration of intravenous fluids and medications. If these horses have concurrent coagulopathies, in association with jugular vein trauma and inflammation occurring with catheterization, they are at increased risk for the development of thrombophlebitis of the jugular vein (13,28). Mair and Smith (29) reported that 8.3% of 252 horses that underwent surgical treatment of colic developed jugular vein thrombophlebitis.

The imbalance leading to thrombus formation may be a result of multiple factors, including vessel injury or other intrinsic vessel wall lesion, a low-flow state or venous stasis, and blood hypercoagulability (6,30). This classic triad, describing the pathogenesis of thrombosis, was first outlined by Virchow in 1856 (cited in reference 30). Experimentally and clinically, it is now recognized that at least 2 of these 3 postulated factors in combination are essential in the progress of venous thrombosis. In humans, decreased blood flow or stasis seems to be the dominant component (31). However in horses, local trauma is

the most important factor of this triad in the development of jugular vein thrombosis (32).

Thrombosis begins with platelets adhering to macromolecules in the subendothelial regions of the injured blood vessel to form the primary hemostatic plug. The platelets then stimulate local activation of plasma coagulation factors, leading to the generation of a fibrin clot that reinforces the platelet aggregate. Within an intact blood vessel, thrombosis is prevented by the body's anticoagulant mechanisms. Prostacyclin (PGI₂), anti-thrombin, heparan sulfate proteoglycans, protein C, protein S, ADPase, and TF pathway inhibitor (TFPI) are examples of natural thrombosis inhibitors (7,9,33,34). Activated protein C and protein S, in the circulation or on the endothelium surface, block the inhibitory effect of PAI-1. Therefore, plasminogen may exert its function leading to fibrinolysis, thereby preventing thrombotic processes (10).

Jugular thrombophlebitis in horses

Thrombophlebitis is defined as venous thrombosis secondary to inflammation of the vessel wall (35–37). Infection can complicate and enhance this venous disorder. In septic thrombophlebitis, there is bacterial or, rarely, fungal colonization of the vessel wall, thrombus, and, occasionally, of the surrounding perivascular tissues (38). Blood flow is impaired due to reduced vascular lumen by partial or complete occlusion (38,39). Thrombophlebitis most commonly affects the jugular veins in horses because they are the most commonly used site to access venous circulation. The disease is associated with poor venipuncture technique, prolonged or improper placement of indwelling catheters, and injections of irritating drugs that lead to mechanical or chemical injury of the vessel wall (30,36,40–44). An atypical etiology of jugular thrombophlebitis, extending directly from a penetrating buccal ulcer in a horse, was described by Matsuda et al (45).

The development of thrombophlebitis following catheterization is dependent on catheter composition, venipuncture technique, cannula size, catheter maintenance, pH of the infusate solution, duration of infusion, and presence of bacteria (46). All of these factors underscore the importance of using aseptic techniques to implant and maintain venous catheters.

A bacteriological study assessing techniques for disinfecting sites prior to the insertion of jugular intravenous catheters in horses reported that chlorhexidine and povidone-iodine were equally effective when used on skin after the hair had been clipped (47). The authors concluded that clipping or shaving the hair over the veins prior to disinfection is recommended, but there were no differences when the hair was left long, clipped, or shaved. Therefore, the skin can be disinfected effectively with either agent without clipping or shaving the hair when rapid intravenous catheterization is a clinical priority.

The pharmaceuticals most frequently associated with the development of thrombophlebitis include glycerol guaiacolate, thiopental, calcium gluconate, phenylbutazone, and oxytetracycline (38,39). Phenylbutazone, widely used for anti-inflammatory therapy of musculoskeletal system injuries of athletic horses, is commonly associated with thrombophlebitis when it is accidentally infused in the perivascular region (39,48).

Clinical signs associated with aseptic jugular vein thrombosis are generally limited to localized firmness and a cord-like jugular vein. Venous distention proximal to the thrombus site is observed when there is complete occlusion. When bacteria are seeded in thrombi resulting in septic thrombophlebitis, horses have intermittent fever, depression, and neck stiffness. Palpation elicits local swelling, heat, pain, and a cord-like jugular vein. Generally, leukocytosis, neutrophilia, and hyperfibrinogenemia are present (49,50). As reported by Ryu et al (51), septic thrombi in the jugular vein may also lead to pleuropneumonia via the pulmonary circulation.

The diagnosis of septic or nonseptic thrombophlebitis is primarily based on history and physical signs (38,39,49). The disease is evaluated with hematology tests, ultrasonography, contrast angiograms, and bacteriologic confirmation (35,49,50,52,53). Ultrasonography of the vein and surrounding tissue can be used to specifically characterize the thrombus and monitor the extent and progress of the lesion (37,54). The jugular vein and its valves can be readily identified (35). In cases of thrombophlebitis, ultrasonography allows an evaluation of vessel walls, blood flow compromise, and presence, extension and shape of the thrombus, as well as compensatory vascularization and recanalization characteristics (55). The sonographic appearance of the normal jugular vein is that of an anechoic circular or tubular structure, with identification of a more hyperechoic vessel wall (38). Inflamed jugular veins often appear thick-walled, and the thrombus is imaged as a partially or totally occlusive hyperechoic structure adhering to the vessel wall. In cases of partial obstruction, the blood flow appears as an anechoic area between the thrombus and opposite vessel wall where the thrombus is connected (38,56,57). If only partial obstruction to blood flow is present, distension of the vein by distal digital occlusion helps to prevent collapse during ultrasonographic evaluation (55). A septic thrombus appears as a hyperechoic heterogeneous cavitating mass in which the anechoic areas represent fluid accumulation secondary to infection and necrosis (38,50,54). Anaerobic bacterial infections often show numerous hyperechoic areas creating an acoustic shadow due to gas production (38). Blood flow across the affected vessel may be evaluated by venography, or with pulsed-wave or color-coded Doppler (50).

If a catheter is still in place when a thrombosis is discovered, the catheter should be carefully withdrawn and the tip cultured (26,35). Identification of the infectious agent and its drug susceptibility is important for treatment (35). While the catheter remains *in situ*, the thrombus will not dissolve, and it may grow (58). Furthermore, the injured vessel should be preserved, and venipuncture should be avoided. The opposite jugular vein should also be preserved to avoid the risk of bilateral thrombophlebitis. Lateral thoracic, cephalic, and saphenous veins are other options for drug administration and venous blood collection (59). In a retrospective study, Dolente et al (26) reported severe intestinal disease, hypoproteinemia, salmonellosis, and endotoxemia as potential risk factors for development of catheter-associated jugular thrombophlebitis in horses.

Both medical (35,43,60,61) and surgical (40,42,62–66) treatments for thrombophlebitis are reported. Local treatment

consists of hot packs and hydrotherapy applied over the swollen vein 3 or 4 times daily and the application of dimethyl sulfoxide (DMSO) solution on the affected area. Non-steroidal anti-inflammatory drugs may be useful in reducing pain and inflammation. Systemic antibiotics are indicated for sepsis (35,43,50,61). Bonagura et al (50) suggested metronidazole at 15 mg/kg body weight (BW), PO, q6h, or at 25 mg/kg BW, PO, q12h in cases of anaerobic infection. If the thrombotic lesion is associated with a generalized coagulopathy, heparin therapy [unfractionated, 40 to 100 IU/kg BW, IV or SQ, q6h; low molecular weight (Dalteparin), 50 to 100 IU/kg BW, SQ, q24h] may be beneficial (67). Efficacy and side effects of low molecular weight heparin (LMWH) compared to unfractionated heparin (UH) have been evaluated in horses with gastrointestinal diseases. At a dose of 50 IU/kg BW, q24h, LMWH decreases the incidence of jugular thrombosis compared to treatment with UH in horses having colic surgery (68). Aspirin at a dose of 20 mg/kg BW every other day is also recommended for the treatment of thrombophlebitis to inhibit platelet activation and aggregation (30). Scott et al (60) reported 2 cases of jugular vein thrombophlebitis successfully treated by warfarin anticoagulation. However, the authors recommend this therapy only in situations in which the coagulation status can be monitored by daily laboratory determinations of prothrombin time.

When jugular vein thrombophlebitis is refractive to medical treatment, surgical techniques including phlebotomy, thrombectomy with Fogarty's catheter, or venous grafts may be performed to restore blood flow (40,42,62–66). Dias et al (57) performed an ultrasonographic evaluation during the acute phase of experimental jugular vein thrombophlebitis in horses and demonstrated that the major thrombus development occurs in the early stages of injury. These findings suggest that the first 24 h may represent the most effective intervention period. In horses, the complications associated with jugular vein thrombophlebitis include pleuropneumonia, bacterial endocarditis, pulmonary thromboembolism, septicemia, and other conditions associated with metastasis of septic thrombi (44).

The long-term outcome for a thrombus is variable. Recanalization of the vein may take place. The thrombus may undergo fibrous organization without recanalization or collateral circulation may develop (44). Hussni et al (69) observed via angiography that collateral vascularization develops within 1 y in horses submitted to a unilateral jugular vein resection that restores the venous drainage of the head and neck. If the jugular venous obstruction persists and collateral vascularization does not occur, especially when both jugular veins are involved, dysphagia and dyspnea due to impaired venous return from the head is likely to limit athletic performance (38,42,50). Moreau and Lavoie (44) suggested that thrombophlebitis did not affect the athletic performance of horses used for pleasure riding and other nonracing activities, even when the horses suffered bilateral occlusion. However, thrombophlebitis in racing Standardbreds was associated with a decreased chance of return to racing.

Thrombolytic therapy and streptokinase

The medical treatments for equine jugular vein thrombophlebitis are often ineffective, and restoration of blood flow

is typically only achieved with complex and expensive surgical procedures. In human medicine, thrombolytic therapy involving fibrinolytic agents has revolutionized the treatment of diverse circulatory disorders, such as pulmonary embolism, deep-vein thrombosis, and myocardial infarction (12). It has been possible to treat intravascular thrombosis and achieve complete dissolution by using drugs capable of stimulating the fibrinolytic system (6). Thrombolytic therapy consists of the pharmacological dissolution of the blood clot by intravenous infusion of plasminogen activators that activate the intrinsic fibrinolytic system components (11,12). Thrombolytic drugs dissolve both pathological thrombi and fibrin deposits at sites of vascular injury, with the risk of hemorrhage as the major side effect (7). Streptokinase (SK) is a nonenzymatic protein produced by strains of β -hemolytic streptococci (6,11,12). The capacity of SK to promote the lysis of blood clots was first described by Tillet in 1933 (cited in reference 70); the effect is thought to be mediated by enzymatic action on fibrin (70). Streptokinase combines with plasminogen to form a stable activator complex that has enzymatic activity (71). This SK-activator complex then activates the fibrinolytic mechanism by converting uncomplexed plasminogen to plasmin. The SK-plasminogen complex is slowly converted to a SK-plasmin form, which can also activate and convert plasminogen. The initial activity is mediated by the SK-plasminogen complex, whereas the later activity is mediated by the SK-plasmin form (6). Streptokinase is a foreign protein, and its introduction into the circulatory system can elicit an anaphylactic response (8). Plasma antibodies against SK are normally present as a result of prior streptococcal infections. Therefore, systemic lytic therapy only becomes effective when enough of the drug has been administered to overcome these antibodies (7). Lytic agents can be administered systemically or regionally (6).

In the attempt to avoid the hemorrhagic consequences of thrombolytic therapy, Dotter et al (72) proposed a low dose, local infusion of SK for the treatment of arterial occlusive disorders. Due to the smaller total dose of SK in local application, there were fewer complications than with systemic therapy. Regional thrombolytic therapy was further developed, and local targeted instillation through a catheter implanted into thrombotic material was proposed (6,73). The technique makes local fibrinolysis possible, and, importantly, this process is partially protected from circulating inhibitors. Regional thrombolytic therapy with SK has been used successfully in human practice for venous thrombotic disorders of superficial veins, such as the axillosubclavian vein (6). The use of SK may be successful for jugular vein thrombophlebitis in horses, given the similarity between horse and human thrombosis development processes (74), and the superficial localization and easy access to the jugular vein in horses. Nevertheless, there are few investigations analyzing SK fibrinolytic activity in horses. The use of SK in horses was first reported in 1966 and 1968 to treat aortic and left iliac thrombosis, respectively. Streptokinase was administered in association with streptodornase, plasminogen, and sodium gluconate. Unfortunately, the authors could not specify which fibrinolytic agent led to case resolution (1,2). Lions et al (3) described the administration of SK to treat jugular

thrombophlebitis in horses, showing evidence of SK fibrinolytic activity; however, their methods are not fully established. According to Dias et al (4), regional thrombolytic therapy using a bolus administration of 100 mL of SK solution (7500 IU of SK per mL of 0.9% sodium chloride solution) may be effective for resolving induced jugular vein thrombosis in horses, and providing transitory recanalization.

Other applications for fibrinolytic therapy have been reported besides jugular thrombophlebitis in horses. Clark-Price et al (75) utilized recombinant tPA in the anterior chamber of each eye of a foal with fibrin accumulation associated with endotoxemia and septicemia, providing fibrin clot clearance and restoring normal vision. Hilton and Pusterla (76) also used fibrinolytic therapy in the management of septic pleuropneumonia in a horse.

Early regional thrombolytic therapy for jugular thrombophlebitis in horses may be effective to achieve sustained recanalization. A thorough understanding of the fibrinolytic system and the potential complications associated with its modification is an essential foundation for advances in thrombolytic therapy. Additional research is needed to expand our knowledge of the fibrinolytic system, and to develop new clinical applications to address coagulation problems in horses. The authors hope to stimulate new investigations analyzing drugs capable of activating the fibrinolytic system in horses, and to promote future development of novel treatments for jugular thrombophlebitis and other diseases associated with fibrin accumulation in horses.

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Answers to Quiz Corner

Les réponses du test éclair

1. e) Conception can occur from a mating more than 7 days before ovulation to 5 days after ovulation.
 - e) La conception peut se produire à partir du premier accouplement plus de 7 jours avant jusqu'à 5 jours après l'ovulation.
2. b) Fractures on one side of the bone, with bending of the opposite side, are called greenstick fractures. They occur primarily in young growing dogs.
 - b) Les fractures sur le côté d'un os avec courbure du côté opposé sont nommées fractures en bois vert. Elles se produisent principalement chez les jeunes chiens en croissance.
3. b) Hemimandibulectomy is most likely to prevent recurrence.
 - b) L'hémimandibulectomie est la plus susceptible de prévenir une récurrence.
4. e) Unlike dogs, cats do not develop diabetic cataracts because of a difference in their lens metabolic pathway.
 - e) Contrairement aux chiens, les chats ne développent pas de cataractes diabétiques à cause d'une différence dans leur voie métabolique du cristallin.
5. a) These signs describe guttural pouch tympany.
 - a) Ces signes décrivent du tympanisme de la poche gutturale.
6. e) This foal had unilateral disease, so fenestration of the median septum would allow trapped air to exit through the normal right guttural pouch.
 - e) Cette pouliche souffre d'une affection unilatérale, de sorte que la fenestration du septum médian permettra à l'air de s'échapper par la poche gutturale droite qui n'est pas atteinte.
7. c) Calves can become infected with *Cryptosporidium* as early as 3 days of age.
 - c) *Cryptosporidium* peut infecter les veaux qui sont âgés de moins de 3 jours.
8. e) Though a good indicator of hepatocellular damage in some species, serum alanine aminotransferase activity is not helpful in the diagnosis of liver disease in cattle.
 - e) Bien qu'un bon indicateur du dommage hépatocellulaire chez certaines espèces, l'activité de l'alanine aminotransférase sérique n'est pas utile pour le diagnostic des maladies hépatiques chez les ruminants.
9. c) Hypotension can be observed following the administration of propofol in healthy patients. The effect is exacerbated by dehydration. Propofol does not directly affect heart rate or myocardial contractility.
 - c) On peut observer de l'hypotension à la suite de l'administration de propofol chez les patients en santé. Les effets sont exacerbés par la déshydratation. Le propofol n'affecte pas directement la fréquence cardiaque ou la contractilité du myocarde.
10. d) Eosinophilia occurs commonly in response to antigen-antibody reactions, as well as with inflammation of certain organs, such as the lungs, which tend to be allergy targets.
 - d) L'éosinophilie se produit communément en réponse aux réactions antigène-anticorps ainsi qu'en présence d'une inflammation de certains organes comme les poumons, qui sont des cibles pour les allergies.