1

Surgical Complications

Luis M. Rubio-Martinez DVM, DVSc, PhD, DACVS, DECVS, DACVSMR, MRCVS[1] *and*
Dean A. Hendrickson DVM, MS, DACVS[2]

[1]*Sussex Equine Hospital, Ashington, West Sussex, United Kingdom and CVet Ltd. Equine Surgery and Orthopedics, United Kingdom*
[2]*College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, Colorado*

Overview

The term "surgical complication" is frequently used in the medical profession, but its definition in the medical literature has been inconsistent over the years. The *World Journal of Surgery* defines "surgical complication" as "any undesirable, unintended, and direct results of an operation affecting the patient that would not have occurred had the operation gone as well as could reasonably be hoped" [1]. This definition suggests that a surgical complication is dependent on the surgical skill of the surgeon, the facilities and equipment available and the condition of the patient.

List of Complications Associated with Surgery:

- Morbidity and mortality
- Surgical checklists
- Perioperative consequences of surgical trauma
- Metabolic and nutritional effects
- Neuroendocrine
- Systemic inflammatory response
- Pain
- Impact of host factors and comorbid conditions

"Surgical complications," otherwise referred to as "operative complications," are not restricted to the time window of the surgical procedure itself but comprise both intra- and postoperative complications [2]. The duration of surgery defines the time window for intraoperative complications; meanwhile, postoperative complications are not restricted to those occurring during hospitalization but are defined according to a time period. A 30-day period after the surgical procedure, either during or after hospitalization, has been used in human medicine [2].

All surgical procedures are associated with a degree of risk and the benefits of any procedure need to be weighed against any potential complications so that the clinician and the patient or animal owner can make a balanced and informed decision. This discussion should also cover complementary techniques that augment results to optimize physical, occupational and societal goals [3]. In veterinary medicine, owners' expectations, engagement and commitment, animal welfare and economics need also to be balanced.

Surgical complications can be classified into patient-related complications (related to patient-specific characteristics, rather than to a procedural error), and practitioner-related complications (arising from errors that directly lead to undesirable and unintended results affecting the patient, but also as a result of a faulty technique) [3]. Although surgical errors may be frequently linked to complications, some errors may not result in complications.

Recognition of errors and complications provide unique instances to learn from and to work toward avoiding or preventing their re-occurrence [4]. To maximize this process the following practitioner's goals have been defined in human medicine [3, 5]:

1) Minimize errors by applying an appropriate surgical technique.
2) Identify and manage errors in a timely manner and in a way that would prevent ensuing complications.
3) Identify and manage complications in a timely manner and appropriately.

Complications in Equine Surgery, First Edition. Edited by Luis M. Rubio-Martinez and Dean A. Hendrickson.

4) Identify and consider patient-related complications in the decision-making process, so that they can be anticipated, prevented or managed correctly.

It is not uncommon for clinicians to adopt routines that prevent and manage complications on the basis of personal experience. However, in some cases this may be associated with "making the same mistakes with increasing confidence over an impressive number of years" [6]. In human medicine, standards of expected outcomes for groups of patients require evidence-based practice, making seniority and individual experience less important [7]. Evidence-based literature in this area has quickly developed over the last decades, and several textbooks and journals dedicated to surgical complications are available in the human field. The application of an evidence-based approach for prevention, identification and management of surgical complications should result in a reduction in mistakes in the clinical decision-making process. In addition, it will also identify areas on which further research is warranted.

Morbidity and Mortality

Morbidity (from Latin *morbidus*, meaning sick, unhealthy) is a diseased state, disability, or poor health due to any cause [8]. Surgical morbidity relates to those morbid states that are related to a surgical procedure performed on a patient. Although traditionally defined by the presence or absence of specific postoperative complications, surgical morbidity represents any clinically significant, non-fatal, adverse outcome associated with a surgical procedure [9]. Morbidity can be divided into local (associated with operation site, e.g. wound dehiscence) or general (related to any operation, e.g. acute renal failure). It can also be subdivided based on timely occurrence as intraoperative or postoperative; the latter being further considered as immediate, early, late or long-term, although these are based on arbitrary time thresholds [9]. These categories overlap and are closely interconnected, as for example a specific, local complication such as surgical site infection may have general or systemic effects such as pyrexia, inappetence and motor dysfunction, which are not procedure specific [9].

Surgical mortality is any death regardless of cause, occurring: (1) within 30 days after surgery in or out of the hospital; or (2) after 30 days during the same hospitalization period subsequent to the operation [10, 11]. In patients undergoing more than one surgical procedure during a single hospitalization, mortality is assigned to the first operation during hospitalization [10].

In human medicine, postoperative morbidity has been shown to have a significant effect on mortality in patients undergoing major surgery; [12] however, the association between general postoperative morbidity and long-term outcome or functionality is not well established [9]. This stems from the inconsistent reporting of morbidity in relation to definition, type and criteria, which leads to a lack of reliability in the recording of complications data [9]. Surgical mortality is a concrete universal outcome measure, but unlike morbidity, mortality recording has traditionally been inconsistent as a result of variable duration of hospitalization, follow-up information, and number of surgical procedures performed during the same hospitalization period or different hospitalization periods [10].

Evidence-based knowledge on complications has rapidly evolved and continues to do so in human medicine. The Morbidity and Mortality Conferences (MMCs) were established in the beginning of the 20th century at the Massachusetts General Hospital in Boston [13], with the aim to improve the quality and safety of human healthcare [14]. The MMCs have become a requirement for all human medicine surgical training programs in high-risk specialties such as surgery, anesthesia, intensive care and oncology, being a key factor in the accreditation of human hospitals [15]. These conferences are associated with improvements in healthcare quality and patient safety through analysis of failures [15]. To further improve the effectiveness of these MMCs, additional structured frameworks such as the Physician Peer Review have been implemented, enabling surgeons to review and evaluate peer surgeons' results and take corrective actions [16, 17]. These systems aim to improve competencies, protect patients from harm and assist institutions in their evaluations of surgical outcomes, with the ultimate goal of improvement of patient outcome through implementation of measures to identify and prevent operative complications.

In 1991, Copeland et al. developed the "**P**hysiological and **O**perative **S**everity **S**core for the nUmeration of **M**ortality and morbidity (POSSUM)" as a representative method for evaluating the result of surgery in patients [18]. This system includes a physiological score and an operation severity score to calculate individual risk for morbidity and mortality. Classification systems for perioperative complications (such as the Clavien–Dindo classification) have been developed [19] and application of these systems has confirmed their prediction of morbidity and mortality rates in humans [20]. Over the last few years, equine studies have focused on identification of prognostic factors, mainly associated with mortality, in patients suffering from certain conditions or undergoing specific surgical procedures. From those studies, risks factors have been identified which provide useful information during the decision-making process between veterinarian and horse owner. However, inconsistent definitions, limited populations and diverse management regimes often limit universal conclusions. Adaptations of POSSUM-like strategies to the equine surgical field warrant consideration.

Surgical Checklists

The Safety Checklist was developed by Dr. Atul Gawande with the intention of improving outcomes, team dynamics and patient safety in an intensive care unit of a human hospital [21]. Based on their successful implementation, in 2008 the World Health Organization (WHO) instituted the Surgical Safety Checklist (SSC) as a global initiative to improve surgical safety of human patients. Since then, SSCs have become standard practice in human hospitals and are slowly being implemented in veterinary hospitals. These checklists cover introduction of surgical and anesthetic teams, identification of patient, consent, procedure to be performed, anatomical location, estimated duration of surgery, availability of equipment, and potential complications among others. Use of SSCs has assisted in prevention of potential safety hazards and errors in the operating room, and improved safety and communication among operating staff [22–24]. Their implementation has been associated with reduced morbidity, length of in-hospital stay and mortality [25]. Sustained use of SSCs seems to be discipline-specific and is more successful when physicians are actively engaged and leading implementation [26]. In addition, implementation of SSCs did not negatively impact the operating room efficiency, whilst reducing overall disposable costs, in a large multispecialty tertiary care human hospital [27].

Perioperative Consequences to Surgical Trauma

Any surgical procedure is associated with some degree of tissue trauma, which results in a stress response by the patient's body. This stress response follows the same pathways as that after accidental trauma or disease; however, the magnitude of the stress response will vary with the severity of the stimulus. The patient's condition, severity of disease, anesthesia and surgical procedure will all contribute to the stimulus of a stress response. Healthy patients undergoing elective minor surgery may not sustain any significant effects, but patients with severe trauma or critical illness can enter prolonged catabolic states with notable consequences to morbidity and mortality.

The stress response is multifactorial and governed by inflammatory, metabolic, neurohormonal and immunologic pathways. As a consequence, it is difficult to categorize the degree of stress response as there is no single variable or combination thereof that define stress in a consistent manner. A combination of variables encompassing all involved pathways, and even variables related to other body systems susceptible to stress-related consequences such as the reproductive system, should be included to define the short- and long-term effects of stress [28]. The pathways involved are totally interrelated and difficult to separate, but for the purpose of this review the stress response in the surgical patient will be divided into four sections: metabolic/nutritional effects, neuroendocrine consequences, inflammatory response, and pain.

Metabolic and Nutritional Effects

In the 1930s, Cuthbertson described the body's post-traumatic response as an immediate "ebb" or shock phase followed by the flow phase [29]. The short-lived (24–48 h) ebb phase is characterized by reductions in blood pressure, cardiac output, body temperature and oxygen consumption, and when associated with hemorrhage, hypoperfusion and lactic acidosis, depending on the severity. The latter flow phase is characterized by hypermetabolism, increased cardiac outputs, increased urinary nitrogen losses, altered glucose metabolism and accelerated tissue catabolism.

The nutritional status of the human surgical patient is well recognized as a factor associated with morbidity and mortality [30, 31]. Malnourished patients show a reduction in survival, immune function, wound healing and gastrointestinal functions, and associated prolonged hospitalization and increased infection [32, 33]. Preoperative fasting, anesthesia, surgery and disease all contribute to the stress hypermetabolic response. Stimulation of the sympathetic nervous system causes release of catecholamines, an increase in oxygen delivery and consumption at the tissue level, and a rise in body temperature. As a consequence, the resting energy expenditure increases. Individual assessment of resting energy expenditure has become an integral part of the management of the human surgical patient. Providing adequate perioperative nutritional support is standard of care in humans, as malnutrition or overfeeding are associated with poorer outcome [34]. Horses undergoing surgery are subject to variable preoperative fasting times, and colic patients may undergo prolonged food and even water restriction perioperatively. However, standard assessment of the nutritional status of the equine patient is not common, and nutritional support is often limited to intravenous and/or oral fluids with electrolytes. Other nutrients such as glucose, aminoacids and lipids are less frequently incorporated in the form of either enteral or parenteral nutrition. [35].

The healthy adult horse can tolerate food deprivation, commonly referred to as simple starvation or pure protein or calorie malnutrition (PPCM), for 24–72 hours with minimal systemic consequences [36]. In this situation, healthy humans sustain neuroendocrine changes leading to a lower metabolic rate and resting energy expenditure. This is associated with decreased blood glucose, insulin, increased glucagon and down-regulation of catecholamines. Initial hepatic glycogenolysis and gluconeogenesis followed by use of fat stores maintain normal blood glucose values and survival, while lean tissue (protein) is spared.

Energy demands are increased in patients with a prior history of malnutrition, increased metabolic rate (i.e. young growing animals), underlying metabolic abnormalities, sepsis, severe trauma, or underweight animals at higher risk of stress response. The effect of fasting on stressed catabolic patients is a hypermetabolic state with increased resting energy expenditure. This is the result of the catecholamine release by the stimulated sympathetic nervous system and the inflammatory cytokines released at the site of injury, inflammation, disease or surgery [37, 38]. The magnitude of this hypermetabolic state relates to the severity of the disease or trauma. Stimulation and/or release of corticotrophin, cortisol, epinephrine, growth hormone and glucagon result in an increased resting metabolic rate characterized by insulin resistance, increased glucocorticoid secretion, gluconeogenesis, dysregulation of glycemia, lipolysis, proteolysis, nitrogen loss and rapid malnutrition [39]. Blood triglycerides should be monitored, and appropriate nutritional support instituted in horses at risk of developing hyperlipemia such as obese animals (especially miniature horses and donkeys), lactating mares, and horses suffering from Cushing's syndrome or equine metabolic syndrome.

The response to an elective surgical procedure will be more limited in a healthy than in a critically ill patient or a patient with severe trauma. However, an increase in metabolic rate occurs postoperatively in humans after simple elective surgery [40]. Anesthesia and midline abdominal exploratory laparotomy increased the postoperative caloric demand in healthy horses by 10% in experimental conditions [41]. Increased demands in critically ill equine patients are expected to be higher but have not been quantified to the editors' knowledge.

Due to the patient's size and weight, local changes in muscle metabolism can also be substantial in the recumbent horse under general anesthesia. Physical compression of muscle groups is associated with restricted local blood perfusion and an increased demand for energy through anaerobic metabolism in the muscle [42]. This can lead to use of adenosine triphosphate and creatinine phosphate as energy sources and production of lactate, which can extend into the recovery period [43, 44]. Because of decreased venous drainage from the muscle, increased muscle lactate is not paralleled by the lower plasma lactate during anesthesia and increases in plasma lactate and potassium extend into the recovery period [42, 44–46]. These metabolic changes can be apparent in healthy horses, especially in the heavy patient and prolonged anesthesia, but changes are more pronounced and commonly recognized in prolonged anesthetics and ill horses such as colic cases [43, 46].

Nutritional supplementation will reverse catabolic processes during simple starvation; however, it will not completely reverse those during metabolic stress, which will remain as long as tissue injury persists. Nutritional support of the critically ill patient aims to minimize the severity of protein loss and morbidity associated with the disease. The goal should be to re-institute food intake as soon as possible and if that is not possible, consider nutritional support. Nutritional support can be provided in the form of enteral or parenteral nutrition. The enteral route is always preferred as it provides a trophic stimulus for the gastrointestinal tract and has a protective effect against bacterial translocation across the intestinal wall [47]. Early enteral nutrition (initiated within 48 h after surgery) significantly decreased morbidity and length in critically ill human patients [48], and lessened the hypermetabolic and catabolic responses to injury in human and animals [49]. When the enteral route is not available, parenteral nutrition can be used in the form of partial (most commonly) or total parenteral nutrition. Although there is a paucity of published studies, there are some reports of clinical application of enteral and parenteral nutrition in foals and adult horses, from which some guidelines can be obtained [35, 47, 48, 50–55]. Parenteral nutrition is not exempt of complications and, therefore, close monitoring of patients receiving it is required [52, 55, 56]. A clinical nutrition counselling service has recently been pioneered at a referral equine hospital [57].

Neuroendocrine

Surgical patients undergo a sympathetic nervous system response with activation of adrenocortical axis and release of catecholamines, cortisol and glucagon. The degree of surgical trauma will determine the magnitude of this endocrine response, with redistribution of blood flow to preserve important organs, splenic contraction to increase blood volume, mobilization of resources to provide substrates such as glucose and fatty acids, and activation of the immune system in more severe cases [58, 59].

General anesthesia itself is associated with a stress response characterized by sympathetic output in healthy horses [45]. Inhalation anesthesia increased adrenocorticotropic hormone and cortisol release in healthy horses [60, 61], and even in glycerol and non-esterified fatty acids in prolonged anesthesia in healthy horses [45]. On the contrary, total intravenous anesthesia seemed to cause a lesser stress response than gas anesthesia, although duration of anesthesia and other factors have important effects [62]. Fasting, re-feeding and anesthetic drugs (i.e. α2-agonists) affect insulin regulation and therefore different drug combinations, and induction and anesthetic protocols contribute to large variability of the hyperglycemic response and circulating levels of these stress markers in the equine patient [63-65].

Laparoscopic surgery under standing sedation and local anesthesia produced increased cortisol and non-esterified fatty acids plasma levels in horses [66]. Minor elective surgery under general anesthesia (skin sarcoid removal or laryngeal surgery) produced minor changes in blood glucose, lactate or plasma non-esterified fatty acid (NEFA) values, beyond those caused by anesthesia [63]. Equine patients undergoing elective arthroscopic surgery showed transient hyperglycemia and increased beta-endorphin and cortisol [67]. Cortisol response in people undergoing surgery correlates with surgical trauma and is higher in abdominal than other minor surgeries [68, 69]. Similarly, a 1.6-fold [67] versus a 10-fold [70] increase in plasma cortisol was observed in horses undergoing arthroscopy or abdominal surgery, respectively. Horses with acute colic showed only a mild increase in plasma cortisol intraoperatively, but already had much higher preoperative cortisol levels, which indicates that the stress response in these patients may be already nearing or at maximum level before undergoing surgery [71]. Postoperative return to baseline of cortisol levels correlates with surgical trauma, being faster after elective arthroscopy than elective abdominal surgery [64]. This return was longest in colic cases (~60 h) compared with 24 hours in the non-colic group [71]. Sustained increased levels of cortisol in the postoperative period may also reflect response to pain or further trauma in this time period [70].

Surveillance of metabolic and endocrine changes in perioperative equine patients is limited. A recent report investigating the metabolic and hepatic changes in 32 surgical adult colic patients, revealed that hepatic dysfunction, hepatobiliary disease and alterations in metabolism are common in equine colic patients [72]. Surgical colic patients showed increased levels of bile acids, bilirubin, triglyceride and glucose concentrations and activities of liver enzymes such as GGT, AST, AP and SDH, whereas plasma ammonia was expected to remain within normal limits [72–74]. This may indicate hepatocellular injury in equine colic patients but could otherwise be associated with underlying diseases, transient bile duct obstruction, vascular compromise of the liver, or ascending infection from intestinal contents into the liver [72, 74, 75]. Increased TG values have the potential to progress organ damage [76], and were in fact negatively associated with survival [72]; however, a return of TG to normal values was observed at the time of re-feeding in most horses [72]. Elevated bile acid concentrations at admission were associated with decreased survival in colic patients, although increased bile acid can also be the result of prolonged fasting (>3 days) [72].

Hypothermia is another factor that occurs during surgery, which in humans has been associated with an adrenergic response [77]. A decrease in the mean core body temperature occurs in horses during standing laparoscopy and horses under general anesthesia with or without surgery [45, 78, 79], but the effects of hypothermia on the stress response in horses are unknown.

In conclusion, the stress response to anesthesia and surgery is multifactorial, with pain, tissue perfusion and energy availability being important determinants of stress. Differences in fasting period, anesthetic protocol, length of anesthesia, anesthetic protocol, surgical procedure, surgical trauma, and systemic condition of the patient will have definite effects on the type and magnitude of stress markers such as glycaemia, and plasma insulin, cortisol and NEFA in horses [67], as has been shown in humans.

Systemic Inflammatory Response

All surgery leads to systemic inflammatory response syndrome (SIRS). The majority of information is found in the human literature. It is assumed that similar effects can be found in the equine patient. The inflammatory response consists of hormonal, metabolic and immunological components. The more severe the surgical insult, the more severe the inflammatory response [80]. The hormonal response is characterized by various stress hormones. In people, adrenaline and cortisol levels are increased in the face of surgery, as are glucagon, growth hormone, aldosterone and antidiuretic hormone. The extent of surgical trauma correlates well with the levels of ACTH and cortisol [81]. If patients develop postoperative complications, other abnormalities can occur. In people, critically ill patients can have a cortisol deficiency. High dose therapy with glucocorticosteroids has been associated with increased mortality, while low doses may have beneficial effects by increasing their response to noradrenaline [82]. The metabolism is decreased in the first few hours after surgery. However, this is soon followed by a catabolic and hypermetabolic phase. This phase is characterized by break down of skeletal muscle and fat [83]. Oxygen delivery to the tissues is important during this hypermetabolic phase. The body reacts by vasodilating, increasing the heart rate, increasing cardiac output, and increasing the respiratory rate [84]. A leukocytosis occurs in the peripheral blood and granulocytes and macrophages accumulate in the damaged tissues [85]. Many pro-inflammatory cytokines are released leading to inflammation. The amount of cytokine release is well correlated with both the magnitude and duration of surgery and the risk of postoperative complications. If the initial pro-inflammatory response is exaggerated, sever systemic inflammatory response syndrome may occur.

Pain

Surgical procedures will lead to a pain response. It is well supported that the more invasive a procedure is, the more pain the patient will experience. Horses are typically stoic animals when it comes to exhibiting pain. It is thought that they mask signs of pain from predators, including humans, to minimize possible predation [86]. In one study, it was determined that horses undergoing surgery paid decreased attention toward novel objects and decreased responsiveness to auditory signals [87]. The relationship between pain, behavioral distress and physiological stress is complex and difficult to determine. Consequently, endocrine measures may not be accurate indicators of pain alone. It is also difficult to separate the inflammatory process associated with surgery and surgical complications from the pain response associated with surgery and surgical complications. The measurement of equine pain is probably best accomplished with multidimensional pain scales [88]. The Horse Grimace Scale has been recently described and is easy to use and has a high reliability between observers [89].

Impact of Host Factors and Comorbid Conditions

Blood loss impairs the body's ability to deliver oxygen to the tissues and oxygen delivery to the tissues is important during injury [84]. Lack of oxygen impairs the body's ability to heal. Diagnosing blood loss in the horse can be challenging due to the large reservoir of red blood cells stored in the spleen. Splenic contraction can maintain packed cell volume and total protein in the acute stages of hemorrhage [90]. Fluid volume expansion can actually reduce the effectiveness of oxygen delivery, making blood transfusions an important aspect of improving oxygen delivery.

Pituitary pars intermedia dysfunction is thought to impair corneal wound healing in horses [91]. There also appears to be an association between PPID and degenerative suspensory ligament desmitis [92]. It seems reasonable then that horses with PPID may have difficulty in healing. This should be considered when operating on horses with PPID.

References

1 Sokol, D.K. and Wilson. J. (2008).What is a surgical complication? *World J. Surg.* 32 (6): 942–944.
2 Jacbos, J.P., Jacbos. M.L., Mavrudis. C. et al. (2007). What is operative morbidity? defining complications in a surgical registry database. *Ann. Thorac. Surg.* 84: 1416–1421.
3 Tsesis, I. and Rosen, E. (2014). Introduction: an evidence-based approach for prevention and management of surgical complications. In: Complications in Endodontic Surgery: Prevention, Identification and Management, 1e (ed. I. Tsesis), 1–6. Berlin: Springer-Verlag.
4 Wooley, C.F. and Boudoulas, H. (1993). Clinician. *Hellenic J. Cardiol.* 34: 241–243.
5 Tsesis, I. and Rosen, E. (2014). Approach for prevention and management of surgical complications. In: Complications in Endodontic Surgery: Prevention, Identification and Management, 1e (ed. I. Tsesis), 1–6. Berlin: Springer-Verlag.
6 Isaacs, D. and Fitzgerald, D. (1999). Seven alternatives to evidence based medicine. *B.M.J.* 319 (7225): 1618.
7 Mulholland, M.W. and Doherty, G.M. (2011). Surgical complciations. In: Complications in Surgery, 2e (ed. M.W. Mulholland and G.M. Doherty), 3–4. Philadelphia: Wolters Kluwer. Lipincott Williams & Wilkins.
8 Dorland, D. (2011). Dorlands Illustrated Medical Dictionary, 32e. Philadelphia: Saunders.
9 William, M.P. (2010). Measuring Morbidity Following Major Surgery. London: University College London.

10 Jacobs, J.P., Mavroudis, C., Jacobs, M.L. et al. (2006). What is operative mortality? Defining death in a surgical registry database: a report of the STS Congenital Database Taskforce and the Joint EACTS-STS Congenital Database Committee. *Ann. Thorac. Surg.* 81 (5): 1937–1941.

11 Sahni, N.R., Dalton, M., Cutler, D.M. et al. (2016). Surgeon specialization and operative mortality in United States: retrospective analysis. *B.M.J.* 354: i3571.

12 Khuri, S.F., Henderson, W.G., DePalma, R.G. et al. (2005). Participants in the VANSQIP: determinants of long-term survival after major surgery and the adverse effect of postoperative complications. *Ann. Surg*. 242 (3): 326–341; discussion 341–323.

13 Kravet, S.J., Howell, E., and Wright, S.M. (2006). Morbidity and mortality conference, grand rounds, and the ACGME's core competencies. *J. Gen. Intern. Med.* 21 (11): 1192–1194.

14 Pierluissi, E., Fischer, M.A., Campbell, A.R. et al. (2003). Discussion of medical errors in morbidity and mortality conferences. *J.A.M.A.* 290 (21): 2838–2842.

15 Lecoanet, A., Vidal-Trecan, G., Prate, F. et al. (2016). Assessment of the contribution of morbidity and mortality conferences to quality and safety improvement: a survey of participants' perceptions. *B.M.C. Health Serv. Res.* 16: 176.

16 Reines, H.D., Trickey, A.W., and Donovan, J. (2017). Morbidity and mortality conference is not sufficient for surgical quality control: processes and outcomes of a successful attending Physician Peer Review committee. *Am. J. Surg.* 214 (5): 780–785.

17 Tignanelli, C.J., Embree, G.G.R., and Barzin, A. (2017). House staff-led interdisciplinary morbidity and mortality conference promotes systematic improvement. *J. Surg. Res.* 214: 124–130.

18 Copeland, G.P., Jones, D., and Walters, M. (1991). POSSUM: a scoring system for surgical audit. *Br. J. Surg.* 78 (3): 355–360.

19 Dindo, D., Demartines, N., and Clavien, P.A. (2004). Classification of surgical complications: a new proposal with evaluation in a cohort of 6,336 patients and results of a survey. *Ann. Surg.* 240 (2): 205–213.

20 Imaoka, Y., Itamoto, T., Nakahara, H. et al. (2017). Physiological and Operative Severity Score for the enumeration of mortality and morbidity and modified Physiological and Operative Severity Score for the enumeration of mortality and morbidity for the mortality prediction among nonagenarians undergoing emergency surgery. *J. Surg. Res.* 210: 198–203.

21 Gawande, A. (2007). The checklist: if something so simple can transform intensive care, what else can it do? *New Yorker*. December 10th: 86–101.

22 Oak, S.N., Dave, N.M., Garasia, M.B. et al. (2015). Surgical checklist application and its impact on patient safety in pediatric surgery. *J. Postgrad. Med.* 61 (2): 92–94.

23 Treadwel, J.R., Lucas, S., and Tsou, A.Y. (2014). Surgical checklists: a systematic review of impacts and implementation. *B.M.J. Qual. Saf.* 23 (4): 299–318.

24 Zingiryan, A., Paruch, J.L., Osler, T.M., et al. (2017). Implementation of the surgical safety checklist at a tertiary academic center: impact on safety culture and patient outcomes. *Am. J. Surg.* 214 (2): 193–197.

25 Haugen, A.S., Softeland, E., Almeland, S.K. et al. (2015). Effect of the World Health Organization checklist on patient outcomes: a stepped wedge cluster randomized controlled trial. *Ann. Surg.* 261 (5): 821–828.

26 Gillespie, B.M. and Marshall, A. (2015). Implementation of safety checklists in surgery: a realist synthesis of evidence. *Implement. Sci.* 10: 137.

27 Papaconstantinou, H.T., Smythe, W.R., Reznik, S.I. et al. (2013). Surgical safety checklist and operating room efficiency: results from a large multispecialty tertiary care hospital. *Am. J. Surg*. 206 (6): 853–859; discussion 859–860.

28 Moberg, G.P. (1985). Biological response to stress: key to assessment of animal well-being? In: Animal Stress, 27–49. Bethesda: American Physiological Society.

29 Cuthbertson, D.P. (1932). Observation on the disturbance of metabolism produced by injury to the limbs. *Quart. J. Med.* 25: 233–246.

30 Keusch, G.T. (2003). The history of nutrition: malnutrition, infection and immunity. *J. Nutr.* 133 (1): 336S–340S.

31 Ward, N. (2003). Nutrition support to patients undergoing gastrointestinal surgery. *Nutr. J.* 2: 18.

32 Robinson, G., Goldstein, M., and Levine G.M. (1987). Impact of nutritional status on DRG length of stay. *J.P.E.N.* 11 (1): 49–51.

33 Shukla, V.K., Roy, S.K., Kumar, J. et al. (1985). Correlation of immune and nutritional status with wound complications in patients undergoing abdominal surgery. *Am. Surg.* 51 (8): 442–445.

34 Mann, S., Westenskow, D.R., and Houtchens, B.A. (1985). Measured and predicted caloric expenditure in the acutely ill. *Crit. Care. Med.* 13 (3): 173–177.

35 Durham, A.E., Phillips, T.J., Walmsley, J.P. et al. (2004). Nutritional and clinicopathological effects of postoperative parenteral nutrition following small intestinal resection and anastomosis in the mature horse. *Equine Vet. J.* 36 (5): 390–396.

36 Carr, E.A. and Holcombe, S.J. (2009). Nutrition of critically ill horses. *Vet. Clin. N. Am. Equine Pract.* 25 (1): 93–108, vii.

37 Lewis, L.D. (1995). Feeding and care of horses with health problems. In: Equine Clinical Nutrition and Feeding and Care, 2e (ed. L.D. Lewis), 289–299. Baltimore (MD): Williams & Wilkins.

38 Campbell, I.T. (1999). Limitations of nutrient intake. The effect of stressors: trauma, sepsis and multiple organ failure. *Eur. J. Clin. Nutr.* 53 Suppl 1: S143–147.

39 Bessey, P.Q., Watters, J.M., Aoki, T.T. et al. (1984). Combined hormonal infusion simulates the metabolic response to injury. *Ann. Surg.* 200 (3): 264–281.

40 Carli, F., Webster, J., Ramachandra, V. et al. (1990). Aspects of protein metabolism after elective surgery in patients receiving constant nutritional support. *Clin. Sci. (Lond).* 78 (6): 621–628.

41 Cruz, A.M., Cote, N., McDonell, W.N. et al. (2006). Postoperative effects of anesthesia and surgery on resting energy expenditure in horses as measured by indirect calorimetry. *Can. J. Vet. Res.* 70 (4): 257–262.

42 Serteyn, D., Pincemail, J., Deby, C. et al. (1991). Equine postanesthetic myositis: an ischaemic reperfusion phenomenon. *J. Vet. Anaesth.* 18 (Supp 1): 319–322.

43 Edner, A., Essen-Gustavsson, B., and Nyman, G. (2005). Muscle metabolic changes associated with long-term inhalation anaesthesia in the horse analysed by muscle biopsy and microdialysis techniques. *J. Vet. Med. A.* 52 (2): 99–107.

44 Edner, A., Nyman, G., and Essen-Gustavsson, B. (2002). The relationship of muscle perfusion and metabolism with cardiovascular variables before and after detomidine injection during propofol-ketamine anaesthesia in horses. *Vet. Anaesth. Analg.* 29 (4): 182–199.

45 Edner, A.H., Nyman, G.C., and Essen-Gustavsson, B. (2007). Metabolism before, during and after anaesthesia in colic and healthy horses. *Acta Vet. Scand.* 49: 34.

46 Edner, A.H., Essen-Gustavsson, B., and Nyman, G.C. (2009). Metabolism during anaesthesia and recovery in colic and healthy horses: a microdialysis study. *Acta Vet. Scand.* 51: 10.

47 Carr, E.A. (2012). Metabolism and nutritional support of the surgical patient. In: Equine Surgery, 4e (ed. J.A. Auer and J.A. Stick), 62–67. St. Louis, Missouri: Saunders Elsevier.

48 Rokyuta, R., Jr., Matekovic,M., Krouzecky, A. et al. (2003). Enteral nutrition and hepatosplanchnic region in critically ill patients – friends or foes? *Physio. Res.* 52 (1): 31–37.

49 Robert, P.R. and Zaloga, G.P. (2000). Enteral nutrition. In: Textbook of Critical Care, 4e (ed. W. C. Shoemaker, S.M. Ayres, and A. Grenvick), 875–882. Philadelphia: Saunders Elsevier.

50 Jose-Cunilleras, E., Viu, J., Corradini, I. et al. (2012). Energy expenditure of critically ill neonatal foals. *Equine. Vet. J. Suppl.* (41): 48–51.

51 McKenzie, H.C. 3rd, and Geor, R.J. (2009). Feeding management of sick neonatal foals. *Vet. Clin. N. Am. Equine Pract.* 25 (1): 109–119, vii.

52 Myers, C.J., Magdesian, K.G., Kass, P.H. et al. (2009). Parenteral nutrition in neonatal foals: clinical description, complications and outcome in 53 foals (1995–2005). *Vet. J.* 181 (2): 137–144.

53 Krause, J.B. and McKenzie, H.C. 3rd. (2007). Parenteral nutrition in foals: a retrospective study of 45 cases (2000–2004). *Equine Vet. J.* 39 (1): 74–78.

54 Durham, A.E. (2006). Clinical application of parenteral nutrition in the treatment of five ponies and one donkey with hyperlipaemia. *Vet. Rec.* 158 (5): 159–164.

55 Lopes, M.A. and White, N.A. 2nd. (2002). Parenteral nutrition for horses with gastrointestinal disease: a retrospective study of 79 cases. *Equine Vet. J.* 34 (3): 250–257.

56 Jeejeebhoy, K.N. (2001). Total parenteral nutrition: potion or poison? *Am. J. Clin. Nutr.* 74 (2): 160–163.

57 Vergnano, D., Bergero, D., and Valle, E. (2017). Clinical nutrition counselling service in the veterinary hospital: retrospective analysis of equine patients and nutritional considerations. *J. Anim. Physiol. Anim. Nutr. (Berlin).* 101 (Suppl 1): 59–68.

58 Clarke, R.S. (1973). Anaesthesia and carbohydrate metabolism. *Br. J. Anaesth.* 45 (3): 237–243.

59 Oyama, T. (1973). Endocrine responses to anaesthetic agents. *Br. J. Anaesth.* 45 (3): 276–281.

60 Luna, S.P., Taylor, P.M., and Wheeler, M.J. (1996). Cardiorespiratory, endocrine and metabolic changes in ponies undergoing intravenous or inhalation anaesthesia. *J. Vet. Pharm. Ther.* 19 (4): 251–258.

61 Taylor, P.M. (1991). Stress responses in ponies during halothane or isoflurane anaesthesa after induction with thiopentone or xyulaxine/ketamine. *J. Assoc. Vet. Anaesth.* 18: 8–14.

62 Wagner, A.E. (2009). Stress associated with anesthesia and surgery. In: Equine Anesthesia Monitoring and Emergency Therapy, 2e (ed. W.W. Muir and J.A.E. Hubbell), 101–108. St. Louis, Missouri: Saunders Elsevier.

63 Robertson, S.A. (1987). Some metabolic and hormonal changes associated with general anaesthesia and surgery in the horse. *Equine Vet. J.* 19 (4): 288–294.

64 Robertson, S.A., Steele, C.J., and Chen, C.L. (1990). Metabolic and hormonal changes associated with arthroscopic surgery in the horse. *Equine Vet. J.* 22 (5): 313–316.

65 Taylor, P.M. (1989). Equine stress responses to anaesthesia. *Br. J. Anaesth.* 63 (6): 702–709.

66 van Dijk, P., Lankveld, D.P., Rijkenhuizen, A.B. et al. (2003). Hormonal, metabolic and physiological effects of laparoscopic surgery using a detomidine-buprenorphine combination in standing horses. *Vet. Anaesth. Analg.* 30 (2): 72–80.

67 Robertson, S.A., Malark, J.A., Steele, C.J. et al. (1996). Metabolic, hormonal, and hemodynamic changes during dopamine infusions in halothane anesthetized horses. *Vet. Surg.* 25 (1): 88–97.

68 Cooper, G.M., Paterson, J.L., Ward, I.D. et al. (1981). Fentanyl and the metabolic response to gastric surgery. *Anaesthesia.* 36 (7): 667–671.

69 Elliott, M. and Alberti, K.G.M.M. (1983). The hormonal and metabolic response to surgery by narcotics and general anaesthesia. *Clin. Anaesth.* 3: 247–270.

70 Taylor, P.M. (1985). Changes in plasma cortisol concentration in response to anaesthesia in the horse. In: *2nd International Congress of Veterinary Anaesthesiology: 1985; Sacramento*, 165–166.

71 Stegmann, G.F. and Jones, R.S. (1998). Perioperative plasma cortisol concentration in the horse. *J. S. Afr. Vet. Assoc.* 69(4): 137–142.

72 Underwood, C., Southwood, L.L., Walton, R.M. et al. (2010). Hepatic and metabolic changes in surgical colic patients: a pilot study. *J. Vet. Emerg. Crit. Care (San Antonio).* 20 (6): 578–586.

73 Gardner, R.B., Nydam, D.V., Mohammed, H.O. et al. (2005). Serum gamma glutamyl transferase activity in horses with right or left dorsal displacements of the large colon. *J. Vet. Intern. Med.* 19 (5): 761–764.

74 Davis, J.L., Blikslager, A.T., Catto, K. et al. (2003). A retrospective analysis of hepatic injury in horses with proximal enteritis (1984–2002). *J. Vet. Intern. Med.* 17 (6): 896–901.

75 Cotovio, M., Monreal, L., Navarro, M. et al. (2007). Detection of fibrin deposits in horse tissues by immunohistochemistry. *J. Vet. Intern. Med.* 21 (5): 1083–1089.

76 Dunkel, B. and McKenzie, H.C. 3rd. (2003). Severe hypertriglyceridaemia in clinically ill horses: diagnosis, *treatment and outcome. Equine Vet. J.* 35 (6): 590–595.

77 Frank, S.M., Higgins, M.S., Fleisher, L.A. et al. (1997). Adrenergic, respiratory, and cardiovascular effects of core cooling in humans. *Am. J. Physiol.* 272 (Pt 2): R557–562.

78 Tomasic, M. (1999). Temporal changes in core body temperature in anesthetized adult horses. *Am. J. Vet. Res.* 60 (5): 556–562.

79 Cruz, A.M., Kerr, C.L., Boure, L.P. et al. (2004). Cardiovascular effects of insufflation of the abdomen with carbon dioxide in standing horses sedated with detomidine. *Am. J. Vet. Res.* 65 (3): 357–362.

80 Toft, P. and Tønnesen, E. (2008). The systemic inflammatory response to anaesthesia and surgery. *Curr. Anaesth. Crit. Care.* 19 (5): 349–353.

81 Choileain, N.N. and Redmond, H.P. (2006). Cell response to surgery. *Arch. Surg.* 141 (11): 1132–1140.

82 Annane, D., Sébille, V., Charpentier, C. et al. (2002). Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. *J.A.M.A.* 288 (7): 862–861.

83 Bessey, P.Q., Jiang, Z.M., Johnson, D.J. et al. (1989). Posttraumatic skeletal muscle proteolysis: the role of the hormonal environment. *World J. Surg.* 13 (4): 465–470.

84 Russell, J.A., Ronco, D., Lockhat, A. et al. (1990). Oxygen delivery and consumption and ventricular preload are greater in survivors than in non-survivors of the adult respiratory distress syndrome. *Am. Rev. Respir. Dis.* 141 (3): 659–665.

85 Toft, P., Tønnesen, E., Helbo-Hansen, H.S. et al. (1994). Redistribution of granulocytes in patients after major surgical stress. *A.P.M.I.S.* 102 (1): 43–48.

86 Ashley, F.H., Waterman-Pearson, A.E., Whay, H.R. (2005). Behavioural assessment of pain in horses and donkeys; application to clinical practice and future studies. *Equine Vet. J.* 37 (6): 565–575.

87 Dodds, L., Knight, L., Allen, K. et al. (2017). The effect of postsurgical pain on attentional processing in horses. *Vet. Anaesth. Analg.* 44 (4): 933–942.

88 de Grauw, J.C. and van Loon, J.P.A.M. (2016), Systematic pain assessment in horses. *Vet. J.* 209: 14–22.

89 Dalla Costa, E., Minero, M., Lebelt, D. et al. (2014). Development of the horse grimace scale (HGS) as a pain assessment tool in horses undergoing routine castration. *PLoS ONE.* 9: e92281

90 Mudge, M.C. (2014). Acute hemorrhage and blood transfusions in horses. *Vet. Clin. N. Am. Equine Pract.* 30 (2): 427–436.

91 Hart, K.A., Kitchings, K.M., Kimura, S. et al. (2016). Measurement of cortisol concentration in the tears of horses and ponies with pituitary pars intermedia dysfunction. *Am. J. Vet. Res.* 77 (11): 1236–1244.

92 Hofberger, S.C., Gauff, F., Thaller, D. et al. (2018). Assessment of tissue-specific cortisol activity with regard to degeneration of the suspensory ligaments in horses with pituitary pars intermedia dysfunction. *Am. J. Vet. Res.* 79 (2): 199–210.