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Systemic inflammatory response syndrome – an overview

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ABSTRACT Systemic inflammatory response syndrome (SIRS) is a poorly understood clinical state that is not restricted to the emergency and critical care environment. This article aims to explain the pathophysiology and causes of SIRS. Veterinary nurses can play a pivotal role with patients at risk of developing SIRS. Our close and frequent monitoring of hospitalised patients mean that veterinary nurses are best placed to recognise the clinical criteria relating to SIRS. Early recognition and aggressive treatment of SIRS maximises the chance of a successful outcome.

Introduction

The systemic inflammatory response syndrome (SIRS) occurs as a response to an infectious or non-infectious insult on the body. SIRS is a complex and serious condition that can affect patients of any age or level of fitness. Early recognition of the condition is vital to maximise the likelihood of a positive outcome and prevent progression of SIRS into shock, multiple organ dysfunction syndrome (MODS) or eventually multi-organ failure (MOF) (Guillaumin, 2010). Basic terminology relating to the condition is outlined in Box 1.

Box 1. Terminology

SIRS – systemic inflammatory response syndrome
Sepsis – SIRS with evidence of infection
MODS – multiple organ dysfunction syndrome
MOF – multiple organ failure
DIC – disseminated intravascular coagulation
ARDS – acute respiratory distress syndrome
ALI – acute lung injury

SIRS is not limited to the hospital, referral or emergency and critical-care environment. Patients that present in first opinion practice with common conditions such as parvoviral enteritis and flystrike are all typical of those at risk of developing SIRS.

Most veterinary nurses see these types of cases on a regular basis, however SIRS still remains poorly understood. This is, in part, because it can be difficult to recognise. Clinical signs differ between species and from patient to patient. Cats with SIRS can be particularly challenging.

The criteria for SIRS are based on a human model which is somewhat unspecific. This can make recognising SIRS difficult and formulating an appropriate treatment plan problematic. Furthermore, instances of SIRS in veterinary patients are less well documented. There is little primary research relating to SIRS but we do know that the mortality rate is high. Howie (2013) states that around 50% of patients with SIRS will not survive. Whilst SIRS is less common in cats than dogs, cats can be more difficult to diagnose, with the mortality rate in feline patients being significantly higher.

The pathophysiology of SIRS

SIRS can be better understood when considered alongside the normal inflammatory process. When an injury or trauma occurs (whether infectious or not), sufficient local cytokine (proteins secreted by cells of the immune system) is produced to incite a localised pro-inflammatory and anti-inflammatory response and promote repair (Neumann, 2012). Pro-inflammatory mediators (macrophages, monocytes and neutrophils) move towards

the area of injury or infection and stem the inflammation (Howie, 2013). These mediators have a noxious element to them to remove or destroy damaged tissue. In a normal patient, inflammation remains localised and eventually the pro-inflammatory mediators decrease. Repair and healing is controlled and self-limiting. In such cases inflammation is a beneficial process. Patients heal and recover.

In patients with SIRS, however, the entire body becomes inflamed. Cytokine production is abnormal, with pro-inflammatory and anti-inflammatory mediators becoming unbalanced. Pro-inflammatory mediators damage normal healthy tissues, often distant from the original site of inflammation. The process becomes totally overwhelming, causing severe and prolonged inflammation in animals that are often already compromised. SIRS causes systemic vasodilatation, distributive shock, organ dysfunction, a fall in blood pressure and initiation of the clotting system (Howie, 2013; Neumann, 2012). If untreated, SIRS continues to destroy healthy tissues, leading to organ failure and death.

Causes of SIRS

The causes of SIRS can be either infectious or non-infectious. When the cause is infectious, this is known as sepsis.

Table 1. Clinical criteria for SIRS (Guillaumin, 2010; Neumann, 2012; Silverstein, 2006)

Parameter	Canine	Feline
Heart Rate	Tachycardia >120 bpm	Bradycardia <140 bpm Tachycardia >225 bpm
Respiration Rate	Tachypnoea >40 bpm and/or PaCO ₂ <30 mmHg	Tachypnoea >30 bpm and/or PaCO ₂ <30 mmHg
Temperature	Hypothermia <38°C Hyperthermia >40°C	Hypothermia <37.7°C Hyperthermia >40°C
WBC	Leukopenia <5,000 WBC/μl Leucocytosis >18,000-20,000 WBC/μl	Leukopenia <5,000 WBC/μl Leucocytosis >19,500 WBC/μl

SIRS and sepsis are common in veterinary practice. Sepsis may be caused by gram-positive or gram-negative bacteria, viral or fungal organisms (Neumann, 2012). One such example is entire bitches diagnosed with pyometra (**Figure 1**). These patients may have been inflamed for a number of days, due to bacteria in the uterus. Karlsson, Hagman, Johannisson, Wang, Karlstam, and Wernersson (2012) state that almost six out of ten dogs diagnosed with a pyometra have SIRS. This is particularly significant in what is a relatively common condition seen in general practice. Other potential causes of sepsis are pyothorax, parvoviral enteritis, flystrike, snake envenomation, peritonitis and bite wounds.

Non-infectious causes of SIRS are wide ranging. They include burns, major trauma, heat stroke, seizures, immune-mediated diseases, hyperthermia, neoplasia and blood pressure issues.

Patients with pancreatitis are also at risk of SIRS. In many cases, the pancreas has been inflamed for a number of days and this severe insult to a small, yet vitally important, organ can result in systemic inflammation (Howie, 2013).

Clinical criteria for SIRS

The American College of Chest Physicians and the Society of Critical Care Medicine first defined SIRS and sepsis in 1991 (Semler & Wheeler, 2014). This definition aimed to assist doctors to identify SIRS and improve the formulation of treatment plans. It has subsequently been developed within both the human and veterinary sector, yet for both it still remains relatively unspecific, especially given the wide range of causes of SIRS.

Whether SIRS is caused by an infectious or non-infectious cause, the clinical criteria remain similar, although they differ between dog and cat and can easily be mistaken for other conditions. It is worth noting that cats are usually more seriously ill and much harder to treat. **Table 1** outlines the parameters at which canine and feline patients may be considered at high risk of SIRS. Most authors agree that a minimum of two of the clinical criteria should be present to suspect SIRS (Aldrich, 2014; Guillaumin, 2010).

There are other documented clinical signs of SIRS that have been observed in veterinary patients that do not form part of the recognised parameters. These include:

- mucous membrane colour
- capillary refill time
- pulse quality
- oliguria
- anaemia

Awareness of these other findings in patients with SIRS may assist veterinary professionals who are concerned about an animal in their care.

It is important to monitor mucous membrane colour and capillary refill time

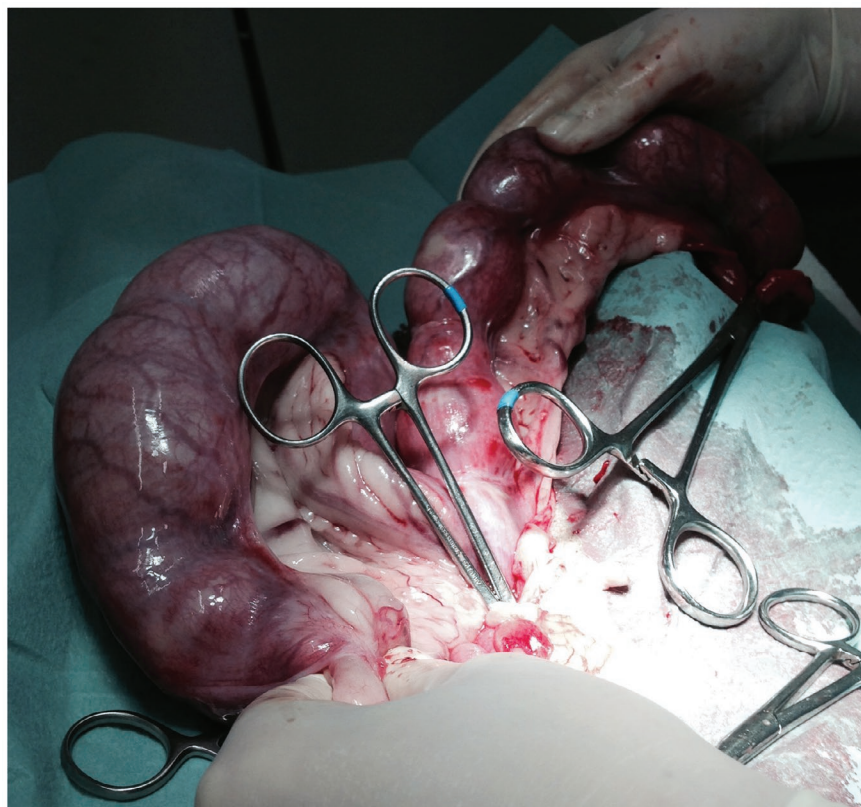


Figure 1. Pyometra

(Howie, 2013). Patients with SIRS commonly have brick-red mucous membranes as a result of vasodilatation and often have a rapid capillary refill time. Cats may alternatively have pale or icteric mucous membranes. In addition, cats have been reported to have poor pulse quality, abdominal pain and anaemia (Silverstein, 2006).

Black (2008) suggests that dogs with SIRS can present with oliguria. The veterinary nurse should consider placement of a urinary catheter to enable urine output to be measured. Daily urine output falling to less than 0.5ml/kg/h is significant and, in conjunction with other clinical signs, can be suggestive of SIRS (Black, 2008).

It is also important to record the demeanour of a patient that is at risk of developing SIRS. A worrying sign would be a patient that has been getting brighter and more alert each day who suddenly becomes lethargic, depressed and inappetent.

Management of SIRS

Monitoring of trends is vital in patients with SIRS. As part of a minimum database it would be prudent to conduct full haematology and biochemistry profiles in suspected SIRS cases. Leukopenia and leucocytosis have already been discussed as part of the clinical criteria for SIRS. In addition, hypoglycaemia, hypoalbuminaemia and hyperbilirubinaemia (in cats) may be seen in septic patients. Bloodwork can easily be compared against previous test results. In addition, packed cell volume (PCV), total solids (TS), lactate and blood gas measurements are vital point-of-care tests that can be effective in determining the extent of the illness and initiation of a treatment plan (Guillaumin, 2010). It is imperative that the source of the injury is found and removed. This may require further diagnostic work-up, for example imaging, echocardiography or urinalysis (Guillaumin, 2010). Surgical intervention may be warranted for example in the case of a pyometra or gastric dilatation volvulus where surgery is necessary to correct the initial cause.

The key to successful treatment of SIRS and sepsis is to improve cardiopulmonary parameters and treat any infection aggressively with broad-spectrum antibiotics at the earliest possible opportunity. Intravenous fluid therapy, taking into account maintenance requirements,

dehydration and on-going losses, is vital. Central venous pressure monitoring would be useful to determine fluid status (Silverstein, 2006). Analgesia and any other supportive care must also be used appropriately and reviewed regularly.

Maintaining adequate oxygen delivery to tissues is paramount. Oxygen therapy is necessary in patients with $SpO_2 < 93\%$ or $PaO_2 < 80\text{mmHg}$ and in patients where SIRS has developed into MODS that is affecting the lungs (Silverstein, 2006). Depending on the injury, vasopressors, blood products and liver protectants may be indicated.

Veterinary nurses should always endeavour to create a bond with each and every patient they deal with, so plenty of TLC and a comfortable environment must be provided for these patients, especially as they may be hospitalised for long periods. Parenteral feeding may be warranted for patients who are vomiting or where enteral feeding is contraindicated (Silverstein, 2006). Ultimately, it is vital that SIRS or sepsis do not develop into MODS or MOF, for which the prognosis significantly worsens.

Multiple organ dysfunction syndrome (MODS)

Failure of one organ system increases the mortality rate by 20% (Guillaumin, 2010). It does not follow that the failing organ system is related to the original site of injury. Indeed, the organ system may be either local or distant to the original site of injury and it is not uncommon for multiple organs to fail. These may include the gastrointestinal system, hepatic system, cardiovascular system and the immune system. The blood-clotting mechanism can also be affected, leading to disseminated intravascular coagulation (DIC), as the pro-inflammatory response leads to abnormal consumption of clotting proteins in the blood. This manifests itself as excessive bleeding, for example at the site of venepuncture, bruising, hypotension or gastrointestinal haemorrhage.

Lung failure in MODS is described as acute lung injury (ALI) or, in more severe cases, acute respiratory distress syndrome (ARDS). Pro-inflammatory mediators damage the alveolar capillary membrane, allowing fluid to leak from the vascular space and into the alveoli (Aldrich, 2014). Patients are

typically dyspnoeic, tachypnoeic and have a low SpO_2 . They may require mechanical ventilation. The prognosis in these types of cases is particularly poor.

The role of the veterinary nurse

Difficulties in identification of SIRS are quite apparent. We regularly see frightened and nervous patients in the hospital environment, and this can increase temperature, heart and respiration rate. This does not necessarily mean that SIRS is present. Conversely, we should not be complacent if the clinical criteria that determine SIRS are met. Veterinary nurses should closely monitor patients at risk of developing SIRS to ensure any changes in trends are rapidly observed and dealt with. Making detailed notes on hospital charts and having good communication across the whole veterinary team is imperative to ensure trends can be monitored effectively.

Vital signs that should be monitored include temperature, pulse and respiration. If they remain within normal limits, it can indicate that inflammation has remained localised. Changes in two of these parameters, for example if the patient becomes tachycardic and hyperthermic, could suggest the patient is developing SIRS and the veterinary surgeon should be advised accordingly. This would be of particular concern if the patient has been hospitalised for a few days and has previously shown signs of improvement. It would then become important to monitor these patients even more vigorously and give any further treatment according to the veterinary surgeon's instructions.

Conclusion

SIRS is a complex state that can be hard to identify in both human and veterinary patients. It would no doubt be beneficial if the medical and veterinary profession could work together to understand the condition better. After reading this article readers may well become aware in hindsight of a number of cases where the patient was at risk of, or may even have developed, SIRS. Veterinary nurses can play a vital role in monitoring their hospitalised patients with a view to preventing SIRS or at least recognising the condition early. Good communication throughout

the veterinary team and comprehensive completion of hospital charts is required to ensure that in a busy environment individual patient trends can be noted and quickly acted upon.

The outcome for these patients depends largely on successful supportive treatment, which is both aggressive and instituted rapidly in response to the nature of the injury presented. These cases are, no doubt, exceptionally interesting and can be very rewarding to nurse.

Disclosure Statement

No potential conflict of interest was reported by the author.

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