The purpose of this lecture is to remind veterinarians in practice that shock is a complex disease with a high mortality and in particular to review the pathophysiology of and interventions needed in the management of hypovolemic shock and SIRS (Systemic Inflammatory Response Syndrome) in the cat and the dog.

Rapid recognition of shock and SIRS with early intervention are key to recovery. Critical cases presented in emergency situations such as post trauma are likely to provoke a determined examination for signs of shock. However signs of shock or SIRS may be missed in animals with a history of non specific clinical signs or animals who develop shock or SIRS during the treatment of a clinical or surgical condition or develop shock after surgery or chemotherapy.

**Classification of Shock**

There a number of ways shock has been classified including based on its underlying cause. Haemorrhagic shock is due to bleeding perhaps as a result of trauma, post operatively and increasingly in practice as a result of neoplasia. Hypovolemic shock can be caused by fluid loss in the GIT or uncompensated renal disease and or third spacing. Cardiogenic shock occurs as a result of heart failure or myocardial depression as in GDV. Cytotoxic shock describes cells which can not use oxygen as a result of mitochondrial damage. Anaphylactic shock occurs as a result of a hypersensitivity reaction. Neurogenic shock is due to a neurologic disease process causing loss of vasomotor tone. Obstructive shock is when reduced venous return as in GDV compression of the vena cava results in reduced cardiac output. Septic shock occurs with serious infection. Shock often has multiple and overlapping causes with dynamic systemic and complex physiologic responses.

The stages of shock are a description of the physiological response to reduced delivery of oxygen to the tissues. They are neatly divided in to an early or compensatory stage, decompensation and then a terminal decompenatory stage which can culminate in multiple organ failure. Physiologic responses can deteriorate to pathology in shock and is not necessarily neatly divided in to stages but rather is a declining continuum. It is important for veterinarians in practice to recognise the clinical presentations of shock and equally essential to intervene and anticipate rapid changes which can lead to multiple organ failure. Delays in recognition of shock and treating with appropriate intervention inevitably increase mortality.
Shock is at a cellular level more uniform and has been succinctly described as a "state in which profound and widespread reduction of effective tissue perfusion leads first to reversible and then if prolonged to irreversible cellular injury." (Kumar A, Parillo JE: Shock Classification, pathophysiology and approach to management CCM 2001).

The identification of key indicators of shock in its various stages and regardless of cause is practical and essential to early intervention. The suspicion of and diagnosis of shock centres around assessment of parameters of perfusion: mucous membrane colour, capillary refill time, oxygen saturation, lactic acid levels, blood gases /pH and the assessment of physiological responses to shock which veterinarians look at in practice every day namely mental alertness, heart rate, respiratory rate, temperature and blood pressure.

The common pathway for all types of shock is:

**Inadequate delivery of oxygen to the tissues to meet tissue demand**

The relationship between oxygen demand, oxygen uptake and oxygen supply is mathematically expressed (derived from Fick’s equation):

\[
DO₂ = CO \times (1.34 \times Hb \times SaO₂ + 0.0003 \times PaO₂)
\]

Oxygen delivery to the tissues (DO₂) = CO Cardiac Output \(\times\) CaO₂ (Total Arterial Oxygen) which is dependant on Haemoglobin uptake of oxygen available in the arteries and capillaries. Cardiac output (CO) is the heart rate \(\times\) stroke volume.

In a normal state Oxygen delivery DO₂ equals Oxygen consumption VO₂. Oxygen demand is relatively constant except in hyper metabolic states or heat stroke and status epilepticus.

If shock is understood as primarily the under perfusion of tissues and under delivery of oxygen to cells it becomes intuitive that physiologic responses of the animal and clinical interventions by veterinarians will involve improving the delivery of oxygen by manipulating cardiac output (heart rate, stroke volume through intravascular volume) and availability of Oxygen. Intravenous fluid therapy and oxygen are almost always indicated once shock is suspected. Intravascular volume fluid replacement using a combination of isotonic crystalloids and hypertonic saline as a first response in situations where tissue demand for oxygen has exceeded tissue delivery. Fluid rates should always be based on assessment of shock parameters and should be tailored to clinical presentations and underlying disease processes. Rates should be lowered if fluid retention as in pulmonary oedema and or heart failure is identified. Other
circumstances where care must be taken with aggressive fluid rates is with a
history of chest trauma and possible pulmonary contusion or with a history of
head trauma or clinical situations with possible increased intracranial pressure.
Oxygen should be available to the cat or dog with clinical signs of shock and
should be delivered without increasing oxygen demand or stressing the patient.

Working towards specific goals (See Section on Goal Directed Therapy) keeps
the veterinarian focussed on monitoring the rapidly changing parameters of
shock and changing therapy or even stopping therapy if the response is not
adequate. The pillars of therapy in all types of shock are to remove the cause if it
has been identified, restore intravascular volume, improve cardiac output and
blood pressure and optimise oxygenation.

In first opinion practice the most common presentations of shock are
hypovolemic shock and septic shock with or without infection as in SIRS.

HYPOVOLEMIC SHOCK
Hypovolemic shock is caused by a reduction in intravascular fluid volume
sufficient to reduce ventricular filling and cardiac output. This can be as a result
of blood loss, vomiting and or diarrhoea, renal losses, wound fluid loss and third
space losses. Third spacing is where fluid is lost from the intravascular space
interstitial space or intracellular space to a third space such as the GIT, chest ,
abdomen or skin, as in ascites, pleural effusion or peripheral oedema.

Hypovolemic shock is recognised as a cause of mortality if untreated.

STAGES OF SHOCK

The early stage or compensatory shock is a physiological response to
hypovolemia or in other words reduced intravascular volume.

Decreased intravascular volume causes reduced cardiac output which is
detected by Baroceptors in the aortic arch and carotid arteries. A
neuroendocrine response results in sympathetic activation and the release of
renin in the kidney. Sympathetic activation increases the circulation of
catecholamines which results in an increased heart rate and and peripheral
vasoconstriction. This is recognized clinically as either pale pink mucous
membranes when blood is diverted to vital organs or injected red mucous
membranes if hypovolemia is accompanied by sepsis or SIRS. The increased
heart rate is the main clinical sign.

The Renin induced Angiotensin and Aldosterone response causes further
vasoconstriction especially in the GIT and increases reabsorption of water and
sodium in the kidney tubules. This is detected clinically as a strong bounding
pulse and a moderate increase in blood pressure. Replacing lost fluid volume at
this point is essential so it is important to look for the subtle signs of shock in an
animal with a history of vomiting, diarrhoea, recent trauma or any fluid loss
leading to hypo perfusion. The dog may appear bright, wagging its tail in
response to attention, temperature in the normal range, slight increase in heart
and respiratory rates, normal to increased blood pressure, the capillary refill time
(CRT) is 1-2 sec and the mucous membrane colour suggests shock. The cat’s response to shock is different and they can have either an abnormally high or low heart rate and often have hypothermia.

Unfortunately because animals are often not presented until they are already in the early stage of decompensatory shock the clinical picture is often already one of depressed mentation, weak rapid pulses, pale mm, prolonged CRT and decreased body temperature, smelly flatulence and lowered urine output.

If shock has not been treated by this stage and tissue demands for energy increase the tissue demand for oxygen exceeds delivery and anaerobic metabolism ensues. This leads to lactic acidosis. This ultimately results in low cell pH and cell death. In the interim cellular acidosis has serious effects on the microcirculation. Vasoactive peptides are released from the cells. Capillary endothelial cells become swollen and the entire capillary bed starts to leak. With increased vascular permeability it becomes even more difficult to hold fluids in the intravascular space. Fluid resuscitation with crystalloids alone at this point is not likely to succeed.

Also in the early decompensatory stage blood continues to be diverted away from the GIT, kidneys, pancreas, muscles and skin. The responses of these underperfused organs leads to a further exacerbation of shock and requires far more intense interventions if terminal shock and mortality is to be prevented.

GIT: Microcirculation and bacterial translocation through compromised mucosa

Pancreas: Myocardial Depressant Factor (MDF) released causing arrhythmias and depressed cardiac contractility which further decreases cardiac output

Lungs: Micro vascular shunting and V/Q mismatch

Kidneys: Reduced GFR as a result of glomerular arteriole constriction leads to tubular necrosis and lowered urine output

Muscles: Blood pooling

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Compensatory</th>
<th>Early Decompensatory</th>
<th>Terminal</th>
<th>Cat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mentation</td>
<td>Normal</td>
<td>Depressed</td>
<td>Coma</td>
<td>Depressed</td>
</tr>
<tr>
<td>HR</td>
<td>Up a little</td>
<td>Tachycardia</td>
<td>Bradycardia</td>
<td>Up or Down</td>
</tr>
<tr>
<td>RR</td>
<td>Up a little</td>
<td>Tachypnea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T</td>
<td>N</td>
<td>Decreasing</td>
<td>Hypothermia</td>
<td>Low</td>
</tr>
<tr>
<td>MM</td>
<td>Pale</td>
<td>Pale</td>
<td>Pale/Cyanos</td>
<td></td>
</tr>
<tr>
<td>CRT</td>
<td>&lt;1 sec</td>
<td>&gt;2 secs</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>BP</td>
<td>Normal</td>
<td>Low</td>
<td>Very Low</td>
<td></td>
</tr>
</tbody>
</table>
Treatment of hypovolemic shock if in early presentation:

IV bolus Crystalloids  
Dog 70-90 ml/Kg/hr  
Cat 40-60ml/kg/hr  
Oxygen  
Ideally resuscitation of hypovolemia (without complications) should be achievable in the first hour.

Treatment of shock if signs of decompensatory stage

Crystalloids 70-90ml/kg/hr  
Colloids  shock dose 20ml/kg followed by 5ml/kg increments  
Hypertonic Saline 4-6ml/kg once only  
Antibiotics if indicated  
Gastric Protectants  
Oxygen

Treatment of terminal shock is unlikely to be reversed without supporting all organs and often requires mechanical ventilation and multi modal therapy including pressors to raise blood pressure. Terminal shock has a mortality rate exceeding 80%. It reinforces the need for early identification and treatment of shock.

**Septic Shock and SIRS (Systemic Inflammatory Response Syndrome)**

In 1992 the American College of Chest Physicians and the Society of Critical Care Medicine defined SIRS sepsis, septic shock and severe sepsis. This allowed for a heightened awareness of the clinical responses to non specific insults of either infectious or non infectious origin. In 2001 the Vet Clinics of North America published the first volume on SIRS. Since then both medics and veterinarians have expanded the definitions. There has been discussion about the need for more sensitive markers for SIRS as at the moment it is perhaps too broad a catchment for dogs and not enough for cats (2007 Hauptman et al). However the observation of signs of SIRS should alert the veterinarian in practice to the possibility of endothelial dysfunction, developing organ dysfunction and the need for a hunt for the inciting cause and for rapid aggressive treatment.

SIRS is not uncommon. A study evaluating the use of serum C reactive protein as a marker for SIRS showed that 45% of Pyometra cases develop SIRS (B.A.Fransson et al JVECC 17( 4) 2007).
SIRS kills. Another study evaluating markers (Gebhardt et al. JVECC 12(3) 2010) demonstrates that there is a mortality rate of about 30% in dogs with SIRS.

SIRS is defined as a severe systemic response to an inciting stimulus provoking an acute inflammatory response with two or more of these clinical signs:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cat</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>&lt;140 &gt;225</td>
<td>Increasing &gt;140</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>&gt;40</td>
<td>Increasing &gt;20</td>
</tr>
<tr>
<td>Temperature</td>
<td>Often Decreased</td>
<td>&lt;38.1 &gt;39.2 C</td>
</tr>
<tr>
<td>MM</td>
<td>Pale or Icteric</td>
<td>Brick Red</td>
</tr>
<tr>
<td>WBC</td>
<td>&lt; 5k &gt;19k</td>
<td>&lt;6k&gt;18k with .5% Bands</td>
</tr>
</tbody>
</table>

Sepsis is the presence of SIRS plus infection with either bacteria, bacterial endotoxin, parasites, virus or fungal organisms. (eg response to Parvo virus infection, Fly Strike)

Severe sepsis is the presence of sepsis or SIRS and one of the following (applies to dog):

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine Output</td>
<td>&lt;1 ml/kg/hr for more than one hour</td>
</tr>
<tr>
<td>Lactic Acid</td>
<td>&gt;2.5 mmol/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>Decreasing</td>
</tr>
<tr>
<td>Blood Glucose</td>
<td>Hyperglycemia</td>
</tr>
<tr>
<td>Mental Status</td>
<td>Abrupt deterioration</td>
</tr>
</tbody>
</table>

Septic Shock/SIRS shock is the signs of severe sepsis/SIRS along with refractory hypotension in spite of adequate fluids and colloids

Examples of non infectious causes of SIRS are pancreatitis, multiple wounds, ischemia, crushing injuries, hyperthermia, seizures.

**Pathophysiology of SIRS**

Following an insult (infection or other cause) local cytokine is produced with the goal of inciting an inflammatory response promoting wound repair and or recruitment of the reticuloendothelial system. Growth Factor is stimulated and macrophages and platelets move to the site of injury or infection. This early stage of inflammatory response is well controlled by a concurrent decrease in proinflammatory mediators and the release of endogenous antagonists. Everything is still normal and in check. However in a hyperdynamic response
(SIRS) the cytokine cascade leads to unchecked activation of numerous humoral cascades, the hyperactivation of the reticuloendothelial system and subsequent loss of circulatory integrity (leaky capillary bed) and at points activation of the clotting system. (There are numerous publications on the full pathophysiology of SIRS which is beyond the scope of this lecture but are well advised reading.) Once SIRS is suspected the diagnostic steps for sepsis or SIRS shock must be started immediately.
The key to preventing the multiple hits from the exaggerated systemic response is to IDENTIFY THE CAUSE and APPROPRIATE RESUCITATION.

**Identifying the cause**

Pay attention to any history that suggests lines of investigation eg possible ingestion of foreign body, last oestrus in an intact female.
Carry out a full and thorough physical examination starting systematically from one end of the animal to the other.
Temperature, pulse strength and rate, respiratory rate (TPR) recorded and monitored every 30-60 minutes so that trends of change in parameters are recognised.

Careful abdominal palpation for signs of acute abdominal pain, a fluid thrill or abnormal masses. It takes very little time and equipment to tap the abdomen in four quadrants and find fluid which may give invaluable insight. Bacteria, white blood cells or vegetable matter warrant the diagnosis of a septic abdomen or perforated bowel. Abdominal fluid with higher than serum levels of pancreatic enzymes suggests acute necrotizing pancreatitis. Abdominal fluid with urea or creatinine implies uroabdomen. In the absence of a history of trauma haemabdomen warrants a search for a coagulopathy or neoplasia.

In intact animals look for pyometra and prostatic abscess

Cat and dog hair hides wounds, burns, crushing injuries and signs of peripheral ischaemia so clip hair if history suggests any of these causes.

Auscultation of a heart murmur in the absence of signs of heart disease suggests looking for bacterial endocarditis.

Cheap and useful blood tests to start with are PCV/TP Blood Glucose, BUN serum electrolytes. These only require a drop of blood from the stylet when placing the IV catheter. They will give invaluable hints such as hypoproteinemia from crushing injuries, anaemia, glucose derangements which are common in sepsis, and potassium alterations which are common with in critical animals. It also allows for immediate stabilization of abnormalities even if the cause has still not been found.

Xrays and Ultrasound to identify source of sepsis/SIRS if still not found
A standard minimal database suggested by most critical care specialists dealing with SIRS are:
Haematology, biochemistry profile, urine analysis and placement of a urinary catheter to monitor urine output.
Coagulation parameters including APTT and platelet counts to monitor for DIC
Blood gases or at least pulse oximetry to monitor for effective reperfusion
Blood lactate levels. This is now very easy to do and gives invaluable guides if managing SIRS according to goal directed therapy. An increasing lactate means a worsening prognosis because of persistent problems with delivery of oxygen to the tissues.
Blood pressure measurement. This is very achievable in practice using a Doppler. It may not give as comprehensive an assessment as gained with a central line but will monitor trends and assist in knowing whether goals of treatment are being achieved.
Take samples for culture if there is infection.

TREATMENT OF SIRS

The goals of treatment of SIRS or Septic Shock are as follows
Stabilization
Identify and remove the source of sepsis or SIRS. This should be carried out as soon as the animal is cardiovascularly stable.
Support organ function
Control infection where sepsis exists

<table>
<thead>
<tr>
<th>Goal Directed therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
</tr>
<tr>
<td>Mental Alertness</td>
</tr>
<tr>
<td>Temperature</td>
</tr>
<tr>
<td>Pulse</td>
</tr>
<tr>
<td>Blood Pressure</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Resp Rate/SpO2</td>
</tr>
<tr>
<td>Heart Rate</td>
</tr>
<tr>
<td>MM colour</td>
</tr>
<tr>
<td>CRT</td>
</tr>
<tr>
<td>Blood Lactate</td>
</tr>
<tr>
<td>Urine Output</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Glucose</td>
</tr>
<tr>
<td>Haemoglobin/PCV</td>
</tr>
</tbody>
</table>
**Stabilization**

There is ongoing discussion in critical care circles on whether to use colloids or not (See lecture on Colloids) and whether to give isotonic crystalloids at shock rates per hour or bolus amounts every 10 minutes over a period of 10 minutes. There is agreement that the goal is hemodynamic stability and that once that is achieved rates should be maintained at at least 30ml/kg/day.

Dog Crystalloids 70-90ml/kg either per hour or 25% of this amount in 10 mins q 10mins
Cat Crystalloids 40-60mls/kg either per hr or 25% of this

Colloids (Voluven) 10-20ml/kg either per hour or 25% of this dose every ten minutes to resuscitate and then 20ml/kg/day

7% Hypertonic saline 4-6 ml/kg once

Oxygen: oxygen cage or via a nasal cannula

Antibiotics: Ideally based on C/S results but imperative to start early if sepsis exists. Broad spectrum cover for Gram positive, Gram negative and anaerobes. Suggested based on common availability but not limited to:
- Enrofloxacin 5mg/kg/12 hr IV and
- Ampicillin or Amoxycillin 20-40mg/kg/8 hr IV and
- Metronidazole 10mg/kg/8hr IV

Gastric Protectants: Cimetidine 5-10mg/kg/IV q 8hr or Famatodine 0.5-1.0mg/kg/12 hr IV

H2 antagonists are more efficacious but Proton pump inhibitors do keep acid levels down and so are indicated as well.

Analgesia: Pain exacerbates the hyperdynamic stress response and increases catecholamine release. It should always be prevented. The choice of analgesia is based on individual circumstances and availability. Some suggestions:
- Morphine 0.2-1mg/kg IV in dogs and 0.05-0.5 mg/kg in cats (See MLK CRI)
- Butorphenol in cats 0.1-0.2 mg/kg/hr CRI
- Fentanyl 2ug-20 ug /kg to effect followed by CRI 5-20ug/kg/hr

NSAIDS are contraindicated
Whole Blood: Transfuse if PCV trend is downward and below 30% once fluid resuscitation achieved. Packed RBC should only be given if Haemoglobin levels fall below 7.0g/dl and target is 7.0-9.0g/dl

Pressors: Pros and cons of each of these need to be considered. However there is consensus that they should be used if urine output is falling in spite of good fluid resuscitation and or the target blood pressure can not be maintained.
Dopamine 5-20mcg/kg/min
Dobutamine 5-20mcg/kg/min
Noradrenaline 0.01-0.4mcg/kg/min

Heparin: Low dose or low molecular weight to prevent a hypercoagulable state
FFP: If available 10ml/kg incubated with heparin 75u/kg in situations of hypocoagulopathy

Hydrocortisone: In animals where resuscitation levels of fluids and pressors have failed to achieve goals of therapy, need to look for relative adrenal insufficiency and treat if diagnosed. There is no other evidence at this stage to use corticosteroids in the treatment of shock or SIRS

Once the inciting cause is found it should be removed if possible. This may require surgery and should ideally be carried out when the animal is hemodynamically stable. However delays in removal of for example a necrotic devitalised section of bowel or a septic source in the abdomen will only further exacerbate the SIRS response. So need to do in the first 1-12 hours in some situations

Infection Control continued based on evidence of sepsis and results of culture and sensitivity

Nursing is essential throughout and the veterinary nurse should be effectively used in the monitoring of vital parameters in the SIRS patient.

Nutrition: Should be started early. Parenteral and enteric feeding tubes if the animal is not being fed orally. Aim to provide 70 (weight in kg) 0.75 calories per day

There are several other therapies under investigation in human trials and they may eventually be analyzed in veterinary patients so further reading is advised.

References available on request