NCSU VTH ICU
SEVERE SEPSIS AND SEPTIC SHOCK PROTOCOL
RED FONT SECTIONS = AN ICU FACULTY OR RESIDENT MUST BE INVOLVED

Definitions:

Systemic Inflammatory Response (SIRS): May be present in animals with a consistent history and clinical characteristics, and with any 3 or more of the following findings:

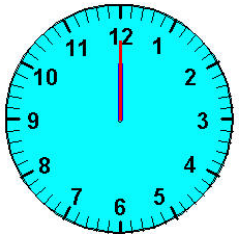
resting HR > 140 (dog) or > 220 (cat) or < 160 (cat)
resting respiratory rate > 30
Injected or pale grey mucous membranes
warm skin
hypo- or hyperthermia
leukocytosis or leucopenia
thrombocytopenia

Sepsis syndrome is a systemic inflammatory response due to bacterial infection and is categorized, in order of increasing severity, as:

Sepsis: A systemic inflammatory response associated with infection. *Protocolized therapy not needed*. Address underlying infection and monitor response.

Severe sepsis: Sepsis with hypotension (MAP < 70 mm Hg) that responds to supportive care and fluid therapy without vasopressors. *Enter protocol*

Septic Shock: Sepsis with hypotension unresponsive to fluid therapy and requiring vasopressors. *Enter protocol*



Follow the clocks for an approximate time line after entering protocol at 12:00!

ACUTE CARE THERAPEUTIC TARGETS

DOGS:

Cardiovascular:

- HR < 140 BPM
- Normal, hyperkinetic, or improved pulse
- Normal-to-injected mucus membrane color
- Warm skin
- CRT < 2 seconds
- Noninvasive arterial pressure systolic (SAP) > 140 mm Hg, mean (MAP) 80-90 mmHg
- (if used) Direct MAP 80-90+ mm Hg, diastolic blood pressure (DBP) 65-80 mm Hg
- (if used) Appropriate CVP response to fluid challenge

Other:

- Temperature > 38^{o} C
- Urine output > 1-2 ml/kg/hour
- Alert, oriented mentation
- Normoglycemia
- Arterial blood gas analysis: pO_2 > 90 mm Hg, pCO_2 25 – 35 mm Hg, lactate concentration < 2.5 mmol

CATS:

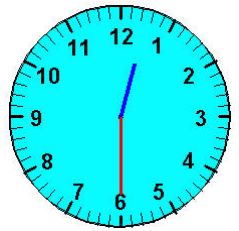
Cardiovascular:

- HR > 160 BPM
- Palpable or improved pulse
- Normal-to-injected mucus membrane color
- Warm skin
- CRT < 2 seconds
- (Noninvasive arterial pressure systolic (SAP) > 120 mm Hg, mean arterial pressure (MAP) 80-90
- (if used) Direct MAP 80-90+ mm Hg, diastolic blood pressure (DBP) 65-80 mm Hg
- (if used) Appropriate CVP response to fluid challenge

Other:

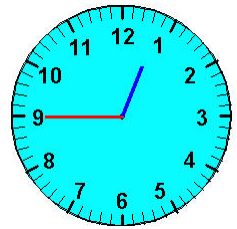
- Temperature > 38^{o} C
- Urine output > 1-2 ml/kg/hour
- Alert, oriented mentation
- Normoglycemia
- Arterial blood gas analysis: pO_2 > 90 mm Hg, pCO_2 25 – 35 mm Hg, lactate concentration < 2.5 mmol

Step 1: Characterize patient condition and begin instrumentation



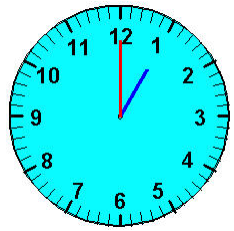
- ☐ Monitor with ECG, pulse oximetry
- ☐ Large-bore peripheral catheter
- ☐ Central venous catheter: Consider a double- or triple-lumen catheter; consider ScvO2 monitor
- ☐ Collect blood for:
  - ☐ CBC
  - ☐ chemistry profile
  - ☐ Big 4 (PCV, TS, glucose, BUN)
  - ☐ Arterial (or central venous) blood gas
  - ☐ Coagulation profile and/or a baseline aPTT on the SCA 2000
  - ☐ FIV/FeLV, 4DX testing
- ☐ If SPO_2 is < 90% or if increased respiratory effort is present: **oxygen** by face mask

Step 2: Identify hypoglycemia, K^{+} or Ca^{++} disorders, and evaluate response to fluid challenge



- ☐ If the baseline glucose is < 60 mg/dl, administer 0.2 ml 50% **dextrose**/kg lean body wt IV to raise blood glucose by 50 mg/dl. If administered peripherally, DILUTE with sterile water to < 12.5%.
- ☐ Evaluate blood gas results for significant hypokalemia (< 3.5 mmol) or ionized hypocalcemia (< 0.9 mmol). If either is present, begin…
  - o 2 mEq/ml KCl infusion, diluted as needed, and administered at a rate of .25 - .5 mEq/kg/hour (faster if warranted and with continuous ECG monitoring and rechecks every 30-60 minutes)
  - o 10% calcium gluconate 1 ml/kg IV as a slow injection (over a couple of minutes) and diluted in saline
- ☐ If hypothermia or shivering (even with a fever) is present:
  - o Insert continuous temperature probe and begin active warming with warm air unit until temperature is normal and/or physical signs that the animal is trying to increase its fever abate.
- ☐ 5 minute fluid challenge
  - ☐ Evaluate HR, RR, mm color, CTR, pulse, +/- ABP, CVP
  - ☐ Administer in < 5 minutes either:
    - ☐ Warm **LRS** (usual) **or saline** (only if hypochloremic): 20 (dog) or 10 (cat) ml/kg
    - ☐ RARE: If marked hypoproteinemia is present, consider warm **hetastarch, Hespan™,** or **Voluven™** 5 (dog) or 2.5 (cat) ml/kg instead of crystalloid
- ☐ Recheck blood glucose if it was low initially
- ☐ Obtain urine sample for C/S & UA prior to antibiotic therapy if there is no other obvious source of sepsis
- ☐ Consider a consultation with the critical care resident. Consider requesting placement of an indwelling arterial catheter now if the hemodynamic response to fluid challenge is ambiguous and/or hypotension is likely.

Step 3: Antibiotic therapy



☐ Start as soon as culture and/or cytology samples are collected.

- ☐ If no source is apparent obtain urine for culture, thoracic radiographs, and consider abdominal ultrasound (but do NOT delay cardiovascular stabilization for these tests!). Aspirate any abdominal fluid or perform transtracheal airway wash based on findings.
- ☐ If no source identified look for systemic infections such as *Rickettsia spp* and *Cytauxzoan.*
- ☐ Gram stain identification of any bacteria seen on cytology
- ☐ Blood cultures if primary source is not identified: See the ICU blood culture protocol

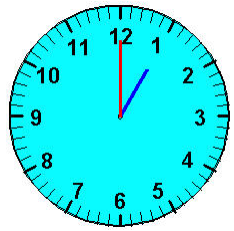
☐ Consider Gram stain results, site of infection, past antibiotic exposure, and current antibiogram data. In 2013 the two most common G+/G- isolates from infected canine and feline patients at NSCU-VHC were *E. coli* and *Staphylococci* species.

- If *E. coli* is suspected: consider
  - **Amikacin** dog: 15-30 mg/kg IV q 24h; cat 9-14 mg/kg IV q24h
  - **Imipenem-cilastatin** dog 5-10 mg/kg IV over 30 min q 6-8 h
  - **Meropenem** dog 9-25 mg/kg SQ, IV q 8-12 hours (low end for E. coli, high end for Pseudomonas)
  - **Cefotaxime** dog 3.2 mg/kg IV loading dose then 5 mg/kg/hour
  - **Ceftazidime** dog 1.2 – 4.4 mg/kg IV loading dose then 1.6 – 4 mg/kg/hour
  - **Cefepime** dog 1.4 mg/kg loading dose, then 1.1 mg/kg/hour
- If *Staphylococcus* is suspected: consider
  - **Gentamicin** dog: 10 mg/kg q 24h
  - **Clindamycin** dog & cat: 11 mg/kg IV q 12 h
  - **TMS** dog & cat: 30 mg/kg q 12 h IV, SQ
  - **Vancomycin** 15 mg/kg IV q 6 h (dog) or 6-8 h (cat)
  - **Florfenicol** dog (unknown safety!): 20 mg/kg IV over 30+ minutes, then 2.5 mg/kg/hr CRI
- If the animal has been on antibiotics in the past 1-2 months the likelihood of MDR infection is increased; in that case strongly consider amikacin or meropenem (Gram negative rods), vancomycin or florfenicol (*Enterococcus faecium*, *Staphylococcus sp*.). Invoke isolation protocol for MDR patients.

☐ Peritonitis: Consider adding **fluconazole** 2.5 mg/kg SQ or IV (SLOWLY) every 24 hours

☐ Recheck blood glucose if it was low initially or if patient deteriorates

Step 4: Verify that ALL the cardiovascular goals on page 2 are met



☐ **YES:** monitor and proceed to step 5.

☐ **NO: DO NOT SEND THE PATIENT TO SURGERY** for source control unless it is essential to control active bleeding! This patient is likely to die if put under general anesthesia and subjected to surgical trauma while in shock

- Measure CVP (if not done already) and repeat fluid bolus until the goals are met, or the CVP increases by 2-3 mm Hg above baseline and remains elevated for > 5 minutes, and/or there is no improvement of hypotension in response to fluid bolus.

➔ Goals still not met? **YOU MUST REQUEST ASSISTANCE FROM THE ECC RESIDENT**

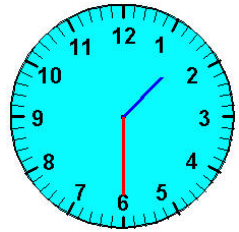
☐ Dog: begin **norepinephrine** 0.1-0.2 mcg/kg/minute. If diastolic hypotension persists (DBP < 60-80 mm Hg with tachycardia) after you are confident the infusion has reached the circulation, increase it by increments of 0.1 – 0.2 mcg/kg/min every 2-5 minutes as needed to a maximum of 2-3 mcg/kg/min

☐ Dog: Consider adding **dobutamine** 5 mcg/kg/min if myocardial systolic dysfunction is suspected (dog only; this will generally not help cats and promotes seizures in that species). Increase in increments of 2.5 mcg/kg/min every few minutes if needed indicated by clinical response.

☐ Cat: If HR < 160, administer **atropine** 0.04 mg/kg IV. If heart rate increases to > 160 bpm, begin **norepinephrine** as for dogs. If heart rate does not increase to > 160, use **epinephrine** instead of norepinephrine, using the same dosing protocol described above.

☐ Insert arterial catheter during this process (if not done already) to allow continuous BP monitoring. Recheck blood glucose if it was low on the last check or if patient deteriorates

☐ If the hematocrit is < 30%, consider transfusion of FWB or pRBC's.



➔ Still not met? (CONTINUED ECC RESIDENT ASSISTANCE REQUIRED)

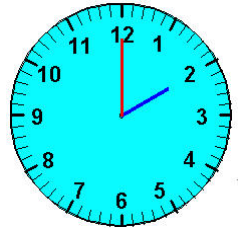
☐ Rule out hypoxemia (SPO_2 or ABG), anemia (PCV), recurrent hypovolemia (recheck CVP response), faulty blood pressure transducer setup, hypoglycemia, ionized hypocalcemia, marked hypokalemia, ongoing hemorrhage, arrhythmia, pericardial effusion with tamponade, pulmonary embolism, gastrointestinal necrosis.

☐ Add **vasopressin.** A test dose of 4 milliunits/kg IV may be administered by rapid injection while observing the BP response. If there is a response, begin 1 milliunit/kg/min; if necessary increase this in increments of 1 milliunit/kg/min to a maximum or 4 milliunits/kg/min.

☐ Consider glucocorticosteroids if relative adrenal insufficiency is suspected OR if the patient shows signs of lethal infection and is unstable despite increasing doses of catecholamines and vasopressin.

- Hydrocortisone 0.4 mg/kg followed immediately by 0.4 mg/kg/hour (lean body weight) CRI
- **Dexamethasone sodium phosphate** at 0.01 mg/kg IV followed immediately by 0.01 mg/kg/hour (lean body weight) CRI
  - consider DOCP 2.2 mg/kg IM
- Continue 3-7 days depending on clinical course

➔ Still not met (refractory hypotension)?



☐ If not already done, consider adding **dobutamine** 5-15 mcg/kg/min and/or milrinone 5-10 mcg/kg/min to the continuing vasopressor therapy if myocardial systolic dysfunction is suspected (dog only).

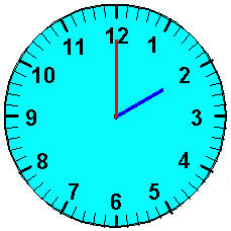
☐ If the diastolic pressure is low despite adequate or high systolic pressure consider transfusion of FWB or pRBC's to increase the Hct to > 30-35%.

☐ Consider **GIP** infusion: **G**lucose (0.75 grams/hour) **I**nsulin (0.25 units/kg/hour) **P**otassium (.3 mEq/kg/hour). To accomplish this:

- Load a 60 ml syringe with **54 ml 50% dextrose, 5.4 ml KCL, and 9 units of regular insulin** and begin an infusion into the central venous catheter at 1.65 ml/kg/hour.
- Administer **0.1 IU/kg of regular insulin** IV, once, at the start of the CRI
- Allow up to an hour of this infusion + other supportive measures to provide benefit

☐ Recommend euthanasia if the patient is not responsive to these measures

Step 5: Nasal oxygen, metabolic monitoring

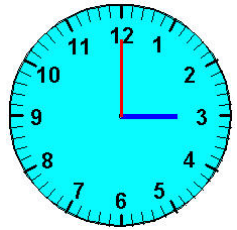


- ☐ Recheck blood glucose and electrolytes if these were abnormal previously.
- ☐ Nasal oxygen: Insert a nasal cannula for continuous nasal **oxygen** administration (see ICU protocol).
  - ☐ If respiration is labored, weak, or relative hypercapnia is present: Contact ICU resident discuss **mechanical ventilation**.
- ☐ Indwelling urinary catheter in obtunded patients with apparent oliguria or very high USG.

Step 6: Source control

- ☐ Surgical treatment: If surgical exploration (peritonitis, deep tissue infections) is indicated, do so ONLY in patients that are able to reach hemodynamic stability and control of hypotension.
  - o Chest tube drainage of pyothorax
  - o Placement of active drains into abscess or cellulitis by ultrasound guidance

Step 7: Continued support of homeostasis



- ☐ Maintain hematocrit if the patient has difficulty compensating for anemia:
  - o Dogs: >30%
  - o Cats: >25%
- ☐ Maintain total solids/oncotic pressure
  - o **FF Plasma**: an expensive source of albumin but indicated to preserve endothelial function and provide coagulation factors (see below)
  - o **Hetastarch** or **Voluven™**: increasing dosages of HS promotes bleeding, both cause TS to trend to 4.5 gm/dl
  - o **25% human albumin**: There is an unknown risk of Type I or Type III allergy: skin test first!
- ☐ Coagulation: For all patients that are not bleeding consider DIC prophylaxis:
  - o **Unfractionated heparin** 10-50 IU/kg IV, then 10-15 IU/kg/hour CRI
  - o Patients with aPTT prolongation: to the heparin therapy above add **fresh frozen plasma** 1-5 ml/kg/hour (faster if hypovolemia is present) with monitoring of aPTT

- Hypercoagulable (on TEG) patients at risk of deep vein thrombosis/PTE: increase the dose of **unfractionated heparin** to 50-100 IU/kg IV, then 25-40 IU/kg/hour adjusted per the ICU heparin nomogram; OR administer **Fragmin™** 150 mg/kg SQ followed immediately by a CRI at 15 - 20 IU/kg/hour.

☐ Glycemic control:
- Maintain blood glucose between 80-160 mg/dl
- Hypoglycemia: CRI of **dextrose** added to maintenance fluid
- Hyperglycemia (> 250 mg/dl in cats or > 180 mg/dl in dogs): discontinue administration of any glucose-containing fluids and consider beginning a CRI of **regular insulin** (1 IU/ml in D5W via syringe pump). Start at 0.05 IU/kg/hour, monitor both glucose and potassium.

☐ Analgesia:
- Use multimodal therapy whenever possible
- Avoid NSAID's until hemodynamically stable and risk of GI/renal injury diminishes

☐ Patient positioning: If the patient is obtunded and at risk of aspiration injury consider either:
- Head elevated, in sternal or semi-sternal to limit risk of aspiration and improve pulmonary gas exchange.
- Whole body tip-up to 20-30^{o} with elevation of one end of a rack under patient, particularly if the animal prefers lateral recumbency
- Institute a plan for position changes and PROM therapy

☐ GI protection/antiemetic therapy
- NG or PEG tube for gastric sump if gastroparesis, regurgitation, or vomiting are concerns (consider remove nasal oxygen and using a mask or put in an oxygen cage).
- **Cerenia™** 1 mg/kg SQ daily (dogs) for vomiting
- **Ondansetron** .5-1 mg/kg SQ/IV
- **Famotidine** 1 mg/kg IV (consider SQ in cats), then 0.2-0.4 mg/kg/hour CRI (lower dose in cats)
- **Pantoprazole** 1 mg/kg IV q 24 hours (dogs)
- Continue famotidine and pantoprazole for at least 2 days together, then consider weaning off the famotidine

☐ Nutrition

- Consider instituting nutritional support within 12-48 hours.
- Placement of NE, esophagostomy, gastrostomy, or jejunostomy: Utilize "**Laci Protocol"** and **Preliminary Nutrition Worksheet** (available in ICU) to determine an initial, short-term (1-2 day) feeding plan.
  - Avoid diets with arginine supplementation
    - Contact the clinical nutritionist for feeding tube diet recommendations
  - **CRI diet** delivery minimizes metabolic and/or physical complications
  - Do not tube feed if patient is vomiting or gastroparesis is present. Discuss parenteral feeding options with nutritionist
- Initiate tube feeding @ 25% RER (day 1), increase to 33% RER (day 2), reassess plan (day 3 or sooner)
- **Submit a nutrition consult** for most appropriate feeding guidelines if daily nutrition consult will not happen in time.