Definitions:

Systemic inflammatory response 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 due to bacterial 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:
- HR < 140 BPM
- Temperature > 38° C
- Normal, bounding, 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
- Direct MAP 80-90 mm Hg, diastolic blood pressure (DBP) > 60 mm Hg
- Urine output > 1-2 ml/kg/hour
- Alert, oriented mentation
- Appropriate CVP response to fluid challenge
- Normoglycemia
- Arterial blood gas analysis: pO2 > 90 mm Hg, pCO2 25 – 35 mm Hg, lactate concentration < 2.5 mmol

CATS:
- HR > 160 BPM
- Temperature > 38° C
- 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
- Direct MAP 80-90 mm Hg, diastolic blood pressure (DBP) > 60 mm Hg
- Urine output > 1-2 ml/kg/hour
- Alert, oriented mentation
- Appropriate CVP response to fluid challenge
- Normoglycemia
- Arterial blood gas analysis: pO2 > 90 mm Hg, pCO2 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
- 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
- If SPO₂ 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

☐ Run glucose immediately.
  - If < 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 (< 0.8 mmol). If either is present, begin…
  - 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)
  - 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:
  - 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 temperature abate.

☐ 5 minute fluid challenge
  - Evaluate HR, RR, mm color, CTR, pulse, +/- ABP, CVP
  - Administer in < 5 minutes either:
    - Warm LRS or saline: 20 (dog) or 10 (cat) ml/kg
    - Warm hetastarch or Voluven™ 5 (dog) or 2.5 (cat) ml/kg

☐ Recheck blood glucose if it was low initially

☐ 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 consider systemic infections such as *Rickettsia* spp.
- 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 antiobiogram data. In 2007 the two most common isolates from infected canine and feline patients 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
    - **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)

- 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 cardiovascular goals are met

□ YES: monitor and proceed to step 4.

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

  o 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.

  ▸ Still not met? REQUEST ASSISTANCE FROM THE ICU RESIDENT

  □ Dog: begin norepinephrine 0.1-0.2 mcg/kg/minute. If diastolic hypotension persists 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 3 mcg/kg/min

  □ 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

  ▸ Still not met? ICU RESIDENT ASSISTANCE REQUIRED

  □ Rule out hypoxemia (SPO₂ 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 the sepsis syndrome has been present for > 8 hours AND if relative adrenal insufficiency is suspected OR if the patient requires both catecholamines and vasopressin
  ○ Use dexamethasone sodium phosphate at 0.01 mg/kg IV followed immediately by 0.01 mg/kg/hour CRI

→ Still not met (refractory hypotension)?

□ If not already done, consider adding dobutamine 5-15 mcg/kg/min to the continuing vasopressor therapy if myocardial systolic dysfunction is suspected (dog only; this will generally not help cats and promotes seizures in that species).

□ If the diastolic pressure is low despite adequate or high systolic pressure and the hematocrit is < 30%, consider transfusion of FWB or pRBC’s to increase the Hct.

□ Consider GIP infusion: Glucose (0.75 grams/hour) Insulin (0.25 units/kg/hour) Potassium (.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: Oxygen, metabolic monitoring, identifying source of infection

☐ 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 drainage: General anesthesia and surgery indicated ONLY in patients that stabilize hemodynamically
  ☐ Where appropriate, consider placement of active drains by ultrasound guidance

Step 7: Continued support of homeostasis

☐ Maintain hematocrit if the patient has difficulty compensating for anemia:
  ☐ Dogs: >30%
  ☐ Cats: >25%

☐ Maintain total solids/oncotic pressure
  ☐ Hetastarch: increasing dosages tend to promote bleeding and TS tends to 4.5 gm/dl
  ☐ Plasma: Poor source of albumin but may be indicated for coagulation factors (see below)
  ☐ 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:
  ☐ Unfractionated heparin 10-50 IU/kg IV, then 10-15 IU/kg/hour CRI
  ☐ Patients with aPTT prolongation: to the heparin therapy above add fresh frozen plasma 10 ml/kg over 1 - 6 hours, repeated as needed to normalize aPTT
  ☐ Patients at risk of deep vein thrombosis/PTE with normal or short aPTT: 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 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 30° 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
- NG or PEG tube for gastric sump if gastroparesis and 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 mg/kg/hour CRI (or 1 mg/kg SQ q 6 hours in cats).
- Pantoprazole 1 mg/kg IV q 24 hours (dogs)
- Continue famotidine and pantoprazole for at least 2 days, 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 (ASAP) for most appropriate feeding guidelines