


The New Science of Sepsis

Julie Menard, DVM, DACVECC

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Charlie 5 yo Great Dane

- Present for painful mass on thigh appeared rapidly
- Temp: 38,5 C HR: 98 RR: 32 pink m m CRT < 2sec
- Large fluctuant mass on right proximal thigh
- Warm and painful on touch
- FNA: Suppurative inflammation à Abscess




- Sedate clip clean lance flush and antibiotics for 5 days
- Full recovery

2

Zeus 7 yo MC Great Dane

- Presenting for NWB left hind limb lameness, lethargy and anorexia
- T: 39.7C HR: 140 bpm RR: 44 pink mm CRT 1 sec bounding pulses
- Swollen 1st digit left hind with purulent material expressed on manipulation
- Painful and erythematous skin
- XR shows no evidence of osteomyelitis
- Started on IVF, pain meds and antimicrobials
- Within 24 hours hypotensive requires vasopressors
- Vasopressors after admission while on antibiotics



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Zeus and Charlie

Both have abscesses
Both got antibiotics

Why didn't he die and the other one die?

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What is sepsis?

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SPECIAL ARTICLE

Defining sepsis in small animals

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Sepsis in humans

2017:

- 49 million cases of sepsis worldwide
- 11 million sepsis-related deaths
- 20% of global mortality

- Heterogeneity in worldwide survival rates
- Improved mortality rates high income countries
- Substantial burden low- and middle-income countries

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Why do we care about the definition of sepsis?

- Definition of sepsis allows to facilitates patient care
- A sepsis definition should describe what sepsis "is"
- Syndrome = A set of symptoms or conditions that occur together and suggest the presence of a certain disease or an increased chance of developing the disease
- Sepsis is a syndrome with clinical heterogeneity

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Parvo puppy

Pyelonephritis elderly cats

Both are septic

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Challenges about sepsis definition

- Cannot be diagnosed using any standardized, validated diagnostic test
- Not easily transferred to the clinic
- Need to codify objective parameters linked to sepsis pathophysiology
- Enable early recognition:
 - Easy
 - Cheap
 - Without costly equipment or specialized laboratories

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Challenges with sepsis definitions

- Competing needs of clinicians and researchers
- Clinicians:
 - Sensitive definition of sepsis
 - Clinical correlation
 - Facilitates early, accurate diagnoses
 - Identifies all patients with sepsis
 - Over-diagnosis (increased false positive rate) is preferable to missing patients with a potentially life-threatening condition.
- Researchers:
 - Specific definition of sepsis
 - Doesn't dismiss promising therapies as inefficacious by testing them in populations containing individuals with no likelihood of response.
 - Research tolerate a higher false negative rate à minimizes enrollment of patients without definitive sepsis
 - Be able to compare study results from various locations (higher specificity à biomarkers)
 - Assessment of illness severity à patient stratified during analysis
 - Ultimate goal: Clinicians might then be better able to assign resources and prognosticate.

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Challenges with sepsis definition

- If stringent criteria:
 - False negatives à missing patients with sepsis
 - Delays in diagnosis – not sick enough... Need to measure a biomarker
 - Increases in cost
 - Limits access to care
 - Prevent research dissemination

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Why sepsis is challenging to diagnose for clinicians?

1. Non-specific clinical symptoms
2. No good easy and reliable biomarker available to help increase clinical suspicion
3. Sepsis is a heterogenous syndrome with no unifying biological characteristic, cause or phenotype.

Any infection has the potential to turn into sepsis....

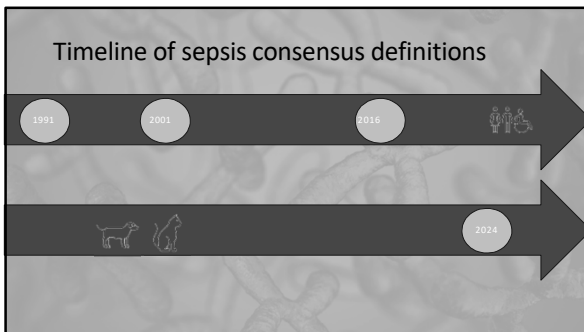
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Let's go back in time...

- How we define sepsis has changed overtime...



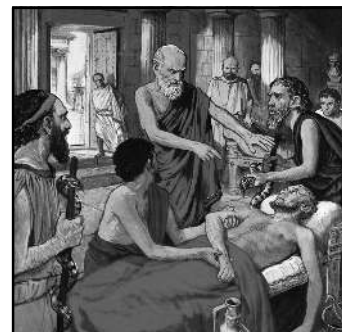
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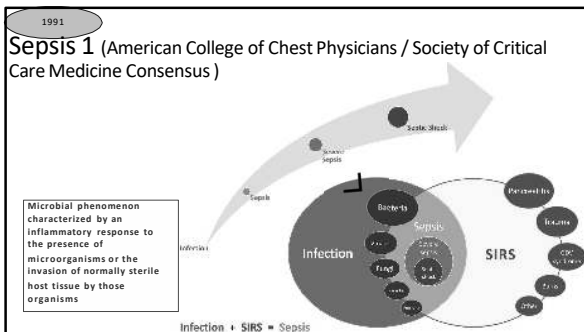
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Sepsis

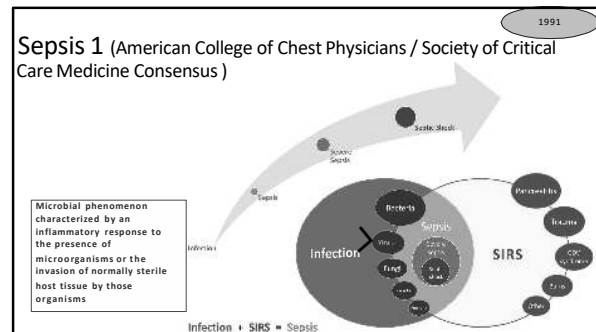
- Derived from the Greek word for "decomposition" or "decay"
- First documented use 2700 years ago in Homer's poem
- Use by Hippocrates and Galen



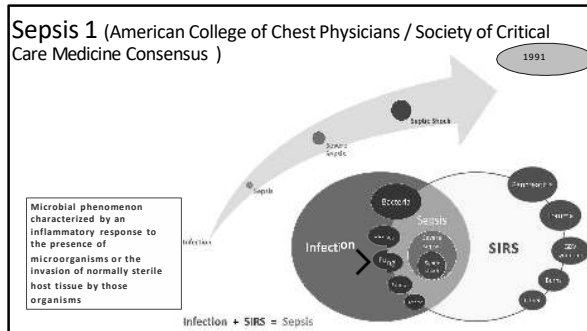
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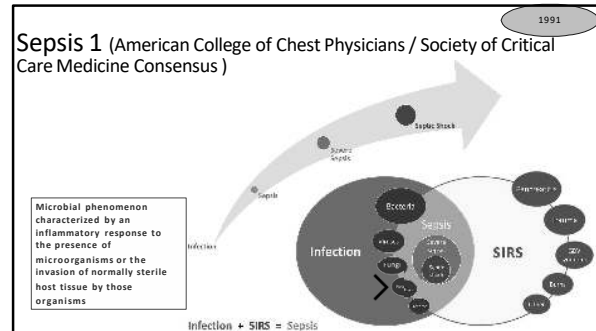
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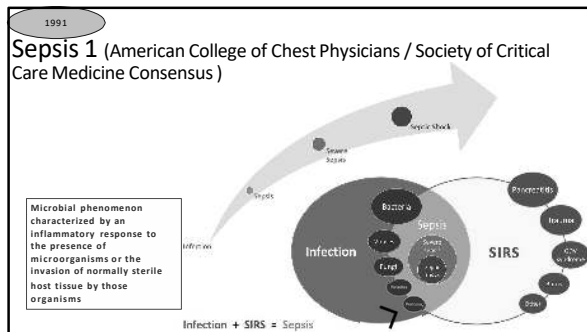
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How do we diagnose an infection?

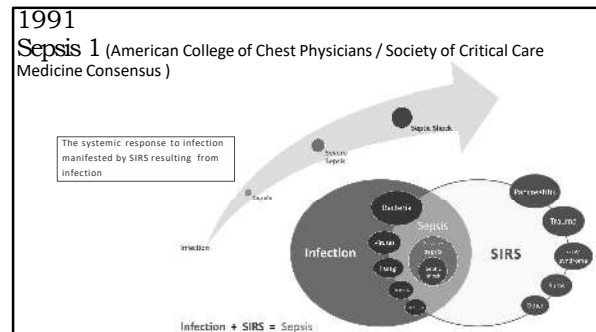
- Culture
 - Culture and susceptibility testing
 - Organism(s) involved
 - Bacterial antimicrobial drug resistance
 - 16S rRNA /metagenomic → limited to research setting
- Cytology
 - Identification of intracellular pathogens
 - Limited sensitivity (high false negative rates)
 - Visual identification of organisms = active infection??
- Viral testing:
 - Antigen tests (canine parvovirus)
- Histopathology : long turn-around time

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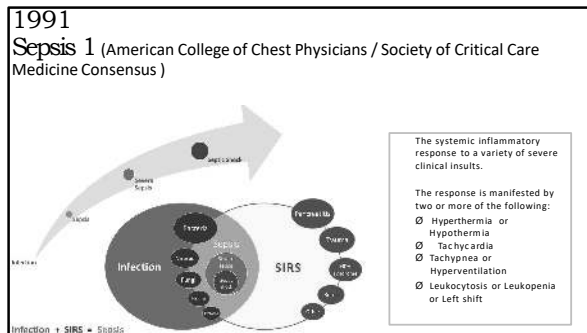
Limitation with infection diagnostic

- Clinically:
 - suspected or highly suspected infection
 - Intensification of diagnostic assessment
 - Therapeutic intervention w
- Research:
 - Bias results
 - Less severe disease
 - Includes patients without sepsis

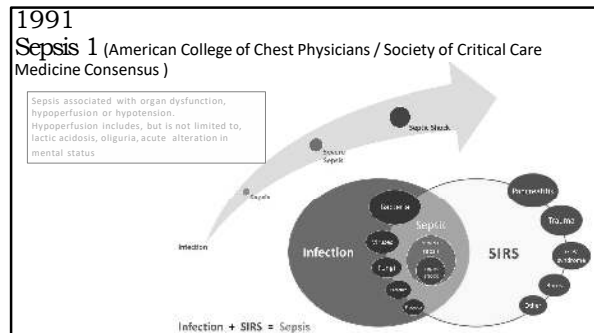
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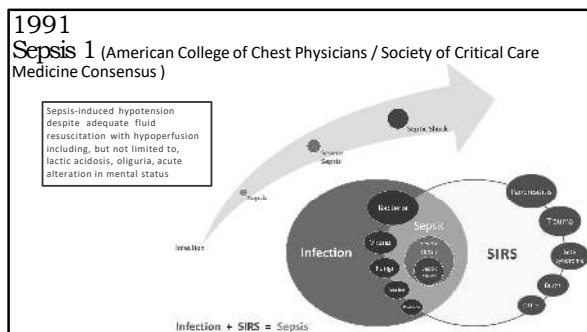
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Other important definitions from 1991- Sepsis 1

Term or Concept	Definition
Infection	Microbial phenomenon characterized by an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by those organisms
Bacteremia	The presence of viable bacteria in the blood
Sepsis-induced hypotension	A systolic blood pressure <90 mmHg or a reduction of ≥40 mmHg from baseline in the absence of other causes for hypotension
Multiple Organ Dysfunction Syndrome (MODS)	Presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention

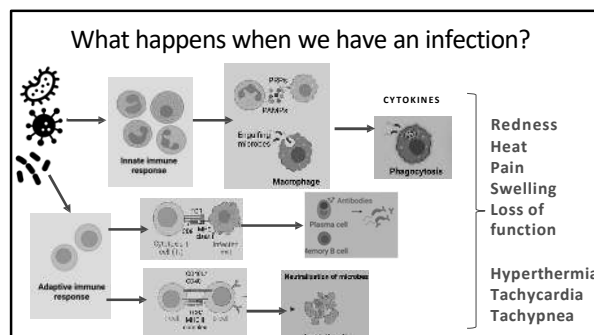
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Systemic inflammatory response- SIRS

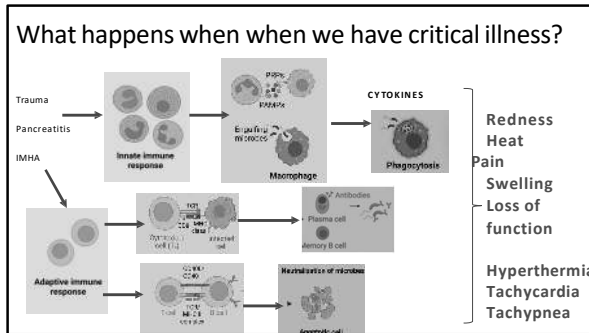
- Central role in the definition
- In 1991 belief that sepsis resulted from a hyperinflammatory response to infection

What is a normal inflammatory response to an infection?

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Limitations with SIRS criterias

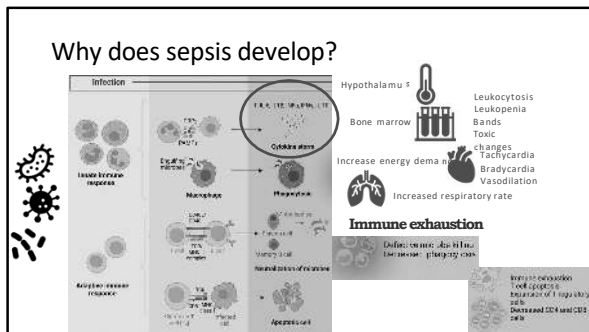
- SIRS secondary to :
 - Trauma
 - Pancreatitis
 - Thrombosis
 - Ischemia

Chemical peritonitis from bile or urine leakage

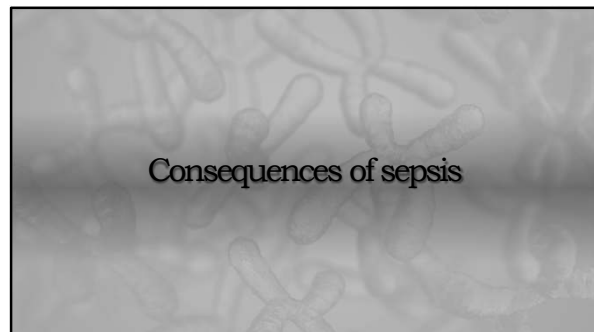
Diagnostic challenges for clinicians to differentiate non-infectious causes of SIRS

Clinically indistinguishable from SIRS incited by an infection caused by bacteria, viruses or fungi for sepsis

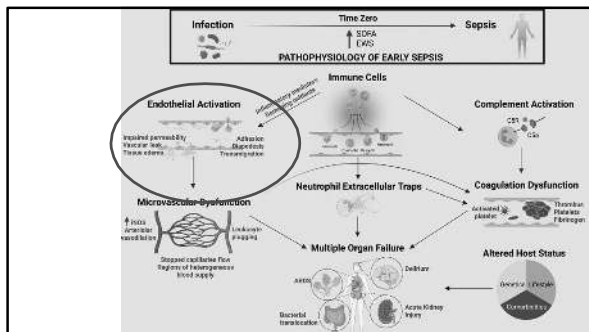
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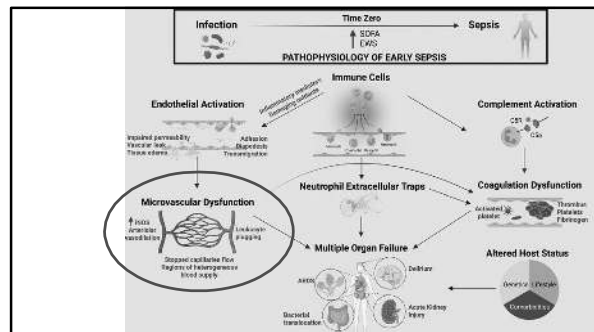
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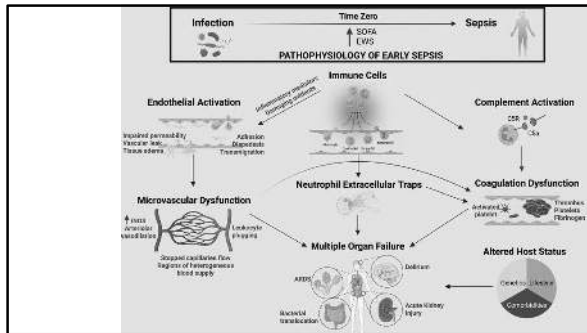
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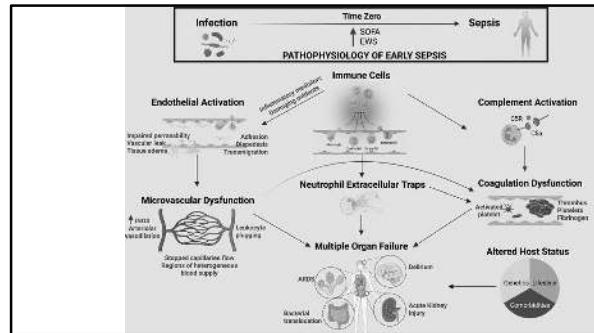
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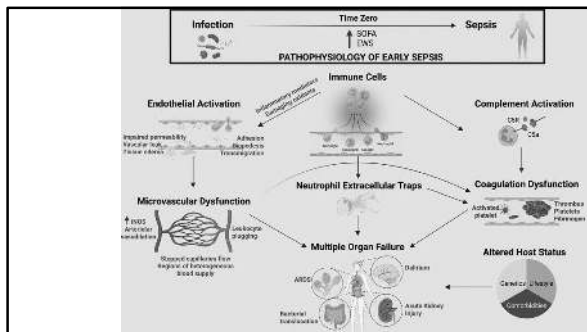
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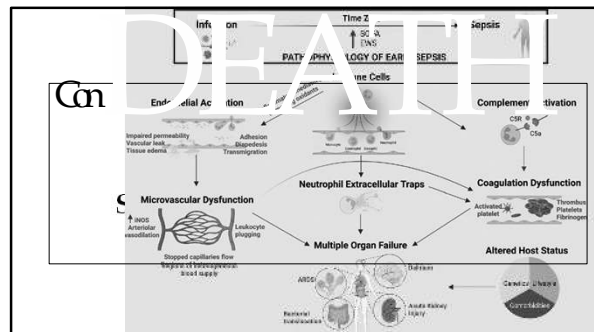
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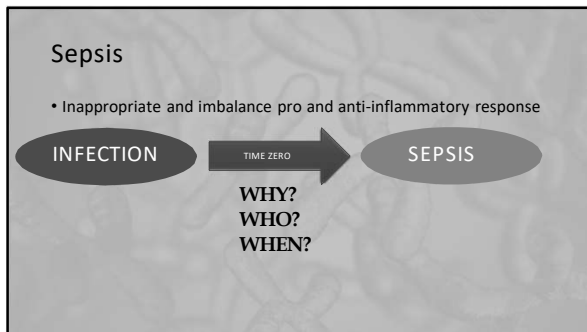
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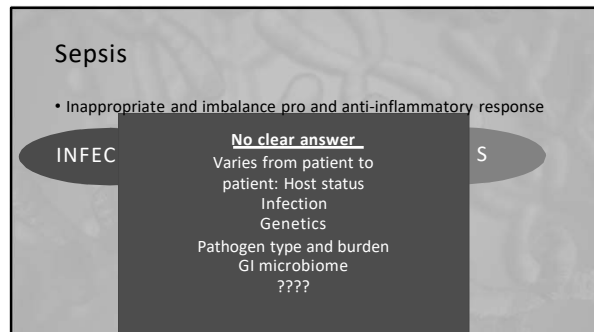
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Up until mid 2000, we believed that sepsis was only a pro-inflammatory disease

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Timeline of sepsis consensus definitions

Sepsis 2
International Sepsis Consensus Definitions 2001
 Society of Critical Care Medicine, European Society of Intensive Care Medicine, American College of Chest Physicians, American Thoracic Society, Surgical Infection Society

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Sepsis 2
International Sepsis Consensus Definitions 2001
 Society of Critical Care Medicine, European Society of Intensive Care Medicine, American College of Chest Physicians, American Thoracic Society, Surgical Infection Society

- Second sepsis definitions conference
- No evidence basis for a change to the definition of sepsis.
- Expansion of the diagnostic criteria
 - Inherently arbitrary in the absence of a gold standard against which to calibrate them.

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	Documented, or suspected, and some of the following
Infection	
General variables	Fever (core temperature >38.3°C) Hypothermia (core temperature <36°C) Heart rate >90/min or >2 standard deviations (SD) above the normal value for age Tachypnea Altered mental status Significant edema or positive fluid balance (>20mL/kg over 24 hours)
Inflammatory variables	Hyperglycemia (Plasma glucose >120mg/dL or 7.7mmol/L) in the absence of diabetes Leukocytosis (white blood cell count [WBC] >12,000/uL) Leukopenia (WBC <4,000/uL) Normal WBC with >10% immature forms
Hemodynamic variables	Plasma C-reactive protein (CRP) >2 SD above the normal value Plasma procalcitonin (PCT) >2 SD above the normal value Arterial hypotension (SBP <90mmHg, MAP <70, or SBP decrease >40mmHg in adults or <2 SD below normal for age) SvO ₂ >70% (adults only)
Organ dysfunction variables	Cardiac index >3.5L/min Arterial hypoxemia (PaO ₂ /FiO ₂ <300) Acute oliguria (urine output [UOP] <0.5mL/kg/hr) Creatinine increase >0.5mg/dL Coagulation abnormalities (INR >1.5 or aPTT >60 seconds) Ileus (absent bowel sounds)
Tissue perfusion variables	Thrombocytopenia (Plt count <100,000/uL) Hyperbilirubinemia (Tbili >4mg/dL or 70mmol/L) Hyperlactatemia (>1mmol/L) Decreased capillary refill time or mottling

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Pediatric definition of sepsis

- Evidence of infection
- Signs and symptoms of inflammation:
 - Hyper- or hypothermia
 - Tachycardia
 - Pediatric Logistic Organ Dysfunction (PELOD):
 - Altered mental status
 - Hypoxemia
 - Hyperlactatemia

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Pediatric definition of septic shock

- Clinical signs of shock in children:
 - Tachycardia
 - Poor peripheral pulses
 - Altered mentation
 - Delayed capillary refill time
 - Mottled or cool extremities
- Children with hypotension is rare à sign of decompensated shock
- BP is not used in pediatrics

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Can we predict which kids will have sepsis and die from it?

- In children with infections, what factors are associated with development of sepsis?
 - Clinical predictors of sepsis
 - Infection
 - Decreased level of consciousness
 - Higher Pediatric Risk of Mortality (PRISM) scores
- In children with sepsis, what factors help predict mortality?
 - Identification of sepsis severity criteria and codified severe forms of the syndrome including septic shock
 - Comorbidities including cancer
 - Blood lactate
 - Platelet count
 - Fibrinogen
 - Procalcitonin
 - Organ dysfunction are all associated with mortality.

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2001-2016

- Limitation of the SIRS criteria
 - Lack discriminant validity and convergent validity
 - Excessive false positives and false negatives
- Sepsis involves activation of both pro- and anti-inflammatory responses
- Sepsis has dysfunction in the cardiovascular, neuronal, autonomic, hormonal, bioenergetic, metabolic, and coagulation systems
- Severe sepsis → stepwise progressive deterioration in status
 - UNTRUE

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Timeline of sepsis consensus definitions

1991 2001 2016

2016 Sepsis 3.0

Society of Critical Care Medicine, European Society of Intensive Care Medicine

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Sepsis 3.0

- Sepsis is life-threatening organ dysfunction due to a dysregulated host response to infection
- “When the body’s response to infection injures its own tissues or organs”*
- Mortality rate= 17-20%

Singer et al. JAMA 2016

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Laymen definition

Sepsis is a life-threatening condition that arises when the body’s response to an infection injures its own tissues and organs

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Identification of organ dysfunction

- SOFA score = Sequential organ function assessment score
- Humans:
 - Suspect sepsis when ≥2 point increase

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SOFA Score Humans

Organ	Measure
Respiratory	PaO ₂ /FIO ₂
Renal	Serum creatinine or urine output mL/kg/hour
Hepatic	Serum bilirubin
Cardiovascular	MAP Need for vasopressors (Dopamine, Dobutamine < Epi or Norepi)
Hematologic	Platelet count
Neurologic	Glasgow coma score

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Organ system [Criterion]	Score				
Respiratory (PaO ₂ /FIO ₂)	0 >400	1 <400	2 <300	3 <200	4 <100
Coagulation (Platelet count, ×10 ³ /μL)	>150	<150	<100	<50	<20
Liver Bilirubin mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	9.0-11.9 (102-204)	>12 (204)
Cardiovascular Blood pressure or Catecholamine usage (μg/kg/min for at least 1 hour)	MAP >70 mmHg	MAP <70 mmHg	Dopamine <5 or Any dobutamine dose	Dopamine 5.1-15 or Epinephrine <0.1 or Norepinephrine <0.1	Dopamine >15 or Epinephrine >0.1 or Norepinephrine >0.1
Central nervous system Glasgow coma scale score	15	13-14	10-12	6-9	<6
Kidney Creatinine mg/dL (μmol/L) or urine output mL/kg/hour	<1.2 (<110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440) <500	>5.0 (≥440) <200

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Identification of sepsis outside of an ICU

- Quick SOFA (qSOFA)
- 2 or more of:
 - Altered mentation (a diminished Glasgow Coma Scale score)
 - Hypotension (systolic blood pressure ≤100mmHg)
 - Tachypnea (respiratory rate ≥22 breaths per minute)
- Rapid screen for **predictors of mortality** rather ID sepsis specifically

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Septic shock 3.0

- Subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.
- Sepsis and despite adequate volume resuscitation:
 - Hypotension requiring vasopressors to maintain MAP ≥65mm^{Hg} AND
 - Lactate ≥2mmol/L
- Mortality >40-60%

Singer et al. JAMA 2016

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Veterinary definition of sepsis

Currently...

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How often do we see sepsis on our patients?

- Incidence of sepsis?
 - Unknown
- Mortality rate?
 - 20%-68%
 - ↑ greater degrees of physiologic parameter disturbance
 - ↑ organ dysfunction

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Current recommendations on how to detect sepsis on small animals

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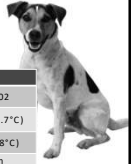
- Suspect or confirm an infection:
 - Bacteria (most common)
 - Viral (parvovirus)
 - Fungal (blastomycosis, candidiasis)
 - Parasitic (rare)
- Clinical signs
 - Fever
 - Pus
 - Pustules
- Cytology
- ELISA
 - Snap test parvo
 - 4Dx
- Culture (takes too long)

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Current recommendations on how to detect sepsis on small animals

2

- Suspect an "inappropriate" immune response :
 - Systemic Inflammatory Response Syndrome




Criteria	Dogs (2/4 criteria)		
	Hauptman 1997	de Laforcade 2003	Okano 2002
Temp.	>102.2°F (>39°C)	>103°F (>39.4°C)	>103.5°F (>39.7°C)
	<100.4°F (<38°C)	<100°F (<37.8°C)	<100°F (<37.8°C)
Heart rate	>120 bpm	>140 bpm	>160 bpm
Resp. rate	>20 rpm	>20 rpm	>40 rpm
Leukocyte count	>16 x10 ³ /μL	>16 x10 ³ /μL	>12 x10 ³ /μL
Band neutrophils	<6 x10 ³ /μL	<6 x10 ³ /μL	<4 x10 ³ /μL

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Current recommendations on how to detect sepsis on small animals

2

- Suspect an "inappropriate" immune response :
 - Systemic Inflammatory Response Syndrome



Criteria	Cats (3/4 criteria)	
	Brady 2000 ¹¹⁰	DeClue 2011 ¹¹¹
Temp.	>103.5°F (>39.7°C)	≥103.5°F (>39.7°C)
	<100°F (<37.8°C)	≤100°F (<37.8°C)
Heart rate	>225 bpm	≥225 bpm
Resp. rate	<140 bpm	≤140 bpm
Leukocyte count	>40 rpm	≥40 rpm
	>19.5 x10 ³ /μL	>19.5 x10 ³ /μL
Band neutrophils	<5 x10 ³ /μL	≤5 x10 ³ /μL
	>5%	≥5%

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Limitation of the SIRS criteria in veterinary patients

- Very non-specific criteria
- SIRS-positive status common for ER and primary care patients
- Weakly associated with outcome

¹⁰Brady et al., JAVMA 2000; ¹¹⁰DeClue et al., JAVMA 2011; ¹¹¹Okano et al., JAVMA 2002. The syndrome criteria in dogs and cats presenting to an emergency department. J Am Vet Assoc 2002; 272:1000-1004.

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Limitations with SIRS criteria in veterinary patients

- Sepsis is NOT an overexuberant pro-inflammatory response
- Hence use of SIRS criteria to ID sepsis is not legitimate

Can we use the SOFA score in dogs and cats?

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Organ dysfunction – complete SOFA score

Organ	Measure
Respiratory	PaO ₂ /FiO ₂ Need for O ₂ supplementation
Renal	Serum creatinine
Hepatic	Serum bilirubin
Cardiovascular	Blood pressure need for vasopressors
Hematologic	Platelet count PT aPTT
Neurologic	Glasgow coma score

Kemmer et al., JAVMA 2010

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qSOFA

- Respiratory rate ≥ 22 /mi
- Systolic blood pressure(SBP) ≤ 100 mmHg
- Altered mentation: Normal or abnormal:
 - able to stand unassisted, responsive but dull
 - can stand only when assisted ,responsive but dull
 - unable to stand, responsive
 - Unable to stand, unresponsive

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Summary of veterinary results

Association between outcome and organ system dysfunction in dogs with sepsis: 114 cases (2003–2007)

- Dysfunction of any organ except hepatic: increase risk of death
- MODS : mortality rate: 70%

Retrospective evaluation of the use of quick Sepsis-related Organ Failure Assessment (qSOFA) as predictor of mortality and length of hospitalization in dogs with pyometra (2013-2019): 52 cases

- Overall mortality rate: 21%
- qSOFA > 2
 - \uparrow Hospital mortality
 - \uparrow Organ dysfunction

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Retrospective evaluation of the prognostic utility of quick sequential organ failure assessment scores in dogs with surgically treated sepsis (2011-2018): 204 cases

- Overall mortality: 30.9%
- qSOFA > 2
 - 7.1 more likely non survivor
 - + septic peritonitis 3.9 more likely postoperative complications

Evaluation of the quick sequential organ failure assessment score plus lactate in critically ill dogs

- Overall mortality: 17.6%
- qSOFA not different between survivor and non survivors
- Lactate : each 1 mmol/L \uparrow lactate \downarrow survival : 1.2 more likely to die

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Take home message

Incorporating organ dysfunction into severity assessments may be useful

May need to modify the parameters or criteria for biological variation between species

Will need to be validated with prospective studies

Current work of the defining sepsis consensus working group

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Current definition veterinary patients

Suspected or known

SIRS = SEPSIS

Cytology: Pus ; ELISA

SEPSIS = Organ failure 20%

Septic shock = Cardiovascular failure 60%

Mean Arterial BP < 65mmHg despite fluids + Lactate > 2 mmol/L \Rightarrow Need for vasopressors

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What are common diseases processes in dogs and cats that can lead to the development of sepsis?

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Diseases associated with sepsis

- Septic peritonitis
- Pylonephritis
- Pneumonia
- Septic arthritis
- Bacterial endocarditis
- Tick borne disease
- Pyothorax
- Septic meningitis
- Pyoderma
- Parvovirus

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Infection sites in dogs and cats

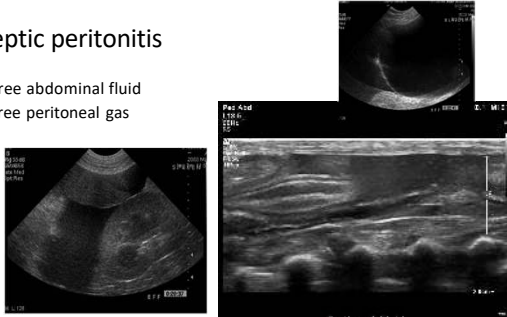
Dogs	Cats
<ul style="list-style-type: none">• Abdominal (35%)• Reproductive (25%)• Respiratory (20%)• Urinary (10%)• Other (10%)	<ul style="list-style-type: none">• Pyothorax (7/29)• Pneumonia (4/29)• Septic peritonitis (5/29)• Bacteremia secondary to GI disease (5/29)• Endocarditis (4/29)• Pylonephritis (2/29)• Osteomyelitis (1/29)• Pyometra (1/29)• Bite Wounds (1/29)

Hauptman et al. 1998.

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Septic peritonitis

- Free abdominal fluid
- Free peritoneal gas



The image contains three ultrasound panels. The top right panel shows a dark, anechoic area, likely representing free fluid. The bottom left panel shows a similar dark area with some internal echoes. The bottom right panel shows a more complex, layered structure, possibly representing peritoneal gas or a specific organ.

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Free gas

Free gas

Free gas

Decreased serosal detail = free fluid

This is a lateral chest X-ray. Three arrows point to dark, radiolucent areas in the thoracic cavity, labeled 'Free gas'. One arrow points to a region with less distinct lung markings, labeled 'Decreased serosal detail = free fluid'.

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Free gas

Decreased serosal detail = free fluid

This is a lateral chest X-ray. One arrow points to a dark, radiolucent area, labeled 'Free gas'. Another arrow points to a region with less distinct lung markings, labeled 'Decreased serosal detail = free fluid'.

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Free gas

Free gas

This is a standard chest X-ray. Two arrows point to dark, radiolucent areas in the lung fields, labeled 'Free gas'.

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Fluid analysis

- TS > 2.5 = EXUDATE
- Fluid Lactate 2 mmol/L > serum lactate
- Fluid Glucose 1.2 mmol < serum glucose
- Look at the feathered edge for intracellular bacteria within neutrophils

Agarose (post) Bile Bile layer Feathered edge

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Septic peritonitis- specific causes

- Uro-septic abdomen
 - Creatinine fluid to serum ratio 2:1
 - Potassium fluid to serum ratio 1.4: 1
 - Intracellular bacteria
- Bile peritonitis
 - Fluid total bilirubin > 2 serum bilirubin
 - **Green brown pigments**
 - Can sometimes be Basophilic amorphous acellular, mucinous material can be seen in clumps of variable diameter
 - Intracellular bacteria

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Summary

Suspected or known

Cytology- pus- + Elisa- + culture

Complete blood count
Biochemistry
Coagulation panel
Urinalysis

SIRS = SEPSIS?

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Diagnosis

- Obtaining appropriate cultures before antimicrobial therapy if **doesn't cause a delay**
 - Urine culture
 - Blood culture
 - Endotracheal wash
 - Peritoneal fluid
 - Pleural fluid
 - CSF
- Imaging
 - Confirm source of potential sepsis

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Complete blood count

Hematologic parameter	Test available	Possible abnormalities
WBC count	WBC count, differential	Leukocytosis or leukopenia
	Blood smear evaluation, cytologic evaluation	Toxic changes, immature neutrophils
	Bone marrow evaluation	Myeloid hyperplasia
Red blood cell count	Hemotocrit	Hemoconcentration or anemia
	Reticulocyte count	Non regenerative anemia
	Blood smear, cytologic evaluation	Heinz body(cats) Schistocytes
	Bone marrow evaluation	Erythroid hyperplasia
Platelets	Platelet count, BS evaluation	Thrombocytopenia

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Coagulation

Hemostatic parameter	Possible abnormalities
PT	Normal (early) or prolonged (late)
PTT	Normal (early) or prolonged (late)
Activated clotting time	Normal (early) or prolonged (late)
FDP	Increased
D dimers	Increased (late)
Antithrombin	Decreased activity
Protein C	Decreased
Fibrinogen	Normal to increase (early) Decreased (late)
Thromboelastography	Increased coagulation index

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Chemistry

Parameter tests	Possible abnormality	Pathophysiology
Albumin	Hypoalbuminemia	Loss (peritonitis, increased vascular permeability) Hepatic dysfunction Negative acute phase protein
Bilirubin	Hyperbilirubinemia	Dogs: sepsis induced cholestasis due to defect in hepatocellular transportation of bile Cats: hemolysis
Glucose	Hyperglycemia (early) Hypoglycemia	Increase counter-regulatory hormones, decrease insulin Depletion of glycogen storage
Ionized calcium	Ionized hypocalcemia	Secondary hypo parathyroidism Hypomagnesemia Decrease vitamin D Elevation pro calcitonin Accumulation of Ca ²⁺ intracellularly

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Bloodwork

- Changes reflective of underlying disease process
- Could reflect progression to organ failure:
 - Important to have baseline and trends..

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Management of sepsis

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Surviving sepsis guideline

- 2005 then 2008; 2012; 2016 publication of Guidelines
 - Based on results of studies
 - Graded based on the quality of evidence
- Creation of "bundles"= packages
 - Resuscitation bundle:
 - Within the first 6 hours
 - Management bundle
 - Within the first 24 hrs
- Aim: decrease mortality



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Initial stabilization:

- Address pain → pure mu opioids
- Address electrolyte derangements if present (hypoglycemia etc..)
- Provide O₂ supplementation if indicated
- Etc...

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Fluid therapy in sepsis

- Usually needs some fluid therapy
- Goal is to restore oxygen delivery

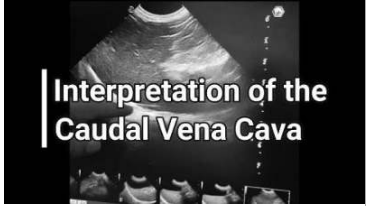


- DO₂ = CO x CaCO₂
 - Judicious fluid volume
 - Small boluses
- Look at end goals for resuscitation (à see triage/ shock lecture)
 - If after 40 mL/kg not reached good perfusion parameters → need to look at other alternatives/ causes

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POCUS findings that can help guide fluid choice


- Assessment of the cardiac filling:
 - Caudal vena cava at the level of the DH site
 - If very collapsible during breathing → hypovolemic
 - If non collapsible during breathing → euvolemic to hypervolemic



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POCUS findings that can help guide fluid choice

- Assessment of ventricular filling:
 - "mushroom" view → if it looks like HCM cat → hypovolemic
 - Normal "mushroom" view → euvolemic



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Antimicrobial Therapy

Surviving Sepsis Campaign

- Administration of effective intravenous antimicrobials within the first hour of recognition of septic shock and severe sepsis without septic shock as the goal of therapy
- Initial empiric anti-infective therapy of one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into tissues presumed to be the source of sepsis

Delinger et al. CCM 2012

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HIT HARD AND HIT FAST

Delinger et al. CCM 2012

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Appropriate Empirical Antimicrobial Therapy

- Antimicrobial therapy with activity against the pathogen that is subsequently identified as the causative agent
- Depends on the:
 - Likely pathogens
 - Susceptibility pattern
 - Pharmacokinetics and pharmacodynamics of the drug




Delinger et al. CCM 2012

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Antimicrobials

- Start IV antibiotics as soon as possible and within 1 hours of recognition of sepsis
- Initial empirical antibiotic effective against all likely pathogens
- COMBINATION therapy = BROAD SPECTRUM
- Gram +, Gram -, anaerobes and aerobes



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Antimicrobials suggested combination therapy for sepsis

- Ampicillin (22 mg/kg q 8 h) + Enrofloxacin (5-20 mg/kg q 24h)
- Ampicillin + Amikacin (15 mg/kg q 24h) +/- metronidazole if suspect anaerobes
- Cefazolin (22 mg/kg q 8h) + Amikacin (15 mg/kg q 24h)
- Ampicillin + Cefotaxime (25 to 50 mg/kg q 4-6 h)
- Ampicillin + Ceftazidime (30-50 mg/kg q6-8h)
- Clindamycin (10 mg/kg q 12h) + Enrofloxacin (5-20 mg/kg q 24h)
- Clindamycin + Amikacin

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Antimicrobials



- Daily reassessment of antimicrobial regimen to prevent formation of resistance
- Empirical antibiotic therapy for NO MORE than 3-5 days then de-escalation based on culture results as soon as possible
- Duration 7-14 days
 - Unless slow clinical response
 - Immunologic deficiencies

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Source control = surgical intervention

Should be done as soon as the patient is stable enough


- If potential for source control
 - Least physiologic insult should be employed
- Wound debridement
- Placement of drains : closed suction >> penrose
- Abdominal exploratory laparotomy
 - Find source of infection
 - Remove if possible (pyometra)
 - Seal (GI perforation)
 - Debride and place drain (Prostatic abscess)

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Important adjunct therapy- post initial stabilization

- Address underlying electrolytes abnormalities
- Nutrition
 - Enteral > parenteral
 - Early nutrition
 - Slow increase in RER
- Analgesia
- Oxygen
- Tender loving care



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Specific therapies for septic shock

Septic shock = Sepsis and despite adequate fluid resuscitation



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Vasopressors recommended for septic shock

- AIM: MAP > 65 mmHg
- Increase blood flow- tissue perfusion
- Increase in CO

Drug(s)	Goal	Indication	Mechanism of action
Dobutamine CRI	Increase cardiac contractility	Decreased cardiac contractility on cardiac POCUS Decreased fractional shortening	Beta agonist
Norepinephrine CRI	Vasoconstriction – increase arterial blood pressure	Hypotension (despite adequate fluid resuscitation)	Alpha agonist > beta agonist

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Summary resuscitation therapy

- Fluid therapy
 - Aggressive but not too much..
 - Goals: MAP, Thoracic POCUS, cardiac filling, ScvO2, UOP,
- Diagnosis- Bloodwork, imaging, cytology
 - CULTURE!
- Antibiotics (Broad spectrum) **within the hour**
- Source control
- Treat the other concerns (O2, glucose, etc...)
- Septic shock ONLY à vasopressors

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Prognosis

- Dogs:
 - 20% to 50% mortality rate
 - Better outcome for closed management septic peritonitis
 - Up to 79% discharge and survival
- Cats:
 - 44% mortality rate



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Questions?




- Those are the 2 questions the consensus statement group is working on to answer...

What variables in infected dogs and cats predict development of sepsis?

What variables in dogs and cats with sepsis predict non-survival?

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12 members
 Experience with sepsis
 International
 Mix of academia and private practice

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