Lactic Acidosis and Sepsis

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Objectives

- To review lactic acidosis
- Update on sepsis statistics
- Overview of sepsis as the disease progresses and treatment plan

What is Lactic Acidosis?

Lactic acidosis

- Accumulation of Lactate and protons in body fluids.

Why is lactic acidosis a concern?

- Often associated with an increase in mortality.
- In sepsis or in low flow states mortality is increased.
- Higher the lactic acidosis, greater the mortality.

Pathophysiology

Glucose breakdown without O_2 is called anaerobic and produces pyruvate

pyruvate + NADH + $H^+ \longleftrightarrow$ lactate + NAD^+

Lactate is produced more in the muscles and converted back to pyruvate in the mitochondria of the liver, kidney, and other tissues

glucose + 2(ADP + inorganic phosphate) $\rightarrow$ 2 lactate + 2 H^+ + 2 ATP.

Hyperlactatemia

1. Lactate production exceeds lactate consumption.
2. Tissue hypoxia, whether global or localized, lactate is overproduced and underutilized as a result of impaired mitochondrial oxidation.
3. If systemic oxygen delivery is not low enough to cause generalized hypoxia, micro-circulatory dysfunction can cause regional tissue hypoxia and hyperlactatemia.
4. Coexisting acidemia contributes to decreased lactate removal by the liver; severe hypoxia and acidemia can convert the liver into a net lactate-producing organ.
5. Hyperlactatemia can also result from aerobic glycolysis (an effective but inefficient mechanism for rapid generation of ATP). This occurs with elevated epinephrine levels in sepsis, severe asthma(overuse of beta agonists), extensive trauma, shock (cardiogenic or hemorrhagic).
6. Aerobic glycolysis and tissue hypoxia are not mutually exclusive.

Causes and Diagnosis

- Major Causes of lactic acidosis are disorders associated with tissue hypoxia (type A) and without tissue hypoxia (type B).
- Evidence of severe cardiopulmonary disease, the systemic inflammatory response syndrome, sepsis, severe trauma, or volume depletion offers important clues for diagnosing lactic acidosis.
- An elevated blood lactate level is essential for confirmation of the diagnosis.

And Now To Sepsis

Sepsis Statistics for Adults

- One of the top 10 leading causes of death in U.S. hospitals
- Inpatient Mortality Risk 25-30%
- Approximately 750,000 cases of severe sepsis
- Kills more than 200,000 people every year
- Numbers continue to grow
  - Hospital admission for **sepsis doubled from 2000 to 2008**
  - In 2008 Patients w/ sepsis had **higher acuity & longer LOS**
  - Cases of Severe Sepsis are estimated to double over the next 25-30 yrs

Definition of Sepsis

- **Surviving Sepsis Campaign**

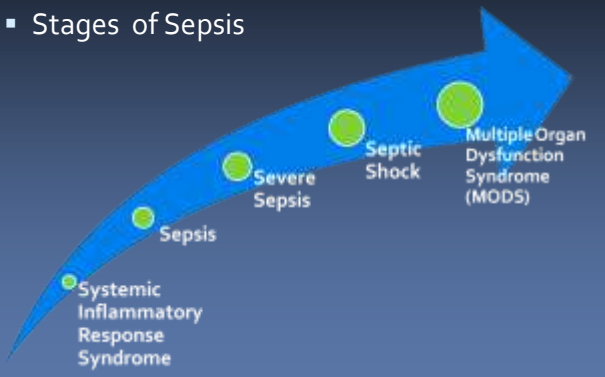
  "Sepsis can be defined as the body's response to an infection. An infection is caused by microorganisms…invading the body, and can be limited to a particular body region…or can be widespread in the bloodstream… Sepsis is a medical emergency just like a heart attack or a stroke because there is an interruption of oxygen and nutrients to the tissues including the vital organs such as the brain, intestines, liver, kidneys and lungs."

- **Global Sepsis Alliance**

  "Sepsis is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs. Sepsis may lead to shock, multiple organ failure and death, especially if not recognized early and treated promptly. Sepsis remains the primary cause of death from infection despite advances in modern medicine, including vaccines, antibiotics and acute care. Millions of people die of sepsis every year worldwide."

Sepsis can be a Progressive Process

- Stages of Sepsis



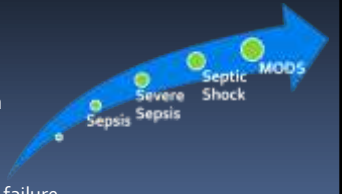
Initial Finding *Commonly* Associated with Sepsis Diagnosis

- **SIRS** (Systemic Inflammatory Response Syndrome)

- Generalized inflammatory response of the body to a variety of clinical conditions including infection, but not limited to infection

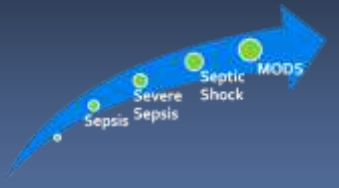
Definition of Sepsis Stages

- **Sepsis:**
  - SIRS+Infection=Sepsis
    Identified or Suspected Infection
- **Severe Sepsis**
  - SIRS + evidence of infection + organ failure
- **Septic Shock**
  - SIRS + evidence of infection + organ failure + refractory hypotension (not responsive to fluid resuscitation)
- **Multi-system Organ Dysfunction Syndrome**
  - More than one organ system failure



Mortality Rates as Sepsis Progresses

- **Sepsis:** Mortality 15%
- **Severe Sepsis:** Mortality 20%
- **Septic Shock:** Mortality 45%



Summary

- Sepsis is a complex disease process
- Mortality increase as the disease progresses

Nursing Implication

- Early detection and treatment are vital to increase patient survival rates
- Knowledge of the early signs & symptoms is the key to early identification

Sepsis

PATHOPYSIOLOGY

Objectives

- Review of pathophysiology
  - Inflammatory Response
  - SIRS
  - Sepsis
  - Severe Sepsis
  - Septic Shock, MultiOrgan Failure

Inflammatory Response

- The key to understanding the **pathophysiology of sepsis** begins w/ understanding the **body's defensive response: Inflammation**
- Inflammation allows the body to release defensive molecules, such as cytokines, hormones, or mediators to begin healing &/or ridding the body of a harmful organism and assist in restoring & maintaining homeostasis
- Inflammation is an essential defense response; *however, **prolonged or excessive inflammation can be harmful***

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS)

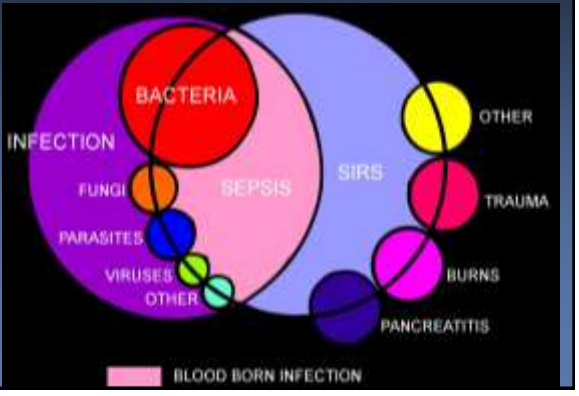
- SIRS occurs when inflammatory state moves beyond the area of insult and begins affecting the whole body; detection based on SIRS criteria
- SIRS Criteria - at least **two** of the following:
  - Temperature > 38°C (100.4°F) or < 36°C (96.8°F)
  - Heart rate (HR) > 90 bpm
  - Respiratory rate (RR) > 20 breaths/min or arterial carbon dioxide tension ($PaCO_2$) < 32 mm Hg
  - WBC count > 12,000/µL or < 4000/µL, or greater than 10% bands

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS)

- Although SIRS is almost always present in the early stages of sepsis, it is not only associated with infections but also other chemical insults, such as injury, organ inflammation, shock, ischemia

SIRS Related Causes

NOTE: Not limited to infection



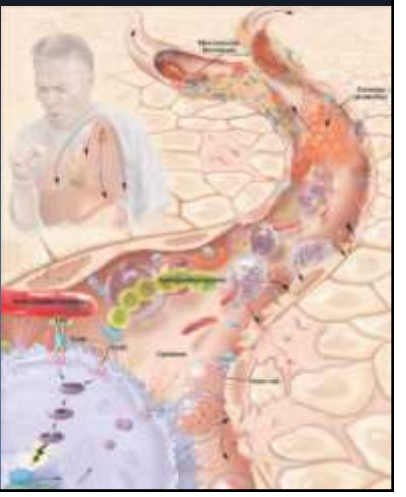
Sepsis

Partly caused directly by the germ/organism which has invaded the body, but by the chemicals released in response to the germ invasion…

SIRS + Infection = Sepsis

In the presence of infections w/ large numbers of microorganisms the inflammatory system often responds by releasing an excessive amount of defensive molecules leading to SIRS.

SIRS is a normal defensive response; however an overactive response leads to disruption of the body's normal homeostasis processes



Progression of Sepsis

- ***Simply Stated:***

"Your systems go into overdrive, overwhelming normal homeostasis processes."

- The end result:
- Blood flow & O_2 transport to vital organs is compromised leading to organ failure and possibly death

Overactive Inflammatory Response

How is blood flow & O_2 transport to vital organs compromised?

Vasodilation & fluid loss (capillary leak) as a response to cytokines release

- Hypotension
- Decreased CO/CI

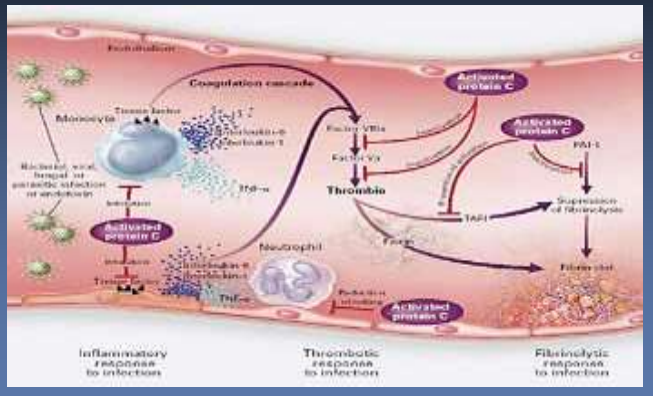
Obstruction from excessive fluid (capillary leak) or defensive molecule (over production of macrophages) accumulation

- Fluid filled alveoli
- Edema

Abnormal coagulation processes

- Impaired fibrinolysis leading to clot formation which causes hypoperfusion, tissue necrosis and organ failure
- DIC (Disseminated Intravascular Coagulation) – clot formation uses up platelets & clotting factors which can lead to uncontrollable bleeding

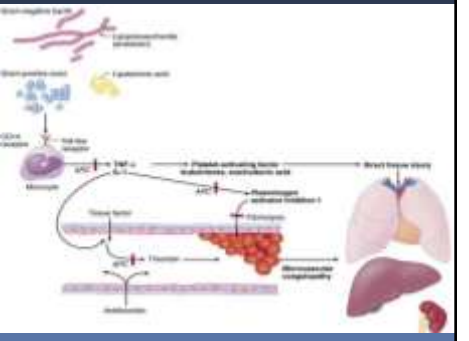
Inflammatory response triggers Coagulation Cascade



Severe Sepsis

Sepsis Complicated by Acute Organ Dysfunction

- Blood flow & O_2 transport to vital organs is compromised by:
  - ✓Hypotension
  - ✓Obstruction
  - ✓Increased clot formation



Septic Shock

- **Severe Sepsis + Persistent hypotension despite aggressive fluid resuscitation**
- NS bolus (≥20 ml/kg)
- Tissue hypoperfusion - Lactic Acid (LA) > 4 mg/dl
  - 1-2 mmol/dl - Normal
  - 2-4 mmol/dl – diminished oxygen perfusion
  - > 4 mmol/dl – **complete tissue hypoxia or Global Tissue Hypoxia**

Persistent Hypotension:
- SBP < 90 or MAP < 65
- LA > 4

Septic Shock Syndrome

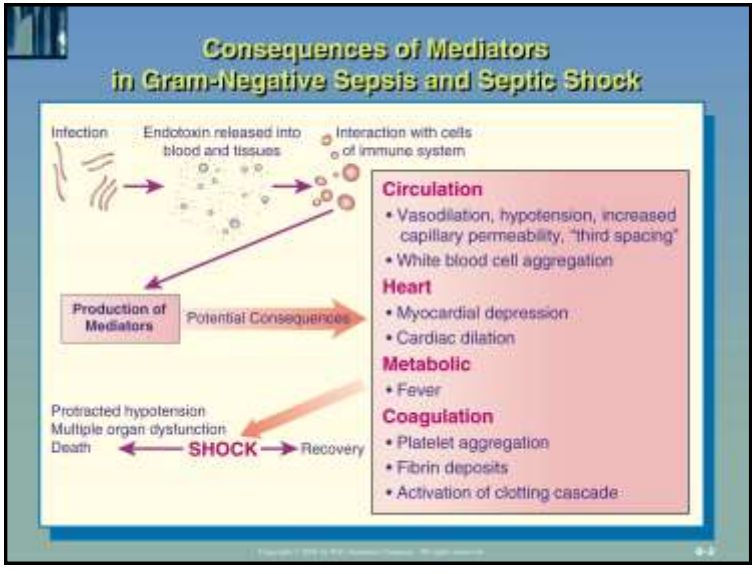
- A complex cycle of compensatory responses resulting in inadequate tissue perfusion, cellular dysfunction & organ failure.
  - Blood flow & O_2 transport to vital organs becomes even more compromised
    - ✓Hypotension
    - ✓Obstruction
    - ✓Increased Clot Formation
- Can lead to further deterioration such as:
  - DIC (Disseminated Intravascular Coagulation) – clot formation uses up platelets and clotting factors which can lead to uncontrollable bleeding
  - Multisystem organ failure
  - Death

Multiple Organ Dysfunction Syndrome (MODS)

- More than one organ system failure
- Presence of altered organ function lasting for > 24 hrs in an acutely ill patient, such that homeostasis cannot be maintained w/out intervention

Summary of Sepsis Patho

- Infection triggers the body's inflammatory response
- The inflammatory response extends beyond the original insult, affecting other distant areas of the body
- Blood flow & O_2 Transport are compromised leading to tissue hypoperfusion causing organ dysfunction
- Homeostasis is disrupted
- Without the normal organ functions, the body progresses to a state of shock
- If not reversed permanent organ damage and death will likely occur



Sepsis

EARLY RECOGNITION

Objectives

- Describe components for early identification
  - Sepsis biomarker *(or lack of)*
  - Awareness of:
    - Risk factors
    - Predisposing factors
    - Preventative measures (when not avoided, becomes a risk factor)
  - Early Warning Signs
    - SIRS Criteria
    - Confirmed or Suspected Infection

      Common Sources

Early Recognition is the Key

Early Diagnosis & Early Treatment = Increased Rate of Survival

However,

SEPSIS IN THE BEGINNING IS DIFFICULT TO RECOGNIZE BUT EASY TO TREAT; LEFT UNATTENDED IT BECOMES EASY TO RECOGNIZE BUT DIFFICULT TO TREAT

Machiavelli

Why is Early Recognition Difficult…

- **SIRS is not always r/t sepsis**
  - Currently no true biomarkers for sepsis to differentiate sepsis from a non-infectious source for SIRS
    - *Purposed* biomarkers

      C-reactive protein (CRP), IL-6, IL-12, Procalcitonin (PCT), CD64, G-CSF, TREM-1, pFN, Complement (C_3, C_4, C_5a)

      ***However, due to the complexity of sepsis, it is unlikely that a single ideal biomarker will ever be found… (Pierrakos & Vincent, 2010)
  - Biomarkers for sepsis are more often used to monitor response to treatment or estimate prognosis rather than for diagnosis (such as Lactic acid)

How to identify Sepsis

- Without a reliable diagnostic marker for Sepsis, clinicians must utilize a screening process to identify patient displaying common early findings associated with sepsis
- SIRS criteria is recommended as the key for sepsis screening *(in RARE cases 2 or more SIRS criteria may not be present)*
- In addition to the SIRS criteria, knowledge of: risk and predisposing factors; prevention techniques; and common sources of infection are also helpful to assist clinicians w/ early recognition of sepsis

Consider Risk & Predisposing Factors

- **Risk factors**
  - Immunosuppressed patients
  - Elderly or Newborns
  - Post-op
  - Alcoholism
  - AIDS
  - Critically Ill
  - Chemotherapy
  - Invasive Lines (Central Lines; Urinary Catheter)
  - Renal Failure
  - Diabetics
  - High Dose Steroids
- **Predisposing factors**
  - Very young or old
  - Prior Antibiotic therapy
  - Injury
  - Surgery or Invasive Procedure
  - Malnutrition
  - Alcohol history
  - Prolonged Intubation
  - Chemotherapy
  - Dialysis

Prevention

- Treat sepsis early to prevent progression
- Avoid invasive procedures
- Limit use of invasive line (central lines, urinary catheters)
- Avoid indiscriminate use of antimicrobials, glucocorticoids
- Control of infections

SIRS Criteria for Sepsis Dx

- **SIRS + Infection = Sepsis**
  - Assess for the presence of at least 2 or more of the following SIRS Criteria:
    - Temp > 38°C (100.4°F) or < 36°C (96.8°F)
    - HR > 90 bpm
    - RR > 20 breaths/min or $PaCO_2$ < 32 mm Hg
    - WBC > 12,000/µL or < 4000/µL, or 10% bands
- If 2 or more SIRS Criteria are found, assess for infection (identified or suspected)

Consider Common Sources

- **Lungs** – pneumonia, aspiration
- **Abdomen** – appendicitis, bowel leak, gallbladder infections, peritonitis
- **Urinary Tract** – UTI (esp. w/ catheter present), pyelonephritis
- **Skin** – wounds, burns, cellulitis, IV devices, incisions
- **Bones** – osteomyelitis (common in children)
- **Central Nervous System** – meningitis, encephalitis
- **Other** –
  - Implantable device
  - around 20 % etiology unknown

Addition Warning Signs

- Early on (not included in SIRS):
  - Delirium, anxiety, restlessness, confusion
  - Change in LOC: SAE (sepsis-associated encephalopathy) Often precedes all other cardinal signs of sepsis
  - Nausea & Vomiting
  - Fatigue, weakness
- Later in the disease process
  - Mottled skin; petechiae; purpura
  - Low urine output; elevated Cr
  - Low platelet count; elevated PT/INR/PTT
  - Elevated Bilirubin or ALT
  - Left ventricular systolic dysfunction (LVSD)
  - ARDS

Clinical Implication

- If 2 criteria for SIRS are found AND infection is confirmed or suspected notify physician of findings
- Use critical thinking skills to r/o other causes which may be r/t SIRS criteria
  - Examples
    - Post-op pt w/ elevated Temp & RR:
    - Excessive beta agonists
    - Assess lung sounds, check CXR, assist/instruct w/ C & DB and Voldyne
    - Assess rhythm, SpO_2, O_2 use, pain level

Sepsis

TREATMENT

Objectives

- Briefly discuss integration of research into practice
- Describe components for early treatment
  - Early Goal Directed Therapy (EGDT)
  - "Time is Tissue"
  - Assessing Responsiveness
- Review of Sepsis Order Set

Why is Sepsis Mortality Rates Still so High?

- Research not yet "common knowledge" among the health-care team; therefore is not "common practice"
- The recommendations for Sepsis Treatment commonly referred to as the Sepsis Bundle or Early Goal Directed Therapy (EGDT) were released in 2001, yet have not been integrated into the standard practice by many providers
- Sepsis *may* become one of the next focus areas from a CMS core measure stand point to enhance compliance with the ultimate goal to improve patient outcomes

Improvements take time

- Think about past advances in medical management with other diseases/injury
  - AMI
  - Stroke
  - Trauma

  Improvement in patient outcomes occurred over time with the compliance with EBP treatment bundles

Now is the time for improvements with Sepsis

Early Goal Directed Therapy (EGDT)

- EGDT includes the application of early diagnosis and time-sensitive treatments ordered as a sepsis bundle
- The treatment regimen is similar to the conditions of that for AMI, Stroke and Trauma
  - Identify ⟶ Treatment w/out delay

Components of EGDT

- Goal: Control cause and restore tissue perfusion

- Within Six Hours of Diagnosis
  - Obtain cultures (blood Cx's 2, urine, respiratory, wound), then appropriate antibiotics-ASAP
  - Monitor hemodynamics - BP, CVP, SVO_2(or $ScVO_2$)
  - Monitor Lactate levels (marker of tissue hypoperfusion)
  - Fluid resuscitation - NS 20-40cc/kg (May require repeated boluses)

- Within 24 hours of Diagnosis (if not sooner)
  - Vasopressors & inotropes (*If unresponsive to fluid resuscitation*)
  - Search for the cause (diagnostics/x-rays)
  - Ventilatory support if needed (maintaining inspiratory plateau pressure of <30 cm H_2O)
  - TGC? (Tight Glucose Control) -No
  - DVT/PUD Prophylaxis
  - Blood Transfusions & steroids as indicated (not standard as other interventions)

Plan of Care/Goals

- Improve tissue perfusion
  - $ScvO_2$ >/= 65-70
    - If not achieved with fluid resuscitation during first 6 hrs, start thinking about pRBC
  - MAP >/=65
    - Consider vasopressor (levophed, vasopressin)
  - CVP >/=8-12
- Improve cardiac pump function
  - If not achieving goals within first 6 hours
    - Think about dobutamine to support pump function
- Improve fluid balance
  - Urinary output >/=0.5 cc/kg/hr

Sepsis Advanced Management

- **Sepsis**
  - ***Time is Tissue***
    - Early Goal Directed Therapy (EGDT) - Dr. Emanuel Rivers

      Cultures, Antibiotics, Baseline LA, Fluid Resuscitation, Central line placement, Vasopressors, Inotropes, Oxygenation, Glycemic Control, PUD & VTE Prophylaxis, Steroids

Sepsis Management

- Recognition & tx during the "golden hours" provides maximal benefits in terms of outcome
  - Each ONE hour of delay in antibiotic administration is associated with a 7.6% increase in mortality
- If you can identify patients early with initial diagnosis *as well as progression of sepsis*, then you can intervene and prevent further tissue damage

Assess for Progression

- **Severe Sepsis:**
- **Sepsis complicated by end-organ failure**

- **Assess for possibilities**
- Renal (Cr or GFR, urine output)
- Respiratory (lung sounds, RR, ABGs, dyspnea, CXR, SOB, PaO_2, SaO_2, SvO_2)
- Hepatic (jaundice, SGPT, SGOT, Bilirubin, albumin, PT/INR, pH)
- Hematological (platelets, PT/INR, D-dimer)
- Central Nervous System (LOC, Delirium)
- Unexplained Metabolic Acidosis
- Cardiovascular (hypotension, CVP, dysrhythmias, CO/CI, troponins, LVSD)
- Coagulation cascade
  - Increased clotting & Decreased Fibrinolysis
  - Leading to Global Tissue Hypoxia (mottled skin)

Global tissue hypoxia

- When there is a threat to the oxygen balance, the body's primary compensatory mechanisms are to increase delivery of O_2 &/or increase extraction of O_2
- When tissue needs more O_2, an increase extraction occurs, which decreases the amount returning to the heart, this results in **low SVO_2 percentages.**

Global Tissue Hypoxia

- A change in SVO_2 of 5% -10% from baseline can be an early indication of physiologic instability
- FYI – In the past decade $ScVO_2$ reading have been utilized in place of SVO_2 readings
  - Research evidence supports no benefit in SVO_2 (saturated venous oxygen) reading over $ScVO_2$ (saturated central venous oxygen)

	SVO_2	$ScVO_2$
Catheter tip location	PA (Pulmonary Artery)	SVC (Superior Vena Cava)
Catheter type	PA Line – offers continuous reading	Central Line (Short- or Long-term; or PICC) – usually a blood draw for an intermittent reading; new short-term catheter offer continuous reading capability
Invasiveness	Highly	Less so
Complications	More Risks	Less Complications
Target Value for Sepsis Tx	65%	70%

Key Points to Treatment

Do NOT delay antibiotics (order & obtain cultures promptly prior to giving antibiotics)

Recognize the relevance of initial fluid boluses – 20-40ml/kg (150 lbs = 68 kg = 1,400 – 2700 ml bolus)

Obtain baseline VS & labs including (MAP, CVP, $ScvO_2$, LA)

Vasopressors are recommended when hemodynamics are unresponsive to fluid resuscitation

- Norepinephrine **(Levophed)** – 1st choice
- Adding or substituting Epinephrine or Vasopressin are additional options
- Dopamine as an alternative - ONLY in highly selected pts who are at very low risk for arrthytmias and w/ low cardiac &/or low heart rate

Inotrope (Dobutamine) should be added when myocardial dysfunction (elevated cardiac filling & low cardiac output) is noted

Key Points to Treatment

- O_2 support may required mechanical ventilation
  - Minimal sedation
- Maintain good glucose control
- Once susceptibility report is available from culture, contact physician for appropriate antibiotic therapy
- Provide VTE (DVT/PE) & PUD prophylaxis
- Close continuous monitoring is essential to avoid further deterioration
- Blood transfusions &/or steroids ordered based on individual patient needs
- The process of Sepsis is difficult for significant others to understand – Provide ongoing emotional support , contact resources such as clergy, social work for additional support

Sepsis Summary

- ✓ Recognize signs & symptoms early and obtain orders for EGDT (Early Goal Directed Therapy)
- ✓ Recognize the signs & symptoms of further deterioration and notify intensivist promptly
- ✓ Implement and follow the guideline for care of septic patients
- ✓ Order sets if available – Severe sepsis/Septic shock order set

Questions?