Sepsis and Septic Shock in Pregnancy

John R. Barton, M.D.
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Comparison of Sepsis With Other Major Diseases

**Incidence of Severe Sepsis**

- AIDS*
- Colon Cancer§
- Breast Cancer
- CHF†
- Severe Sepsis‡

**Mortality of Severe Sepsis**

- AIDS*
- Breast Cancer§
- AMI†
- Severe Sepsis‡

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The fundamental clinical problem of sepsis was readily apparent even to the casual observer over 500 years ago.

“Hectic fever (sepsis) at its inception is difficult to recognize but easy to treat. Left untended, it becomes easy to recognize but difficult to treat.”

- Circa 1498

Niccolo Machiavelli
The Prince, Book III

Steven M. Opal, MD
International Sepsis Forum Symposium
Sept. 27, 2007
1840’s: Lying-in Hospital
Vienna
Divided into two clinics-
alternating admissions
every 24 hours:
1. First Clinic: Doctors
and medical students-
did autopsies between
deliveries
2. Second Clinic: Midwives-came in off
the street to deliver-
wore gloves outside

Ignaz Semmelweis (1818-1865)

“It is not by chance that a single obstetrician has 16 fatal cases in a single month - I can only dispel the sadness which falls upon me by gazing into that happy future when the infection will be banished”

Maternal mortality, 1842
- Circa 1858

Observed: Doctors’ hands smelled like corpses (putrefied) but not midwives; death rate went down when students on vacation- no autopsies
Hand antisepsis reduces the frequency of postpartum sepsis. 

The Intervention:
Hand scrub with chlorinated lime solution.
Removed the putrefying smell from the hands of students and doctors.

What was Semmelweis's reward in 1848 for this major contribution?
- Fired by the hospital board for enforcing hand washing requirement for doctors
Systemic Inflammatory Response Syndrome (SIRS or SSI)

• Inflammatory process
  – Infection
  – Noninfectious (burns, trauma)

• Requires 2 or more of following:
  – Temp > 38\(^0\) C or < 36\(^0\) C
  – HR > 90 bpm
  – RR > 20/min or PaCO\(_2\) < 32 mmHg
  – WBC > 12,000, < 4,000 or > 10% bands

• Criteria may differ with physiology of pregnancy
  – HR >110 bpm, RR >24/min, Temp > 39\(^0\) C
  – WBC > 15,000
Definitions

- **Sepsis**
  - SIRS due to infection

- **Severe Sepsis**
  - Sepsis associated with:
    - Organ dysfunction
    - Hypotension
    - Hypoperfusion
  - Hypoperfusion abnormalities include:
    - Lactic acidosis
    - Oliguria
    - Acute alteration in mental status
Definitions

• Septic Shock
  – A subset of severe sepsis
  – Sepsis-induced hypotension persisting despite adequate fluid resuscitation
  – Requirement for vasoactive medications

Bone et al. Chest 1992
Case History

- 31 wks, sore throat, refuses antibiotics
  - “It might hurt the baby”
- Presents 24 hours later
  - Tachypnea (RR 70 / min)
  - Tachycardia (HR 140 / min)
  - Hypotension (SBP 70 mmHg)
  - Hypoxic ($O_2$ sat 82%)
  - Anuria
  - Febrile (101.2 F)
  - Ammonia level 98 micro mol / L
  - IUFD
Case History

• Organ dysfunctions
  – Cardiac
  – Respiratory
  – Gastroenterologic
  – Neurologic

• Intubation, Swan-Ganz, Pacemaker
• Dopamine, Dobutamine, Levophed
• CPR

• Death 8 hrs from admission
The Etiology, Concept and Prophylaxis of Childbed Fever
Case History

• Class B IDDM at 37 wks gestation
• Previous cesarean section x 1
• Maternal weight 200 kg (BMI 65)
• TOLAC: 7 cm cx dilatation for 5 hrs
  – “we wanted to avoid c/s with obesity”
• Necrotizing fasciitis post op day 5
• Organ dysfunction
  – Cardiac
  – Respiratory
  – Hematologic
  – Gastroenterologic
  – Hepatic
  – Renal
Mortality By Number of Organ Dysfunctions

Mortality %

- One
- Two
- Three
- Four

Angus DC, et al, Crit Care Med 2001

76%
Early Goal Directed Therapy

- Early provision of time sensitive therapies (within 6 hrs)
- Aggressive hydration
- Initiation of antibiotics
- If indicated
  - Vasoactives
  - Transfusion
  - Inotropes

For flow diagram see Rivers E et al, N Eng J Med 2001
Later Goal Directed Therapy

• Complete within 24 hours
• Initially recommended
  – Administer “physiologic” steroids
  – Administer drotrecogin alpha
    • WRONG per PROWESS-SHOCK Trial 2011
  – Tight glucose control (80-110 mg/dl)
    • WRONG per NICE-SUGAR study 2009 and VISEP Trial 2008

The Importance of Early Goal-Directed Therapy (EGDT) for Sepsis Induced Hypoperfusion


NNT to prevent 1 event (death) = 6 to 8

<table>
<thead>
<tr>
<th>Mortality (%)</th>
<th>In-hospital mortality (all patients)</th>
<th>28-day mortality</th>
<th>60-day mortality</th>
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<tbody>
<tr>
<td>Standard therapy</td>
<td><img src="#" alt="Graph" /></td>
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<tr>
<td>EGDT</td>
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Septic Shock Standard Orders

- Your hospital should have them
  - But do you know where they are?
- Central hemodynamic monitoring
  - CVP, Arterial line
- Involvement of
  - Pharmacy
  - Infectious disease specialists
  - Critical care specialists
Algorithm for Septic Shock in Pregnancy

- Assess airway
  - Intubation if needed

- Assess breathing
  - Administer oxygen

- Initiate IV fluid bolus
  - 20 ml NS/kg over 1 hour

- Assess volume status
  - Obtain central venous access (CVP, ScvO₂)

- Activate Septic Shock Standard Orders
  - Stat cultures, labs and antibiotics (within 1st hour)
  - Identify source of infection

Barton, Sibai. Obstet Gynecol 2012
Fluid Resuscitation

- Central line placement
- Bolus fluids early in resuscitation
  - Substantial volumes needed (6-10 L NS)
- Colloids are not superior to crystalloids
- Warm IV fluids
- CVP and PCWP “normal” do not exist
- Physiologic perfusion endpoints
  - MAP > 65 mmHg
  - UOP > 25 ml/hr
Antimicrobial Therapy

• Infection prevention
• Prompt cultures
  – Don’t delay therapy
  – Often (1/3) blood cultures negative
• Prompt empiric antibiotic therapy
  – Survival differences seen in delay of therapy of only 1 hr
• Source control
  – Debridement of infected tissue
  – Search for surgically correctable origin infection (abscess, appendicitis, etc.)
Vulvar necrotizing fasciitis
Post-op C/S

- Multilocular abscess
- Displaced uterus
Lap sponge count correct?
Postpartum necrotizing fasciitis
Cultures

- Urine
- Endometrium
- Wound or episiotomy site
- Blood
  - Minimum 2 blood cultures
    - 1 percutaneous
    - 1 from each vascular access (>48 hr)
- Amniotic fluid
- Other (e.g., sputum, drains)
Empiric Antimicrobial Therapy

- Gentamycin 1.5 mg/kg IV, then 1 mg/kg IV every 8 hours
- Clindamycin 900 mg IV every 8 hours
- Penicillin 3,000,000 units IV every 4 hours
  or
- Vancomycin 15 mg/kg IV then dosing by pharmacy
- Zosyn 4.5 gm IV STAT, then every 6 hrs
  or
- Your hospital’s septic protocol
Vasoactive Therapy

• “Fill the tank before you squeeze the pipes”
  – William C. Mabie, M.D. 1990
Vasoactive Therapy

• **Indication**
  – Hypoperfusion despite fluid resuscitation
  – Initial treatment of profound hypotension

• **Administration and monitoring**
  – Central venous access
  – Invasive arterial blood pressure
  – Pulmonary artery catheter (rarely)

• **GOAL: Evidence of increased perfusion**
  – Mental status, UOP, Capillary refill

• **Drug of choice**
  – Not what you might think
Norepinephrine

- **First** line therapy
- Increases MAP
  - Significant $\alpha$-mediated vasoconstriction
  - Mild $\beta$-mediated increase in stroke volume
- Successfully improved hemodynamics and $O_2$ delivery in 93% pts (Dopamine 31% pts)
- Effectively decreases lactate
- Improves UOP
- Dopamine renal enhancing effects a myth
Corticosteroids

• Treat patients who still require vasopressors despite fluid replacement.
  – Hydrocortisone 200-300 mg/day, for 7 days in three or four divided doses or by continuous infusion.
• Wean steroid dose if septic shock resolves.
• ACTH stimulation test not required

Bone, et al. NEJM 1987; 317-658
VA Systemic Sepsis Cooperative Study Group. NEJM 1987; 317:659-65
MAP < 50 mmHg?
Consider vasopressors

MAP 50-65 mmHg or CVP below 8 mmHg?

MAP > 65 mmHg?

Yes

Supportive treatment for shock

No

NS 500 mL over 30 minutes

Repeat bolus until 30 mL/kg NS IV over 3 hours

MAP > 65 mmHg?

No

MAP > 65 mmHg;
urine output > 25 mL/hr?

Yes

Observe need for further IV fluid bolus

No

Evaluate need for delivery

Barton, Sibai 2012

Norepinephrine

Vasopressin

Steroids for refractory shock
Presentation: Temp 103.5, severe flank pain, N and V

Diagnosis: Pyelonephritis

Treatment: IV Fluids, Acetaminophen, IV Antibiotics
3 hrs post therapy: Note resolution of tachycardia and tachysystole
Maintenance Phase
Anticipation of complications

- Fetal heart rate, uterine activity monitoring
- Lung protective ventilation for pts with ARDS
- Transfuse PRBC Hgb < 7.0 gm/dl
- Glucose >180 mg/dl, initiate insulin

- Reassess antibiotics, narrow spectrum
- Stress ulcer prophylaxis
- DVT prophylaxis
- Consider inotropic agent

Barton, Sibai
Obstet Gynecol 2012
Viral Etiologies for Sepsis in Pregnancy

Herpes Simplex Hepatitis
H1N1 influenza-associated ARDS: Bilateral infiltrates
Kill as Few Patients as Possible

AND FIFTY-SIX OTHER ESSAYS ON HOW TO BE THE WORLD'S BEST DOCTOR

by Oscar London M.D., WILD
Indications for surgical intervention in Severe sepsis / Septic shock

- Cholecystitis with bile duct obstruction
- Necrotizing pancreatitis
- Perinephric abscess
- Acute appendicitis
- Obstructing renal stone
- Retained products of conception
- Uterine microabscess / gas gangrene
- Bowel infarction
- Pelvic abscess
- Necrotizing fasciitis
- Infected episiotomy site
Indications for Delivery

• Maternal
  – Intrauterine infection
  – Development of DIC
  – Compromised cardiopulmonary function by uterine size and/or peritoneal fluid
    • Compartment syndrome
    • Multifetal gestation
  – Severe ARDS/ barotrauma
  – Cardiopulmonary arrest

• Fetal
  – Fetal demise
  – Gestational age associated with low neonatal morbidity / mortality
Prevention of Surgical Site Infection

- Treat infections remote to surgical site before elective surgery
- Shower with antiseptic agent the night prior to surgery
- Abstain from smoking (30 d)
- Glycemic control in diabetics
- Hair removal around incision by electric clippers not razor
- Antiseptic skin prep

www.cdc.gov/ncidod/dhqp/gl_surgicalsite.htmL.
Obesity Trends* Among U.S. Adults

*BMI $\geq 30$

Don’t mess with Texas!

Prevention of Surgical Site Infection

• Preoperative antibiotics
  – 1-2 gm cefazolin
  – 1-2 gm cefotetan
• Higher dose for obese patients
  – BMI > 30
  – Weight >100 kg
• Up to 60 min before skin incision
  – Compared to Ab at cord clamping
  – 48% reduction in surgical site infection*

*Kitter et al Obstet Gynecol 2012
DEATH
It's permanent.

Outcome

THE NEWS & OBSERVER

17 REMAIN DEAD
IN MORGUE
SHOOTING SPREE

Trial on hold
3 years

Microsoft breakup
won't be pursued
References


References

References

References


References


• Use of prophylactic antibiotics in labor and delivery. Practice Bulletin No. 120. ACOG Obstet Gynecol 2011:117:1472-83.
Learning Objectives

• Discuss the causes and pathophysiology of sepsis
• Discuss goal-directed therapy in the treatment of severe sepsis and septic shock
• Review indications for surgery or delivery in the setting of severe sepsis
• Review prevention strategies of surgical site infection and sepsis
Historical Guidelines for Sepsis Therapy

- Society of Critical Care Medicine (1991)
  - Definitions of sepsis/septic shock
- Society of Critical Care Medicine (1999)
  - Practice parameters for hemodynamic support of sepsis in adult patients
- The Surviving Sepsis Campaign
  - Phase I (2001): Goal directed therapy in the treatment of severe sepsis to reduce mortality
  - Phase II (2004): Guidelines published for management
  - Phase III (2008): Guidelines translated into clinical practice
The Yang-Ying of Systemic Response to Injury

- Pro-Inflammatory Response
- Massive Systemic Response
- Mild Systemic Response
- Local Response
- Insult
- Compensatory Anti-Inflammatory Response

Diagram illustrates the balance between pro-inflammatory and anti-inflammatory responses in response to an insult.
Fluid Resuscitation
Severe Sepsis

Death rate at 90 days
43% Ringer’s acetate
51% HES 130

Probability of Survival

Days since randomization

No. at Risk
HES 130/0.4  398
Ringer’s acetate  400

HES 130 / 0.4
Ringer’s acetate

Perner, et al
NEJM 2012
"Except on few occasions, the patient appears to die from the body's response to infection rather than from it."

Sir William Osler-
in
“The Evolution of Modern Medicine”-1904
Drotrecogin Alfa (Xigris)

- Decreases microvascular thrombosis
- Decreases duration of hypotension
- **BUT**
  - Increases risk of fatal bleeding (1.5-5%)
  - Very expensive
- *FDA market withdrawal* (10/25/2011)
  - PROWESS-SHOCK trial
  - Failure to show survival benefit
Septic Shock in Pregnancy

• Case series of 18 patients
  – 13 survivors
  – 5 non-survivors

• Causes of shock
  – Pyelonephritis (n = 6)
  – Chorioamnionitis (n = 3)
  – Postpartum endometritis (n = 2)
  – Toxic shock (n = 2)

Mabie W, Barton J, Sibai B. Obstet Gynecol 1997
Ventricular Function

Group I
Normal

Group II
Mildly Depressed

Group III
Markedly Depressed

Mabie et al 1997
Dopamine

- Renal enhancing effects are a myth
- 1st line use in sepsis increases death
  - Tachyarrhythmias
  - CNS effect
- Use in sepsis increases cost
  - Increased sedation requirements
  - Increase ventilator duration
  - Increased ICU and hospital LOS
Varicella-Zoster in Pregnancy

Photo Courtesy of CDC - Joe Miller
Predisposing Factors for Surgical Site Infection in Obese Women

- Tissue hypoxia
  - Decreased vascularity of SQ fat
  - Higher risk of hypoxemia
- Increased risk of hematoma / seroma
- Persistent skin moisture
- Decreased tissue antibiotic levels
- Increased prevalence of diabetes
- Difficult exposure
  - Longer operative time
  - Trauma from retractors

Walsh et al, Obstet Gynecol 2009
BACKGROUND

Global

- Puerperal sepsis
  - 75,000 maternal deaths / year
- Puerperal infections
  - 16 % of maternal deaths
  - 5-10 % of maternal morbidity