97 Seconds for Sepsis
Increasing the Awareness of World Sepsis Day

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September 13th

https://www.youtube.com/watch?v=GNz3S3tvYLA

https://www.facebook.com/WorldSepsisDay

http://www.sepsisalliance.org/sepsisawarenessmonth/
The Challenge: Understanding Sepsis

In 2002, the European Society of Intensive Care Medicine and the Society of Critical Care Medicine conducted an international survey on 1,050 physicians worldwide.

The goal was to investigate:

- Physicians’ views on sepsis
- Satisfaction with current definitions
- Routes to diagnosis
- Treatment options

Survey conducted by Yankelovich Partners, Inc. 2002.
The Challenge: Understanding Sepsis

Most physicians found sepsis challenging and frustrating to diagnose and treat.

86% said that symptoms of sepsis can easily be misattributed to other conditions.

89% said doctors are eager for a breakthrough in treating sepsis.

81% said that a common definition for sepsis among the medical community would be a significant step toward better treatment.

Survey conducted by Yankelovich Partners, Inc. 2002.
The Response: Surviving Sepsis Campaign

A six point action plan to reduce global mortality from severe sepsis by 25% by 2009:

- Building awareness of sepsis among healthcare professionals, governments, health and funding agencies, and the general public
- Improving early and accurate diagnosis
- Increasing the use of appropriate treatments and interventions
- Educating all healthcare professionals about diagnosis, treatment, and management of sepsis
- Improving access to post-ICU care for sepsis patients
- Developing global standards of care

Sepsis: Treatment Improvements

2004 Surviving Sepsis Campaign (SSC) Guidelines

2006 Surviving Sepsis Campaign Implementation

2008 An updated version of SSC Guidelines

2012 The revised SSC Guidelines contain two bundles, a resuscitation bundle for the first 3 hours and a management bundle for the following 6 hours

Early goal-directed therapy (EGDT)

European Society of Intensive Care Medicine (ESICM), the Society of Critical Care Medicine (SCCM), and the International Sepsis Forum (ISF)

Early Goal Directed Therapy

To be completed within 3 hours
- Measure lactate level
- Obtain blood cultures before administration of antibiotics
- Administer broad-spectrum antibiotics
- Administer 30 ml/kg crystalloid for hypotension or lactate ≥ 4 mmol/L

To be completed within 6 hours
- Apply vasopressors (for hypotension that does not respond to fluid resuscitation) to maintain a MAP ≥ 65 mm Hg
- In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥ mmol/L:
  - measure CVP*
  - Measure central SvO₂
- Remeasure lactate if initial lactate was ↑

* Targets for quantitative resuscitation
  Included in the guidelines are CVP of ≥ 8 mm Hg, SvO₂ of ≥ 70% and normalization of lactate

Early Goal Directed Therapy

Protocolised Care for Early Septic Shock trial ProCESS - USA


Australasian Resuscitation in Sepsis Evaluation trial ARISE


Protocolised Management in Sepsis trial ProMISE - UK


The three published studies reported no benefit for EGDT

The addition of continuous ScvO$_2$ monitoring and strict protocolisation did not improve outcomes in the EGDT group

EGDT was not superior to usual care
Sepsis: Incidence and Costs

Severe sepsis is the leading cause of death in the non-coronary ICU.

More than 27 million cases of sepsis occur each year.

19 million sepsis victims survived 2014/ at least 1 million more could.

Sepsis kills some 1,400 people worldwide every day.

The number of sepsis cases is projected to grow at a rate of 1.5% per year as the population ages and medicine become more aggressive (2007 18 mill cases vs. 2014 27 mill cases).

The mortality rates are: 12-17% for sepsis, 30-50% for severe sepsis and 50-60% for septic shock.

Average cost for sepsis treatment is approximately $22,000.
2013 US Sepsis mortality rate was more than the mortality rate of:

- Breast cancer,
- Prostate cancer, and
- AIDS

COMBINED
Sepsis

2735 BC Chinese emperor Sheng Nung described use of herbal tonic for fever treatment

Two millennia of plague, cholera, measles, tuberculosis and gonorrhea took millions of lives and changed the course of history and civilizations

1546 Hieronymus Fracastorius: cause of infection is living organism
Sepsis

In 19th century introduction od antiseptic measures among woman at birth reduced maternal mortality from 13.6% on 1.5% in one year!

1879 Louis Paster: Streptococcus is the cause of puerperal sepsis

1892 Richard Pfeiffer: toxin is a cause of shock in infective disease

1928 Alexander Fleming: blue mold Penicillium notatum inhibits bacterial growth in Petri dish

1914 Schottmueller: septicemia is presence of living organism in the blood of humans
Infection-SIRS-Sepsis

Sepsis-SIRS Definition

- **Sepsis**, Greek word meaning blood poisoning

- Profound inflammatory response to an underlying infection

- Living microorganisms activate and stimulate release of inflammation mediators and nitric oxide (NO) leading to profound vasodilatation and **HYPOTENSION**

- Results in endothelial injury, creates a procoagulant state and impaired fibrinolysis

SIRS-Sepsis: Clinical Presentation

SIRS
Agent
T >38.3 °C or <36 °C
HR>90/min or
pCO₂<4,26 kPa
L>12/<4×10³
bands>10%
(immature neutrophils)

SEPSIS
SIRS + infection
bacteria, virus, fungi, parasites
+ Oedema or positive fluide balance
>20mL/kg/24 hours
Blood glucose >6.5 mmol/L
CRP>2SD above normal
PCT>2SD above normal
Alterated mental status

SEVERE SEPSIS
Sepsis+Organ hypoperfusion
SBP<90 mmHg or drop >40
MAP <65 mmHg
laktat >2mmol/L
PaO₂/FIO₂ <300
Diuresis <0.5mL/kg/h⁻¹
creatinine >136 μmol/L
INR >1.5; T<100
bilirubine >35 mmol/L

SEPTIC SHOCK
Persistent hypotension refractory to fluide resuscitation

MODS/MOF
Multiple organ dysfunction syndrome
Multiple organ failure

Sepsis: Increased Nitric Oxide Synthases (NOSs)

Endothelial (eNOS), neuronal (nNOS) and inducible (iNOS)

- Macrophages + invading bacteria
- Vasodilatation
- Hypotension
- Decreased heart contractility
- Rapid conversion in peroxynitrite
- Peroxidation of lipids, depletion of glutathione and ATP-a
- Mitochondrial dysfunction and cell damage

Sepsis: Capillary Leakage Syndrome
SIRS-Sepsis: Pathogenesis

**Triad:** SIRS, prothrombosis, impaired fibrinolysis

**Infection:** host response, immunity, invading microorganism virulence

**Proinflammatory markers:** TNF-\(\alpha\), IL-1, IL-6, IL-8, IFN-\(\gamma\), PAI-1

**Endothelial cell dysfunction:** capillary leakage syndrome, vasodilatation, transudation, organ damage

**Anti-inflammatory markers:** IL-4, IL-10, IL-11, IL-13, IL-1ra, TGF-\(\beta\)

**Immunomodulation impairment:** monocyte deactivation

Disseminated Intravascular Coagulation DIC

1. Is there a risk for DIC development?
   If YES continue  If NO drop

2. Laboratory investigations:
   Platelets  PT  Fibrinogen  DPF

3. Points:
   P > 100  0  P < 100  1  P < 50  2
   DPF ≈ 0  DPF ↑  2  DPF ↑↑↑ 3
   PT < 3s  0  PV 3-6 s  1  PV > 6 s  2
   FIB>1g/L 0  FIB<1g/L 1

4. Calculate sum

5. ≥ 5 DIC < 5 follow patient and repeated in 1-2 days

Disseminated intravascular coagulation DIC
Disseminated intravascular coagulation DIC
Acute lung injury: Septic ARDS
Septic shock + ARDS = Deadly duo

- Common organ system affected in sepsis MODS
- Bilateral airspace infiltration
- Absence of cardiomegaly, vascular redistribution and Kerley B lines

Degoricija V. ICU. UH Sisters of Charity. 2010.
ARDS

✓ Organizing phase of diffuse alveolar damage
✓ Infiltration with inflammatory cells
✓ Disorganization of pulmonary architecture
✓ Hyaline membrane deposits
Sepsis: Renal Impairment

- A continuum of severity from sepsis to septic shock exists
- The cause of acute renal injury (ARI) is multifactorial
- Decrease in effective intravascular volume
- Systemic hypotension
- Direct renal vasoconstriction
- Release of cytokines
- Activation of neutrophils and endotoxins
Degoricija V. ICU. UH Sisters of Charity. 2013.
Central role in GI dysfunction have TB, ischemia of the gut and decrease in intarmucosal pH.

The normal barrier function of the gut is affected.

Gut-associated lymphoid tissue (GALT) is affected with bacteria and endotoxins.
Translocation of Bacteria + Ischemia of the Gut

Sepsis: Gastrointestinal Dysfunction

- Overgrowth of bacteria in the upper GI tract may be aspirated into lungs ending with nosocomial pneumonia.
- Paralytic ileus leads to a delay in the institution of enteral feeding.
- Nutritional intake is interfered with in the face of high protein and calorie requirements.
- Narcotics and muscle relaxants worse GI tract motility.
Sepsis: Gastrointestinal dysfunction
Sepsis: Gastrointestinal dysfunction

Degoricija V. ICU. UH Sisters of Charity. 2013.
Sepsis: MODS

- Development of MODS is not connected with first hours of septic shock
- ALI/ARDS develops early and lasts for days
- Septic shock develops early, is reversible or leads to poor outcome in early stage of sepsis
- DIC, ARI, hepatic insufficiency and septic encephalopathy are developed hours and days in the natural course of sepsis and last for days
- Mortality from MODS remains high: ARDS alone 40-50% plus one additional organ system, usually ARI increases to 90%
Sepsis: MODS

The precise mechanism of cell injury and resulting organ dysfunction in sepsis is not fully understood.

Widespread endothelial and parenchymal cell injury.

Four proposed mechanisms:
1. Hypoxic hypoxia
2. Direct cytotoxicity
3. Apoptosis (programmed cell death)
4. Immunosuppression
Sepsis: Treatment

**STEP ABC - Airway Breathing Circulation**

- Resuscitation, volume resuscitation, mechanical ventilation
- Keeping tissue perfusion and oxygen delivery
- Keeping hydrostatic pressure in the lungs low with adequate oxygenation and oxygen delivery to tissues

**STEP D - Diagnosis**

- Define sepsis, obtain blood cultures

**STEP E - Empiric antimicrobial therapy**

- Administer empiric broad spectrum antibiotic

**STEP F - Find and control the source of infection**

- Define the source of sepsis, eliminate the nidus of infection

**STEP G - Gut**

- NG suction, paralytic ileus treatment
Sepsis: Treatment

**STEP H - Hemodynamics**
Volume resuscitation, norepinephrine, dobutamine, vassopresine

**STEP I - Iatrogenic injuries**
Nosocomial infection, iatrogenic pneumothorax

**STEP J - Justify your therapeutic plan and reassess**
Reassess the patient

**STEP KL - Keep Looking: secondary source of infection?**
Reassess the patient

**STEP MN - Metabolic and Neuroendocrine control**
Blood glucose control, electrolytes, nutrition, calories, elements
FAST HUG Protocol

- Feeding
- Analgesia
- Sedation
- Thromboembolic Prophylaxis

- Head of Bed Elevation
- Ulcer Prophylaxis
- Glycemic Control

Sepsis: Treatment

Four main components:

- Early recognition
  HISTORY & PHYSICAL, VITALS

- Initial priority is hemodynamic stabilization by IV fluids and vasopressors
  FLUID RESUSCITATION GOALS: CVP 8 - 12 mmHg, MAP > 65 mmHg, ScVO2 > 70%
  CRYSTALLOID VS. COLOID; NOREPHINEPHRINE
  FLUID OVERLOAD LINKED WITH POOR OUTCOME; 30 mL/kg

- Identification and elimination (surgical drainage and/or antibiotics) of the nidus of infection
  EVERY DELAY IN 1 HOUR DECREASES SURVIVAL BY 8%

- Interruption of the pathogenic sequence leading to septic shock
  LACTATE, PROCALCITONIN
Sepsis: Failed Novel Treatment Protocols

- Anti-LPS treatment
- Anti TNF treatment
- Anti IL-1 treatment
- Anti PAF treatment
- rTFPI treatment
- Prostaglandin synthase blocking treatment
- iNOS blocking treatment
- AT III treatment
- Tight glucose control (NO/ NICE - SUGAR TRIAL/GLU < 10mmol/L)
- Activated protein C (NO/ PROWESS - SHOCK TRIAL)
- Corticosteroids low, medium, high dose (NO/ CORTICUS TRIAL)
Sepsis: Treatment Options with Increased Survival

2003 Garnacho-Montero et al.
2006 Degoricija et al.

Mortality of sepsis 11.4%, severe sepsis 50%, and septic shock 68.1%

Adequate choice of empiric antibiotic decreased mortality for:

- 43.4% in septic shock
- 23.1% in severe sepsis
- 19.8% in sepsis

Sepsis Six in Emergency Department

- Deliver high-flow oxygen
- Take blood cultures
- Administer empiric IV antibiotic
- Measure serum lactate and CBC
- Start intravenous fluid resuscitation 30 mL/kg
- Commence accurate urine output measurement

Daniels, Nutbeam, Laver et al. 2006.
Sepsis

- Any kind of infection can lead to sepsis
- Quick diagnosis and treatment are the difference between life and death
- Know the symptoms, suspect sepsis, save lives!

3 R: Recognize, Resuscitate, Refer

www.SepsisAlliance.org /2015

Zagreb, UH Sisters of Charity
Solar eclipse on March, 20th 2015
Photo by Karlo Stemberger