# SEPSIS

**Baxter Larmon, PhD, MICP**

**Professor Medicine**

**David Geffen School of Medicine**


ONE WAY
ONE WAY
No
Conflict of
Interest to
Declare

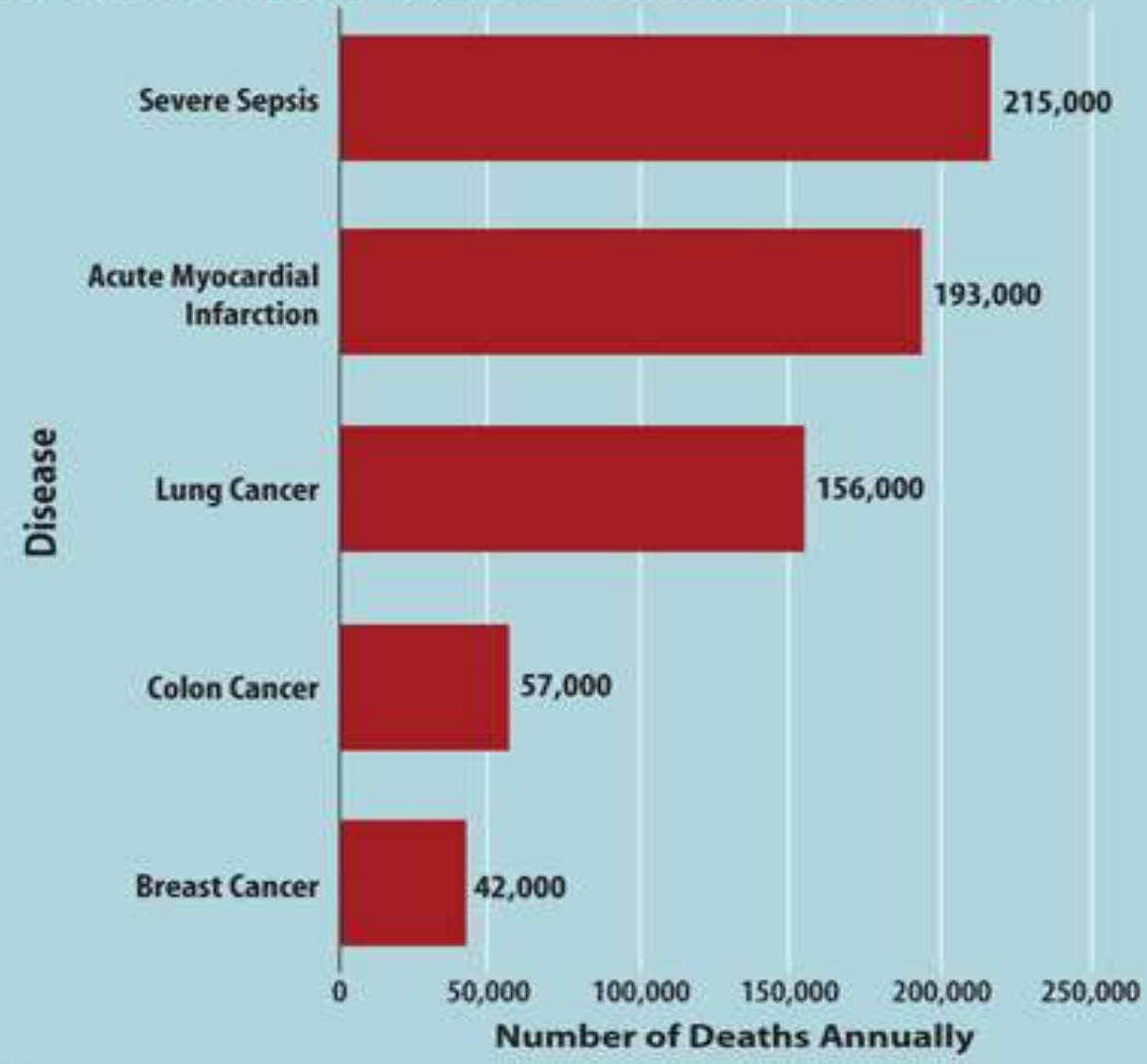
**750,000 cases each year in the United States**

More than 2/3 are seen in the Emergency Department

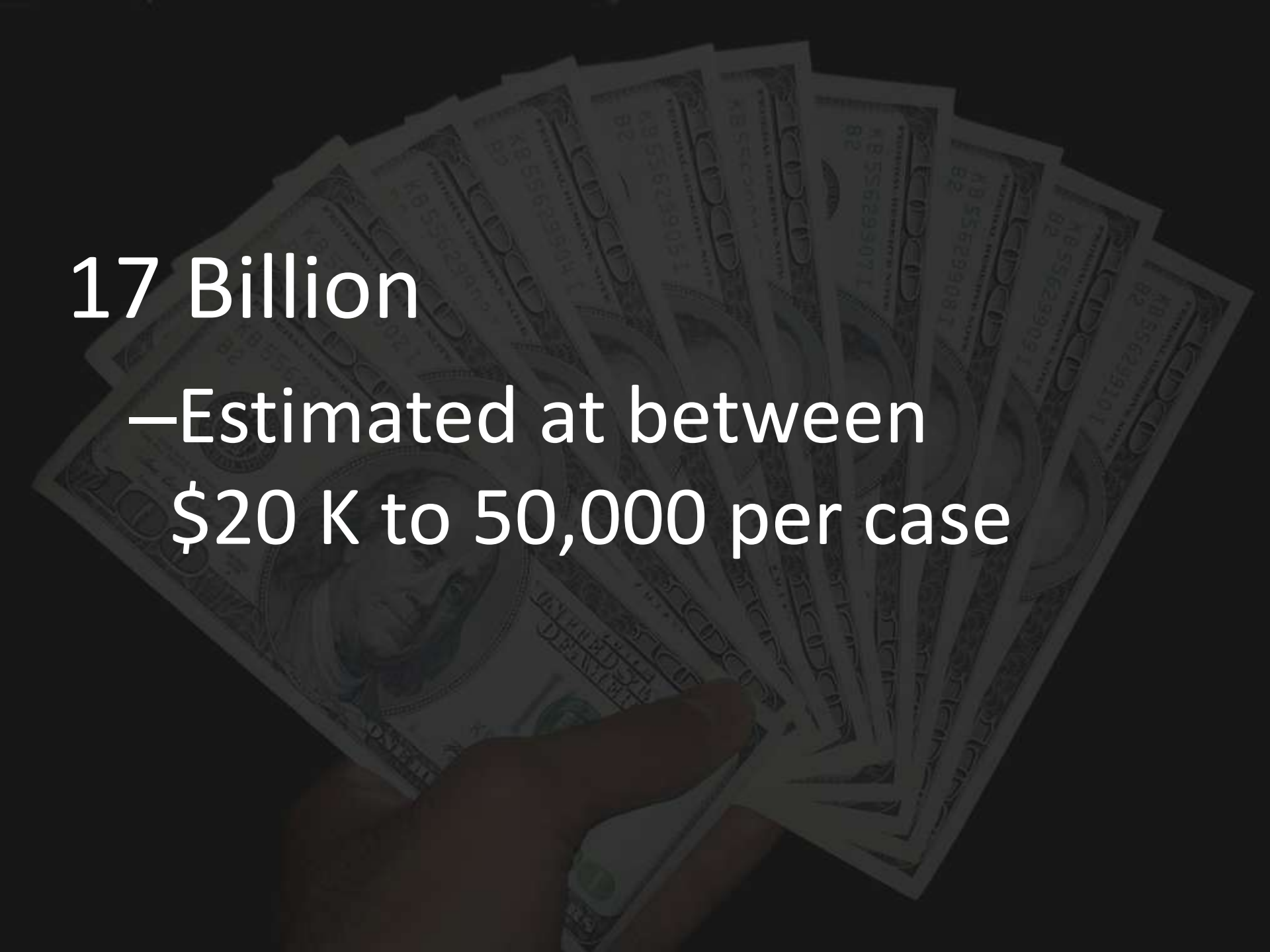
- 10th leading cause of death in the U.S.
  - –215,000 per year
  - –Mortality rate estimated at 25-50%

# How Deadly is Sepsis?

Despite advances in treatment of infectious diseases and clinical care, severe sepsis remains a major killer. U.S. mortality rates for severe sepsis exceed those for acute myocardial infarction and common cancers.




*Source: www.sepsis.com*



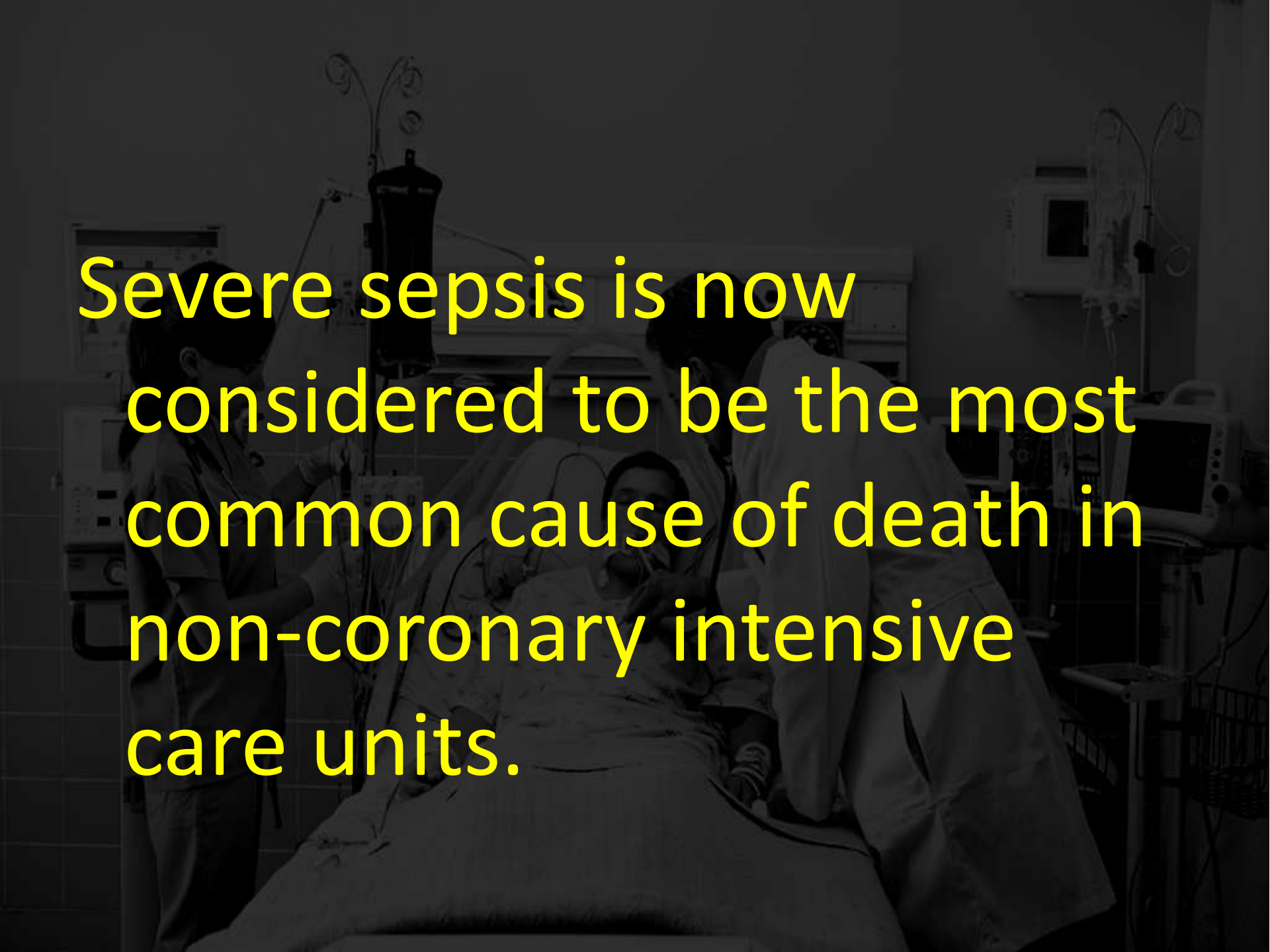
# 17 Billion

- Estimated at between $20 K to 50,000 per case

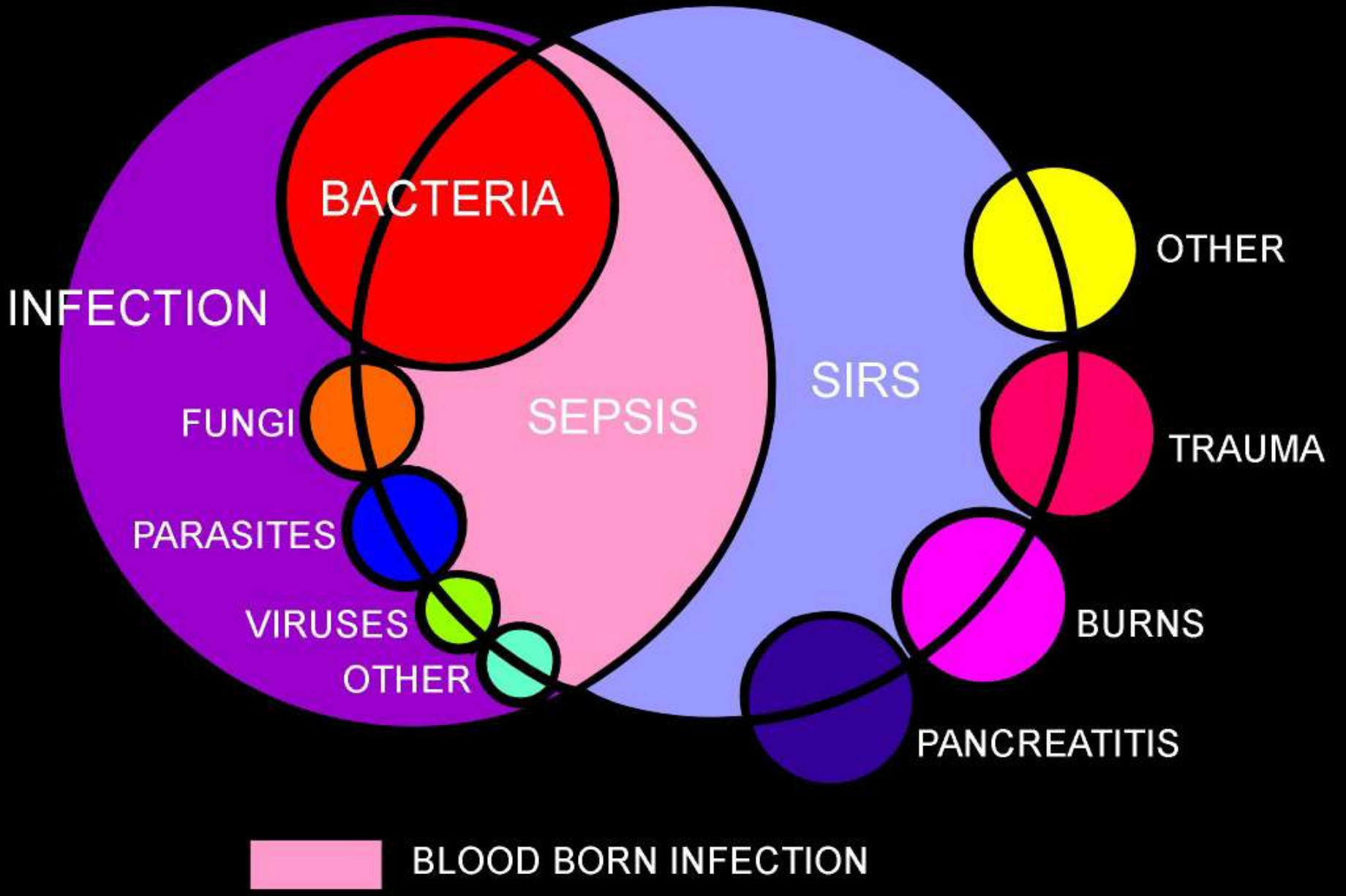
From 1979 to 2000, there was an increase of annual incidence of sepsis from 83 per 100,000 to 240 per 100,000

- In European countries it is 367 cases per 100,000
- Age related sepsis is even higher

- Greater than 1/3 of Emergency departments with infections and patients with sever sepsis and septic shock receive their initial care from EMS System.
- Patients that arrive by EMS have higher mortality rates

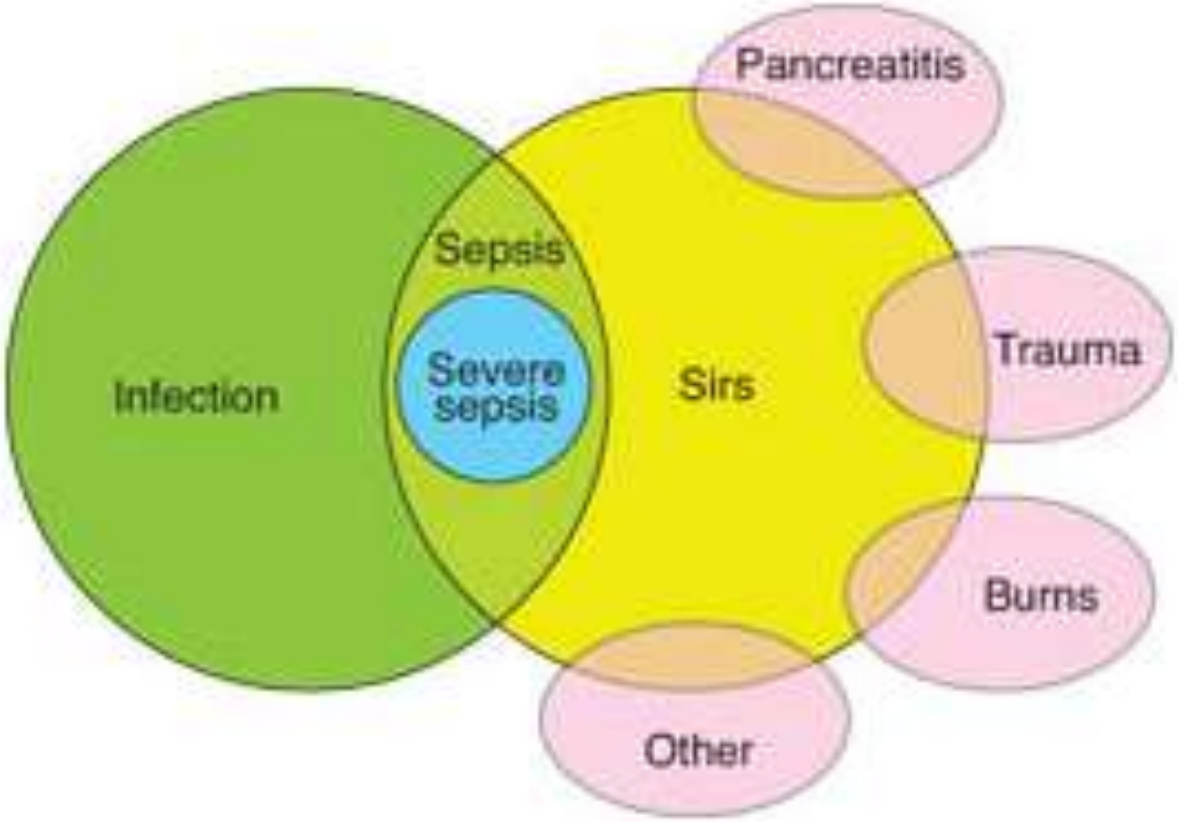


Severe sepsis is now considered to be the most common cause of death in non-coronary intensive care units.

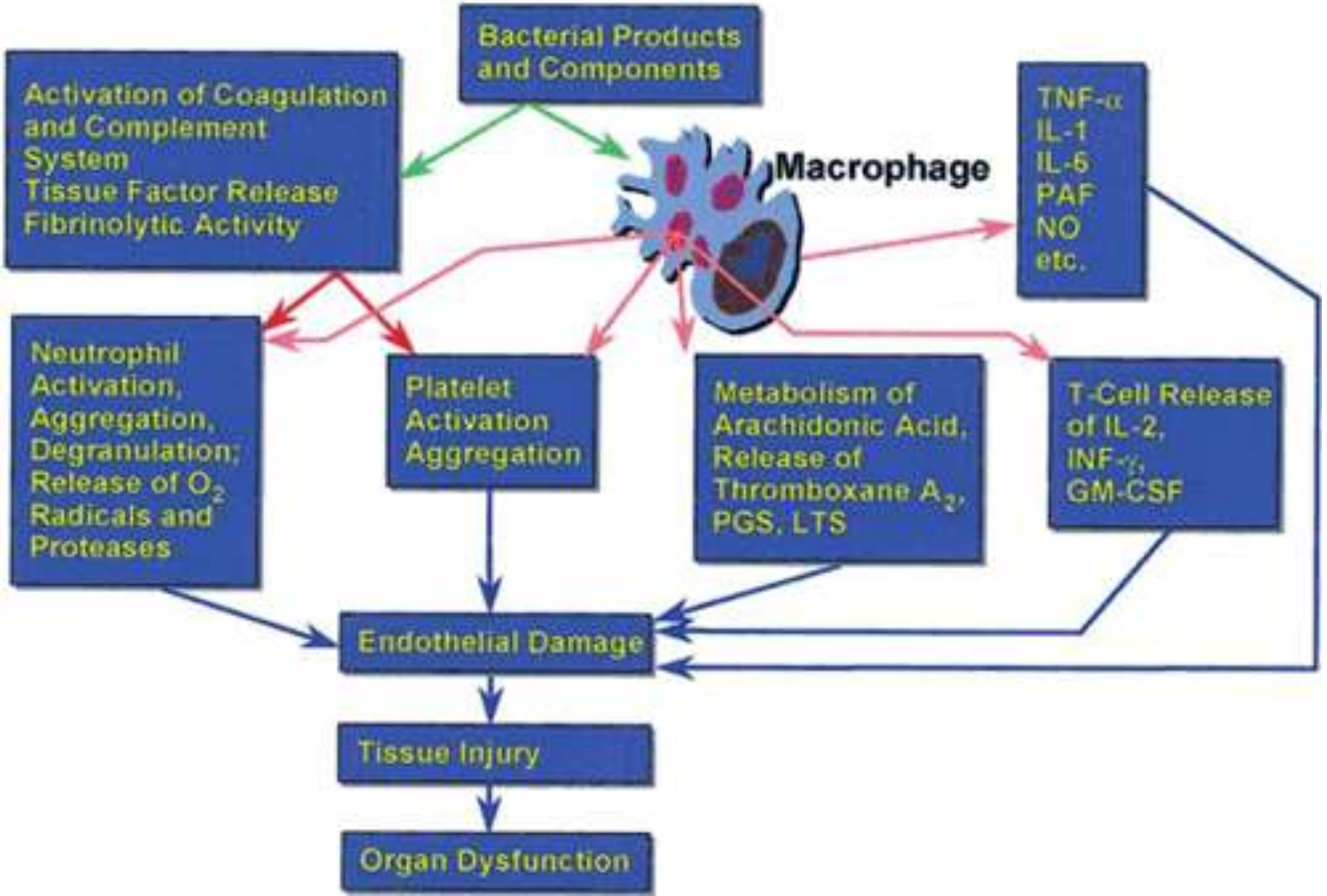

BACTERIA
INFECTION
FUNGI
SEPSIS
SIRS
OTHER
TRAUMA
PARASITES
VIRUSES
OTHER
BURNS
PANCREATITIS
BLOOD BORN INFECTION

# SIRS

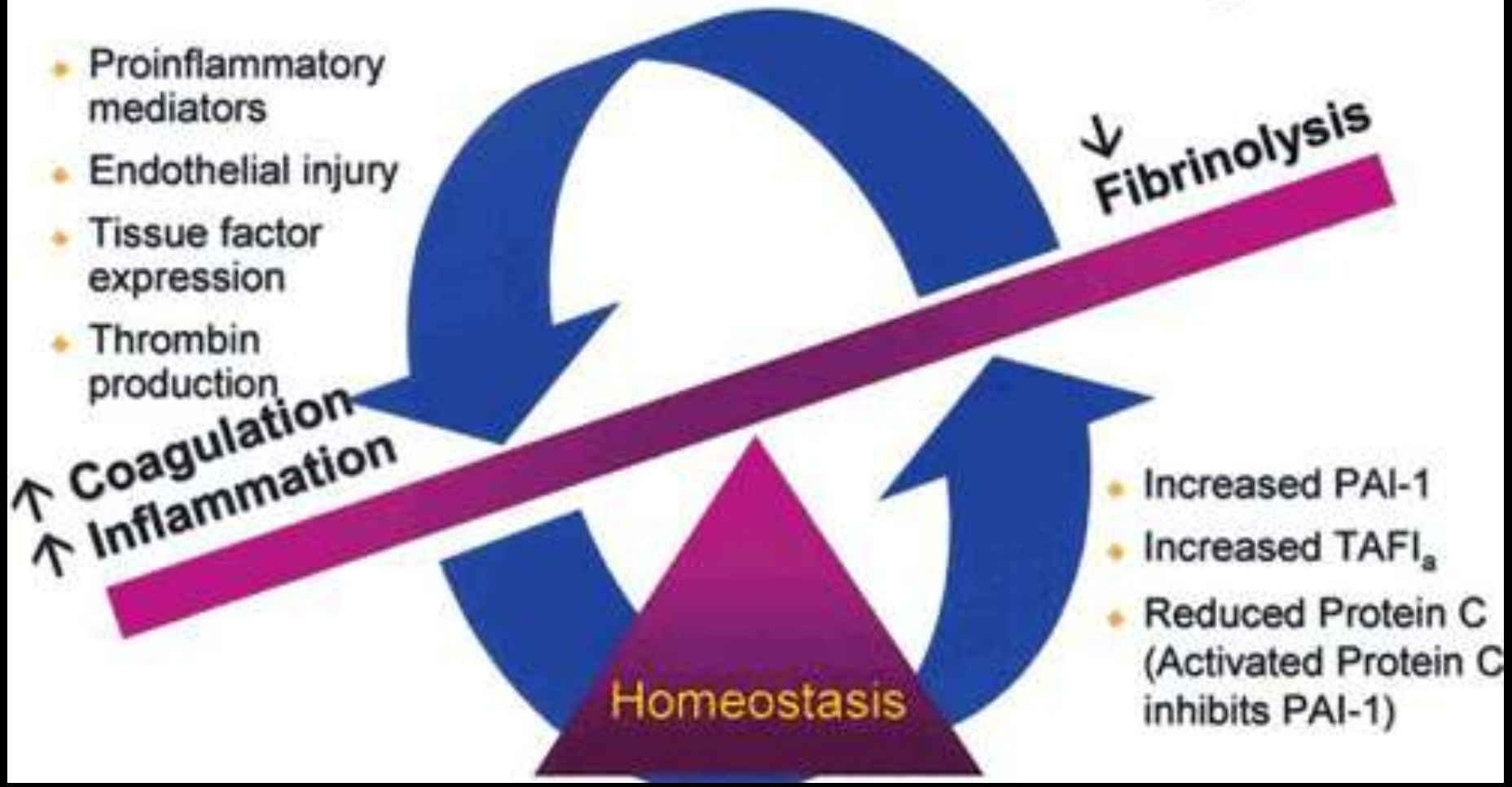
- Systemic Inflammatory Response Syndrome
- Some consider it a self-defense mechanism

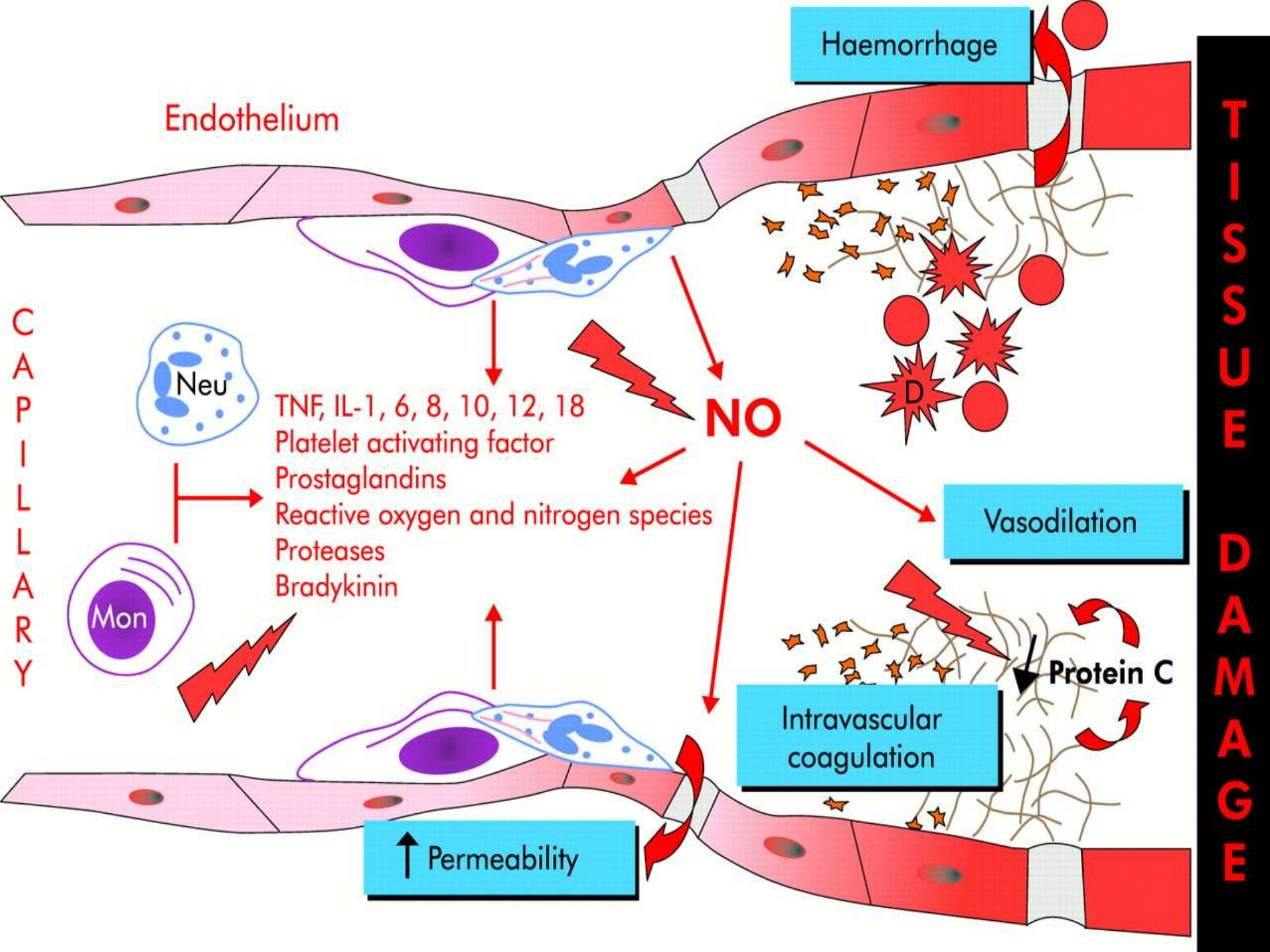

Pancreatitis
Sepsis
Infection
Severe sepsis
Sirs
Trauma
Burns
Other

# The Sepsis Cascade



# Homeostasis Is Lost In Sepsis




Haemorrhage
Endothelium
CAPILLARY
Neu
Mon
TNF, IL-1, 6, 8, 10, 12, 18
Platelet activating factor
Prostaglandins
Reactive oxygen and nitrogen species
Proteases
Bradykinin
NO
D
Vasodilation
Protein C
Intravascular coagulation
Permeability
TISSUE DAMAGE

# Clinical Findings

- At least two of the following;
  - Fever of more than 38 degrees C (100.4 F)or less than 36 degrees (96.8F)
  - Heart rate > 90
  - Respiratory Rate >20 or assisted
  - White blood Cell Count > 12,000 or <4,000
- Suspected or documented infection
- Hypoperfusion
  - Systolic  < 90mm Hg
- Serum Lactate levels > or = 4mmol/L

# Surviving Sepsis Campaign

Critical Care Medicine 2008, vol 36, #1

Special Article

# Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Jean M. Carlet, MD; Julian Bion, MD; Margaret M. Parker, MD; Roman Jaeschke, MD; Konrad Reinhart, MD; Derek C. Angus, MD, MPH; Christian Brun-Buisson, MD; Richard Beale, MD; Thierry Calandra, MD, PhD; Jean-Francois Dhainaut, MD; Herwig Gerlach, MD; Maurene Harvey, RN; John J. Marini, MD; John Marshall, MD; Marco Ranieri, MD; Graham Ramsay, MD; Jonathan Sevransky, MD; B. Taylor Thompson, MD; Sean Townsend, MD; Jeffrey S. Vender, MD; Janice L. Zimmerman, MD; Jean-Louis Vincent, MD, PhD; for the International Surviving Sepsis Campaign Guidelines Committee

*Objective:* To provide an update to the original Surviving Sepsis Campaign clinical management guidelines, "Surviving Sepsis Campaign Guidelines for Management of Severe Sepsis and Septic Shock," published in 2004.

*Design:* Modified Delphi method with a consensus conference of 55 international experts, several subsequent meetings of subgroups and key individuals, teleconferences, and electronic-based discussion among subgroups and among the entire committee. This process was conducted independently of any industry funding.

*Methods:* We used the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) system to guide assessment of quality of evidence from high (A) to very low (D) and to determine the strength of recommendations. A strong recommendation (1) indicates that an intervention's desirable effects clearly outweigh its undesirable effects (risk, burden, cost) or clearly do not. Weak recommendations (2) indicate that the tradeoff between desirable and undesirable effects is less clear. The grade of strong or weak is considered of greater clinical importance than a difference in letter level of quality of evidence. In areas without complete agreement, a formal process of resolution was developed and applied. Recommendations are grouped into those directly targeting severe sepsis, recommendations targeting general care of the critically ill patient that are considered high priority in severe sepsis, and pediatric considerations.

*Results:* Key recommendations, listed by category, include early goal-directed resuscitation of the septic patient during the first 6 hrs after recognition (1C); blood cultures before antibiotic therapy (1C); imaging studies performed promptly to confirm potential source of infection (1C); administration of broad-spectrum antibiotic therapy within 1 hr of diagnosis of septic shock (1B) and severe sepsis without septic shock (1D); reassessment of antibiotic therapy with microbiology and clinical data to narrow coverage, when appropriate (1C); a usual 7–10 days of antibiotic therapy guided by clinical response (1D); source control with atten- pressure is identified to be poorly responsive to fluid and vasopressor therapy (2C); recombinant activated protein C in patients with severe sepsis and clinical assessment of high risk for death (2B except 2C for postoperative patients). In the absence of tissue hypoperfusion, coronary artery disease, or acute hemorrhage, target a hemoglobin of 7–9 g/dL (1B); a low tidal volume (1B) and limitation of inspiratory plateau pressure strategy (1C) for acute lung injury (ALI)/acute respiratory distress syndrome (ARDS); application of at least a minimal amount of positive end-expiratory pressure in acute lung injury (1C); head of bed elevation in mechanically ventilated patients unless contraindicated (1B); avoiding routine use of pulmonary artery catheters in ALI/ARDS (1A); to decrease days of mechanical ventilation and ICU length of stay, a conservative fluid strategy for patients with established ALI/ARDS who are not in shock (1C); protocols for weaning and sedation/analgesia (1B); using either intermittent bolus sedation or continuous infusion sedation with daily interruptions or lightening (1B); avoidance of neuromuscular blockers, if at all possible (1B); institution of glycemic control (1B), targeting a blood glucose <150 mg/dL after initial stabilization (2C); equivalency of continuous veno-veno hemofiltration or intermittent hemodialysis (2B); prophylaxis for deep vein thrombosis (1A); use of stress ulcer prophylaxis to prevent upper gastrointestinal bleeding using H2 blockers (1A) or proton pump inhibitors (1B); and consideration of limitation of support where appropriate (1D). Recommendations specific to pediatric severe sepsis include greater use of physical examination therapeutic end points (2C); dopamine as the first drug of choice for hypotension (2C); steroids only in children with suspected or proven adrenal insufficiency (2C); and a recommendation against the use of recombinant activated protein C in children (1B).

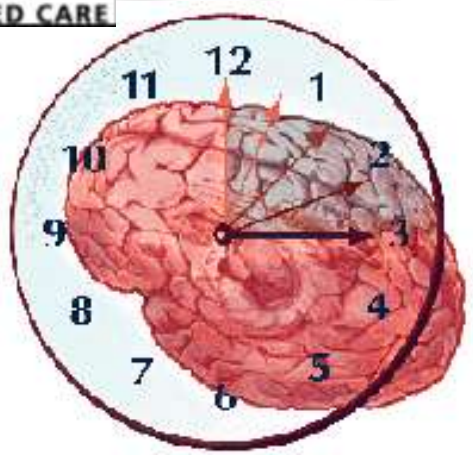
*Conclusions:* There was strong agreement among a large cohort of international experts regarding many level 1 recommendations for the best current care

International Group, meets every 2-4 years and develops evidence based guidelines for the treatment of Sepsis, much like the AHA BLS, ACLS, PALS guidelines

- Studies show that the more proximal treatment and identification can reduce morbidity and mortality of severe sepsis
  - Up to 20%
- Early EMS detection has been shown to decrease time to diagnosis and treatment in-hospital

# Sound Familiar



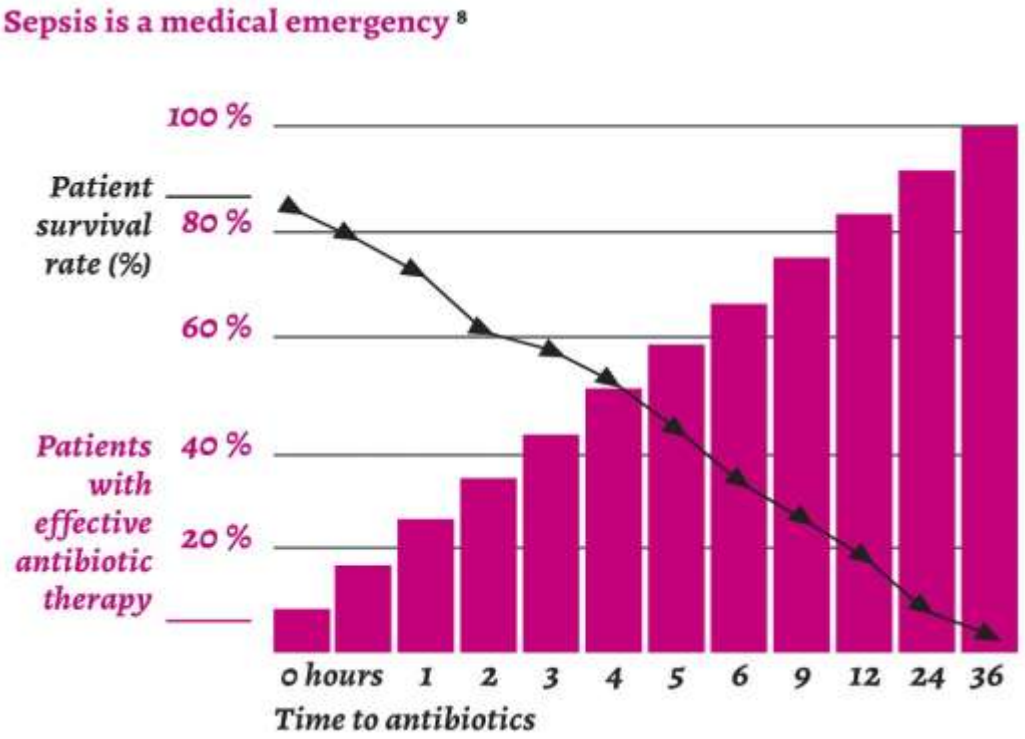



# Early Goal Directed Therapy (EGDT)

16 % reduction in Mortality when compared to traditional therapy

# Treatment Time

- Early fluid delivery
  - Within 1 hour
- Early antibiotic administration

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EMS

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

# Opportunities for Emergency Medical Services care of sepsis☆

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ABSTRACT

*Objective:* Emergency Medical Services (EMS) systems play key roles in the rapid identification and treatment of critical illness such as trauma, myocardial infarction and stroke. EMS often provides care for sepsis, a life-threatening sequelae of infection. In this study of Emergency Department patients admitted to the hospital with an infection, we characterized the patients receiving initial care by EMS.

*Methods:* We prospectively studied patients with suspected infection presenting to a 50,000 visit urban, academic ED from September 16, 2005–September 30, 2006. We included patients who had abnormal ED vital signs or required hospital admission. We identified patients that received EMS care. Between EMS and non-EMS patients, we compared patient age, sex, nursing home residency, vital signs, comorbidities, source of infection, organ dysfunction, sepsis severity and mortality. We analyzed the data using univariate odds ratios, the Wilcoxon rank-sum test and multivariate logistic regression.

*Results:* Of 4613 ED patients presenting with serious infections, 1576 (34.2%) received initial EMS care. The mortality rate among those transported by EMS was 126/1576 (8.0%) compared to 67/3037 (2.2%) in those who were not. Adjusted mortality was higher for EMS (OR 1.8, 95% CI: 1.3–2.6). Of patients who qualified for protocolized sepsis care in the ED, 99/162 (61.1%) were transported via EMS. EMS patients were more likely to present with severe sepsis (OR 3.9; 3.4–4.5) or septic shock (OR 3.6; 2.6–5.0). EMS patients had higher sepsis acuity (mortality in ED sepsis score 6 vs. 3, $p < 0.001$).

*Conclusions:* EMS provides initial care for over one-third of ED infection patients, including the majority of patients with severe sepsis, septic shock, and those who ultimately die. EMS systems may offer important opportunities for advancing sepsis diagnosis and care.

- Looked at the opportunity of EMS to make a difference in sepsis
- Describes 4,613 septic patients that arrived at a suburban/urban ED
- 34% of all sepsis was received by EMS
- Mortality rate is 8% versus 2% for patients transported by EMS
  - Much sicker patients in EMS (60%)

- EMS Patients were more likely to
  - Elderly
  - Female
  - From Nursing home
  - Abnormal vital signs
    - Tachycardia
    - Hypoxia
    - Hypotension
  - Higher serum Lactate Levels
  - Higher comorbid conditions
  - Organ Dysfunction
  - 4 times great chance of presenting in severe sepsis

- Conclusion by Authors:
  - EMS does provide initial care to 1/3 of Septic patients
  - EMS cares for the sickest of septic patients
  - Systems should consider the opportunity of EMS for advanced sepsis diagnosis and care

SCANDINAVIAN JOURNAL OF
trauma, resuscitation
& emergency medicine

REVIEW Open Access

# Suspicion and treatment of severe sepsis. An overview of the prehospital chain of care

Johan Herlitz[1,3*], Angela Bång[1], Birgitta Wireklint-Sundström[1], Christer Axelsson[1], Anders Bremer[1], Magnus Hagiwara[1], Anders Jonsson[1], Lars Lundberg[1], Björn-Ove Suserud[1] and Lars Ljungström[2]

## Abstract

**Background:** Sepsis is a life-threatening condition where the risk of death has been reported to be even higher than that associated with the major complications of atherosclerosis, i.e. myocardial infarction and stroke. In all three conditions, early treatment could limit organ dysfunction and thereby improve the prognosis.

**Aim:** To describe what has been published in the literature a/ with regard to the association between delay until start of treatment and outcome in sepsis with the emphasis on the pre-hospital phase and b/ to present published data and the opportunity to improve various links in the pre-hospital chain of care in sepsis.

**Methods:** A literature search was performed on the PubMed, Embase (Ovid SP) and Cochrane Library databases.

**Results:** In overall terms, we found a small number of articles (n = 12 of 1,162 unique hits) which addressed the prehospital phase. For each hour of delay until the start of antibiotics, the prognosis appeared to become worse. However, there was no evidence that prehospital treatment improved the prognosis.
Studies indicated that about half of the patients with severe sepsis used the emergency medical service (EMS) for transport to hospital. Patients who used the EMS experienced a shorter delay to treatment with antibiotics and the start of early goal-directed therapy (EGDT). Among EMS-transported patients, those in whom the EMS staff already suspected sepsis at the scene had a shorter delay to treatment with antibiotics and the start of EGDT.
There are insufficient data on other links in the prehospital chain of care, i.e. patients, bystanders and dispatchers.

**Conclusion:** Severe sepsis is a life-threatening condition. Previous studies suggest that, with every hour of delay until the start of antibiotics, the prognosis deteriorates. About half of the patients use the EMS. We need to know more about the present situation with regard to the different links in the prehospital chain of care in sepsis

- Collective review article
  - 12 articles that look at PHC of sepsis
- Describes a system of care for sepsis that looks like, STEMI, STROKE

- Conclusion: EMS System designers should consider the development of Sepsis Protocols

American Journal of Emergency Medicine (2012) 30, 51–56

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The
American Journal of
Emergency Medicine

www.elsevier.com/locate/ajem

Original Contribution

# The impact of emergency medical services on the ED care of severe sepsis☆

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[b]*Mecklenburg Emergency Medical Services Agency, USA*

Received 19 July 2010; revised 8 September 2010; accepted 9 September 2010

**Abstract**

**Objective:** The identification and treatment of critical illness is often initiated by emergency medical services (EMS) providers. We hypothesized that emergency department (ED) patients with severe sepsis who received EMS care had more rapid recognition and treatment compared to non-EMS patients.

**Methods:** This was a prospective observational study of ED patients with severe sepsis treated with early goal-directed therapy (EGDT).We included adults with suspected infection, evidence of systemic inflammation, and either hypotension after a fluid bolus or elevated lactate. Prehospital and ED clinical variables and outcomes data were collected. The primary outcome was time to initiation of antibiotics in the ED.

**Results:** There were 311 patients, with 160 (51.4%) transported by EMS. Emergency medical services–transported patients had more organ failure (Sequential Organ Failure Assessment score, 7.0 vs 6.1; $P = .02$), shorter time to first antibiotics (111 vs 146 minutes, $P = .001$), and shorter time from triage to EGDT initiation (119 vs 160 minutes, $P = .005$) compared to non–EMS-transported patients. Among EMS patients, if the EMS provider indicated a written impression of sepsis, there was a shorter

- Urban Emergency Department
- Looked at severe sepsis patients
  - EMS versus non EMS patient outcomes
- 311 severe sepsis patients
  - 52 % were transported by EMS
  - Patients cared by EMS had a reduced Time to early goal directed therapy (EGDT) of 41 minutes.
  - Patients cared by EMS had a 35 minute reduction to administration of antibiotic care

- If EMS Dx'ed sepsis in the field the reduction in time to antibiotic was reduced at an average of 52 minutes and a EGDT reduction of 62minutes

- Authors conclusion;
  - Several relatively simple and inexpensive changes to EMS care could effect sepsis care in the hospital

Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

# Arriving by Emergency Medical Services Improves Time to Treatment Endpoints for Patients With Severe Sepsis or Septic Shock

Roger A. Band, MD, David F. Gaieski, MD, Julie H. Hylton, Frances S. Shofer, PhD, Munish Goyal, MD, and Zachary F. Meisel, MD, MPH

## Abstract

***Objectives:*** The objective was to evaluate the effect of arrival to the emergency department (ED) by emergency medical services (EMS) on time to initiation of antibiotics, time to initiation of intravenous fluids (IVF), and in-hospital mortality in patients with severe sepsis and septic shock.

***Methods:*** The authors performed an evaluation of prospectively collected registry data of patients with a diagnosis of severe sepsis or septic shock who presented to an urban academic ED during a 2-year period from January 1, 2005, to December 31, 2006. Descriptive and multivariate analytic methods were used to analyze the data. Using unadjusted and adjusted models, out-of-hospital patients who presented to the ED by ambulance (EMS) were compared to control patients who arrived by alternative means (non-EMS). Primary outcomes measured were ED time to initiation of antibiotics, ED time to initiation

ACADEMIC EMERGENCY MEDICINE 2011; 18:934–940 a 2011 by the Society for Academic Emergency Medicine

- Urban ED in Pennsylvania
- 963 patients with Sepsis and sever sepsis
- > 35 minute difference between EMS and non-EMS for I.V. Fluids
- >40 minutes difference between EMS and non- EMS for treatment with antibiotics

Prehospital and Disaster Medicine, April 2013

ORIGINAL RESEARCH

# Prehospital Sepsis Project (PSP): Knowledge and Attitudes of United States Advanced Out-of-Hospital Care Providers

Amado Alejandro Báez, MD, MPH;[1] Priscilla Hanudel, MD;[2] Maria Teresa Perez, RN;[3] Ediza M. Giraldez, MD;[4] Susan R. Wilcox, MD[5]

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Correspondence:

Abstract

**Introduction:** Severe sepsis and septic shock are common and often fatal medical problems. The Prehospital Sepsis Project is a multifaceted study that aims to improve the out-of-hospital care of patients with sepsis by means of education and enhancement of skills. The objective of this Project was to assess the knowledge and attitudes in the principles of diagnosis and management of sepsis in a cohort of United States out-of-hospital care providers.

**Methods:** This was cross-sectional study. A 15-item survey was administered via the Web and e-mailed to multiple emergency medical services list-servers. The evaluation consisted of four clinical scenarios as well as questions on the basics of sepsis. For intra-rater reliability, the first and the fourth scenarios were identical. Chi-square and Fisher's Exact testing were used to assess associations. Relative risk (RR) was used for strength of association. Statistical significance was set at .05.

**Results:** A total of 226 advanced EMS providers participated with a 85.4% (n = 193) completion rate, consisting of a 30.7% rural, 32.3% urban, and 37.0% suburban mix; 82.4% were paramedics and 72.5% had worked in EMS >10 years. Only 57 (29.5%) participants scored both of the duplicate scenarios correctly, and only 19 of the 193 (9.8%) responded to all scenarios correctly. Level of training was not a predictor of correctly scoring scenarios ($P = .71$, RR = 1.25, 95% CI = 0.39-4.01), nor was years of service ($P = .11$, RR = 1.64, 95% CI = 0.16-1.21).

**Conclusions:** Poor understanding of the principles of diagnosis and management of sepsis was observed in this cohort, suggesting the need for enhancement of education.

- Development of a tool to look at knowledge and attitudes in the principal diagnosis and management of sepsis by EMS Providers.
- 226 EMS Providers
  - 83% paramedics
  - 73% worked in EMS >10years
- 15 item evaluation
  - Includes 4 clinical scenarios
    - 1st and 4th were the same for IRR

- 10% got the 4 scenarios correct
- Conclusion: EMS Providers need additional knowledge in Sepsis

SEPSIS ALLIANCE
STAMP OUT SEPSIS

Journal of Critical Care (2010) 25, 553–562

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Journal of Critical Care

# Out-of-hospital characteristics and care of patients with severe sepsis: A cohort study ☆

Christopher W. Seymour MD[a,*], Roger A. Band MD FACEP[b], Colin R. Cooke MD, MSc[a], Mark E. Mikkelsen MD MSCE[c], Julie Hylton BS[b], Tom D. Rea MD, MSc[d], Christopher H. Goss MD, MSc[a], David F. Gaieski MD[b]

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**Keywords:**
Emergency medical services;
Hypotension;
Out-of-hospital;
Sepsis;
Lactic acid;
Multiple organ failure

**Abstract**

**Purpose:** Early recognition and treatment in severe sepsis improve outcomes. However, out-of-hospital patient characteristics and emergency medical services (EMS) care in severe sepsis is understudied. Our goals were to describe out-of-hospital characteristics and EMS care in patients with severe sepsis and to evaluate associations between out-of-hospital characteristics and severity of organ dysfunction in the emergency department (ED).

**Materials and Methods:** We performed a secondary data analysis of existing data from patients with severe sepsis transported by EMS to an academic medical center. We constructed multivariable linear regression models to determine if out-of-hospital factors are associated with serum lactate and sequential

- Urban Hospital , Pennsylvania
- Looked at severe sepsis patients
- 216 patients were transferred by EMS that meet criteria for severe sepsis
  - 24 % mortality rate
  - EGDT was performed 1/3 of patients
- Vital sign abnormalities were very common
  - Although on 25% had SBP < 90mm Hg
  - Serial vital signs were either not taken or poorly documented

- Only 30% of the time was an I.V. started
  - Lees tan 1/3 had volume documented
    - Average delivered was 300mL
  - In documented septic shock patients only 38% had an IV
    - Only 8% documented problems in starting
- In severe sepsis without shock, cardiac monitoring was done < 50%

- Authors Conclusions:
  - Interventions like cardiac monitoring, serial vital signs and fluid resuscitation occurred less than half of the severe septic patients transported by EMS.
  - Further studies are needed to improve the role of EMS Interventions and recognition of sepsis

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0736-4679/$ - see front matter

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http://dx.doi.org/10.1016/j.jemermed.2012.11.003

## Selected Topics: Prehospital Care

# EARLY DETECTION AND TREATMENT OF PATIENTS WITH SEVERE SEPSIS BY PREHOSPITAL PERSONNEL

Wayne F. Guerra, MD, MBA, Thomas R. Mayfield, MS, NREMT-P, Mary S. Meyers, MS, EMT-P, Anne E. Clouatre, MHS, EMT-P, and John C. Riccio, MD

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☐ **Abstract—Background: Severe sepsis is a condition with a high mortality rate, and the majority of patients are first seen by Emergency Medical Services (EMS) personnel. Objective: This research sought to determine the feasibility of EMS providers recognizing a severe sepsis patient, thereby resulting in better patient outcomes if standard EMS treatments for medical shock were initiated. Methods: We developed the Sepsis Alert Protocol that incorporates a screening tool using point-of-care venous lactate meters. If severe sepsis was identified by EMS personnel, standard medical shock therapy was initiated. A prospective cohort study was conducted for 1 year to determine if those trained EMS providers were able to identify 112 severe sepsis patients**

☐ **Keywords—prehospital; Emergency Medical Services; sepsis; venous lactate**

## INTRODUCTION

Severe sepsis and septic shock combined are the 10th leading cause of death, resulting in 215,000 deaths annually and 50.37 deaths per 100,000 people in the United States (US) (1). There are an estimated 751,000 cases of sepsis every year, and age-related, sepsis-associated mortality continues to rise (2,3). The cost of caring for

- Developed a Prehospital Care Sepsis ALERT Protocol
- 3 hospitals in a suburban community
- Two part study
  - Feasibility of EMS Providers to early identify severe sepsis
  - Any improvement in outcomes for those treated early for sever sepsis

- Paramedics used standard SIRS screening tool
  - Except WBC
  - Including venous lactate levels
    - Positive = > or equal to 4mmol/L

- EMS Treatment protocol included
  - High flow Oxygen
  - IV, fluid delivered at 20cc/Kg bolus
    - BP and Respiratory assessment every 500 cc
  - Continuous monitored
    - Vitals, including breath sounds
    - Cardiac monitor
    - Pulse oximetry
    - Glucose

- Study results
  - Transported 67 severe septic patients
  - EMS Identified 32 of 67 (47.8) correctly
    - In 8 patients the paramedics didn't have Lactate monitors available yet ????
    - 13 patients were identified by WBC
  - Overall Sepsis mortality was 26%
    - Only 14% in EMS ALERT patients (**SIGNIFICANT**)
  - 11 EMS ALERT False –positive
    - All were critical patients and had serious medical conditions requiring emergent treatment.

- There was a “trend” in favor of EMS Alert for;
  - Greater fluid volume
  - Shorter time to ED Antibiotics
  - Shorter hospital stays

  - Conclusion:
    - Better education for EMS Providers
    - Venous Lactate seems to be a benefit
    - EMS Sepsis Alert and protocol may have merit
      - 48% identified
      - Reduced Mortality and intubation
      - “Trends” might not be trends with greater numbers


“So what?”

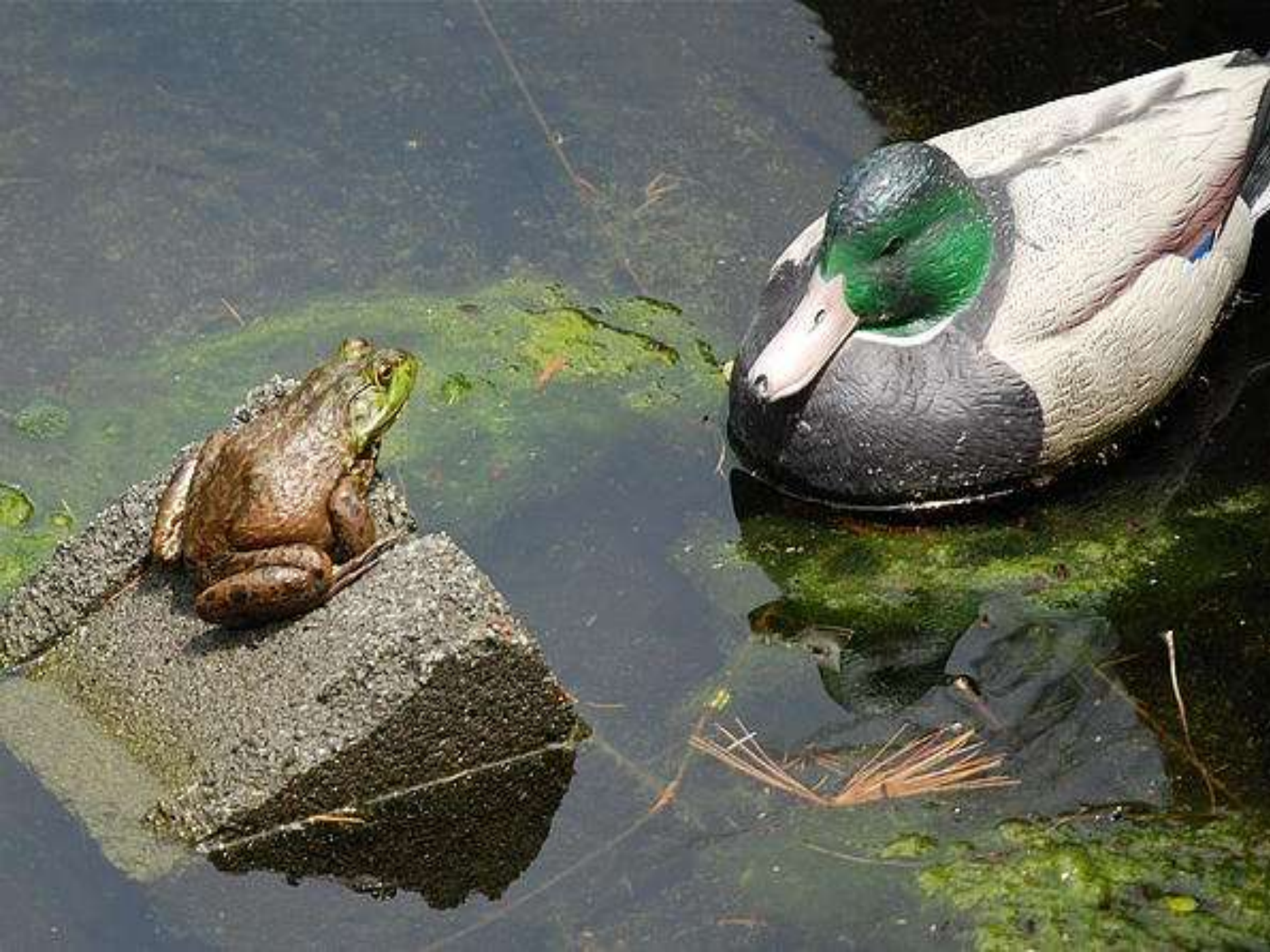
- Education to Providers
- Development of Assessment Guidelines
- Development of Treatment Protocols
- EMS Sepsis Alert
- Alternate transport
  - Sepsis Centers ???


How can we
make a DIFFERENCE ?

# Sepsis Chain of Survivability

- Early Access
- Early Recognition
- Early Treatment
- More Evidence


Knock Out
Sepsis!



# Thanks for Listening

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