UPDATE IN SEPSIS.

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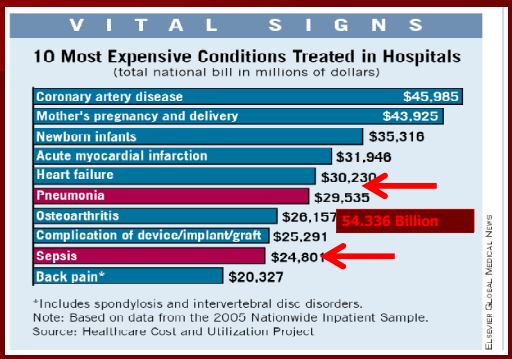
President-Elect of European Society for Emergency Medicine.
Faculty of Medicine and University Hospital of Rennes, France.

Significant Healthcare Challenge

- **Major cause of morbidity and mortality worldwide**
  - Leading cause of death in noncoronary ICU (US)
  - 10th leading cause of death overall (US)
  - more than 500 patients die of severe sepsis daily (US)
  - Mortality = 28.7%
- **More than 750,000 cases of severe sepsis in the US annually**
- **Sepsis in ED: 458,200 cases (61% of severe sepsis/septic shock)**

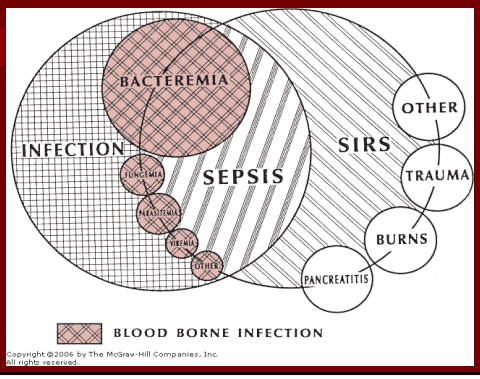
Based on data for septicemia
Reflects hospital-wide cases of severe sepsis as defined by infection in the presence of organ dysfunction
Sands KE, Bates DW, Lanken PN, et al. Epidemiology of sepsis syndrome in 8 academic medical centers. *JAMA* 1997;278:234-40.
National Vital Statistics Reports. 2005.
Angus DC, Linde-Zwirble WT, Lidicker J, et al. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome and associated costs of care. *Crit Care Med* 2001;29:1303-10.

Costs of Sepsis in US

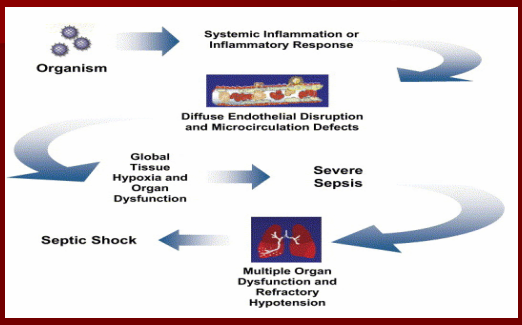


Comparable Global Epidemiology

- 95 cases per 100,000
  - 2 week surveillance
  - 206 French ICUs
- 95 cases per 100,000
  - 3 month survey
  - 23 Australian/New Zealand ICUs
- 51 cases per 100,000
  - England, Wales and Northern Ireland.

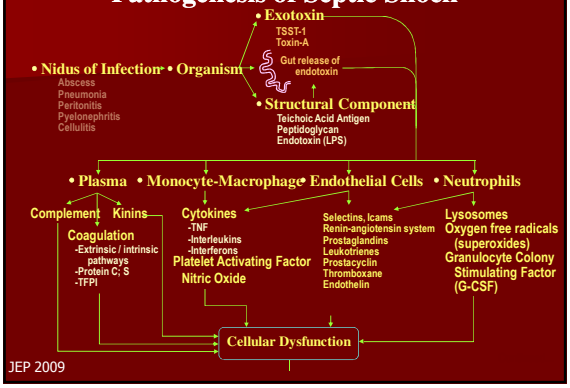


Pathogenesis of Sepsis



Nguyen H et al. Severe Sepsis and Septic Shock: Review of the Literature and Emergency Department Management Guidelines. Ann Emerg Med. 2006;42:28-54.

Pathogenesis of Septic Shock



JEP 2009

Balance between Pro-inflammatory and Anti-inflammatory Responses.

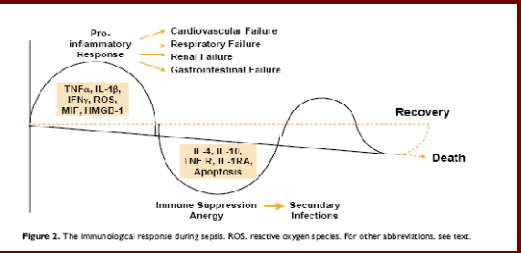
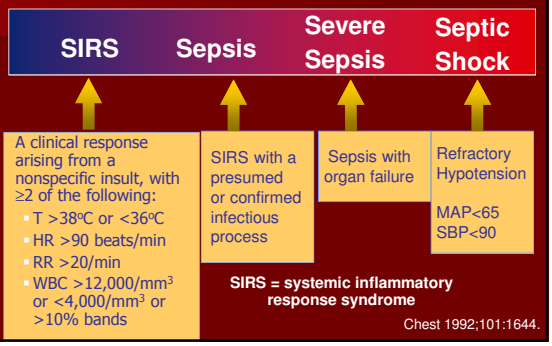


Figure 2. The immunological response during sepsis. ROS, reactive oxygen species. For other abbreviations, see text.

Sepsis Continuum



SIRS = systemic inflammatory response syndrome

Chest 1992;101:1644.

Surviving Sepsis Campaign

- Launched in Fall 2002 as a collaborative effort of European Society of Intensive Care Medicine, the International Sepsis Forum, and the Society of Critical Care Medicine
- Goal: reduce sepsis mortality by 25% in the next 5 years
- Guidelines revealed at SCCM in Feb 2004
  - *Critical Care Medicine* March 2004 32(3):858-87.
  - Website: survivingsepsis.org

The Severe Sepsis Bundles: Surviving Sepsis Campaign/IHI

Resuscitation Bundle (ED)

(To be accomplished as soon as possible over first 6 hours):

- ✓ Serum lactate measured.
- ✓ Blood cultures obtained prior to antibiotics administered. (1C)
- ✓ Perform imaging studies promptly to fine source (1C)
- ✓ From the time of presentation, broad- spectrum antibiotics within 3 hours for ED admissions and 1 hour for non-ED ICU admissions. (1D/1B)
- ✓ For hypotension and/or lactate > 4 mmol/L:
  - ✓ Deliver an initial minimum of 20 mL/kg of crystalloid (or colloid equivalent) (1C)
  - ✓ Apply vasopressors for hypotension not responding to initial fluid resuscitation to maintain MAP ≥ 65 mmHg.
- ✓ For persistent hypotension despite initial fluid resuscitation (septic shock) and/or lactate > 4 mmol/L: 1C
  - ✓ Achieve CVP ≥ 8 mmHg & MAP ≥ 65 mmHg & UO >0.5mL/kg/hr
  - ✓ Achieve $ScvO_2$ of ≥ 70% or SvO_2 ≥ 65%.
  - ✓ if $ScvO_2$ not ≥ 70% blood or dobutamine (2C)

Management Bundle (ICU)

(To be accomplished as soon as possible over first 24 hours):

- ✓ Low-dose steroids administered for septic shock in accordance with a standardized ICU policy. (Given to patients who respond poorly to fluids or vasopressors) (2C)
- ✓ Drotrecogin alfa (activated) administered in accordance with a standardized ICU policy. (Given to patients with sepsis induced organ dysfunction at high risk of death (2B)
- ✓ Glucose control maintained to < 150 mg/dL (8.3 mmol/L). (2C)
- ✓ Tidal volume 6 ml/kg (1B) Inspiratory plateau pressures < 30 cmH_2O for mechanically ventilated patients. (1C)

Adapted from the revised guidelines: CCM 2008;36:296-327.

What is a Bundle?

Specifically selected care elements

- From evidence based guidelines
- Implemented together provide improved outcomes compared to individual elements alone

6 Hour Resuscitation Bundle

- Early Identification
- Early Antibiotics and Cultures
- Early Goal Directed Therapy

VOLUME 345 NOVEMBER 8, 2001 NUMBER 19

The New England Journal of Medicine

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

Early Appropriate Antibiotics and Source Control

- Gram positive organisms have replaced gram negatives as the most common source of sepsis
- Lung (35%), abdomen (21%), Urinary tract (13%), skin and soft tissue (7%), other site (8%), unknown primary site (7%)
- Therapy targeted to the suspected site (eg, CAP, intra-abdominal source)
- Drainage, debridement and device removal as indicated

Empirical antimicrobial recommendations for adults patients

Unknown source:

Vancomycin (1g/12h) + Levofloxacin (750mg/24h) + Gentamicin (7mg/kg/24H)

Community acquired pneumonia:

Vancomycin (1g/12h) + levofloxacin (750mg/24h)

Meningitis:

Vancomycine (1g/12h) + ceftriaxone (2g/12h)

Urinary tract infection:

Piperacillin/Tazobactam (3.375g/6h) + Gentamicin (7mg/kg/24H)

Intrabdominal/pelvic infection:

Piperacillin/Tazobactam (3.375g/6h) + Gentamicin (7mg/kg/24H)

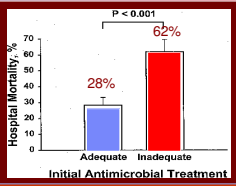
Skin and soft tissue infection/necrorizing infection:

Vancomycine (1g/12h) + Piperacillin/Tazobactam (3.375g/6h)+ Clindamycin 900mg/8h

Therapy Across the Sepsis Continuum

SIRS → Sepsis → Severe Sepsis → Septic Shock

- Drainage
- Debridement
- Device removal
- Definitive control
- • resection
- • amputation



Antibiotics and Source Control

Chest 2000;118(1):146
Chest 1992;101:1644.

Goal Directed Therapy

Restore systemic oxygen delivery through a manipulation of preload (volume), afterload (blood pressure), and contractility (stroke volume) to preserve effective tissue perfusion while avoiding excessive increase in myocardial oxygen consumption and maintaining coronary perfusion pressure.

Administration of fluids, pressors and transfusion based upon targets for CVP, blood pressure, urine output, mixed venous oxygen saturation and hematocrit.

In patients with severe sepsis/septic shock, EGDT should be used as the first means of resuscitation within the first 6 hours, with simultaneous prioritization of appropriate empirical antimicrobials and source control (Grade 1C)

Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Critical Care Medicine, 2008.

Patient randomized N=263

Early goal directed therapy N=130

CVP ≥ 8-12 mm Hg
MAP ≥ 65 mm Hg
Urine Output ≥ 0.5 ml/kg/hr
$ScvO_2$ ≥ 70%
SaO_2 ≥ 93%
Hct ≥ 30%

Antibiotics given at discretion of treating clinicians

Standard therapy N=133

CVP ≥ 8-12 mm Hg
MAP ≥ 65 mm Hg
Urine Output ≥ 0.5 ml/kg/hr

At least 6 hours of EGDT Mean 8hrs

Transfer to ICU

ICU MDs blinded to study treatment

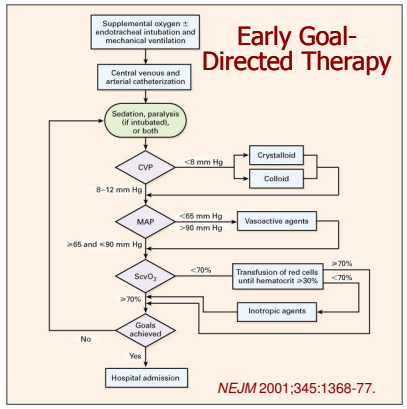
As soon as possible Mean 6.2hrs

NEJM 2001;345:1368-77.

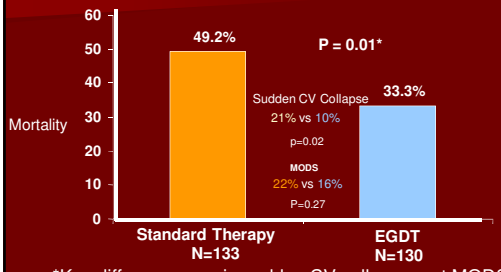
CVP: central venous pressure

MAP: mean arterial pressure

$ScvO_2$: central venous oxygen saturation



Early Goal-Directed Therapy Results: 28 Day Mortality

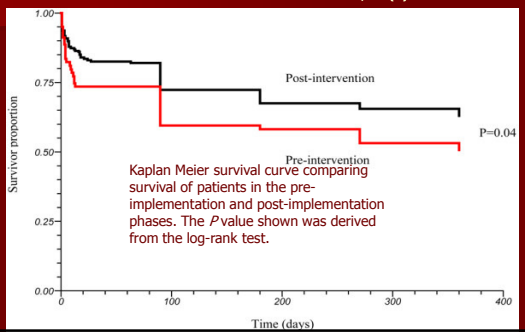


*Key difference was in sudden CV collapse, not MODS

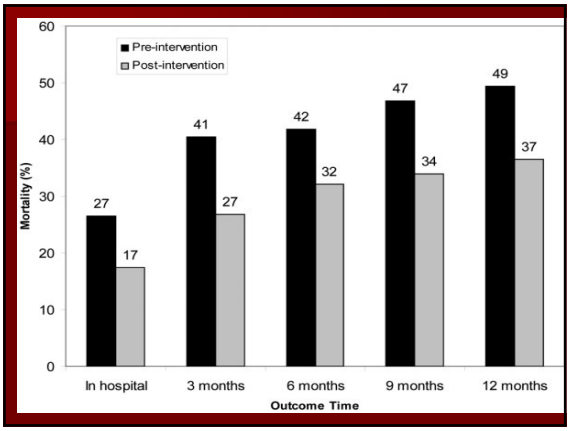
NEJM 2001;345:1368-77.

One year mortality of patients treated with an emergency department based early goal directed therapy protocol for severe sepsis and septic shock: a before and after study.

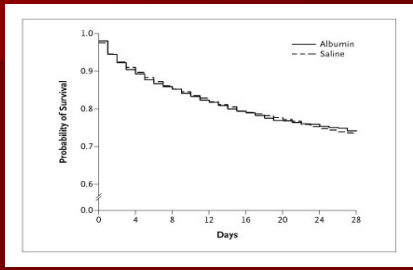
Michael A Puskarich et al. Crit Care. 2009; 13(5): R167.



Kaplan Meier survival curve comparing survival of patients in the pre-implementation and post-implementation phases. The *P* value shown was derived from the log-rank test.



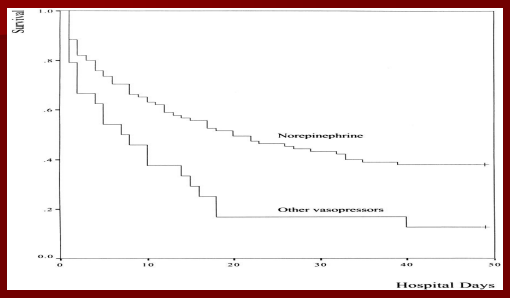
Fluid Resuscitation



Crystalloids and colloids are equally effective in restoring intravascular volume

The SAFE Study Investigators, N Engl J Med 2004;350:2247-2256
Primary Endpoint was 28 day mortality

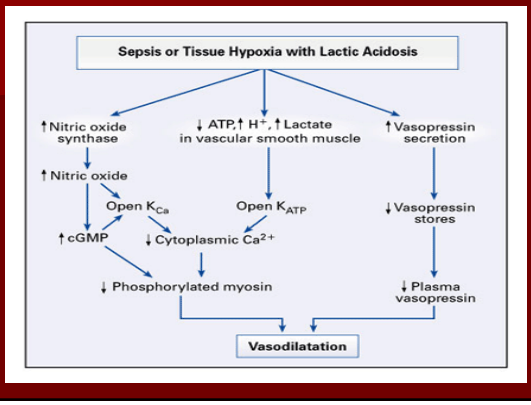
Vasopressors for Septic Shock



Claude, Critical Care Med 2000;28:2758

However

- If cardiac output is inadequate with norepinephrine, as indicated by a reduced mixed venous oxygen saturation, dobutamine may be added
- Vasopressin is emerging as a valuable addition to therapy for septic shock in patients with catecholamine refractory hypotension



Why Vasopressin ?

- Patients with septic shock have increased sensitivity to its pressor effects
- Vasopressin restores vascular tone in catecholamine resistant shock by several mechanisms including potentiation of adrenergic agents
- Low dose vasopressin increases urine output in septic patients, and increases creatinine clearance

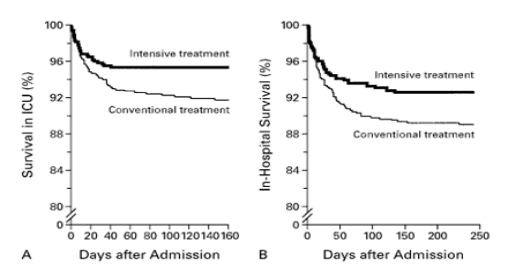
Low-dose vasopressin did not reduce mortality rates as compared with norepinephrine among patients with septic shock who were treated with catecholamine vasopressors.

Russel JA et al: N Engl J Med, 2008

KEY MESSAGES

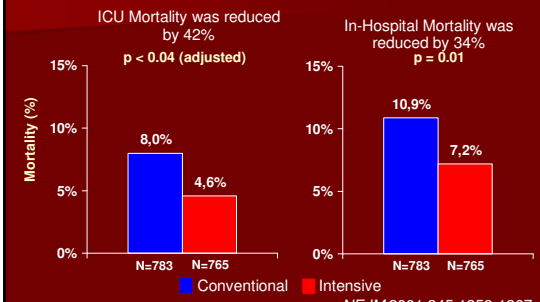
- Early resuscitation of severe sepsis in the ED was associated with a lower mortality.
- The long-term survival association found with EGDT remained significant after adjusting for confounding in a multivariable model.
- Clinical research data suggest a number needed to treat of eight subjects with EGDT to save one life at one year.

Tight Glucose Control Improved Survival



van den Berghe G, et al. *NEJM* 2001;345:1359-1367.

Intensive Insulin Therapy in Critically Ill Patients: Mortality



NEJM 2001;345:1359-1367.

Institution of glycemic control is recommended (1B) with targeting a blood glucose < 150 mg/dL after initial stabilization (2C)

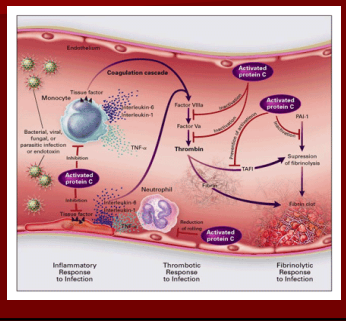
Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Critical Care Medicine, 2008.

BUT

The use of intensive insulin therapy placed critically ill patients with sepsis at increased risk for serious adverse events related to hypoglycemia.

Brunkhorst FM et al. *NEJM* 2008.

Activated Protein C in Sepsis



Protein C:
1. Inactivates clotting factors limiting the generation of thrombin
2. Inhibits prodn of inflammatory cytokines

PROWESS Study Design

1690 Patients :
- Known or suspected infection
- ≥ 3 of the SIRS criteria
- ≥ 1 acute (< 24hr in duration) organ failures

RANDOMIZED

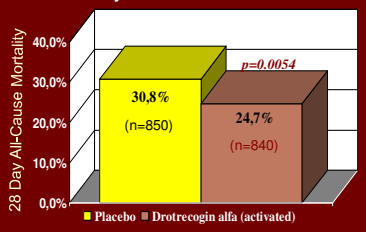
Placebo	Drotrecogin (xigris)
96 hr infusion + standard treatment	24 mcg/kg/hr 96 hour infusion + standard treatment

Primary Endpoint: All-Cause Mortality at 28 days

NEJM 2001;344:699-709.

PROWESS Results

Primary Stratified Intention-to-Treat Analysis



- 6.1% ↓ in absolute mortality
- 19.4% ↓ in RR of death

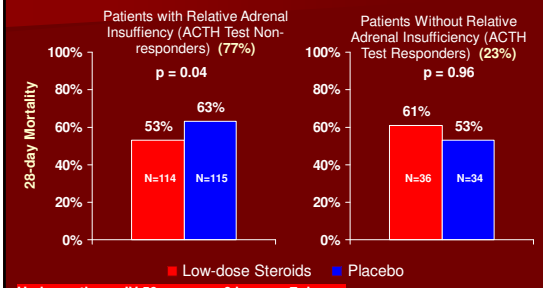
NEJM 2001;344:699-709.

« Patients who do not respond to institution of EGDT, antibiotics, and source control (ie, persistent hypotension, lactic acidosis, low ScvO2, or sepsis related dysfunction) and high risk of death, reflected by APACHE II score, should be considered for drotrecogin alfa (activated) administration » (Grade IIb)

Usually in ICU (24h-bundle) but in real life some patients stay more than 24 h in the ED!

Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Critical Care Medicine, 2008.

Low Dose Steroid Treatment in Septic Shock: 28 Day Mortality (Non-responders vs. Responders)



Hydrocortisone IV 50mg every 6 hours x 7 days + Fludrocortisone 50mcg daily x 7 days

Annane D, et. al. *JAMA* 2002;288(7):862.

« Patients who have refractory shock (ie, require vasopressors after adequate volume resuscitation) or organ dysfunction and are receiving mechanical ventilation should have an adrenocorticotropic hormone-stimulation test and be given low-dose replacement corticosteroid therapy »

Surviving Sepsis Campaign Phase 3 Data

- Study Sample
  - For a site to be included into data set, they had to have collected data for more than 3 months and included more than 20 patients.
  - 15,775 charts >>>>>> 15,022 included in final analysis
  - 252 sites >>>>>> 166 sites included in final analysis
  - 18 Countries represented
    - North America = 59%
    - Europe = 31%
    - South America = 10%

Surviving Sepsis Campaign Phase 3 Data Results

Entry Point	% of Subjects	Mortality (hosp)
ED	52%	27.6
ICU	12.8%	41.3
Ward	34.8%	46.8

Hospital mortality went from 37% to 30%
7% ARR; 19% RRR; p< 0.007

Surviving Sepsis Campaign Phase 3 Data Bundle Compliance

Bundle	Baseline	2 year
Resuscitation	10.9 %	31.3 %
Management	18 %	36 %

Risk Adjusted Hospital Mortality decreased by 5.4%
20 % improvement in compliance with bundles

Levy, M Presented at SCCM meeting 2-09

Surviving Sepsis Campaign Phase 3 Data

- Specific Sub-Group Mortality Results
  - Septic Shock: 71% of charts with 38% Mortality
  - Hypotension Only: 36.7% Mortality
  - Lactate > 4 Only: 5.5% of charts with 30% Mortality
  - SBP < 90 and Lactate > 4: Mortality of 46.1%


Before–after study of a stand
management of septic shock

Scott T. Micek, PharmD; Nareg Roubinian, MI

SHOCK, Vol. 26, No. 6, pp. 551 557, 2006

A MODIFIED GOAL-DIRECTED PROTOCOL IMPROVES CLINICAL OUTCOMES IN INTENSIVE CARE UNIT PATIENTS WITH SEPTIC SHOCK: A RANDOMIZED CONTROLLED TRIAL

Research

CLINICAL INVESTIGATIONS

Outcome of Septic Shock in Older Adults After Implementation of the Sepsis "Bundle"

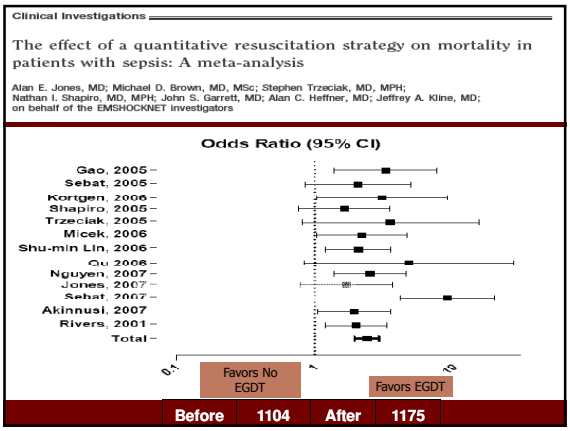
Ali A. El Solh, MD, MPH, Morobunfolu E. Akinnusi, MD, Leith N. Alsawalha, MD, and Lilibeth A. Pineda, MD

Implementati

Alan E. Jones, MD; Anne Focht, RN, MSN; James M. Horton, MD; and Jeffrey A. Kline, MD

Therapies (MUST) protocol*

Nathan I. Shapiro, MD, MPH; Michael D. Howell, MD; Daniel Talmor, MD, MPH; Dermot Lahey; Long Ngo, PhD; Jon Buras, MD, PhD; Richard E. Wolfe, MD; J. Woodrow Weiss, MD; Alan Lisbon, MD


Clinical Investigations

The effect of a quantitative resuscitation strategy on mortality in patients with sepsis: A meta-analysis

Alan E. Jones, MD; Michael D. Brown, MD, MSc; Stephen Trzeciak, MD, MPH; Nathan I. Shapiro, MD, MPH; John S. Garrett, MD; Alan C. Heffner, MD; Jeffrey A. Kline, MD; on behalf of the EMSHOCKNET investigators

Odds Ratio (95% CI)

Gao, 2005
Sebat, 2005
Kortgen, 2006
Shapiro, 2005
Trzeciak, 2005
Micek, 2006
Shu-min Lin, 2006
Qu 2006
Nguyen, 2007
Jones, 2007
Sebat, 2007
Akinnusi, 2007
Rivers, 2001
Total

0.1 1 10

Favors No EGDT | Favors EGDT

Before 1104 After 1175

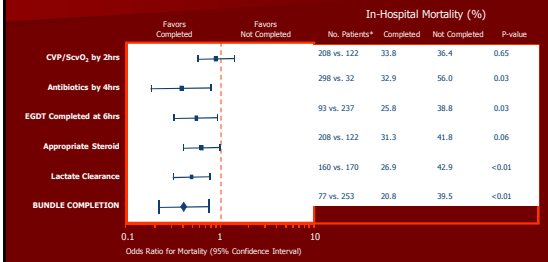
Bundle Implementation: Decreased Mortality

Results:

- In hospital mortality in patients who completed the bundle was significantly lower than those who did not complete the bundle (20.8 vs. 39.5; p<0.01)
- Completing EGDT in 6 hours was the only quality indicator with a significant odds ratio for decreased mortality using multivariate regression analysis
- After 2 years, achieved 51% compliance with all five indicators

Nguyen HB et al. *Crit Care Med.* 2007;35 (4):1-8.

Bundle Component Compliance and Impact on Mortality



* Number of patients (out of 330 total patients) completing vs. not completing the quality indicator
Nguyen HB et al. *Crit Care Med.* 2007;35 (4):1-8.

Sepsis Bundles: Significant Impact on Hospital Outcomes

- Two acute National Health Service Trust Teaching Hospitals in England performed a prospective observational study with 101 adult patients with severe sepsis or septic shock
- Outcomes measures
  - Rate of compliance with 6-hour and 24-hour bundles adapted from 2004 SSC guidelines
  - Hospitality mortality between compliant and noncompliant groups

Compliance with bundles
6-hour bundle 52%
24-hour bundle 30%

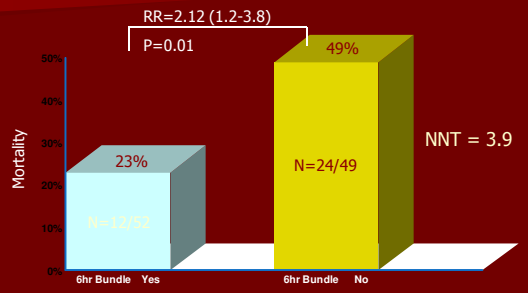
Bundle Mortality
Noncompliant 49% (p=.001)
Compliant 23% (p=.001)

- **More than two-fold increase in hospital mortality associated with noncompliant group**
- **Assessed compliance as "all or none" for the bundle elements**

Source: Gao F et al. *Crit Care Med.* 2005;9(6):R764-R770.

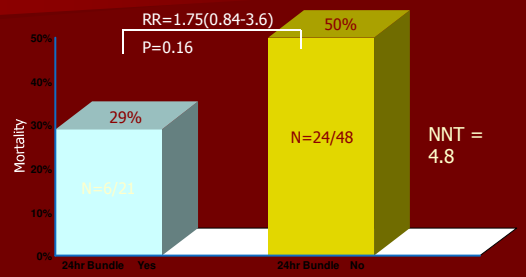
6-Hour Bundle and Hospital Mortality

Gao F et al. *Crit Care Med.* 2005;9 (6):R764-R770.



24-Hour Bundle and Hospital Mortality

Gao F et al. *Crit Care Med.* 2005;9 (6):R764-R770.



Median Costs per Patient for Treating Sepsis

	Median per-patient cost	Range	p-value
Before protocol initiation	$21,985	$3,610–99,795	0.008
After protocol initiation	$16,103	$3,445–102,440	

- Median saving of **$5,882**
  - 18.3% more survivors following protocol initiation
- Receipt of care under the protocol associated with decreased costs (adjusted HR: 1.70; 95% CI, 1.03–2.80)

CI = confidence interval; HR = hazard ratio

Shorr AF et al. *Crit Care Med.* 2007;35:1257–1262.

Costs Among Survivors

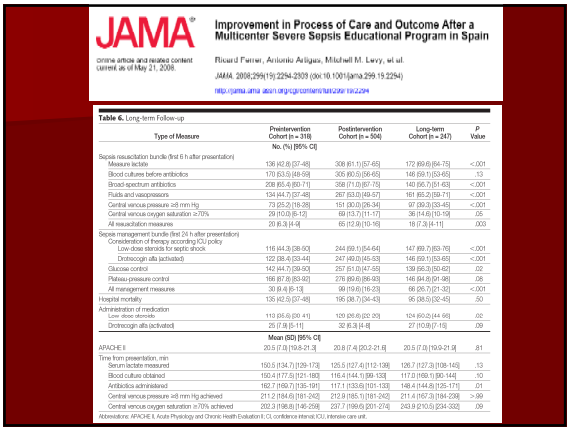
- Survivors
  - Pre-protocol 51.7%, post-protocol 70.0% (p=0.04)

Median total costs among survivors varied significantly following protocol initiation

	Pre-protocol		Post-protocol		p-value
		Range		Range	
Median total costs	$21,985	$3,610–99,795	$16,103	$3,445–102,440	0.008
Hospital LOS	13 days	3–37 days	8 days	2–35 days	0.001

LOS = length of stay

Shorr AF et al. *Crit Care Med.* 2007;35:1257–1262.



JAMA

Improvement in Process of Care and Outcome After a Multicenter Severe Sepsis Educational Program in Spain

Ricard Ferrer, Antonio Artigas, Mitchell M. Levy, et al.

JAMA. 2008;299(19):2294-2303 (doi:10.1001/jama.299.19.2294)

Table 6. Long-term Follow-up

Type of Measure	Preintervention Cohort [n = 318] No. (%) [95% CI]	Postintervention Cohort [n = 504]	Long-term Cohort [n = 247]	P Value
Sepsis resuscitation bundle (first 6 h after presentation)				
Measure lactate	136 (42.8) [37-48]	308 (61.1) [57-65]	172 (69.6) [64-75]	<.001
Blood cultures before antibiotics	170 (53.5) [48-59]	305 (60.5) [56-65]	146 (59.1) [53-65]	.13
Broad-spectrum antibiotics	208 (65.4) [60-71]	358 (71.0) [67-75]	140 (56.7) [51-63]	<.001
Fluids and vasopressors	134 (44.7) [37-48]	287 (63.0) [49-57]	161 (65.2) [59-71]	<.001
Central venous pressure ≥8 mm Hg	73 (25.2) [18-28]	151 (30.0) [26-34]	97 (39.3) [33-45]	<.001
Central venous oxygen saturation ≥70%	29 (10.0) [6-12]	69 (13.7) [11-17]	36 (14.6) [10-19]	.05
All resuscitation measures	20 (6.3) [4-4]	65 (12.9) [10-16]	16 (7.3) [4-11]	.003
Sepsis management bundle (first 24 h after presentation)				
Consideration of therapy according ICU policy				
Low-dose steroids for septic shock	116 (44.3) [38-50]	244 (69.1) [64-64]	147 (69.7) [63-76]	<.001
Drotrecogin alfa (activated)	122 (38.4) [33-44]	247 (49.0) [45-53]	146 (59.1) [53-65]	<.001
Glucose control	142 (44.7) [39-50]	257 (51.0) [47-55]	139 (56.3) [50-62]	.02
Plateau pressure control	166 (67.8) [62-72]	276 (69.6) [66-73]	146 (64.9) [58-71]	.08
All management measures	30 (9.4) [6-13]	99 (19.6) [16-23]	66 (26.7) [21-32]	<.001
Hospital mortality	135 (42.5) [37-48]	195 (38.7) [34-43]	95 (38.5) [32-45]	.50
Administration of medication				
Low dose steroids	113 (35.5) [30 41]	120 (26.6) [22 30]	124 (50.2) [44 56]	.02
Drotrecogin alfa (activated)	25 (7.9) [5-11]	32 (6.3) [4-8]	27 (10.9) [7-15]	.09
	Mean (SD) [95% CI]			
APACHE II	20.5 (7.0) [19.8-21.3]	20.8 (7.4) [20.2-21.5]	20.5 (7.0) [19.9-21.5]	.81
Time from presentation, min				
Serum lactate measured	150.5 (134.7) [129-173]	125.5 (127.4) [112-138]	126.7 (127.3) [108-142]	.13
Blood culture obtained	150.4 (177.5) [121-180]	116.4 (144.1) [99-133]	117.0 (160.1) [90-144]	.10
Antibiotics administered	162.7 (169.7) [135-191]	117.1 (133.6) [101-133]	148.4 (144.8) [125-171]	.01
Central venous pressure ≥8 mm Hg achieved	211.2 (184.6) [181-242]	212.9 (185.1) [181-242]	211.4 (167.3) [184-239]	>.99
Central venous oxygen saturation ≥70% achieved	202.3 (196.8) [149-259]	237.7 (189.6) [201-274]	243.9 (210.5) [234-332]	.09

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; CI, confidence interval; ICU, intensive care unit.

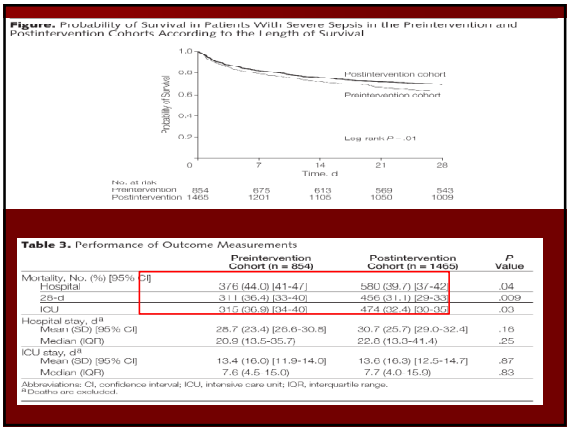


Figure. Probability of Survival in Patients With Severe Sepsis in the Preintervention and Postintervention Cohorts According to the Length of Survival

Table 3. Performance of Outcome Measurements

	Preintervention Cohort (n = 854)	Postintervention Cohort (n = 1463)	*P* Value
Mortality, No. (%) [95% CI]			
Hospital	376 (44.0) [41-47]	580 (39.7) [37-42]	.04
28-d	311 (36.4) [33-40]	456 (31.1) [29-33]	.009
ICU	315 (36.9) [34-40]	474 (32.4) [30-35]	.03
Hospital stay, d[a]			
Mean (SD) [95% CI]	28.7 (23.4) [26.6-30.8]	30.7 (25.7) [29.0-32.4]	.16
Median (IQR)	20.9 (13.5-35.7)	22.6 (13.3-41.4)	.25
ICU stay, d[a]			
Mean (SD) [95% CI]	13.4 (16.0) [11.9-14.0]	13.6 (16.3) [12.5-14.7]	.87
Median (IQR)	7.6 (4.5-15.0)	7.7 (4.0-15.0)	.83

Abbreviations: CI, confidence interval; ICU, intensive care unit; IQR, interquartile range.
[a] Deaths are excluded.

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Online article and related content current as of May 21, 2008.

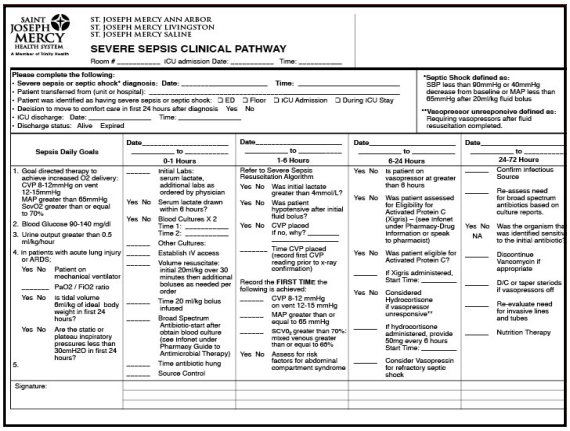
Improving Sepsis Care: The Road Ahead

Jeremy M. Kahn; David W. Bates

JAMA. 2008;299(19):2322-2323 (doi:10.1001/jama.299.19.2322)

http://jama.ama-assn.org/cgi/content/full/299/19/2322

Furthermore, this study should be a wake-up call to policy makers, a challenge to the leaders of professional societies, and a road map for the path ahead. No longer is it acceptable to simply publish practice guidelines and hope that quality improvement happens at the local level. Development of these guidelines should be followed by rigorous testing, and, when results are positive, by dedicated regional, national, and even international implementation efforts. Such broad-based efforts are needed to achieve population-level benefits from interventions known to be effective.



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SEVERE SEPSIS CLINICAL PATHWAY

Room # _____ ICU admission Date: _____ Time: _____

Please complete the following:
- Severe sepsis or septic shock* diagnosis: Date: _____ Time: _____
- Patient transferred from (unit or hospital): _____
- Patient was identified as having severe sepsis or septic shock: ☐ ED ☐ Floor ☐ ICU Admission ☐ During ICU Stay
- Decision to move to comfort care in first 24 hours after diagnosis Yes No
- ICU discharge: Date: _____ Time: _____
- Discharge status: Alive Expired

*Septic Shock defined as: SBP less than 90mmHg or 40mmHg decrease from baseline or MAP less than 65mmHg after 20ml/kg fluid bolus

**Vasopressor unresponsive defined as: Requiring vasopressors after fluid resuscitation completed.

Sepsis Daily Goals	Date _____ to _____ 0-1 Hours	Date _____ to _____ 1-6 Hours	Date _____ to _____ 6-24 Hours	Date _____ to _____ 24-72 Hours
1. Goal directed therapy to achieve increased O2 delivery: CVP 8-12mmHg on vent 12-15mmHg MAP greater than 65mmHg ScvO2 greater than or equal to 70%.	_____ Initial Labs: serum lactate, additional labs as ordered by physician Yes No Serum lactate drawn within 6 hours? Yes No Blood Cultures X 2 Time 1: _____ Time 2: _____ _____ Other Cultures: _____ Establish IV access _____ Volume resuscitate: initial 20ml/kg over 30 minutes then additional boluses as needed per order _____ Time 20 ml/kg bolus infused _____ Broad Spectrum Antibiotic-start after obtain blood culture (see infonet under Pharmacy Guide to Antimicrobial Therapy) _____ Time antibiotic hung _____ Source Control	Refer to Severe Sepsis Resuscitation Algorithm Yes No Was initial lactate greater than 4mmol/L? Yes No Was patient hypotensive after initial fluid bolus? Yes No CVP placed if no, why? _____ _____ Time CVP placed (record first CVP reading prior to x-ray confirmation) Record the **FIRST TIME** the following is achieved: _____ CVP 8-12 mmHg on vent 12-15 mmHg _____ MAP greater than or equal to 65 mmHg _____ $ScvO_2$ greater than 70% mixed venous greater than or equal to 65% Yes No Assess for risk factors for abdominal compartment syndrome	Yes No Is patient on vasopressor at greater than 6 hours Yes No Was patient assessed for Eligibility for Activated Protein C (Xigris) – (see infonet under Pharmacy-Drug information or speak to pharmacist) Yes No Was patient eligible for Activated Protein C? _____ If Xigris administered, Start Time: _____ Yes No Considered Hydrocortisone if vasopressor unresponsive** _____ If hydrocortisone administered, provide 50mg every 6 hours Start Time: _____ _____ Consider Vasopressin for refractory septic shock	_____ Confirm infectious Source _____ Re-assess need for broad spectrum antibiotics based on culture reports. Yes No NA Was the organism that was identified sensitive to the initial antibiotic _____ Discontinue Vancomycin if appropriate _____ D/C or taper steroids if vasopressors off _____ Re-evaluate need for invasive lines and tubes _____ Nutrition Therapy
2. Blood Glucose 80-140 mg/dl				
3. Urine output greater than 0.5 ml/kg/hour				
4. In patients with acute lung injury or ARDS: Yes No Patient on mechanical ventilator _____ PaO2 / FiO2 ratio Yes No Is tidal volume 6ml/kg of ideal body weight in first 24 hours? Yes No Are the static or plateau inspiratory pressures less than 30cmH2O in first 24 hours?				
5.				
Signature:				

SUMMARY: 6 - hour Severe Sepsis/ Septic Shock Bundle

- **Early Detection:**
  Obtain serum lactate level.
- **Early Blood Cx/Antibiotics:**
  within 3 hours of presentation. In fact during The first hour.
- **Early EGDT:**
  Hypotension (SBP < 90, MAP < 65) or lactate > 4 mmol/L:
  initial fluid bolus 20-40 ml of crystalloid (or colloid equivalent) per kg of body weight.
- **Vasopressors:**
  Hypotension not responding to fluid
  Titrate to MAP > 65 mmHg.
- **Septic shock or lactate > 4 mmol/L:**
  CVP and $ScvO_2$ measured.
  CVP maintained >8 mmHg.
  MAP maintain > 65 mmHg.
- **ScvO2<70%with CVP > 8 mmHg, MAP > 65 mmHg:**
  PRBCs if hematocrit < 30%.
  Inotropes.

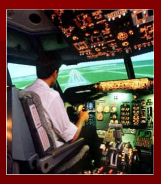
Clinical Inertia: Low Levels of Compliance at Research Centers

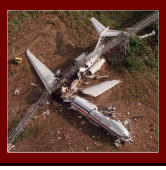
Surviving Sepsis

"If those who generated the evidence are slow to translate it into practice, it is unlikely that passive forms of dissemination can improve the quality of care. To accelerate adoption of new evidence, we need to understand factors other than knowledge and awareness that influence practice".

Majumdar SR, et al. *Am J Med* 2002;113:140-5

A Sepsis Pilot





- Recognizes trouble before it start
- Follows standard operating procedures (SOP) for managing sepsis.
- Does not take little things for granted.
- Understands the consequences:
  – Immediate
  – Long term
- Holds everyone accountable
  – takes personal responsibility for outcomes.