Importància del tractament precoç i adequat a la sèpsia greu

Ricard Ferrer
Intensive Care Department
Mutua Terrassa University Hospital
Barcelona. SPAIN
Outline

• Epidemiology of Sepsis.
• Time-to-treatment in Sepsis.
• Interventions. Sepsis Code.
Epidemiology of sepsis

Use of Retrospective Administrative Data

ICD-9 Infection + ICD-9 Organ Dysfunction OR ICD-9 Severe Sepsis Code = Severe Sepsis

Martin, Angus

Wang, Dombrovskiy
Two Decades of Mortality Trends Among Patients With Severe Sepsis: A Comparative Meta-Analysis

Elizabeth K. Stevenson, MD, MS\textsuperscript{1,2}; Amanda R. Rubenstein, MD\textsuperscript{3}; Gregory T. Radin, MD\textsuperscript{3}; Renda Soylemez Wiener, MD, MPH\textsuperscript{1,2,4,5}; Allan J. Walkey, MD, MSc\textsuperscript{1,2}

Control group in 36 RCT vs Administrative data

- RCT
- Angus
- Martin

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>% Mortality</td>
<td>544</td>
<td>863</td>
<td>1682</td>
<td>1554</td>
<td>1148</td>
<td>97</td>
<td>882</td>
<td>1799</td>
<td>1537</td>
<td>537</td>
<td>648</td>
<td>91</td>
<td>509</td>
<td>545</td>
<td>834</td>
<td>400</td>
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<td>5.83</td>
<td>6.59</td>
<td>7.27</td>
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<td>8.22</td>
<td>9.02</td>
<td>9.29</td>
<td>9.51</td>
<td>10.3</td>
<td>11.8</td>
<td>13.4</td>
<td>15.1</td>
<td>17.0</td>
<td>18.8</td>
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<td>3.12</td>
<td>3.36</td>
<td>3.48</td>
<td>3.55</td>
<td>3.94</td>
<td>4.49</td>
<td>5.13</td>
<td>6.09</td>
<td>6.90</td>
<td>7.91</td>
<td>8.89</td>
<td>10.2</td>
<td>10.8</td>
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</table>
Mortality Related to Severe Sepsis and Septic Shock Among Critically Ill Patients in Australia and New Zealand, 2000-2012

Australian and New Zealand Intensive Care Society adult ICU patient database

Mortality Reduction: 50%
Mortality Related to Severe Sepsis and Septic Shock Among Critically Ill Patients in Australia and New Zealand, 2000-2012

Australian and New Zealand Intensive Care Society adult ICU patient database

<table>
<thead>
<tr>
<th></th>
<th>2000</th>
<th>2012</th>
<th>Risk Reduction</th>
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<tr>
<td></td>
<td>No. of Events</td>
<td>No. of Patients</td>
<td>Mortality, % (95% CI)</td>
</tr>
<tr>
<td>All patients with severe sepsis</td>
<td>949</td>
<td>2708</td>
<td>35.0 (33.2-36.8)</td>
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<tr>
<td>Without comorbidities(^b)</td>
<td>529</td>
<td>1800</td>
<td>29.4 (27.2-31.6)</td>
</tr>
<tr>
<td>With comorbidities(^b)</td>
<td>420</td>
<td>908</td>
<td>46.3 (43.0-49.6)</td>
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<tr>
<td>Severe sepsis without shock</td>
<td>426</td>
<td>1411</td>
<td>30.2 (27.8-32.6)</td>
</tr>
<tr>
<td>Septic shock</td>
<td>523</td>
<td>1297</td>
<td>40.3 (37.6-43.0)</td>
</tr>
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</table>

Age, y

<table>
<thead>
<tr>
<th>Age, y</th>
<th>No. of Events</th>
<th>No. of Patients</th>
<th>Mortality, % (95% CI)</th>
<th>Absolute</th>
<th>Relative</th>
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<tbody>
<tr>
<td>≤44</td>
<td>98</td>
<td>443</td>
<td>22.1 (18.2-26.0)</td>
<td>14.8 (11.0-19.1)</td>
<td>66.9 (58.0-74.0)</td>
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<tr>
<td>45-64</td>
<td>226</td>
<td>742</td>
<td>30.5 (27.2-33.8)</td>
<td>16.1 (12.7-19.7)</td>
<td>53.0 (46.2-58.9)</td>
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<tr>
<td>65-84</td>
<td>537</td>
<td>1326</td>
<td>40.5 (38.0-43.0)</td>
<td>18.8 (16.0-21.7)</td>
<td>46.4 (41.9-50.6)</td>
</tr>
<tr>
<td>≥85</td>
<td>88</td>
<td>197</td>
<td>44.7 (37.6-51.8)</td>
<td>14.2 (7.0-21.6)</td>
<td>31.9 (18.7-42.9)</td>
</tr>
</tbody>
</table>

Mortality Reduction > 50% in young and healthy
Mortality Reduction: +++
Discharged Home: ++
Discharged to Another Hospital: -
Discharged to Rehabilitation: ++++
• 42 ICUs in Spain.

• All episodes of severe sepsis or septic shock in two periods of time.
  – 2 months in 2005, before EDUSEPSIS intervention.
  – 3 months in 2011, before ABISS intervention.

• 2011 patients were:
  – Older: 62.1±16.7 vs 64.9±14.9 years; p=0.023
  – More severe: APACHE II 20.7±7.2 vs 22.4±7.9; p=0.001
Evolution of Sepsis Mortality in Spain

Adjusted mortality: OR 0.638 (0.49-0.831); p=0.001

ESICM Congress 2013
Evolución Mortalidad Sepsis Grave
CMBD Cataluña

Ferrer R et al. SCCM Congress 2014
Evolución Mortalidad Sepsis Grave

CMBD Cataluña

Ferrer R et al. SCCM Congress 2014
Outline

• Epidemiology of Sepsis.
• Time-to-treatment in Sepsis.
• Sepsis Code.
• Cost-effectiveness.
SEVERE ANTI-INFLAMMATORY RESPONSE: HARMFUL

MODERATED ANTI-INFLAMMATORY RESPONSE: BENEFICIAL

MACROPHAGE

ENDOTOXIN (PAMP)

TLR-4 (PRR)

LYMPHOCYTES

↑ Treg %

ENDOTHELIUM NEUTROPHILS

ANTINFECTIONOUS RESPONSE

DIC COAGULOPATHY

MICROVASCULAR DYSFUNCTION

NITRIC OXIDE

CAPILARY LEAK INTERSTICIAL EDEMA

NITRIC OXIDE

VASODILATATION HYPOTENSION MYOCARDIAL DYSFUNCTION

↓ VO₂, Cell Death, Multi-organ failure

MODERATED PRO-INFLAMMATORY RESPONSE: BENEFICIAL

SEVERE PRO-INFLAMMATORY RESPONSE: SEPTIC SHOCK

ANTI-INFLAMMATORY CYTOKINES IL-10, IL-11...

PRO-INFLAMMATORY CYTOKINES (IL-1, IL-6, TNFα)

HMGB1 COMPLEMENT ACTIVATION

CORTISOL CATECHOLAMINES VASOPRESSIN GLUCAGON

↑ VO₂, ↑ DO₂

LIPID MEDIATOR FACTORS PG, LEUCOTRIENS...

PAF TISSUE FACTOR

↑ PLATELET AGGREGATION ↓ FIBRINOLISIS ↑ COAGULATION

THROMBIN

DIC COAGULOPATHY

PAI-1

PLATELET

Endothelial Injury Neutrophils

NEUTROPHILS

APoptosis

TNFα
Stages of sepsis

Infection

↑ Microvascular Dysfunction

↑ Tissue dysoxia

Time is Tissue

The biphasic VO$_2$ – DO$_2$ model

- Critical point: DO$_2$ crit
- Independence zone: Variable O$_2$ Extraction Ratio
- VO$_2$ and impaired OER

Dependence zone: Max O$_2$ ER

Sepsis

Normal

- $\approx$10 ml/min·kg
- $\approx$15 ml/min·kg

$\uparrow$ VO$_2$ and impaired OER
$\text{VO}_2 - \text{DO}_2$ model: $O_2$ Debt

$O_2$ Debt = $O_2$ Deficit x Time

Independence zone

Dependence zone

$O_2$ Deficit & Anaerobic Metabolism

Lactate

$\text{DO}_2$

$\text{VO}_2$
Markers of dysoxia: **Lactate**

**Anaerobic Glycolysis**
- **Glycogen** → **Glucose** → **Pyruvate** → **Lactate**
  - Equation: $1 \text{Glu} + 2 \text{ADP} + 2 \text{Pi} 
  \downarrow \quad \text{2 Lactate + 2 ATP + Hydrogen ion}$

**Aerobic Glycolysis**
- **O$_2$** → **Citric Acid Cycle** → **CO$_2$** + **H$_2$O**
  - Equation: $1 \text{Glu} + 6 \text{O}_2 + 38 \text{ADP} + 38 \text{Pi} 
  \downarrow \quad 6 \text{CO}_2 + 6 \text{H}_2\text{O} + 38 \text{ATP}$

High initial serum lactate associated with ↑ mortality regardless of presence of shock (hypotension despite fluid resuscitation).

Improving Lactate: a Good Prognostic Sign

VO$_2$ and alteration of microvascular flow
VO$_2$ and alteration of microvascular flow

Principal mechanisms implicated in the development of microcirculatory alterations

- Endothelial dysfunction (impaired sensitivity of vasoconstrictive/vasodilating substances)
- Impaired RBC deformability
- Rolling and adhesion of RBC and WBC to endothelium
- Altered glycocalyx
- Impaired backward communication

- Flow $>>$ O$_2$ needs $\Rightarrow$ High SvO$_2$
- Flow $<<$ O$_2$ needs $\Rightarrow$ Hypoxia

$\downarrow$ Capillary density
$\uparrow$ number of stopped-flow and intermittent-flow capillaries

$\downarrow$ surface for O$_2$ exchange

Metabolic failure

Mervyn Singer, MD


INSULT
(infection, trauma, burns, haemorrhage...)

systemic inflammatory response

early circulatory hypoxia

mitochondrial inhibition

bioenergetic ‘failure’

metabolic ‘shutdown’

biochemical & functional abnormalities characteristic of MULTI-ORGAN FAILURE
Treatment strategies: balanced $\text{DO}_2/\text{VO}_2$
Decrease \( \text{VO}_2 \)

1 Septic Shock
2 Balanced \( \text{DO}_2/\text{VO}_2 \)

\( \text{VO}_2 \) vs \( \text{DO}_2 \)

Lactate

1
2
Decrease VO$_2$

- Infection control: Adequate empirical antibiotics and Source Control.
- Normothermia (or hypothermia)
- Analgesia
- Mechanical Ventilation.
- Titrate minimum dose of Termogenic drugs like inotropes.
Increase $\text{DO}_2$

1. Septic Shock
2. Resuscitated Shock
   Restored $\text{VO}_2$
3. Supranormal Resuscitation
   $\text{DO}_2 > 600 \text{ ml/min} \cdot \text{m}^2$

$\text{VO}_2$ vs. $\text{DO}_2$

- Sepsis
- Lactate
\[ \text{DO}_2 = \text{CO} \times \text{CaO}_2 \]

**TREATMENTS**
- Fluids
- Inotropes
- Vasopressors

\[ \text{CaO}_2 \approx \text{Hb} \times 1.34 \times \text{SaO}_2 \times 100 \]

\[ \text{O}_2 \]
- PRBC
First 6H

Protocol Based EGDT:
Requires Continuous Central Venous Monitoring
Indications to ↑ DO$_2$ if ScvO$_2$ < 70%
Protocol similar to Rivers

Protocol Based Standard Therapy:
Protocolized resuscitation without CV monitoring
No special indications to ↑ DO$_2$

Usual care
If Hgb < 7.5, transfuse PRBC

Lactate > 4, oliguria, mottled skin
Monitorization

A

Central venous catheter insertion

B

Catheter insertion for ScvO2 monitoring

![Cumulative percentage vs. Hours](image)

- **Protocol-based EGDT**
- **Protocol-based Standard Therapy**
- **Usual care**

\[ p < 0.0001 \]
Treatments
Outcome

P = 0.52 by log-rank test

Mortality (%) vs. Days

- Orange: Protocol-based EGDT
- Blue: Protocol-based standard therapy
- Green: Usual care
Conclusions

• Tissue dysoxia is playing an important role in the patho-physiology of sepsis:
  – Inadequate DO$_2$ to VO$_2$
  – Alterations in the microcirculation
  – Mitochondrial dysfunction.

• Early hemodynamic resuscitation based in a balanced DO$_2$/VO$_2$. The ideal protocol and goal are not well established.
Pillars of Sepsis Treatment

ABX  Source Control  HMDC Resusc.

YOUR speed is LIFE!
Timing of surgery in NSTI

The administration of **effective intravenous antimicrobials** within the **first hour of recognition** of septic shock (grade 1B) and severe sepsis without septic shock (grade 1C) should be the goal of therapy.

**Remark:** Although the weight of the evidence supports prompt administration of antibiotics following the recognition of severe sepsis and septic shock, the **feasibility** with which clinicians may achieve this ideal state has not been scientifically evaluated.
We recommend that initial empiric antimicrobial therapy include one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into the tissues presumed to be the source of sepsis (grade 1B).
Effective empirical antibiotics

Impact of adequate empirical antibiotic therapy on the outcome of patients admitted to the intensive care unit with sepsis*

Crit Care Med 2003;31:2742–2751

Jose Garnacho-Montero, MD, PhD; Jose Luis Garcia-Garmendia, MD, PhD; Ana Barrero-Almodovar, MD;

Risks:
- Mortality
- Morbidity
- Length of hospital stay
- Resistance selection
- Cost burden
Early antibiotic treatment

Median time to effective antimicrobial therapy was 6 hrs

Mortality Risk with Increasing Delays in Initiation of Effective Antimicrobial Therapy

Septic shock secondary to *Candidemia*: importance of empiric therapy and source control

- 224 patients with septic shock and candidemia
- Multivariate logistic regression analysis showed as independently associated with hospital mortality
  - delayed antifungal therapy
    (AOR, 33.75; 95% CI, 9.65 – 118.04; p = 0.005)
  - failure to achieve timely source control
    (AOR, 77.40; 95% CI, 21.52 – 278.38; p = 0.001)

*Kollef MH. Clin Infect Dis 2012; 54:1739-46*
Objective: To analyze the impact on hospital mortality of severe sepsis treatments included in the SSC guidelines in a prospective multicenter observational study (n= 2,796 adult patients with severe sepsis in 77 Spanish ICUs).

Method: The effectiveness of each sepsis treatment was estimated by using PS.

AJRCCM 2009;180:861–866.
Propensity Score. **Antibiotics.**
Effectiveness of APC in MOF
Final Model: All risk factors + Other TTM + PS

2,796 patients with severe sepsis or septic shock

Broad spectrum AB:
- 0-1 Hour
- 1-3 Hour
- 3-6 Hour
- Previous AB
- No AB first 6H

Fluid challenge:
Fluid challenge, only severe sepsis

Steroids in septic shock

APC in MOF

Ferrer R et al. AJRCCM 2009;180:861–866
Empiric Antibiotic Treatment Reduces Mortality in Severe Sepsis and Septic Shock From the First Hour: Results From a Guideline-Based Performance Improvement Program

Severe Sepsis and Septic Shock

Surviving Sepsis campaign database
N = 28,150

N = 19,279

N = 18,447

N = 17,990

Empirical antibiotics after sepsis recognition

Remove patients with previous antibiotic administration prior to suspected severe sepsis N = 8,871

Remove patients who received antibiotic, but missing antibiotic timing N = 832

Remove patients with no antibiotic administration N = 457

CCM 2014;42:1749-55
Predicted hospital mortality and 95% CIs for time to first antibiotic administration

Results adjusted by the sepsis severity score, ICU admission source ([ED], ward, vs ICU), and geographic region (Europe, United States, and South America)
TABLE 1. Patient Characteristics by Timing in Hours to the First Antibiotic

<table>
<thead>
<tr>
<th>Patient Characteristic, ( n (%) )</th>
<th>0.0–1.0</th>
<th>1.0–2.0</th>
<th>2.0–3.0</th>
<th>3.0–4.0</th>
<th>4.0–5.0</th>
<th>5.0–6.0</th>
<th>&gt; 6.0</th>
<th>( p^a )</th>
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<tbody>
<tr>
<td>( n )</td>
<td>4,728</td>
<td>4,595</td>
<td>3,020</td>
<td>1,734</td>
<td>1,037</td>
<td>640</td>
<td>2,239</td>
<td></td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>1,512 (32.0)</td>
<td>1,292 (28.1)</td>
<td>863 (28.6)</td>
<td>517 (29.8)</td>
<td>337 (32.5)</td>
<td>234 (36.6)</td>
<td>885 (39.6)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Severity sepsis score, median (IQR)</td>
<td>58 (42–73)</td>
<td>50 (36–66)</td>
<td>49 (35–64)</td>
<td>49 (35–66)</td>
<td>51 (37–68)</td>
<td>53 (38–69)</td>
<td>57 (40–71)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Nosocomial infection</td>
<td>812 (17.2)</td>
<td>357 (7.8)</td>
<td>229 (7.8)</td>
<td>173 (10.0)</td>
<td>128 (12.3)</td>
<td>89 (13.9)</td>
<td>403 (18.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Septic shock</td>
<td>3,289 (69.6)</td>
<td>2,880 (62.7)</td>
<td>1,847 (61.2)</td>
<td>1,047 (60.4)</td>
<td>684 (66.0)</td>
<td>441 (68.9)</td>
<td>1,370 (61.3)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Hospital LOS, median days (IQR)</td>
<td>13 (6.4–25)</td>
<td>10 (5.6–19)</td>
<td>10.0 (5.6–19)</td>
<td>11 (5.9–20)</td>
<td>12 (5.9–23)</td>
<td>12 (6.3–22)</td>
<td>14 (7.3–29)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ICU LOS, median days (IQR)</td>
<td>5.1 (2.4–11)</td>
<td>4.1 (2.1–8.9)</td>
<td>4.2 (2.1–8.8)</td>
<td>4.3 (2.0–9.5)</td>
<td>4.0 (2.4–11)</td>
<td>4.6 (2.1–10)</td>
<td>6.7 (2.8–15)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LOS prior to ICU, median days (IQR)</td>
<td>0.1 (0.0–0.8)</td>
<td>0.1 (0.0–0.3)</td>
<td>0.1 (0.0–0.3)</td>
<td>0.1 (0.0–0.4)</td>
<td>0.2 (0.0–0.5)</td>
<td>0.2 (0.0–0.7)</td>
<td>0.2 (0.0–1.4)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Median time to empiric antibiotics

26.3%  51.8%  68.6%  78.2%  84.0%  87.5%  100%
Adequate empirical antibiotics en less than 1H

Not so easy!
Selection of Antibiotics in Sepsis

Antibiotic

- Sensibility
- Resistance

Pathogen

- Pharmacology
- Toxicity

Host

Infection

Immunity
Selection of Antibiotics in Sepsis

**Pathogen**
Source
Recognition of the Source of Infection

- Lungs
- Bilis
- Abdomen
- Skin and soft tissue
- Urinary Tract
- Meningitis
- Endovascular Catheters
# Selection of Antibiotics in Sepsis

**Pathogen**

Source

Setting: Community vs Nosocomial.
Setting and Adequate empiric antibiotics

RISK OF RESISTANCE

ICU

HOSPITAL

HEALTHCARE

COMMUNITY

RISK OF INAPPROPRIATE TREATMENT
HCAI: Risk factors

- Received intravenous therapy at home; received wound care or specialized nursing care.
- Attended a hemodialysis clinic or received intravenous chemotherapy in the 30 days before the infection.
- Was hospitalized in an acute care hospital for 2 or more days in the 90 days before the infection.
- Resided in a nursing home or long-term care facility.

[Health Care–Associated Bloodstream Infections in Adults: A Reason To Change the Accepted Definition of Community-Acquired Infections]

N. Deborah Friedman, MBBS; Keith S. Kaye, MD, MPH; Jason E. Stout, MD, MHS; Sarah A. McGarry, MD; Sharon L. Trivette, RN; Jane P. Briggs, RN; Wanda Lamm, RN; Connie Clark, RN; Jennifer MacFarquhar, RN; Aaron L. Walton, MD; I. Barth Reller, MD; and Daniel J. Sexton, MD
Selection of Antibiotics in Sepsis

**Pathogen**
Source
Setting: Community vs Nosocomial.
Biofilms
Local susceptibility patterns.
Outbreak?
Clinical syndrome:
  Shock
Initial microbiological information
## Selection of Antibiotics in Sepsis

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Host</th>
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</thead>
<tbody>
<tr>
<td>Source</td>
<td>Drug intolerances</td>
</tr>
<tr>
<td>Setting: Community vs Nosocomial.</td>
<td>Previous colonization or infection.</td>
</tr>
<tr>
<td>Biofilms</td>
<td>Recent antibiotics</td>
</tr>
<tr>
<td>Local susceptibility patterns.</td>
<td>Comorbidities</td>
</tr>
<tr>
<td>Outbreak?</td>
<td>Immune Status</td>
</tr>
<tr>
<td>Clinical syndrome: Shock</td>
<td></td>
</tr>
<tr>
<td>Initial microbiological information</td>
<td></td>
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</table>
# Selection of Antibiotics in Sepsis

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Host</th>
<th>Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>Drug intolerances</td>
<td>Broad spectrum</td>
</tr>
<tr>
<td>Setting: Community vs Nosocomial.</td>
<td>Previous colonization or infection.</td>
<td></td>
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<tr>
<td>Biofilms</td>
<td>Recent antibiotics</td>
<td></td>
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<tr>
<td>Local susceptibility patterns.</td>
<td>Comorbidities</td>
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<tr>
<td>Outbreak?</td>
<td>Immune Status</td>
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<tr>
<td>Clinical syndrome:</td>
<td></td>
<td></td>
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<tr>
<td>Shock</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial microbiological information</td>
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</tbody>
</table>
### Broad-/extended-spectrum antimicrobials available for monotherapy

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Gram-negative</th>
<th>Gram-positive</th>
<th>Resistant Gram-negative</th>
<th>Resistant Gram-positive</th>
<th>Anaerobe</th>
<th><em>P. aeruginosa</em></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>![No Proteus]</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Carbapenems</td>
<td>![In vitro activity]</td>
<td>![In vitro activity]</td>
<td>![Varies by product within class]</td>
<td>![Varies by product within class]</td>
<td>![In vitro activity]</td>
<td>![Varies by product within class]</td>
</tr>
<tr>
<td>Quinolones</td>
<td>![In vitro activity]</td>
<td>![In vitro activity]</td>
<td>![Varies by product within class]</td>
<td>![Varies by product within class]</td>
<td>![In vitro activity]</td>
<td>![Varies by product within class]</td>
</tr>
</tbody>
</table>

*In vitro* activity does not necessarily correlate with clinical efficacy.
## Selection of Antibiotics in Sepsis

<table>
<thead>
<tr>
<th><strong>Pathogen</strong></th>
<th><strong>Host</strong></th>
<th><strong>Antibiotic</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Source</strong></td>
<td>Drug intolerances</td>
<td>Broad spectrum</td>
</tr>
<tr>
<td>Setting: Community vs Nosocomial.</td>
<td>Previous colonization or infection.</td>
<td>Bactericidal Activity</td>
</tr>
<tr>
<td>Biofilms</td>
<td>Recent antibiotics</td>
<td>Post-Antibiotic effect</td>
</tr>
<tr>
<td>Local susceptibility patterns.</td>
<td>Comorbidities</td>
<td>PK/PD. Tissue penetration</td>
</tr>
<tr>
<td>Outbreak?</td>
<td>Immune Status</td>
<td>Elimination by CRRT</td>
</tr>
<tr>
<td>Clinical syndrome:</td>
<td>Shock</td>
<td></td>
</tr>
<tr>
<td>Initial microbiological information</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Antifungals and CRRT

Treatment with echinocandins during continuous renal replacement therapy

González de Molina et al. Critical Care 2014, 18:218
http://ccforum.com/content/18/2/218

Francisco Javier González de Molina*, Maria de Los Ángeles Martínez-Alberici and Ricard Ferrer

- Fluconazol is removed by hemofiltration.
- All equinocandins are NOT removed by hemofiltration but can be adsorbed to filters.
- High dose of Fluconazol (800 mg/d).
- The removal of echinocandins by adsorption to the synthetic surfaces of hemofilters is unlikely to have clinical relevance. Same dose.
## Selection of Antibiotics in Sepsis

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Host</th>
<th>Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
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</tr>
<tr>
<td>Local susceptibility patterns.</td>
<td>Comorbidities</td>
<td>PK/PD. Tissue penetration</td>
</tr>
<tr>
<td>Outbreak?</td>
<td>Immune Status</td>
<td>Elimination by CRRT</td>
</tr>
<tr>
<td>Clinical syndrome: Shock</td>
<td></td>
<td>Toxicity</td>
</tr>
<tr>
<td>Initial microbiological information</td>
<td></td>
<td>Availability</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cost</td>
</tr>
</tbody>
</table>
Antibiotic Combination Therapy

Antibiotic prescription patterns in the empiric therapy of severe sepsis: combination of antimicrobials with different mechanisms of action reduces mortality.

Ana Díaz-Martin¹,²,³*, María Luisa Martinez-González⁴, Ricard Ferrer⁵,⁶, Carlos Ortiz-Leyba¹,²,³, Enrique Piacentini⁵, María Jesus Lopez-Pueyo⁷, Ignacio Martín-Loeches⁵,⁶, Mitchell M Levy⁸, Antoni Artigas⁴,⁶, José Garnacho-Montero¹,²,³ and for the Edusepsis Study Group

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Non-DCCT group n = 984 (71.7%)</th>
<th>DCCT group n = 388 (28.3%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-Lactams</td>
<td>582 (59.1%)</td>
<td>320 (82.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>269 (27.3%)</td>
<td>76 (19.6%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Quinolones</td>
<td>96 (9.8%)</td>
<td>186 (47.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>25 (2.5%)</td>
<td>158 (40.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Macrolides</td>
<td>7 (0.7%)</td>
<td>53 (13.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anti-gram-positive</td>
<td>120 (12.2%)</td>
<td>41 (10.6%)</td>
<td>0.456</td>
</tr>
<tr>
<td>Antifungals</td>
<td>21 (2.1%)</td>
<td>17 (4.4%)</td>
<td>0.028</td>
</tr>
<tr>
<td>Others</td>
<td>121 (12.3%)</td>
<td>30 (7.7%)</td>
<td>0.016</td>
</tr>
<tr>
<td>Factors</td>
<td>OR</td>
<td>CI (95%)</td>
<td>P</td>
</tr>
<tr>
<td>------------------------------</td>
<td>------</td>
<td>-------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.023</td>
<td>(1.014-1.032)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>1.350</td>
<td>(1.041-1.750)</td>
<td>0.024</td>
</tr>
<tr>
<td>APACHE II</td>
<td>1.099</td>
<td>(1.099-1.141)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Community-acquired</td>
<td>1.487</td>
<td>(1.119-1.974)</td>
<td>0.006</td>
</tr>
<tr>
<td>DCCT</td>
<td>0.699</td>
<td>(0.522-0.936)</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Focus of infection

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>CI (95%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>0.784</td>
<td>(0.358-1.718)</td>
<td>0.543</td>
</tr>
<tr>
<td>Abdominal</td>
<td>0.595</td>
<td>(0.269-1.317)</td>
<td>0.200</td>
</tr>
<tr>
<td>Urologic</td>
<td>0.241</td>
<td>(0.102-0.569)</td>
<td>0.001</td>
</tr>
<tr>
<td>Meningitis</td>
<td>0.357</td>
<td>(0.122-1.046)</td>
<td>0.060</td>
</tr>
<tr>
<td>Skin and soft-tissue</td>
<td>0.424</td>
<td>(0.157-1.141)</td>
<td>0.089</td>
</tr>
<tr>
<td>Catheter</td>
<td>0.441</td>
<td>(0.135-1.445)</td>
<td>0.177</td>
</tr>
<tr>
<td>Others</td>
<td>0.772</td>
<td>(0.330-1.806)</td>
<td>0.551</td>
</tr>
<tr>
<td>More than one focus</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Outline

• Epidemiology of Sepsis.
• Time-to-treatment in Sepsis.
• Interventions. Sepsis Code.
ABISS Edusepsis Study
Antibiotic Intervention in Severe Sepsis
Objectives

• Efficacy:
  – Reduce time to empiric antibiotic in severe sepsis.
  – Increase appropriateness of antibiotic treatment
  – Reduce hospital mortality.

• Safety:
  – Increase antibiotic deescalation.

By a multifaceted quality-improvement intervention in patients with severe sepsis/septic shock admitted to the Spanish ICUs.
Gamification

EN SEPSIS, TU VELOCIDAD ES VIDA ACTÚA RÁPIDO

PRACTICA CÓMO TRATAR LA SEPSIS EN NUESTRA WEB

edusepsis.org/formacion
Results

• 72 hospitals in Spain.
• 2576 patients: PRE 1,325, POST: 1,251
• Age 64.1 ± 15.1 years, 54.1% male.
• CHARLSON 2.7 ± 2.2
• Septic Shock 67.6%, 32.4% severe sepsis.
• Bacteriemia: 33%
• APACHE-II 22 ± 8.
• SOFA 9 ± 3
• PCT 25 ± 35
Results: Antibiotics

- Time to ABX: $p < 0.001$
- Time to Adequate ABX: $p = 0.020$
Results

- Inadequate ABX: p = 0.002
- De-escalate 72h: p = 0.001
Results

$p = 0.422$

$p = 0.182$

Mortality

Mortality, adequate ABX
# Time-dependent Diseases

<table>
<thead>
<tr>
<th></th>
<th>AMI</th>
<th>STROKE</th>
<th>TRAUMA</th>
<th>SEPSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Recognition</strong></td>
<td>Easy</td>
<td>Easy</td>
<td>Easy</td>
<td>Complex</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>Homogeneous</td>
<td>Homogeneous</td>
<td>Heterogeneous</td>
<td>Heterogeneous</td>
</tr>
<tr>
<td><strong>Biomarker</strong></td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td>YES/NO</td>
</tr>
<tr>
<td><strong>Complex Treatment Algorithms</strong></td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Multidisciplinary Approach</strong></td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Well established guidelines</strong></td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td><strong>Code</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>+/-</td>
</tr>
</tbody>
</table>
Other Strategies

• Sepsis Code: The health care system is organized to provide early treatment in all the area.

• Sepsis Unit, sepsis team: Hospitals are organized to warrant early delivery of treatments.

• Prescription support. Local guidelines.

• Innovation in the microbiology lab: early and precise information.
Ordenación Atención de la Sepsis 
Comunidad Autónoma

• Agentes implicados:
  – Primaria
  – Transporte
  – Hospitales

• Niveles asistenciales y requisitos: Quien pude hacer que.

• Sectorización: Donde

• Evaluación: Registro e Indicadores
<table>
<thead>
<tr>
<th>A</th>
<th>Anamnesi</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Breathing</td>
</tr>
<tr>
<td>C</td>
<td>Circulació</td>
</tr>
<tr>
<td>D</td>
<td>Discapacitat</td>
</tr>
<tr>
<td>EL</td>
<td>Elevació analítica</td>
</tr>
</tbody>
</table>

**Síndrome febril compatible amb infecció**

- FR > 24x'
- Sat art O2 < 90%
- FC > 110x'
- Maixa Perfusió Cutània
- TAS < 90
- TAM < 65
- Afectació Estat General
- Disminució nivell consciència
- Meningisme
- Hiperxicèmia no explicada
- Lactat > 2

**Infecció sense criteris de sepsia greu**

**Valoració mèdica**

**SEPSIA GREU**

**Activació CODI**

Diagrama de conceptes relacionats amb la sepsia i la sepsia greu, inclouent anamnesi, síndrome febril compatible amb infecció, breathing, circulation, disability, elevació analítica, inflamació sense criteris de sepsia greu, valoració mèdica i activació CODI.
Atención de la Sepsis en los Hospitales

- Early detection
- Rapid response teams
- Audit: Quality indicators
- Quality improvement interventions

Kumar A et al. 
Current Opinion in Critical Care 2009, 15:301–307
### Septic Shock

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Historical Group, $n = 96$ (20%)</th>
<th>Intervention Group, $n = 384$ (80%)</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>$62.2 \pm 16.3$</td>
<td>$64.5 \pm 15.1$</td>
<td>.328</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>$55$ (57.3)</td>
<td>$255$ (66.4)</td>
<td>.097</td>
</tr>
<tr>
<td>Sequential Organ Failure Assessment score</td>
<td>$10.2 \pm 3.2$</td>
<td>$9.4 \pm 3.2$</td>
<td>.036</td>
</tr>
<tr>
<td>Acute Physiology and Chronic Health Evaluation II score</td>
<td>$24.6 \pm 7.8$</td>
<td>$23.2 \pm 7.3$</td>
<td>.136</td>
</tr>
<tr>
<td>Mechanical ventilation, n (%)</td>
<td>$83$ (86.4)</td>
<td>$254$ (66.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Central venous oxygen saturation (%) at ICU admission</td>
<td>$67.1 \pm 13.8$</td>
<td>$68.3 \pm 13.7$</td>
<td>.410</td>
</tr>
<tr>
<td>Location before ICU admission, n (%)</td>
<td></td>
<td></td>
<td>.007</td>
</tr>
<tr>
<td>Emergency department</td>
<td>$19$ (19.8)</td>
<td>$126$ (32.8)</td>
<td></td>
</tr>
<tr>
<td>Medical ward</td>
<td>$32$ (33.3)</td>
<td>$76$ (19.8)</td>
<td></td>
</tr>
<tr>
<td>Surgery department</td>
<td>$26$ (27.1)</td>
<td>$123$ (32.0)</td>
<td></td>
</tr>
<tr>
<td>Another hospital</td>
<td>$19$ (19.8)</td>
<td>$59$ (15.4)</td>
<td></td>
</tr>
<tr>
<td>Source of infection, n (%)</td>
<td></td>
<td></td>
<td>.850</td>
</tr>
<tr>
<td>Intra-abdominal infection</td>
<td>$28$ (29.2)</td>
<td>$134$ (35.3)</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>$42$ (43.8)</td>
<td>$136$ (35.8)</td>
<td></td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>$8$ (8.3)</td>
<td>$45$ (11.8)</td>
<td></td>
</tr>
<tr>
<td>Skin/soft tissue infection</td>
<td>$5$ (5.2)</td>
<td>$15$ (4.0)</td>
<td></td>
</tr>
<tr>
<td>Other infections</td>
<td>$7$ (7.3)</td>
<td>$25$ (6.5)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>$6$ (6.2)</td>
<td>$25$ (6.5)</td>
<td></td>
</tr>
<tr>
<td>Hospital mortality, n (%)</td>
<td>$55$ (57.3)</td>
<td>$144$ (37.5)</td>
<td>.001</td>
</tr>
</tbody>
</table>
Septic shock: A multidisciplinary response team and weekly feedback to clinicians improve the process of care and mortality

Garrett E. Schramm, PharmD; Rahul Kashyap, MBBS; John J. Mullen, MD; Ognjen Gajic, MD; Bekele Afessa, MD

Crit Care Med 2011; 39:252–258

The sepsis response team members

<table>
<thead>
<tr>
<th>Multidisciplinary Member</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU attending physician</td>
<td>24/7 bedside supervision of the ICU team in implementing the sepsis protocol, acts as team leader, allocating tasks to individual team members, supervises ICU residents during the resuscitation, including placement of central venous catheter and implementation of the sepsis protocol.</td>
</tr>
<tr>
<td>ICU fellow</td>
<td>Identifies patients who meet criteria for sepsis protocol, responsible for the primary management of the patient in the ICU, including placement of central venous catheter and the implementation of the sepsis protocol.</td>
</tr>
<tr>
<td>ICU resident</td>
<td>Identifies patients who meet criteria for sepsis protocol, responsible for the primary management of the patient in the ICU, including placement of central venous catheter and the implementation of the sepsis protocol.</td>
</tr>
<tr>
<td>ICU nurse</td>
<td>Identifies patients who meet criteria for sepsis protocol, implements the sepsis protocol following the computerized physician standing orders, including fluid boluses triggered by central venous pressure measurement.</td>
</tr>
<tr>
<td>ICU pharmacist</td>
<td>Identifies patients who meet criteria for sepsis protocol, responsible for timely order processing and administration of antibiotics, vasopressors, and inotropes.</td>
</tr>
<tr>
<td>Respiratory therapist</td>
<td>Assists in central venous catheter placement and calibration, arterial line placement and calibration, assists in the management of mechanical ventilation.</td>
</tr>
<tr>
<td>Vascular access technician</td>
<td>Timely bedside blood lactate measurements and drawing blood samples as ordered.</td>
</tr>
<tr>
<td>Unit secretary</td>
<td>Aids in activation of sepsis response team paging system, notifies portable radiology technician if needed.</td>
</tr>
<tr>
<td>Portable radiology technician</td>
<td>Immediate chest radiograph performed when needed.</td>
</tr>
</tbody>
</table>

Elements of the sepsis resuscitation bundle

<table>
<thead>
<tr>
<th>Element</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate</td>
<td>Measured before or within 1 hr after blood culture.</td>
</tr>
<tr>
<td>Blood culture</td>
<td>Drawn before antibiotics administered.</td>
</tr>
<tr>
<td>Antibiotic</td>
<td>Administered within 1 hr of sepsis recognition and intensive care unit admission.</td>
</tr>
<tr>
<td>Fluid resuscitation</td>
<td>In the event of hypotension and/or lactate ≥4 mmol/L, an initial bolus of 20 mL/kg (crystalloid or equivalent colloid) administered followed by subsequent fluid challenges until one of the following: Central venous pressure ≥8 mm Hg (≥12 mm Hg if mechanical ventilation). Mean arterial pressure ≥65 mm Hg without vaspressors and lactate &lt;2.5 mmol/L and urine output &gt;0.5 ml/kg/hr.</td>
</tr>
<tr>
<td>Appropriate vasopressor use</td>
<td>Vasopressor administered for one of the following two: Persistent MAP &lt;65 mm Hg despite fluid challenge 20 mL/kg of crystalloid. Life-threatening hypotension with MAP &lt;50 mm Hg for ≥15 mins. Vasopressor not administered when one of the two not met.</td>
</tr>
<tr>
<td>Red blood cell administration</td>
<td>Transfused if hematocrit &lt;30% and ScvO2 &lt;70% or mixed venous O2 &lt;65% despite fluid resuscitation.</td>
</tr>
<tr>
<td>Inotrope utilization</td>
<td>Started if Hct ≥30% and ScvO2 &lt;70% or mixed venous oxygen saturation &lt;65% despite fluid resuscitation.</td>
</tr>
</tbody>
</table>
### Compliance with sepsis bundles

<table>
<thead>
<tr>
<th>Bundle Element</th>
<th>Baseline (n = 268)</th>
<th>Weekly Feedback (n = 284)</th>
<th>Sepsis Response Team Activation (n = 432)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate measured</td>
<td>202 (75.4%)</td>
<td>259 (91.2%)</td>
<td>419 (97.0%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Blood culture before antibiotics</td>
<td>235 (87.7%)</td>
<td>264 (93.0%)</td>
<td>422 (97.7%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Timely antibiotics</td>
<td>207 (77.2%)</td>
<td>238 (83.8%)</td>
<td>393 (91.0%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Adequate fluid</td>
<td>153 (57.1%)</td>
<td>182 (64.1%)</td>
<td>329 (76.2%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Appropriate vasopressor</td>
<td>264 (93.0%)</td>
<td>252 (94.0%)</td>
<td>385 (89.1%)</td>
<td>.046</td>
</tr>
<tr>
<td>Appropriate red blood cell transfusion</td>
<td>221 (82.5%)</td>
<td>245 (86.3%)</td>
<td>370 (85.6%)</td>
<td>.397</td>
</tr>
<tr>
<td>Appropriate inotrope use</td>
<td>96 (35.8%)</td>
<td>158 (55.6%)</td>
<td>266 (61.6%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>All 7 elements</td>
<td>24 (12.7%)</td>
<td>107 (37.7%)</td>
<td>232 (53.7%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mortality</td>
<td>81 (30.3%)</td>
<td>78 (28.7%)</td>
<td>93 (22.0%)</td>
<td>.029</td>
</tr>
</tbody>
</table>

### Independent predictors of mortality

<table>
<thead>
<tr>
<th>Predictor Variable</th>
<th>Odds Ratio (95% Confidence Interval)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>1.329 (0.983–1.796)</td>
<td>.065</td>
</tr>
<tr>
<td>Acute Physiology and Chronic Health</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evaluation comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Hepatic cirrhosis</td>
<td>3.313 (1.509–7.275)</td>
<td>.003</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>3.113 (1.598–6.066)</td>
<td>.001</td>
</tr>
<tr>
<td>Leukemia or multiple myeloma</td>
<td>1.677 (1.079–2.608)</td>
<td>.022</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1.486 (0.441–5.006)</td>
<td>.523</td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>6.872 (0.556–84.961)</td>
<td>.133</td>
</tr>
<tr>
<td>Metastatic tumor</td>
<td>1.097 (0.564–2.134)</td>
<td>.784</td>
</tr>
<tr>
<td>Intensive care unit admission source</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Same hospital emergency department</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Same hospital ward</td>
<td>2.088 (1.476–2.953)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Other hospital emergency department</td>
<td>1.050 (0.666–1.654)</td>
<td>.835</td>
</tr>
<tr>
<td>Other hospital ward</td>
<td>1.241 (0.705–2.187)</td>
<td>.455</td>
</tr>
<tr>
<td>Do not resuscitate at recognition of severe sepsis or septic shock</td>
<td>1.492 (1.011–2.202)</td>
<td>.044</td>
</tr>
<tr>
<td>Lactate level</td>
<td>1.076 (1.012–1.144)</td>
<td>.019</td>
</tr>
<tr>
<td>Study period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Weekly feedback</td>
<td>1.013 (0.685–1.497)</td>
<td>.950</td>
</tr>
<tr>
<td>Sepsis response team</td>
<td>0.657 (0.456–0.945)</td>
<td>.023</td>
</tr>
</tbody>
</table>

European expert opinion on the management of invasive candidiasis in adults

**Help for Prescription: Algorithm**

**Factores de riesgo CI**
- Hospitalización >10 d y ± 2 de los siguientes:
  - ATB de amplio espectro
  - Nutrición Parenteral y/o vía central
  - APACHE II >25 puntos
  - Neoplasia
  - Corticoides
  - PAG
  - Vía femoral
  - IR con TRR

**Paciente Médico UCI con Sospecha Infección y sin foco evidente**

**Factores de Riesgo CI**

- SÍ

**Shock o SG**

- NO

**IC >0,4**

- NO

**RTA clínica 72 H**

- SÍ

**Hemocultivos**

- NO

**Técnica NO basada cultivo**

- No disponible

**Positiva**

**Negativa**

**Hemocultivos**

- SÍ

**Inicio Antifúngicos**

**HDFVVC Azoles Previos Riesgo Candida R**

- SÍ

**Fluconazol (Considerar suspensión según Recomendaciones ÉPICO.2)**

**Equinocandina (Considerar suspensión o desescalado según Recomendaciones ÉPICO.2)**

**SÍ**

**No infección fúngica**

**No**

**Estudio Colonización Semanal**

- SÍ

**Desconocida**

**NO**

**RCAT clínica 72 H**

**Hemocultivos**

- Positiva

**No disponible**

**NO**

**Negativa**

**SÍ**

**IC >0,4**

**Hemocultivos Valorar retirar catéteres Muestras Resp, Orina, Heridas**

*Hospitalización >1 mes, colonización Candida R*
Help for Prescription

Clinical Decision Support System

Please evaluate the patient’s condition:

- Hypothermia ≤ 36 °C or Hyperthermia ≥ 38 °C
- Tachycardia ≥ 90/min
- Tachypnoea ≥ 20/min or pCO₂ ≤ 4.3 kPa [32 mmHg]
- Leukocytosis ≥ 12,000/μl or Leukopenia ≤ 4000/μl
- Inflammatory markers, CRP > 0.5 mg/dl or PCT > 0.5 ng/dl or pathological IL-6

Additional signs of acute organ dysfunction due to infection

There are signs of circulatory failure due to infection:

There are additional complicating risk factors:

Please now choose the focus of the suspected or confirmed infection, which is believed to be responsible for the changes in the clinical status of the patient:

- Intravascular catheters
- Lungs
- Endocarditis
- Abdomen
- Pancreas
- Genitourinary system
- Bones & Joints
### Help for Prescription: Local Guidelines

**Catalan Sepsis Code**

<table>
<thead>
<tr>
<th>SOURCE</th>
<th>COMMUNITY</th>
<th>RISK FACTORS FOR MULTIRESISTANT MO INTOLERANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>RESPIRATORY</td>
<td>3rd-Generation cephalosporins + macrolide</td>
<td>Levofloxacin</td>
</tr>
<tr>
<td></td>
<td>3rd-Generation cephalosporins + amikacin + metronidazol</td>
<td>Ertapenem</td>
</tr>
<tr>
<td>ABDOMINAL</td>
<td>3rd-Generation cephalosporins + amikacin</td>
<td>Ertapenem</td>
</tr>
<tr>
<td>UTI</td>
<td>3rd-Generation cephalosporins + amikacin</td>
<td>Ertapenem</td>
</tr>
<tr>
<td>SKIN</td>
<td>Piperacillin tazobactam + clindamycin</td>
<td>Aztreonam + clindamycin</td>
</tr>
<tr>
<td>MENINGITIS</td>
<td>Cefotaxima +/- Vancomycin +/- Ampicillin</td>
<td>Vancomycin +/- aztreonam +/- Cotrimoxazol</td>
</tr>
<tr>
<td>UNKNOWN</td>
<td>meropenem + Vancomycin</td>
<td></td>
</tr>
</tbody>
</table>
Local Antibiotic Guide

CISTITIS NO COMPLICADA:
- Cefuroxima 250mg/12h o Ciprofloxacino 250mg/12h (3-5 d) o Fosfomicina 3g/dosi única.

CISTITIS COMPLICADA:
- Cefuroxima 250mg/12h 7d, Fosfomicina 3g/48h (2 dosis)

PELONEFRITIS AGUDA NO COMPLICADA (10-14d):
- Ceftriaxona 2g IV (dosis inicial) seguit de Cefuroxima 500mg/8h VO o Ceftriaxona 2g/d IM (si intolerància oral) 10-14d

PELONEFRITIS COMPLICADA (14d)/ PROSTATITIS (4 setmanes):
- Amb criteris d'inèntriga sense risc de microorganismes multiresistents o sepsis greu: Ceftriaxona 2g/24h o Cefotaxima 2g/8h IV
- Amb criteris d'inèntriga i amb risc de microorganismes multiresistents o sepsis greu: Piperacilina-tazobactam 4g/8h IV + Amikacina 1g/24h o Imipenem 500mg/6h.

INFECCIÓ DEL TRACTA URINARI EN EL PACIENT SONDAT (7-14d):
- Cefazidima 1g/8h + Amoxicil·lina 1g/6h o Piperacil·lina-tazobactam 4g/6h o Imipenem 500mg/6h IV
- En pacients al·lèrgics a B-lactàmics amb ITU (excepte en tractament ambilitatari): Aztreonam 1g/8h + Vancomicina 1g/12h IV

PNEUMÒNIA NO GREU (FINE 1-2-3, CURB 0-2) (5-7d):
- Clínica típica: Amoxicil·lina 1g/8h o Amoxicil·lina-clavulànic 875/125 mg/8h si MPDC i risc d'infecció per H. influenzae. VO
- Clínica atípica o inespecífica: Levofloxacino 500mg/24h (5d) o Moxiﬂoxacino 400mg/d (5d) Azitromicina 500mg/24h (3d) VO

PNEUMÒNIA GREU (FINE 4-5, CURB 6-5 >2) 7-14d:
- Ceftriaxona 2 g/d + Levoﬂoxacino 500 mg/12h IV (48 h de biteràpia)
Rapid Diagnosis of Bloodstream Infections with PCR Followed by Mass Spectrometry

Elena Jordana-Lluch¹, Heather E. Carolan², Montserrat Giménez¹, Rangarajan Sampath², David J. Ecker², M. Dolores Quesada¹, Josep M. Mòdol³, Fernando Arméstar⁴, Lawrence B. Blyn², Lendell L. Cummins², Vicente Ausina¹,⁵*, Elisa Martró¹,⁶

<table>
<thead>
<tr>
<th>Blood culture gold standard</th>
<th>Clinical infection criterion</th>
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<tr>
<td>Conventional methods</td>
<td>Conventional methods</td>
</tr>
<tr>
<td>----------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Total</td>
<td>Total</td>
</tr>
<tr>
<td>A) PCR/ESI-MS in blood culture</td>
<td>89</td>
</tr>
<tr>
<td>Positive</td>
<td>78</td>
</tr>
<tr>
<td>Negative</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>89</td>
</tr>
<tr>
<td>B) PCR/ESI-MS in whole blood</td>
<td>224</td>
</tr>
<tr>
<td>Positive</td>
<td>37</td>
</tr>
<tr>
<td>Negative</td>
<td>25</td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
</tr>
</tbody>
</table>

Better sensitivity
Better time-to-diagnosis
Take Home Messages

• Incidence of sepsis is increasing.
• Mortality is decreasing.
• Tissue dysoxia is playing an important role in the pathogenesis.
• Early identification is crucial.
Take Home Messages

Sepsis is time dependent: TEMPUS FUGIT
Take Home Messages

Early Treatment based on:

• Correct stratification
• Bundles and guidelines.
• Infection Setting and local resistance pattern.
• Source of infection
• Microbiological information.
Ricard Ferrer
Intensive Care Department
Mutua Terrassa University Hospital
Barcelona. SPAIN