Sobreviviendo a la sepsis
Guías 2013

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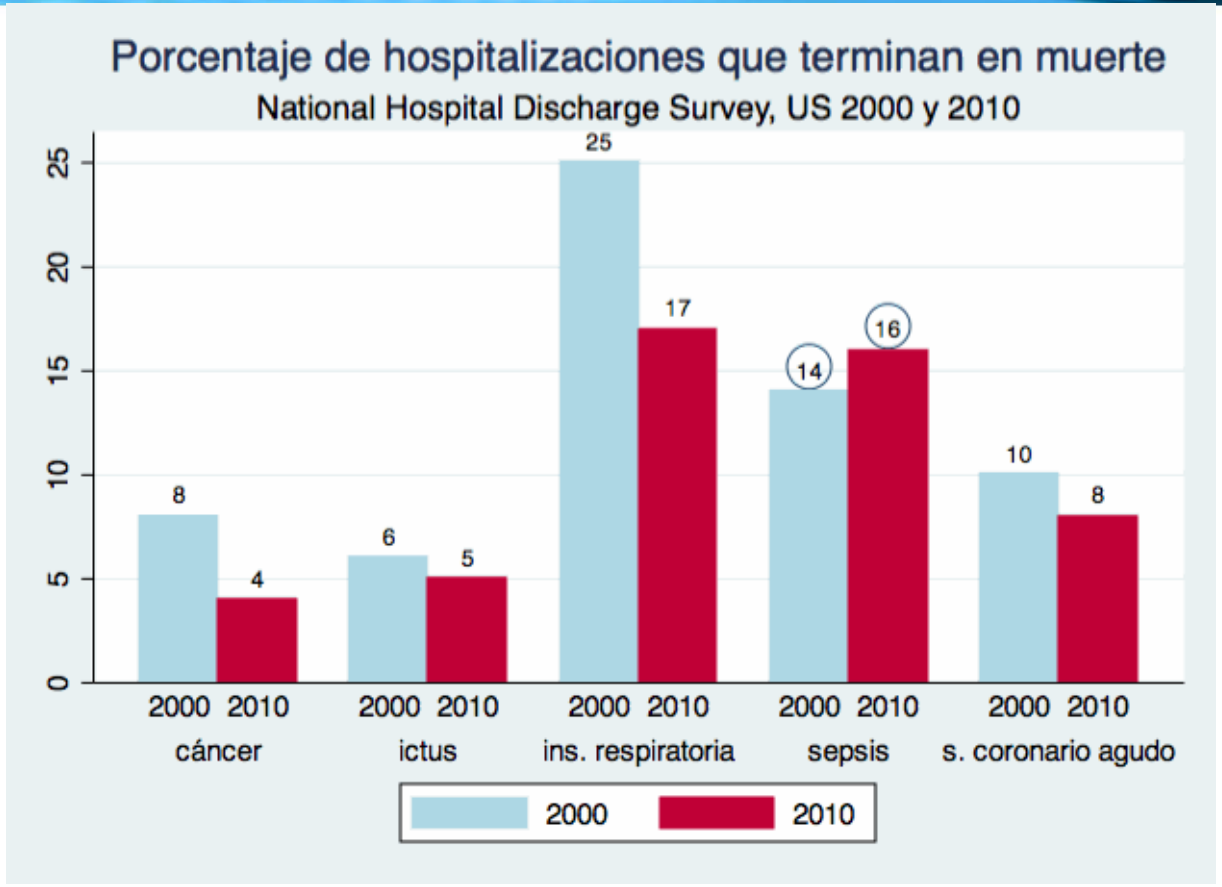
10 de mayo 2013



From the National Center for Health Statistics. Percentage of Hospitalizations Ending in Death, by Selected First-Listed Diagnoses*—National Hospital Discharge Survey, United States, 2000 and 2010. JAMA 2013; 309(1): 26. MMWR 2012; 61(40): 822.

CDC National Hospital Discharge Survey [http://www.cdc.gov/nchs/nhds.htm]

Hall MJ, Williams SN, DeFrances CJ, Golosinskiy A.Inpatient care for septicemia or sepsis: a challenge for patients and hospitals. NCHS data brief 2011; 62): 1-8.

ESTUDIO EPIDEMIOLÓGICO DE SEPSIS SEVERA EN URUGUAY S.U.M.I. 2005

- Prevalencia sepsis severa en UCI: 8.8%
- Shock séptico en 31% de las sepsis severas
- Mortalidad en UCI: 55%

Seguimiento de egresados vivos de UCI (la mitad de los estudiados):

- Fallecidos al alta hospitalaria: 20%
- Fallecidos al año: 11%

TABLE 1. Diagnostic Criteria for Sepsis

Infection, documented or suspected, and some of the following:
General variables
Fever (> 38.3°C)
Hypothermia (core temperature < 36°C)
Heart rate > 90/min^{-1} or more than two SD above the normal value for age
Tachypnea
Altered mental status
Significant edema or positive fluid balance (> 20 mL/kg over 24 hr)
Hyperglycemia (plasma glucose > 140 mg/dL or 7.7 mmol/L) in the absence of diabetes

Levy MM, Fink MP, Marshall JC, et al: 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med 2003; 31:* 1250–1256.

Inflammatory variables

- Leukocytosis (WBC count > 12,000 μL^{-1})
- Leukopenia (WBC count < 4000 μL^{-1})
- Normal WBC count with greater than 10% immature forms
- Plasma C-reactive protein more than two SD above the normal value
- Plasma procalcitonin more than two SD above the normal value

Hemodynamic variables

- Arterial hypotension (SBP < 90 mm Hg, MAP < 70 mm Hg, or an SBP decrease > 40 mm Hg in adults or less than two SD below normal for age)

Organ dysfunction variables

- Arterial hypoxemia ($Pao_2/FIO_2 < 300$)
- Acute oliguria (urine output < 0.5 mL/kg/hr for at least 2 hrs despite adequate fluid resuscitation)
- Creatinine increase > 0.5 mg/dL or 44.2 µmol/L
- Coagulation abnormalities (INR > 1.5 or aPTT > 60 s)
- Ileus (absent bowel sounds)
- Thrombocytopenia (platelet count < 100,000 μL^{-1})
- Hyperbilirubinemia (plasma total bilirubin > 4 mg/dL or 70 µmol/L)

Tissue perfusion variables

- Hyperlactatemia (> 1 mmol/L)
- Decreased capillary refill or mottling

TABLE 2. Severe Sepsis

Severe sepsis definition = sepsis-induced tissue hypoperfusion or organ dysfunction (any of the following thought to be due to the infection)
Sepsis-induced hypotension
Lactate above upper limits laboratory normal
Urine output < 0.5 mL/kg/hr for more than 2 hrs despite adequate fluid resuscitation
Acute lung injury with Pao_2/Fio_2 < 250 in the absence of pneumonia as infection source
Acute lung injury with Pao_2/Fio_2 < 200 in the presence of pneumonia as infection source
Creatinine > 2.0 mg/dL (176.8 μmol/L)
Bilirubin > 2 mg/dL (34.2 μmol/L)
Platelet count < 100,000 μL
Coagulopathy (international normalized ratio > 1.5)

Levy MM, Fink MP, Marshall JC, et al: 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med 2003; 31:* 1250–1256.

Special Articles

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4]; Herwig Gerlach, MD, PhD[5]; Steven M. Opal, MD[6]; Jonathan E. Sevransky, MD[7]; Charles L. Sprung, MD[8]; Ivor S. Douglas, MD[9]; Roman Jaeschke, MD[10]; Tiffany M. Osborn, MD, MPH[11]; Mark E. Nunnally, MD[12]; Sean R. Townsend, MD[13]; Konrad Reinhart, MD[14]; Ruth M. Kleinpell, PhD, RN-CS[15]; Derek C. Angus, MD, MPH[16]; Clifford S. Deutschman, MD, MS[17]; Flavia R. Machado, MD, PhD[18]; Gordon D. Rubenfeld, MD[19]; Steven A. Webb, MB BS, PhD[20]; Richard J. Beale, MB BS[21]; Jean-Louis Vincent, MD, PhD[22]; Rui Moreno, MD, PhD[23]; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

Surviving Sepsis Campaign - International Guidelines for Management of Severe Sepsis and Septic Shock. Crit Care Med 2013; 41(2): 580-637

- Comité de consenso de 68 expertos en representaciónde 30 organizaciones
- Política de confilicto de intereses
- No financiación de la industria (Eli Lilly de Brasil???)
- Reuniones presenciales y teleconferencias
- Principios del sistema GRADE para evaluar la calidad de la evidencia (A – D) y la fortaleza de las recomendaciones (1 o 2)
- 3 grupos de recomendaciones:
- 1) directa relación con la sepsis severa, 2) relación con los cuidados generales y consideradas de alta prioridad en la sepsis; 3) pediátricas.

TABLE 3. Determination of the Quality of Evidence

Underlying methodology

- A (high) RCTs
- B (moderate) Downgraded RCTs or upgraded observational studies
- C (low) Well-done observational studies with control RCTs
- D (very low) Downgraded controlled studies or expert opinion based on other evidence

Factors that may decrease the strength of evidence

1. Poor quality of planning and implementation of available RCTs, suggesting high likelihood of bias
2. Inconsistency of results, including problems with subgroup analyses
3. Indirectness of evidence (differing population, intervention, control, outcomes, comparison)
4. Imprecision of results
5. High likelihood of reporting bias

Main factors that may increase the strength of evidence

1. Large magnitude of effect (direct evidence, relative risk > 2 with no plausible confounders)
2. Very large magnitude of effect with relative risk > 5 and no threats to validity (by two levels)
3. Dose-response gradient

TABLE 4. Factors Determining Strong vs. Weak Recommendation

What Should be Considered	Recommended Process
High or moderate evidence (*Is there high or moderate quality evidence?*)	The higher the quality of evidence, the more likely a strong recommendation.
Certainty about the balance of benefits vs. harms and burdens (*Is there certainty?*)	The larger the difference between the desirable and undesirable consequences and the certainty around that difference, the more likely a strong recommendation. The smaller the net benefit and the lower the certainty for that benefit, the more likely a weak recommendation.
Certainty in or similar values (*Is there certainty or similarity?*)	The more certainty or similarity in values and preferences, the more likely a strong recommendation.
Resource implications (*Are resources worth expected benefits?*)	The lower the cost of an intervention compared to the alternative and other costs related to the decision–ie, fewer resources consumed–the more likely a strong recommendation.

TABLE 5. Recommendations: Initial Resuscitation and Infection Issues

A. Initial Resuscitation

1. Protocolized, quantitative resuscitation of patients with sepsis- induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood lactate concentration ≥ 4 mmol/L). Goals during the first 6 hrs of resuscitation:
   a) Central venous pressure 8–12 mm Hg
   b) Mean arterial pressure (MAP) ≥ 65 mm Hg
   c) Urine output ≥ 0.5 mL/kg/hr
   d) Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively (grade 1C).
2. In patients with elevated lactate levels targeting resuscitation to normalize lactate (grade 2C).

B. Screening for Sepsis and Performance Improvement

1. Routine screening of potentially infected seriously ill patients for severe sepsis to allow earlier implementation of therapy (grade 1C).
2. Hospital–based performance improvement efforts in severe sepsis (UG).

C. Diagnosis

1. Cultures as clinically appropriate before antimicrobial therapy if no significant delay (> 45 mins) in the start of antimicrobial(s) (grade 1C). At least 2 sets of blood cultures (both aerobic and anaerobic bottles) be obtained before antimicrobial therapy with at least 1 drawn percutaneously and 1 drawn through each vascular access device, unless the device was recently (<48 hrs) inserted (grade 1C).
2. Use of the 1,3 beta-D-glucan assay (grade 2B), mannan and anti-mannan antibody assays (2C), if available and invasive candidiasis is in differential diagnosis of cause of infection.
3. Imaging studies performed promptly to confirm a potential source of infection (UG).

D. Antimicrobial Therapy

1. Administration of effective intravenous antimicrobials within the first hour of recognition of septic shock (grade 1B) and severe sepsis without septic shock (grade 1C) as the goal of therapy.

2a. Initial empiric anti-infective therapy of one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into tissues presumed to be the source of sepsis (grade 1B).

2b. Antimicrobial regimen should be reassessed daily for potential deescalation (grade 1B).

3. Use of low procalcitonin levels or similar biomarkers to assist the clinician in the discontinuation of empiric antibiotics in patients who initially appeared septic, but have no subsequent evidence of infection (grade 2C).

4a. Combination empirical therapy for neutropenic patients with severe sepsis (grade 2B) and for patients with difficult-to-treat, multidrug-resistant bacterial pathogens such as *Acinetobacter* and *Pseudomonas* spp. (grade 2B). For patients with severe infections associated with respiratory failure and septic shock, combination therapy with an extended spectrum beta-lactam and either an aminoglycoside or a fluoroquinolone is for *P. aeruginosa* bacteremia (grade 2B). A combination of beta-lactam and macrolide for patients with septic shock from bacteremic *Streptococcus pneumoniae* infections (grade 2B).

4b. Empiric combination therapy should not be administered for more than 3–5 days. De-escalation to the most appropriate single therapy should be performed as soon as the susceptibility profile is known (grade 2B).

5. Duration of therapy typically 7–10 days; longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with *S. aureus;* some fungal and viral infections or immunologic deficiencies, including neutropenia (grade 2C).

6. Antiviral therapy initiated as early as possible in patients with severe sepsis or septic shock of viral origin (grade 2C).

7. Antimicrobial agents should not be used in patients with severe inflammatory states determined to be of noninfectious cause (UG).

E. Source Control

1. A specific anatomical diagnosis of infection requiring consideration for emergent source control be sought and diagnosed or excluded as rapidly as possible, and intervention be undertaken for source control within the first 12 hr after the diagnosis is made, if feasible (grade 1C).

2. When infected peripancreatic necrosis is identified as a potential source of infection, definitive intervention is best delayed until adequate demarcation of viable and nonviable tissues has occurred (grade 2B).

3. When source control in a severely septic patient is required, the effective intervention associated with the least physiologic insult should be used (eg, percutaneous rather than surgical drainage of an abscess) (UG).

4. If intravascular access devices are a possible source of severe sepsis or septic shock, they should be removed promptly after other vascular access has been established (UG).

F. Infection Prevention

1a. Selective oral decontamination and selective digestive decontamination should be introduced and investigated as a method to reduce the incidence of ventilator-associated pneumonia; This infection control measure can then be instituted in health care settings and regions where this methodology is found to be effective (grade 2B).

1b. Oral chlorhexidine gluconate be used as a form of oropharyngeal decontamination to reduce the risk of ventilator-associated pneumonia in ICU patients with severe sepsis (grade 2B).

TABLE 6. Recommendations: Hemodynamic Support and Adjunctive Therapy

G. Fluid Therapy of Severe Sepsis

1. Crystalloids as the initial fluid of choice in the resuscitation of severe sepsis and septic shock (grade 1B).
2. Against the use of hydroxyethyl starches for fluid resuscitation of severe sepsis and septic shock (grade 1B).
3. Albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids (grade 2C).
4. Initial fluid challenge in patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia to achieve a minimum of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients (grade 1C).
5. Fluid challenge technique be applied wherein fluid administration is continued as long as there is hemodynamic improvement either based on dynamic (eg, change in pulse pressure, stroke volume variation) or static (eg, arterial pressure, heart rate) variables (UG).

H. Vasopressors

1. Vasopressor therapy initially to target a mean arterial pressure (MAP) of 65 mm Hg (grade 1C).
2. Norepinephrine as the first choice vasopressor (grade 1B).
3. Epinephrine (added to and potentially substituted for norepinephrine) when an additional agent is needed to maintain adequate blood pressure (grade 2B).
4. Vasopressin 0.03 units/minute can be added to norepinephrine (NE) with intent of either raising MAP or decreasing NE dosage (UG).
5. Low dose vasopressin is not recommended as the single initial vasopressor for treatment of sepsis-induced hypotension and vasopressin doses higher than 0.03-0.04 units/minute should be reserved for salvage therapy (failure to achieve adequate MAP with other vasopressor agents) (UG).
6. Dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (eg, patients with low risk of tachyarrhythmias and absolute or relative bradycardia) (grade 2C).
7. Phenylephrine is not recommended in the treatment of septic shock except in circumstances where (a) norepinephrine is associated with serious arrhythmias, (b) cardiac output is known to be high and blood pressure persistently low or (c) as salvage therapy when combined inotrope/vasopressor drugs and low dose vasopressin have failed to achieve MAP target (grade 1C).
8. Low-dose dopamine should not be used for renal protection (grade 1A).
9. All patients requiring vasopressors have an arterial catheter placed as soon as practical if resources are available (UG).

I. Inotropic Therapy

1. A trial of dobutamine infusion up to 20 micrograms/kg/min be administered or added to vasopressor (if in use) in the presence of (a) myocardial dysfunction as suggested by elevated cardiac filling pressures and low cardiac output, or (b) ongoing signs of hypoperfusion, despite achieving adequate intravascular volume and adequate MAP (grade 1C).
2. Not using a strategy to increase cardiac index to predetermined supranormal levels (grade 1B).

J. Corticosteroids

1. Not using intravenous hydrocortisone to treat adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (see goals for Initial Resuscitation). In case this is not achievable, we suggest intravenous hydrocortisone alone at a dose of 200 mg per day (grade 2C).
2. Not using the ACTH stimulation test to identify adults with septic shock who should receive hydrocortisone (grade 2B).
3. In treated patients hydrocortisone tapered when vasopressors are no longer required (grade 2D).
4. Corticosteroids not be administered for the treatment of sepsis in the absence of shock (grade 1D).
5. When hydrocortisone is given, use continuous flow (grade 2D).

Reanimación inicial

- Reanimación protocolizada y cuantitativa de los pacientes con hipoperfusión tisular por sepsis (definida como hipotensión persistente después del bolo inicial de fluidos o láctico elevado). Se debe iniciar lo antes posible (antes del ingreso a la UCI). Los objetivos en las primeras 6 horas son:
- Presión venosa central de 8-12 mmHg
- Presión arterial media >= 65 mmHg
- Diuresis >= 0,5 ml/kg/hr
- Saturación venosa central >= 70% o mixta >= 65%
- En los pacientes con láctico elevado, se debe agregar el objetivo de la normalización de ese parámetro.

- **Búsqueda de sepsis y mejoras en el sistema**

- Se recomienda realizar una evaluación rutinaria de los pacientes potencialmente infectados graves en búsqueda de sepsis severa, para lograr una implementación temprana de la terapia.
- Cada hospital debe implementar sistemas para el manejo adecuado de estos pacientes.

- **Diagnóstico**

- Los cultivos se deben realizar antes del inicio de los antibióticos, siempre que no retrasen significativamente (> 45 minutos) el inicio de los antibióticos. Se deben tomar por lo menos 2 series de hemocultivos (aeróbicos y anaeróbicos), como mínimo 1 percutáneo y 1 de cada acceso vascular que lleve más de 48 horas instalado. Los cultivos se pueden realizar al mismo tiempo si son realizados en diferentes lugares. Se deben tomar otros cultivos (orina, líquido cefalorraquídeo, etc.) según el caso.
- Se recomienda utilizar examen para la búsqueda de candidiasis invasiva si éstos están disponibles.
- Realice estudios de imágenes rápidamente para confirmar la fuente probable de infección.

- **Fluidos**

- Los cristaloides son el fluido de elección en la reanimación. No se recomienda el uso de hidroxietilalmidones. Si el paciente requiere grandes volúmenes de cristaloides se puede administrar albúmina.
- El bolo inicial de fluidos es de 30 ml/kg de cristaloides. Algunos pacientes pueden requerir mayores volúmenes. Los bolos de fluidos se deben repetir si estos mejoran las variables hemodinámicas dinámicas (variación de presión de pulso o volumen sistólico) o estáticas (presión arterial).

Vasopresores e inotrópicos

- El uso de vasopresores es vital en pacientes con hipotensión refractaria. La mantención de presión arterial media >= 65 mmHg ha demostrado mantener la perfusión tisular.
- El uso de noradrenalina (comparado con dopamina) se asocia a 9% menor mortalidad, 53% menos arritmias supraventriculares y 65% menos arritmias ventriculares.
- La adrenalina es la segunda opción, ya que diversos estudios randomizados han demostrado que no se asocia a un peor pronóstico que el uso de noradrenalina, a pesar que algunos datos indican una mayor producción de ácido láctico y alteraciones del flujo esplácnico.

Corticoides

- Controversial
- Avoiding use of intravenous hydrocortisone in adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (2C)
- In case this is not achievable, we suggest intravenous hydrocortisone alone at a dose of 200 mg per day (grade 2C).
- when hydrocortisone is given, use continuous flow (grade 2D).

Casserly B, Gerlach H, Phillips GS, Lemeshow S, Marshall JC, Osborn TM, Levy MM. Low-dose steroids in adult septic shock: results of the Surviving Sepsis Campaign. Intensive Care Med (38) 2012; 38: 1946-1954

Moreno R, Sprung CL, Annane D, Chevret S, Briegel J, Keh D, Singer M, Weiss YG, Payen D, Cuthbertson BH, Vincent JL. Time course of organ failure in patients with septic shock treated with hydrocortisone: results of the Corticus study. Intensive Care Med 2011; 37: 1765-1772

- Globalmente estas guías:

- Modifican los paquetes de medidas ("*bundles*") recomendados hasta ahora.
- El "antiguo" conjunto de medidas de tratamiento se elimina
- Las medidas de resucitación se desdoblan en dos grupos
- Aumenta el énfasis en el reconocimiento y tratamiento precoces de la sepsis.
- Los dos nuevos paquetes de medidas se deben cumplir en las 3 y en las 6 primeras horas.
- Cumplimiento de los paquetes de medidas como indicadores de calidad .

Resumen de medidas

A completar en las primeras 3 horas:

- Medir lactato
- Hemocultivos antes de la administración de antibióticos
- Antibióticos de amplio espectro
- Administrar 30 ml/kg de cristaloides en caso de hipotensión o lactato ≥ 4 mmol/L

A completar en las primeras 6 horas:

Vvasopresores (para la hipotensión que no responde a la administración inicial de líquidos) para mantener una PAM ≥ 65 mmHg

- En caso de hipotensión persistente a pesar de la administración de volumen (shock séptico) o lactato inicial ≥ 4 mmol/L:
  - Medir la presión venosa central [PVC]
  - Medir la saturación venosa central de oxígeno [SvcO2]
- Volver a medir el lactato si el lactato inicial estaba elevado
- Objetivos cuantitativos de la resucitación:
  PVC ≥ 8 mmHg , SvcO2 ≥ 70%, Normalización del lactato

Antibioticoterapia

El objetivo de la terapia es la admistración de antimicrobianos efectivos intravenosos dentro de la primera hora de reconocido el shock séptico (grade 1B) y de la sepsis severa sin shock (grade 1C)

Nota:

Aunque el peso de la evidencia apunta a la admisitración precoz de antibióticos dentro de las primeras 4 horas

La primera prioridad via y volumen

Tratamiento precoz y adecuado disminuye la mortalidad

Sugieren uso de antibióticos prediluidos, según estabildiad de moléculas.

Optimizando según PK/PD

Kollef et al. Chest 1999; 115:462

Paradigma uso de antibiótico

- Golpear duro y precoz con tratamiento antimicrobiano apropiado

- Duración corta de antibioticoterapia de ser posible

- Descalar de ser posible

Se recomienda que tratamiento inicial incluya uno o más antimicrobianos que tengan actividiad sobre los patógenos probables (bacterias, hongos o virus)

Y que penetren en concentraciones adecuadas en los tejidos presumiblemente comprometidos que sean el foco. (grade 1B)

La antibioticoterapia debe ser reevaluada en forma diaria para un potencial decalamiento en vistas a prevenir resistencia, reducir toxicidad y costos (grade 1B).

Elección de antimicrobiano

Historia del pacientes, alergias, Atb previo reciente (3 meses), comorbilidades, síndrome clínico, patrones de susceptinilidad de microorganismos de la comunidad y nosocomiales documentados previamente en colonización o infecciones

- Cocos +, BGN, FPMB
- Candidiasis, síndromes de shock tóxico, etc
- Neutropénicos
- Riesgo de multirresistentes
- Antifúngicos: echinocandin, triazoles, amphotericin B)
- Recent Infectious Diseases Society
- Restricción Atb apropiada pero no en el paciente séptico grave
- Monitorización de niveles de antimicrobianos

Se recomienda el uso de niveles de procalcitonina u otro biomarcador similar para asistir al clínico en la decisión de la suspensión de antimicrobianos (grade 2C).

Heyland DK, Johnson AP, Reynolds SC, et al: Procalcitonin for reduced antibiotic exposure in the critical care setting: A systematic review and an economic evaluation. *Crit Care Med 2011;* 39:1792–1799

Tang BM, Eslick GD, Craig JC, et al: Accuracy of procalcitonin for sepsis diagnosis in critically ill patients: Systematic review and metaanalysis. *Lancet Infect Dis 2007; 7:210–217*

La terapia empírica debería cubrir los patógenos que más probablemente estén involucrados

Se sugiere el uso de terapia combinada en pacientes neutrpénicos con sepsis severa (grade 2B) y en pacientes con microorganismos multirresistentes como *Acinetobacter y Pseudomonas spp. (grade 2B).*

En pacientes determinados con bacteriemia a Pseudomonas con infección grave con falla respiratoria y shock se sugiere combinar un beta lactámico + aminoglucósido o quinolona (grade 2B).

Se sugiere la combinación de un bealactámico y un macrólido en pacientes con shock séptico y bacteriemia por *Streptococcus pneumoniae (grade 2B)*

Micek ST, et al: Empiric combination antibiotic therapy is associated with improved outcome against sepsis due to Gram-negative bacteria: A retrospective analysis. *Antimicrob Agents Chemother 2010; 54:1742–1748*

Predictors of Mortality in Bloodstream Infections Caused by *Klebsiella pneumoniae* Carbapenemase–Producing *K. pneumoniae*: Importance of Combination Therapy

Mario Tumbarello,[1] Pierluigi Viale,[2] Claudio Viscoli,[3] Enrico Maria Trecarichi,[1] Fabio Tumietto,[2] Anna Marchese,[4] Teresa Spanu,[5] Simone Ambretti,[6] Francesca Ginocchio,[3] Francesco Cristini,[2] Angela Raffaella Losito,[1] Sara Tedeschi,[2] Roberto Cauda,[1] and Matteo Bassetti[3,7]

Methods. In this multicenter retrospective cohort study, conducted in 3 large Italian teaching hospitals, we examined 125 patients with bloodstream infections (BSIs) caused by KPC-producing Kp isolates (KPC-Kp) diagnosed between 1 January 2010 and 30 June 2011. The outcome measured was death within 30 days of the first positive blood culture. Survivor and nonsurvivor subgroups were compared to identify predictors of mortality.

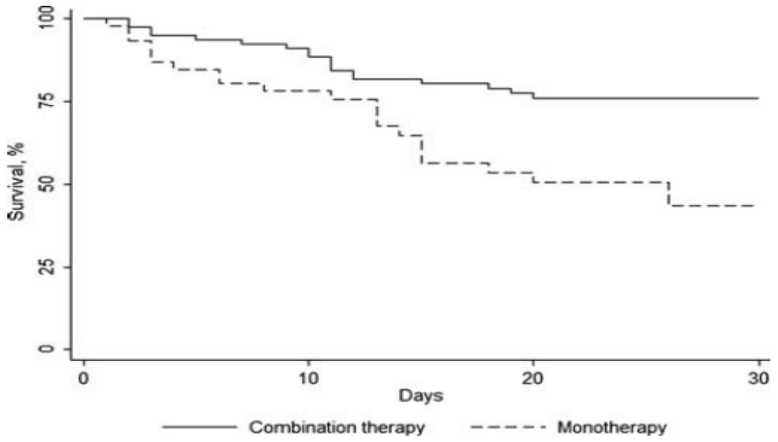


Figure 2. Kaplan-Meier curves showing the impact of combination therapy (solid line) versus monotherapy (dotted line) on 30-day mortality of patients with *Klebsiella pneumoniae* carbapenemase–producing *K. pneumoniae* isolate bloodstream infections ($P = .002$).

Table 4. Outcomes of the 36 Bloodstream Infections Treated With Combination Therapy Including Meropenem Stratified by Meropenem Minimum Inhibitory Concentration

		No. (%)	
Meropenem MIC (mg/L)	Total	Nonsurvivors	Survivors
1	1	0	1 (100)
2	4	0	4 (100)
4	10	2 (20)	8 (80)
8	4	1 (25)	3 (75)
≥16	17	6 (35.2)	11 (64.7)
Total	36	9 (25)	27 (75)

Abbreviation: MIC, minimum inhibitory concentration.

Table 3. Multivariate Analysis of Risk Factors for Mortality in Patients With Bloodstream Infection Caused by *Klebsiella pneumoniae* Carbapenemase–Producing *K. pneumoniae*

Variable	*P* Value	OR (95% CI)
Presentation with septic shock	.008	7.17 (1.65–31.03)
Inadequate initial antimicrobial treatment	.003	4.17 (1.61–10.76)
High APACHE III score	<.001	1.04 (1.02–1.07)
Postantibiogram therapy with tigecycline + colistin + meropenem	.01	0.11 (.02–.69)

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; CI, confidence interval; OR, odds ratio.

Se sugiere una duración de 7 a 10 días según la clínica.

Cursos más prolongados pueden ser apropiados en pacientes con repuesta clíncia lenta, focos no drenables, bacteriemia por *S.aureus*, algunos hongos e infecciones virales, e inmunodeprimidos incluyendo neutropénicos (grade 2C).

Se sugiere el inicio de antivirales en forma precoz en pacientes con sepsis severa o shock de causa viral (grade 2C).

L. Immunoglobulins

1. Not using intravenous immunoglobulins in adult patient[illegible] sev[illegible]sis or septic shock[illegible]e 2B).

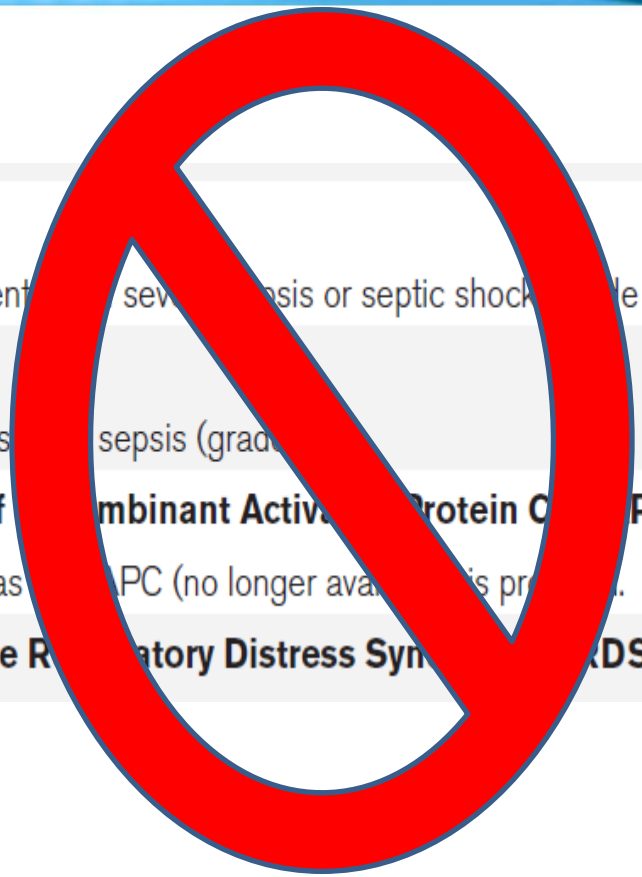
M. Selenium

1. Not using intravenous selenium for the treatment of s[illegible] sepsis (grad[illegible]

N. History of Recommendations Regarding Use of [illegible]mbinant Activ[illegible]rotein C[illegible]PC)

A history of the evolution of SSC recommendations as [illegible]PC (no longer ava[illegible]is pr[illegible].

O. Mechanical Ventilation of Sepsis-Induced Acute R[illegible]atory Distress Syn[illegible]RDS)



Conclusiones

- Guías no son rígidas pero si estáticas hasta la próxima versión
- Evidencia cambiante a veces contradictoria: corticoides, proteina C, tratamiento combinado
- Precoz y fuerte: 1 hora, amplio espectro, de ser necesario combinado
- Plan antibiótico a la medida
- Reevaluación del plan antibiótico
- Sepsis por bacterias, virus, hongos…
- Crítica a las guías: nivel de evidencia
- Financiamiento de la industria