XIV curso

Gestión Integral de los Medicamentos en los servicios de URgencias

GIMUR

CÓDIGO SEPSIS: Fisiopatología, diagnóstico y manejo del paciente séptico

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ORGANIZA:

sefh Sociedad Española de Farmacia Hospitalaria · fefh Fundación Española de Farmacia Hospitalaria · redfaster Grupo de trabajo de Atención Farmacéutica en Urgencias de la sefh · Parc Taulí Hospital Universitari

Introducción

- Definiciones
- Epidemiología
- Fisiopatología
- Guias Clínicas (Surviving Sepsis Campaing SSC)
- Scores Diagnósticos
- Biomarcadores
- Código Sepsis

Definiciones

- El término sepsis proviene de la antigua palabra griega **sepein**, que indica putrefacción o descomposición celular como resultado de una infección invasiva.

- La sepsis sigue representando una de las principales causas de morbilidad y mortalidad mundial anualmente, con más de 50 millones de niños y adultos afectados y más de 10 millones de muertes.

Definiciones

- Concepto de SIRS (respuesta inflamatòria sistèmica).
- 2016:Sistema puntuación SOFA (Sequential Organ Failure Assessment).
- Necesidad de Criterios Diagnósticos con alta Sensibilidad y especificidad para facilitar sospecha precoz.

Definiciones

- **SiRS:** Respuesta inflamatória sistémica.

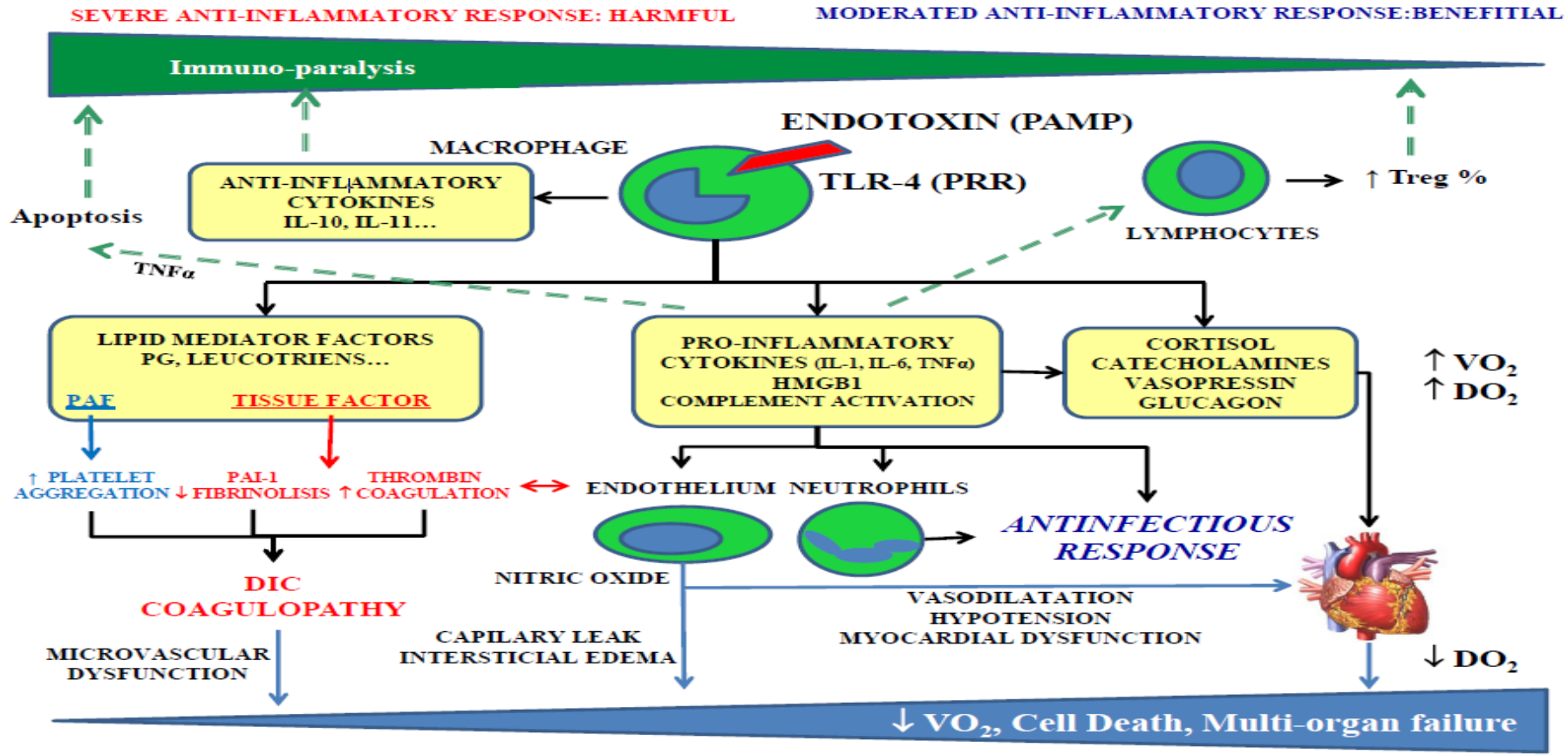
- **Sepsis**: Disfunción orgánica potencialmente mortal causada por una respuesta disregulada del huésped a la infección.

- **Shock séptico**:hipotensión mantenida con requerimiento sostenido de vasopresores para mantener PAM >=65mmHg y /o lactacidémia > 2 mmol/L.

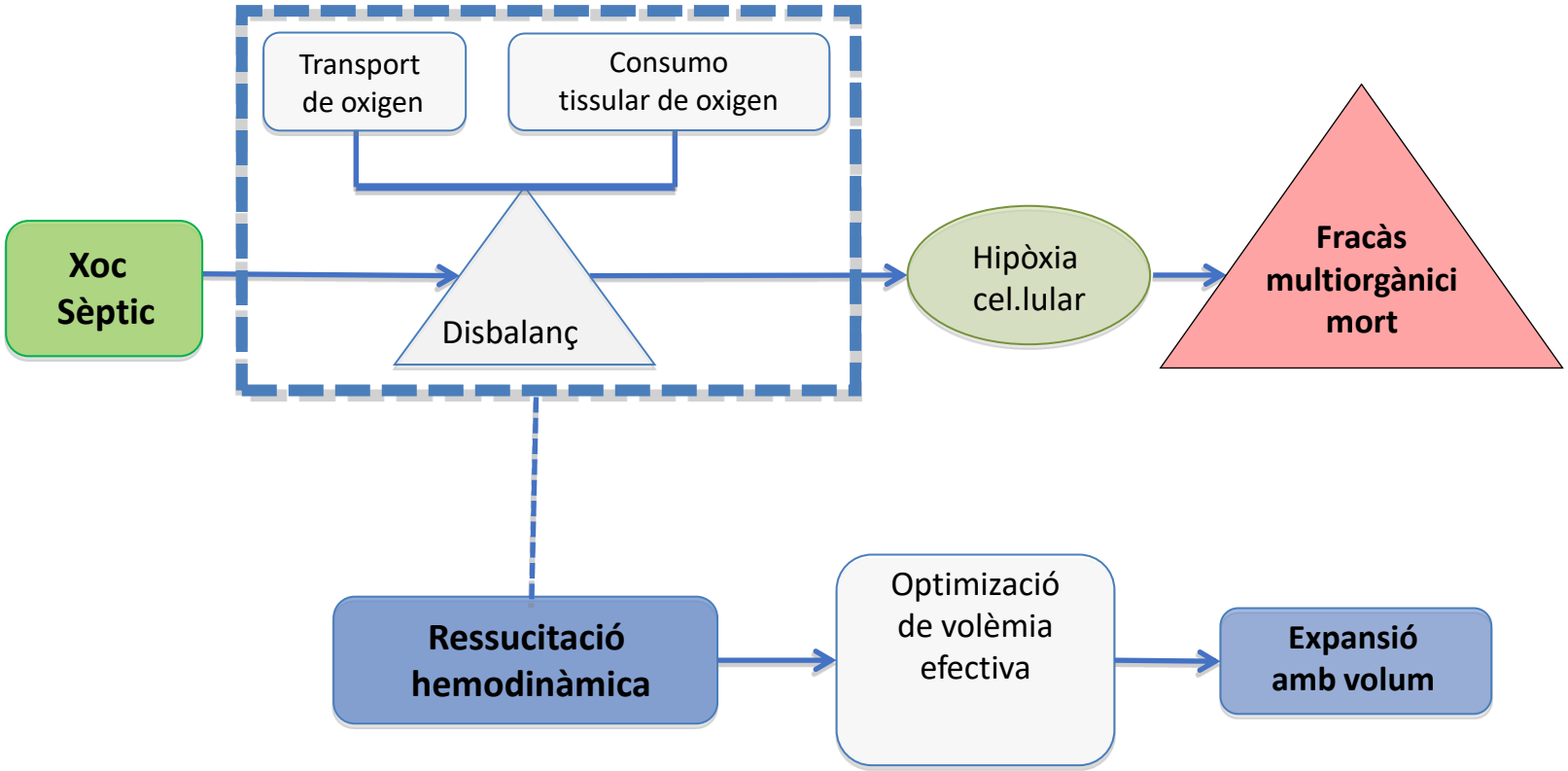
Epidemiología

- El **30% de las infecciones** que ingresan en el hospital tienen criterios de sépsis.
- 1/3 evolucionaran a shock séptico.
- Se estiman **50 ingressos a UCI /100.000 habitantes /año** (una por cada cinco sepsis atendidas).
- La **mortalidad global es del 20%.** Cada insuficiéncia de órgano añadida augmenta la mortalidad un 15%.

Fisiopatología



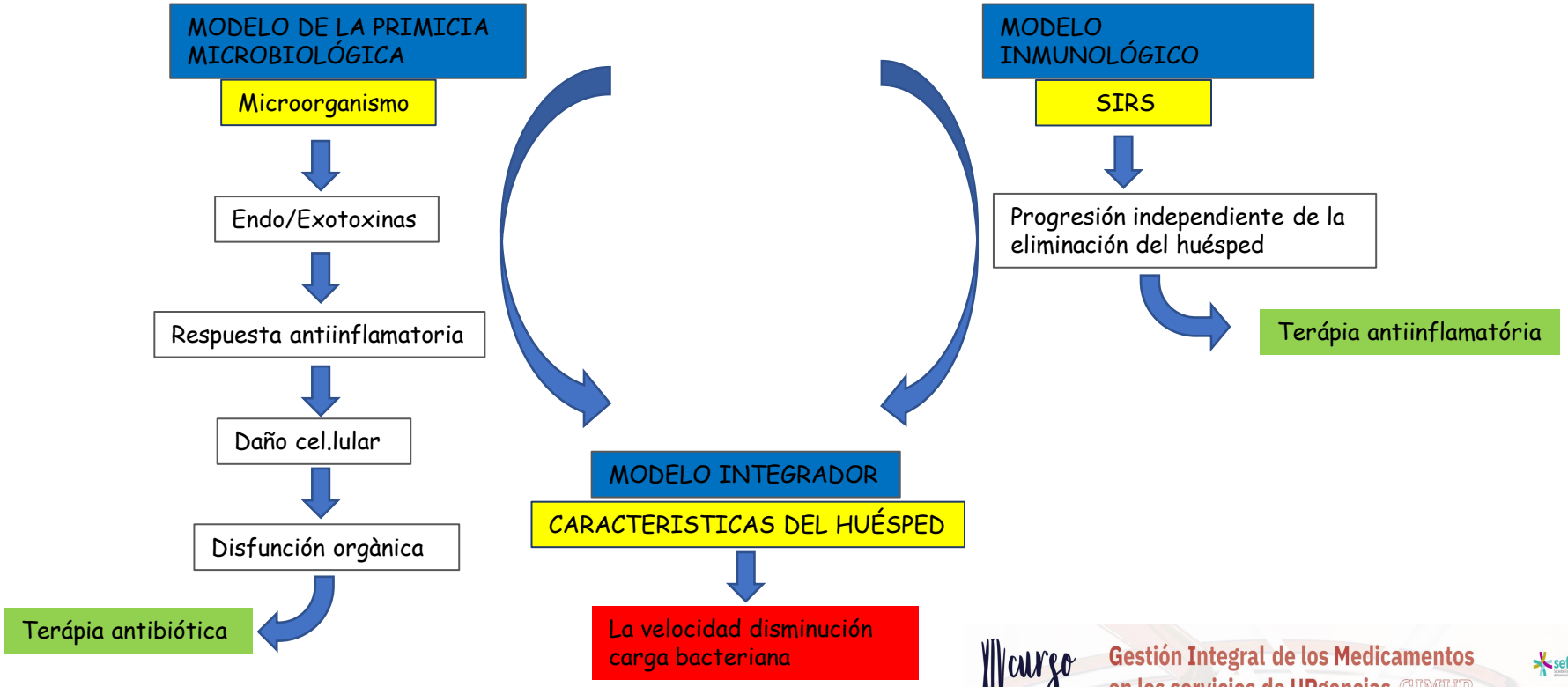
Fisiopatología



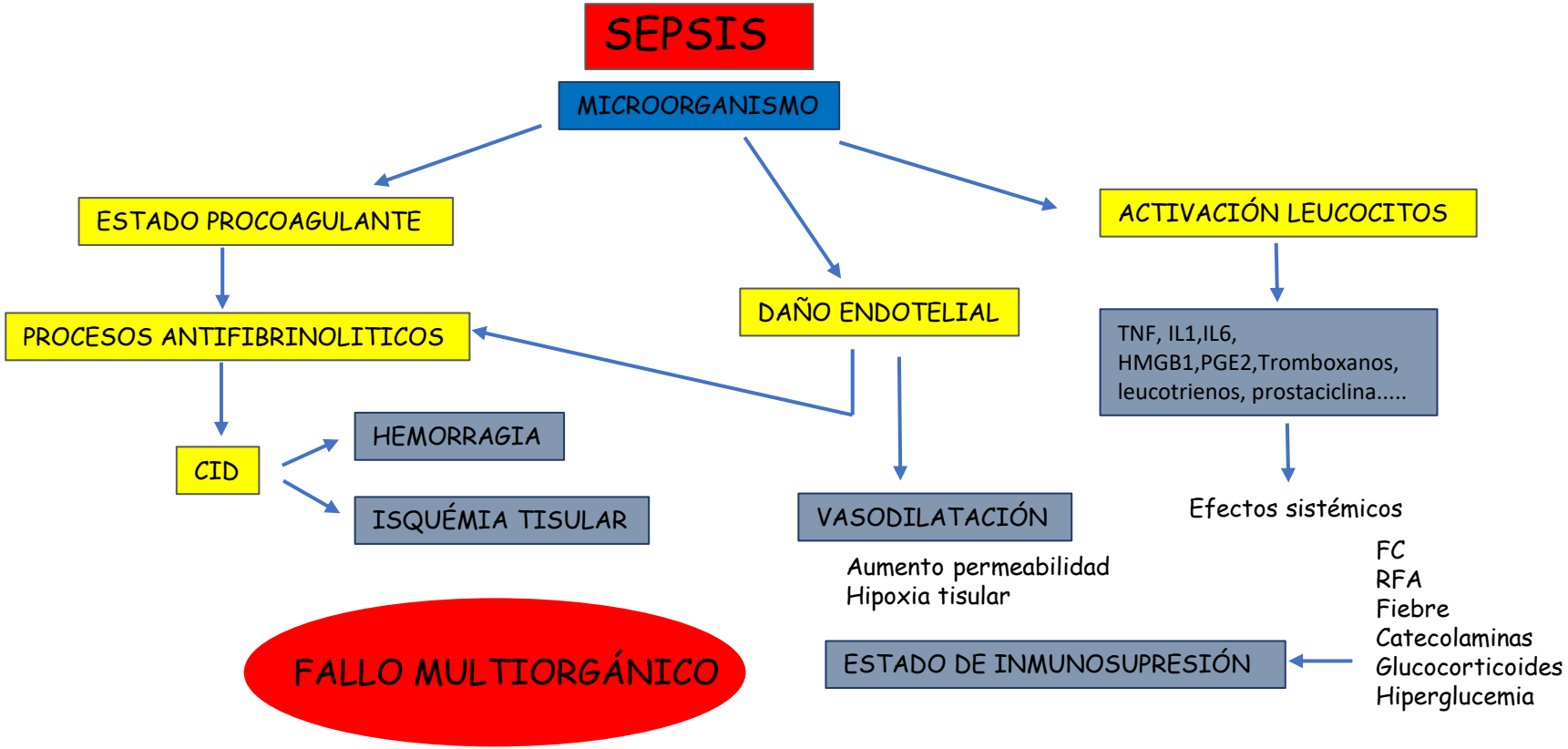
Fisiopatología

- Modelos
- Fisiopatologia
- Alteracions inflamatorias/ inmunológicas

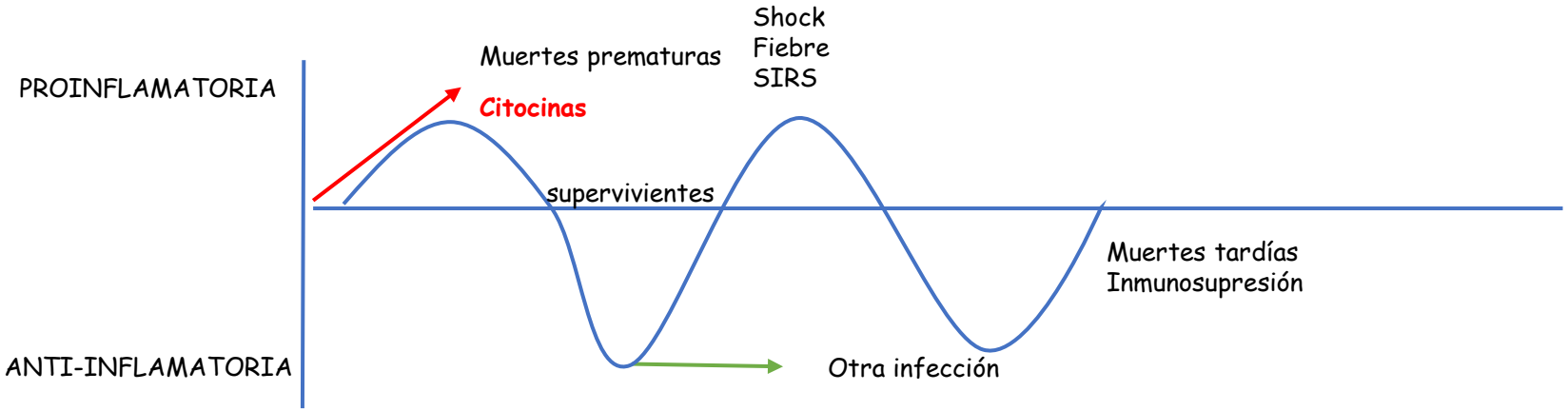
Fisiopatología



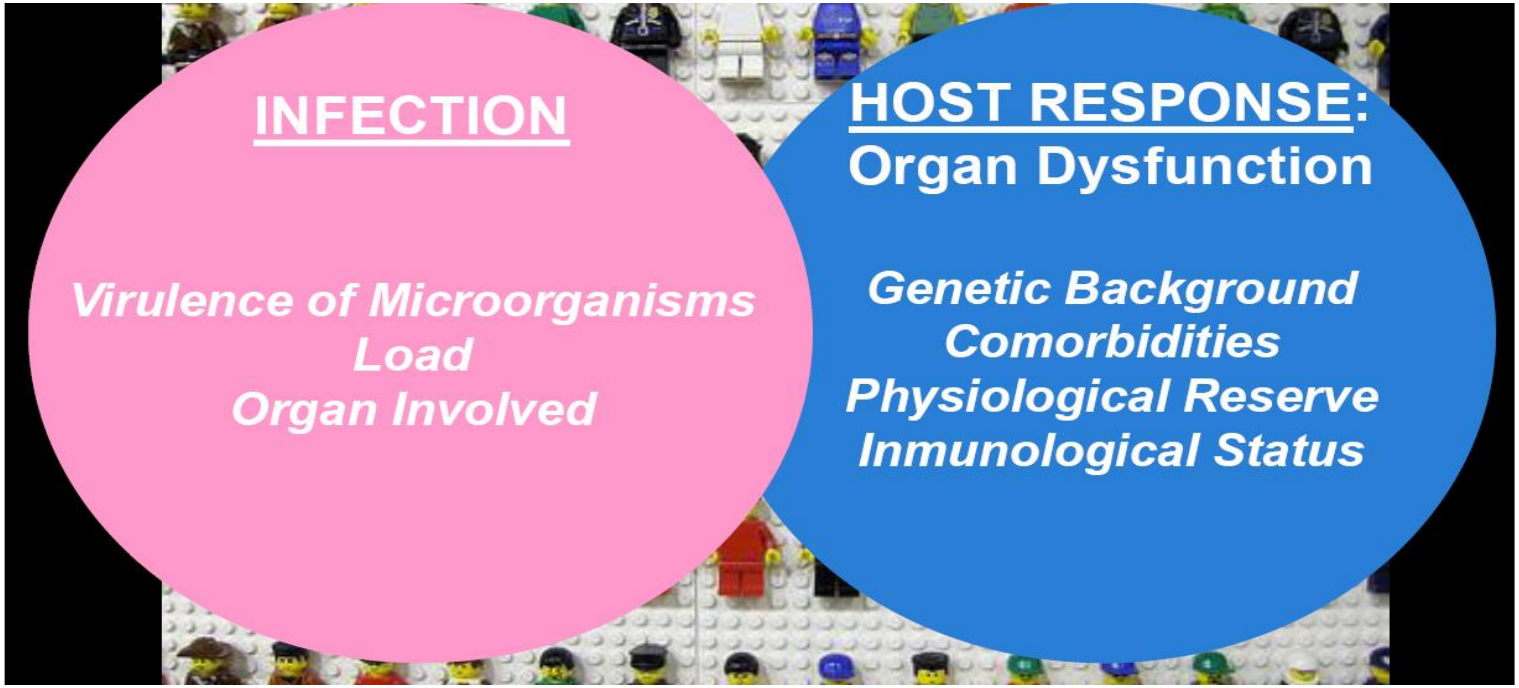
Fisiopatología



Fase Inflamatoria/Inmunológica



FASE INMUNOSUPRESIÓN


INFECTION
Virulence of Microorganisms
Load
Organ Involved
HOST RESPONSE:
Organ Dysfunction
Genetic Background
Comorbidities
Physiological Reserve
Inmunological Status

- Factores NO modificables:
    - Características del paciente
    - Foco de infección
    - Microorganismo responsable

- Factores modificables:
    - Tiempo es restablecer la hipoperfusión tissular
    - Adecuación en control del foco

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

INSTITUTE FOR HEALTHCARE IMPROVEMENT

SEPSIS RESUSCITATION BUNDLE 6h

SURVIVING SEPSIS CAMPAIGN BUNDLES

TO BE COMPLETED WITHIN 3 HOURS:

1) Measure lactate level
2) Obtain blood cultures prior to administration of antibiotics
3) Administer broad spectrum antibiotics
4) Administer 30 mL/kg crystalloid for hypotension or lactate ≥4mmol/L

TO BE COMPLETED WITHIN 6 HOURS:

5) Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mm Hg
6) In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥4 mmol/L (36 mg/dL):
   - Measure central venous pressure (CVP)*
   - Measure central venous oxygen saturation ($Scvo_2$)*
7) Remeasure lactate if initial lactate was elevated*

*Targets for quantitative resuscitation included in the guidelines are CVP of ≥8 mm Hg, $Scvo_2$ of ≥70%, and normalization of lactate.

Figure 1. Surviving Sepsis Campaign Care Bundles.

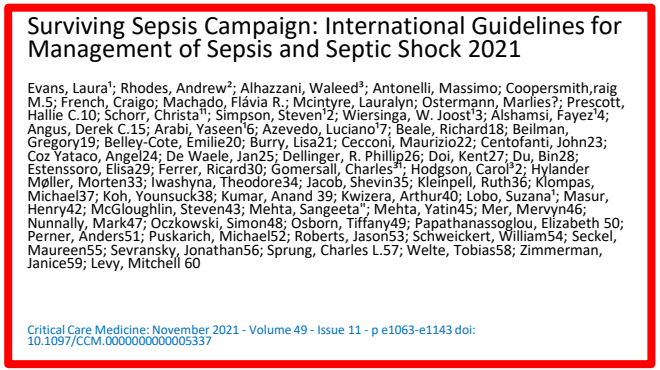
SEPSIS MANAGEMENT BUNDLE 24h

1. Administer low-dose steroids* for septic shock in accordance with a standardized ICU policy.
2. Administer drotrecogin alfa (activated) in accordance with a standardized ICU policy.
3. Maintain glucose control ≥ lower limit of normal, but < 150 mg/dl (8.3 mmol/L).
4. Maintain inspiratory plateau pressures < 30 cm H_2O for mechanically ventilated patients.

Guias Clínicas SSC 2021

Surviving Sepsis Campaign

- **Surviving Sepsis Campaign 2021 Adult Guidelines**
  The new "Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021" provides guidance for the clinician caring for adult patients with sepsis or septic shock.
- *Critical Care Medicine* | *Intensive Care Medicine*

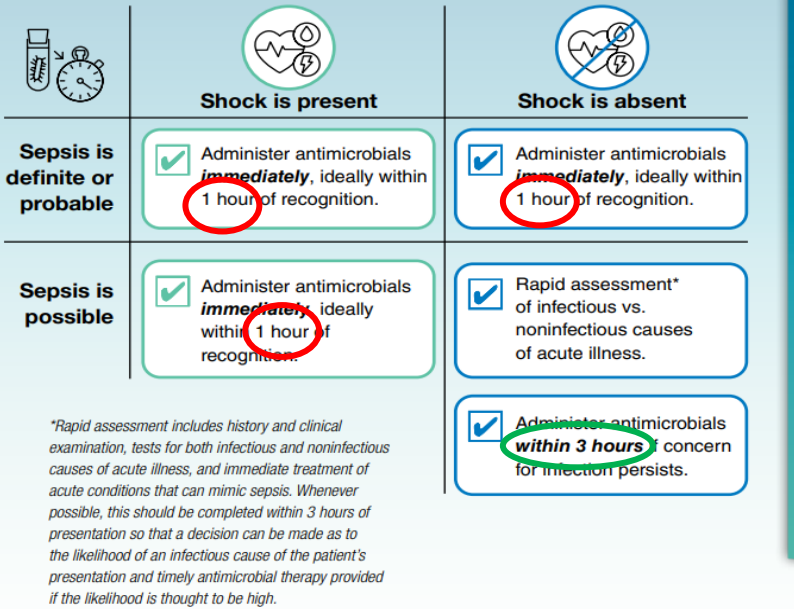


Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021

Evans, Laura[1]; Rhodes, Andrew[2]; Alhazzani, Waleed[3]; Antonelli, Massimo; Coopersmith,raig M.5; French, Craigo; Machado, Flávia R.; Mcintyre, Lauralyn; Ostermann, Marlies?; Prescott, Hallie C.10; Schorr, Christa[11]; Simpson, Steven[12]; Wiersinga, W. Joost[13]; Alshamsi, Fayez[14]; Angus, Derek C.15; Arabi, Yaseen[16]; Azevedo, Luciano[17]; Beale, Richard18; Beilman, Gregory19; Belley-Cote, Emilie20; Burry, Lisa21; Cecconi, Maurizio22; Centofanti, John23; Coz Yataco, Angel24; De Waele, Jan25; Dellinger, R. Phillip26; Doi, Kent27; Du, Bin28; Estenssoro, Elisa29; Ferrer, Ricard30; Gomersall, Charles[31]; Hodgson, Carol[32]; Hylander Møller, Morten33; Iwashyna, Theodore34; Jacob, Shevin35; Kleinpell, Ruth36; Klompas, Michael37; Koh, Younsuck38; Kumar, Anand 39; Kwizera, Arthur40; Lobo, Suzana[1]; Masur, Henry42; McGloughlin, Steven43; Mehta, Sangeeta[11]; Mehta, Yatin45; Mer, Mervyn46; Nunnally, Mark47; Oczkowski, Simon48; Osborn, Tiffany49; Papathanassoglou, Elizabeth 50; Perner, Anders51; Puskarich, Michael52; Roberts, Jason53; Schweickert, William54; Seckel, Maureen55; Sevransky, Jonathan56; Sprung, Charles L.57; Welte, Tobias58; Zimmerman, Janice59; Levy, Mitchell 60

Critical Care Medicine: November 2021 - Volume 49 - Issue 11 - p e1063-e1143 doi: 10.1097/CCM.0000000000005337

Antibiotic Timing

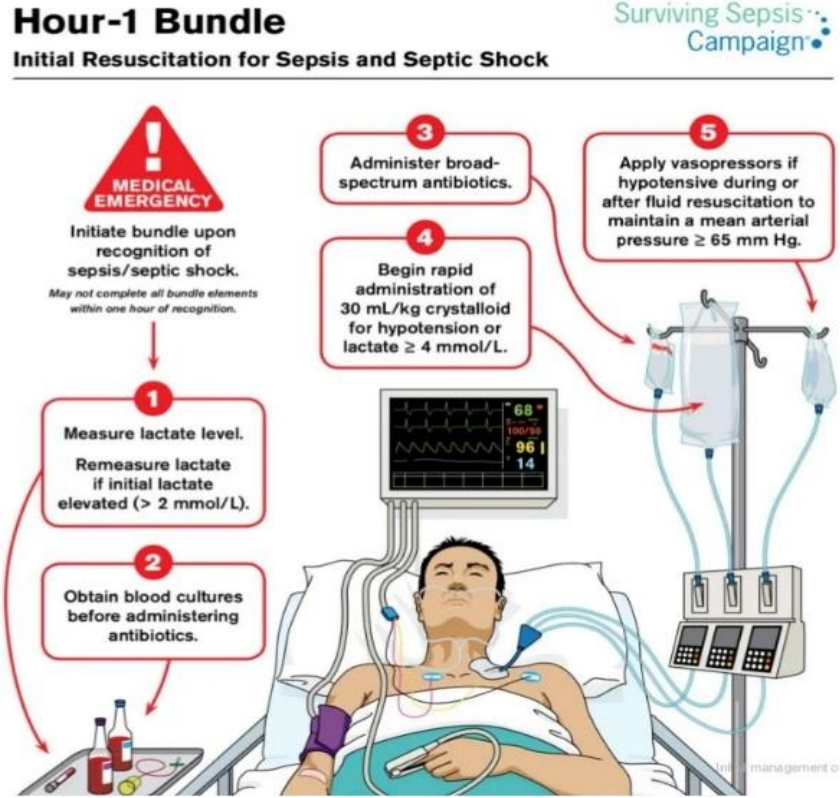


Society of Critical Care Medicine
The Intensive Care Professionals

Surviving Sepsis Campaign

Institute for Healthcare Improvement

Reconocimiento precoz



Predicting sepsis severity at first clinical presentation: The role of endotypes and mechanistic signatures

Arjun Baghela,[a,b] Olga M. Pena,[a] Amy H. Lee,[c] Beverlie Baquir,[a] Reza Falsafi,[a] Andy An,[a] Susan W. Farmer,[a] Andrew Hurlburt,[d] Alvaro Mondragon-Cardona,[e,f] Juan Diego Rivera,[e,f] Andrew Baker,[g] Uriel Trahtemberg,[g] Maryam Shojaei,[h] Carlos Eduardo Jimenez-Canizales,[e,f] Claudia C. dos Santos,[g] Benjamin Tang,[h] Hjalmar R. Bouma,[i,j] Gabriela V. Cohen Freue,[k] and Robert E.W. Hancock[a,*]

Diagnosis and Management of Bloodstream Infections With Rapid, Multiplexed Molecular Assays

Sherry A. Dunbar*, Christopher Gardner and Shubhagata Das

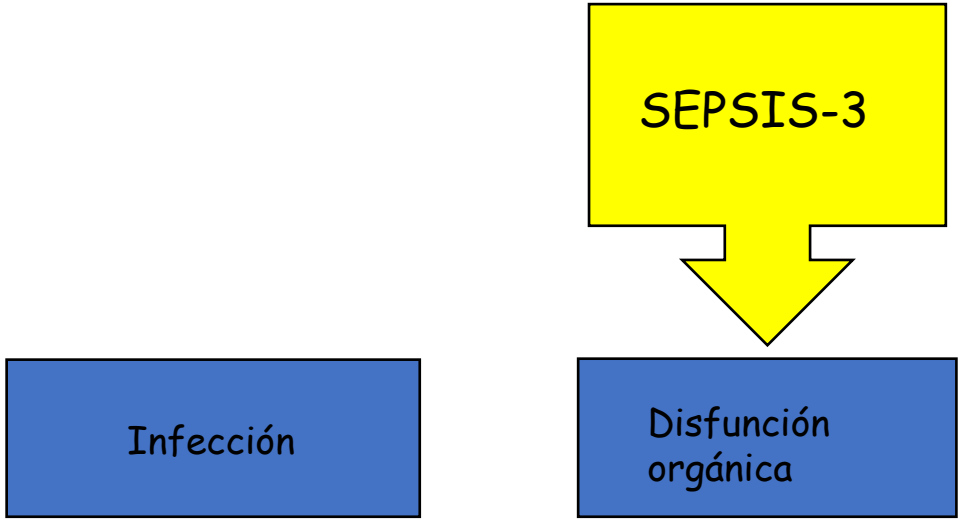
DIAGNOSTIC EXCELLENCE

Achieving Diagnostic Excellence for Sepsis

Predictive Value of Immune Cell Subsets for Mortality Risk in Patients With Sepsis

Ying Zhang, MM, Jia Wang, MM, Le Hu, MM, Jingchao Xuan, MM, Yifan Qu, MM, Yixuan Li, MM, Xinghua Ye, MM, Long Yang, MM, Jun Yang, MM, Xiangqun Zhang, MM, Junyu Wang, MD, and Bing Wei, MM

Reconocimiento precoz



Reconocimiento precoz

Diagnóstico de infección

↓

Signos y sintomas locales
Contexto clínico

Diagnóstico de Sepsis

↓

Respuesta del huesped
Disfunción orgànica

Scores

Escala SOFA (*Sepsis related Organ Failure Assessment*)					
CRITERIOS	0	1	2	3	4
SNC Escala de Glasgow	15	13-14	10-12	6-9	< 6
Renal Creatinina (mg/dl) Diuresis (ml/día)	< 1,2	1,2-1,9	2-3,4	3,5-4,9 ou < 500	> 5 ou < 200
Hepático Bilirrubina (mg/dl)	< 1,2	1,2-1,9	2-5,9	6-11,9	> 12
Coagulación Plaquetas $10^3/mm^3$	≥ 150	< 150	< 100	< 50	< 20
Respiratorio PaO_2/FiO_2 (mmHg)	≥ 400	< 400	< 300	< 200 y soporte ventilatorio	< 100 y soporte ventilatorio
Cardiovascular TAM (mmHg) Drogas vasoactivas (µg/kg/min)	≥ 70	< 70	Dopamina a < 5 o dobutamina a cualquier dosis	Dopamina 5-15 Noradrenalina o adrenalina ≤ 0,1	Dopamina > 15 Noradrenalina o adrenalina > 0,1

SNC: sistema nervioso central; PaO_2: presión arterial de oxígeno; FiO_2: fracción de oxígeno inspirado; TAM: tensión arterial media.

SOFA > o = 2

Sequential Organ Failure Assessment

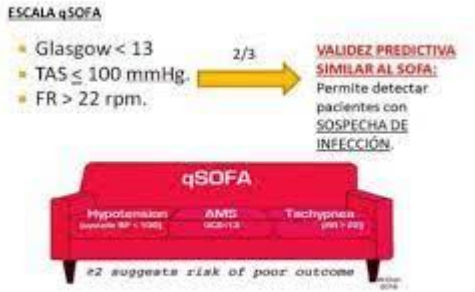
Scores

Box 4. qSOFA (Quick SOFA) Criteria

Respiratory rate ≥22/min

Altered mentation

Systolic blood pressure ≤100 mm Hg



qSOFA

E ↑

S ↓

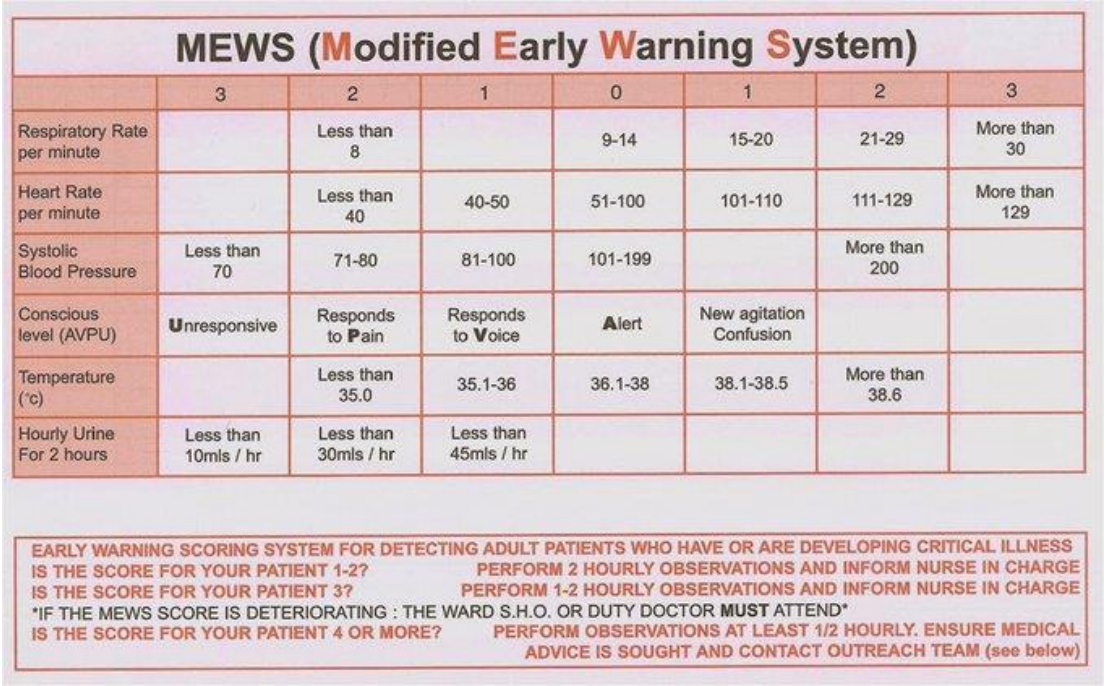
Scores

Physiological parameter	Score 3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9–11	12–20		21–24	≥25
SpO_2 Scale 1 (%)	≤91	92–93	94–95	≥96			
SpO_2 Scale 2 (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91–100	101–110	111–219			≥220
Pulse (per minute)	≤40		41–50	51–90	91–110	111–130	≥131
Consciousness				Alert			CVPU
Temperature (°C)	≤35.0		35.1–36.0	36.1–38.0	38.1–39.0	≥39.1	

News

National Early Warning Score

Scores



MEWS (Modified Early Warning System)							
	3	2	1	0	1	2	3
Respiratory Rate per minute		Less than 8		9-14	15-20	21-29	More than 30
Heart Rate per minute		Less than 40	40-50	51-100	101-110	111-129	More than 129
Systolic Blood Pressure	Less than 70	71-80	81-100	101-199		More than 200	
Conscious level (AVPU)	**U**nresponsive	Responds to **P**ain	Responds to **V**oice	**A**lert	New agitation Confusion		
Temperature (°c)		Less than 35.0	35.1-36	36.1-38	38.1-38.5	More than 38.6	
Hourly Urine For 2 hours	Less than 10mls / hr	Less than 30mls / hr	Less than 45mls / hr				

EARLY WARNING SCORING SYSTEM FOR DETECTING ADULT PATIENTS WHO HAVE OR ARE DEVELOPING CRITICAL ILLNESS

IS THE SCORE FOR YOUR PATIENT 1-2? PERFORM 2 HOURLY OBSERVATIONS AND INFORM NURSE IN CHARGE

IS THE SCORE FOR YOUR PATIENT 3? PERFORM 1-2 HOURLY OBSERVATIONS AND INFORM NURSE IN CHARGE

*IF THE MEWS SCORE IS DETERIORATING : THE WARD S.H.O. OR DUTY DOCTOR **MUST** ATTEND*

IS THE SCORE FOR YOUR PATIENT 4 OR MORE? PERFORM OBSERVATIONS AT LEAST 1/2 HOURLY. ENSURE MEDICAL ADVICE IS SOUGHT AND CONTACT OUTREACH TEAM (see below)

MEWS

Scores

Table 1. *SIRS criteria and qSOFA score*	
SIRS criteria (≥ 2)	Body temperature > 38.0 °C or < 36.0 °C
	Heart rate of > 90/min
	Respiratory rate of > 20 breaths/min or $PaCO_2$ of < 4.3 kPa
	White blood cell count of < 4000 cells/mm³ or > 12,000 cells/mm³ or > 10% immature bands
qSOFA score (≥ 2)	Respiratory rate ≥ 22 breaths/min
	Systolic blood pressure ≤ 100 mmHg
	Altered mental state

SIRS = systemic inflammatory response syndrome; qSOFA = quick sequential organ failure assessment.

-NEWS to be more accurate when compared with both SIRS and qSOFA for the early detection of severe sepsis and septic shock, septic shock alone and sepsis-related mortality.
-NEWS outperforms SIRS is likely due to the inclusion of mental status, blood pressure and oxygenation, which are all readily available indicators of end-organ dysfunction.
-Unlike SIRS, NEWS is immediately available at triage and does not require any laboratory testing and may allow quicker recognition and treatment of sepsis.

Area Under Receiving Operating Characteristic for Primary & Secondary Outcomes				
	Severe Sepsis & Septic Shock	Septic Shock	Sepsis Related Mortality	All-cause mortality
SIRS	0.88	0.88	0.89	0.79
qSOFA	0.81	0.84	0.87	0.79
NEWS	0.91	0.93	0.95	0.88

	Severe Sepsis & Septic Shock		Septic Shock		Sepsis Mortality	
	Sens.	Spec.	Sens.	Spec.	Sens.	Spec.
SIRS (Cutoff ≥ 2)	86	79	87	79	89	79
qSOFA (Cutoff ≥ 2)	29	99	33	99	43	99
NEWS (Cutoff ≥ 4)	84	85	88	85	92	85

Scores

Table 6. *Sensitivity and specificity for in-hospital mortality (n = 577)*

	In-hospital mortality (n = 21)	
	Sensitivity	*Specificity*
SIRS ≥ 2	61.9% (38.4-81.9)	56.9% (52.7-61.1)
qSOFA ≥ 2	33.3% (14.6-57.0)	93.7% (91.3-95.6)
SOFA ≥ 2	66.7% (43.0-85.4)	79.8% (76.2;83.1)
qSOFA ≥ 2 + SOFA ≥ 2	28.6% (11.3-52.2)	96.4% (94.5;97.8)
MEWS ≥ 5	23.8% (8.2-47.2)	87.0% (83.9-89.7)
SIRS ≥ 2 + SOFA ≥ 2	42.9% (21.8-66.0)	87.4% (84.3-90.0)

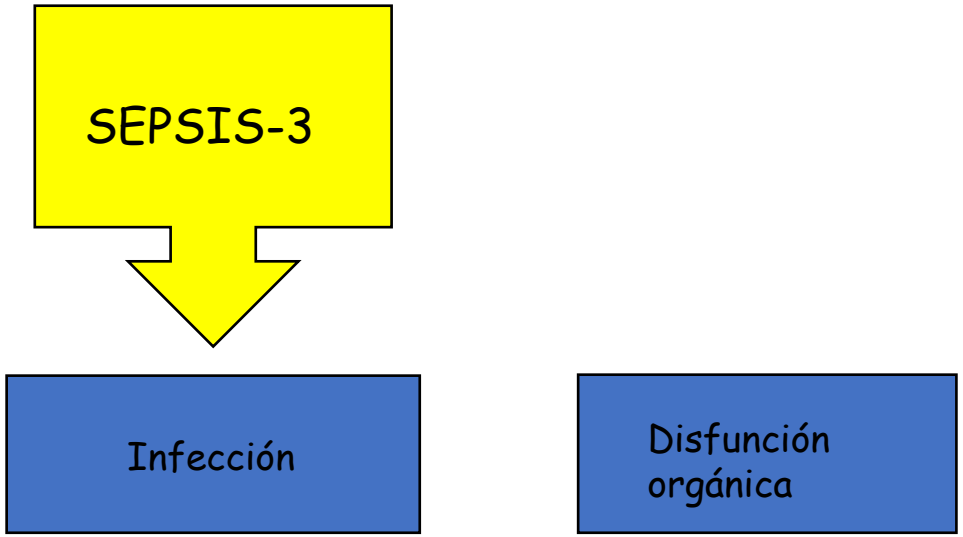
Sensitivity and specificity expressed as percentage with (95% exact Clopper-Pearson confidence intervals). SIRS = Systemic inflammatory response syndrome, qSOFA = (quick) Sequential Organ Failure Assessment, MEWS = Modified Early Warning Score.

Scores

Variables	Cut off value	Sensitivity	Specificity
SIRS	2.5	0.71	0.5
SOFA	7	0.79	0.69
qSOFA	2.5	0.64	0.86

The mean scores of SIRS, qSOFA and SOFA on expired patients are 3.4, 2.8 and 12, respectively. While the scores in recovered patients are 3.2, 2 and 9 for SIRS, qSOFA and SOFA scores respectively (Table 4).

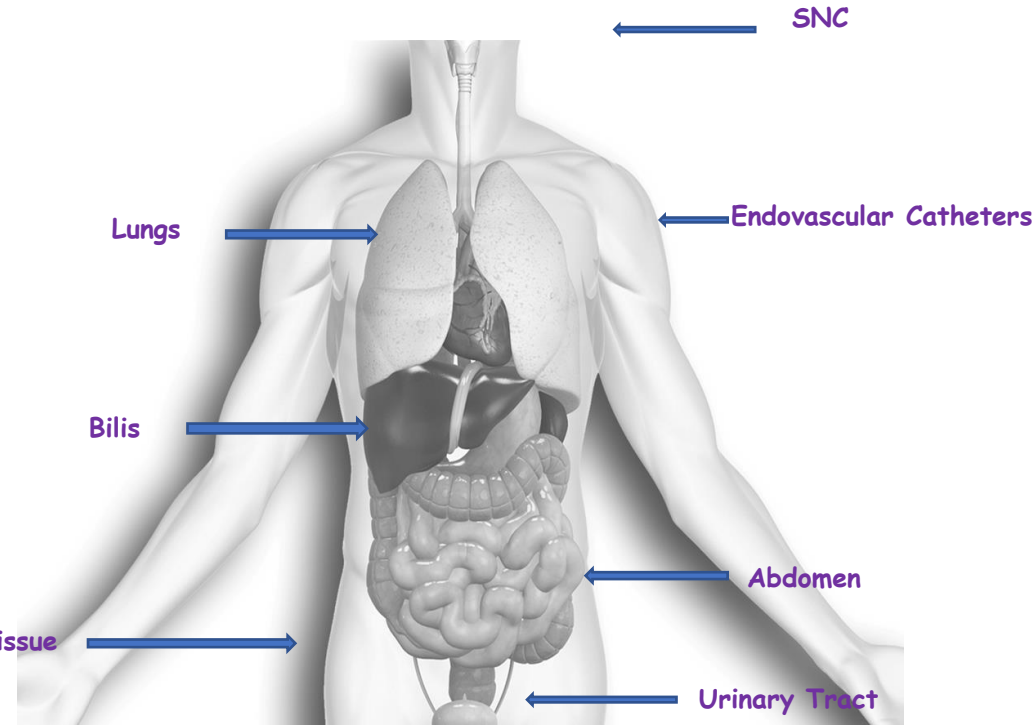
Reconocimiento precoz



Detección infección

Anamnesis dirigida por aparatos

- Comorbilidades
- Estados de inmunosupresión
- Ingresos/ Cirugia recinte
- Presencia de Cultivos previos

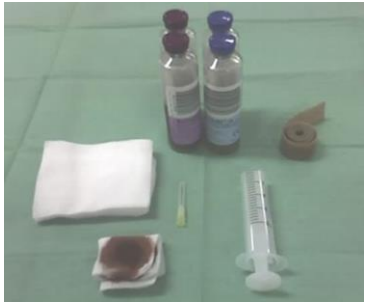


Detección infección

Exploración física:

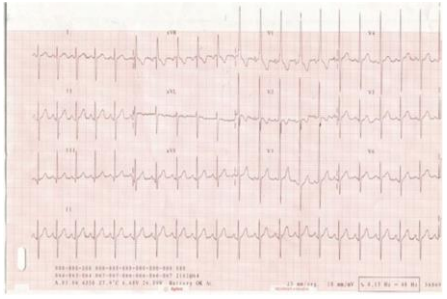
- Por sistemas
- Catéteres / port a cach/ material protésico
- Constantes vitales. Control diuresis.

Detección infección



Pruebas complementarias

- Analítica (perfil sepsis: GSA / Ac. Láctico)
- Sedimento orina
- Hemocultivos/ Urinocultivo/ cultivos frotis heridas
- Pruebas de imagen dirigidas: Rx tórax/Eco/ Tac



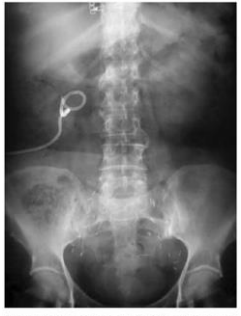
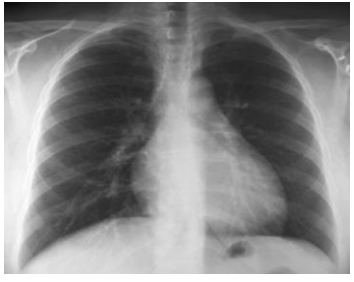


FIGURA 2B. Nefrostomía a través de la cual se extrajo el catéter migrado y que se utilizó para introducir un nuevo catéter ureteral.



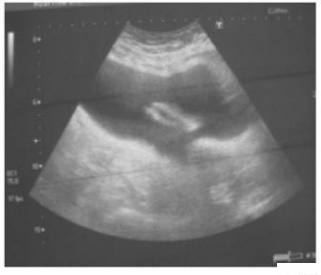


FIGURA 1

Biomarcadores

- Lactat (N < 2mmol/L)
- PCR (N < 10 mg/ L) , inflamatori inespecífic
- Procalcitonina (N< 0,1 ng/ mL), més específic per sepsis que pcr per > 10 ng/mL.
- Pancreatic Stone Protein (PSP)
- Pro Adrenomodulina

Biomarcadores

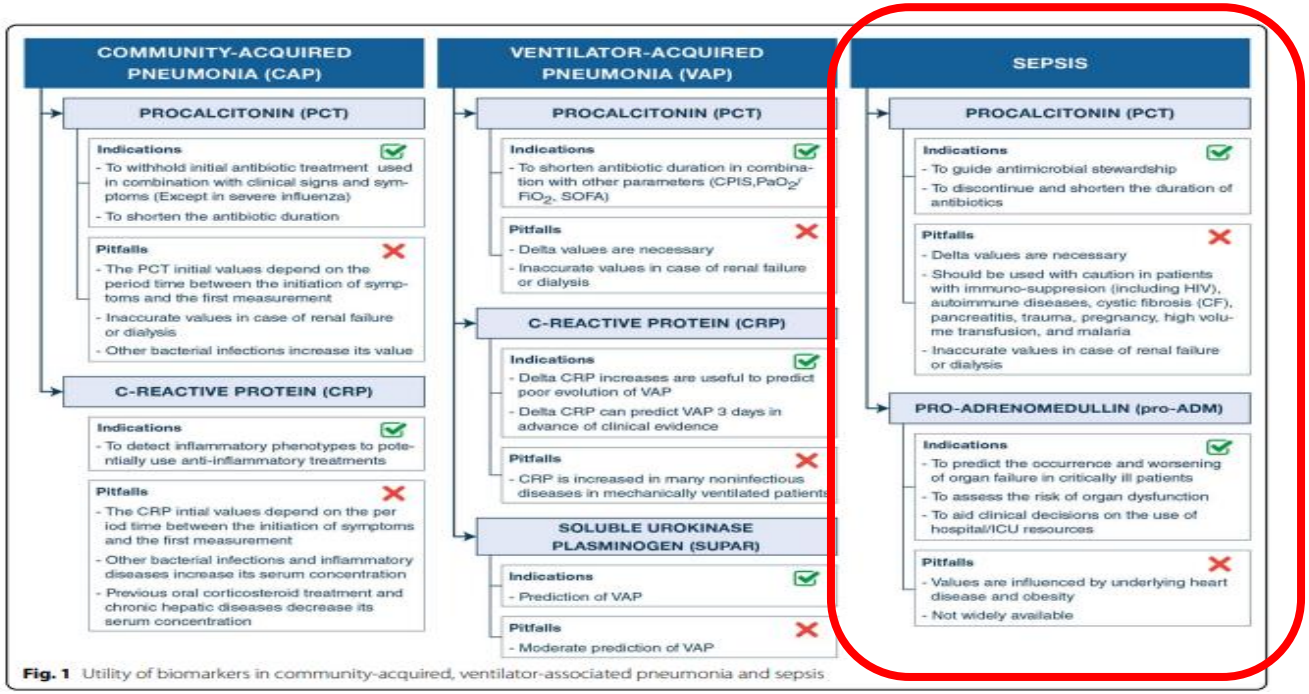


Fig. 1 Utility of biomarkers in community-acquired, ventilator-associated pneumonia and sepsis

Antoni Torres1,2* , Antoni Artigas3 and Ricard Ferrer4,5. Intensive Care Med (2021) 47:97–100. https://doi.org/10.1007/s00134-020-06271-4 . LESS IS MORE IN INTENSIVE CAR

Biomarcadores

Alta sospecha de infección

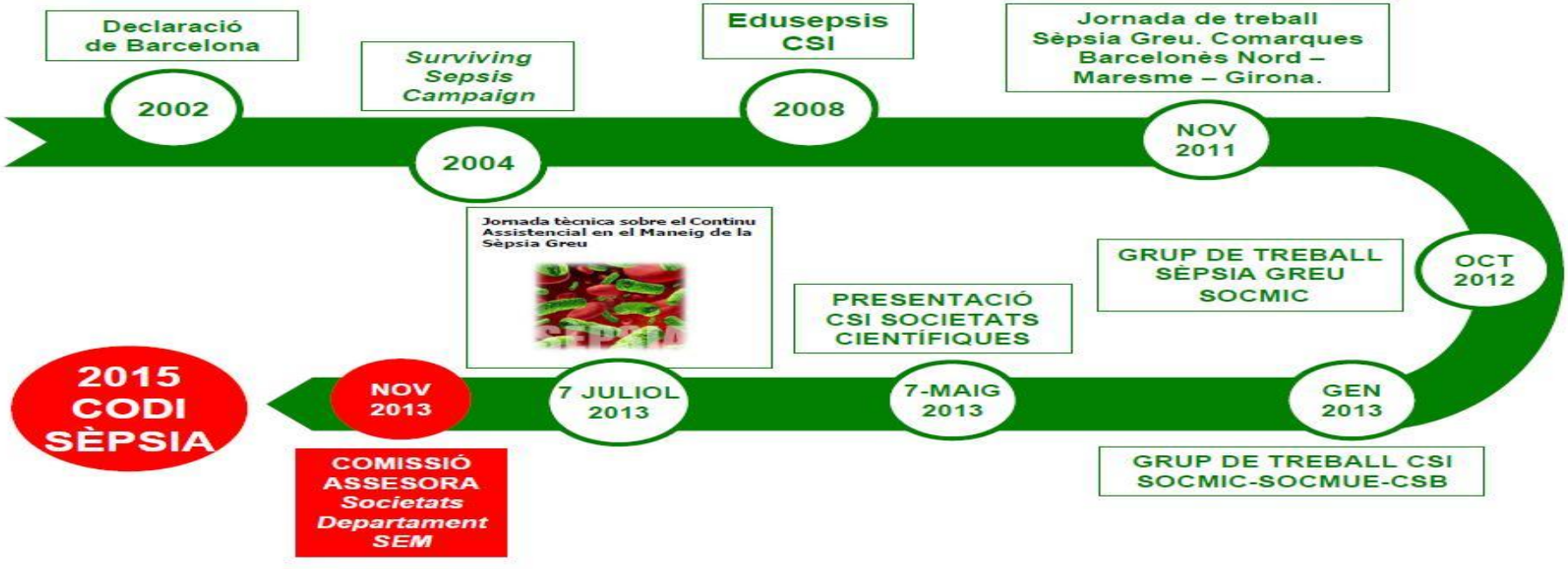
Poca utilidad

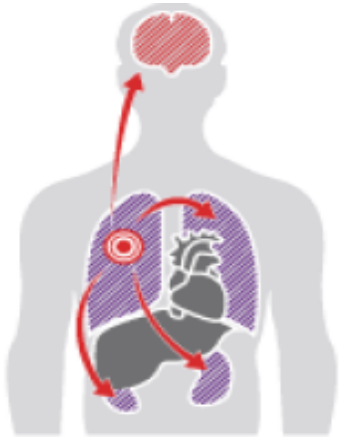
Baja sospecha de infección

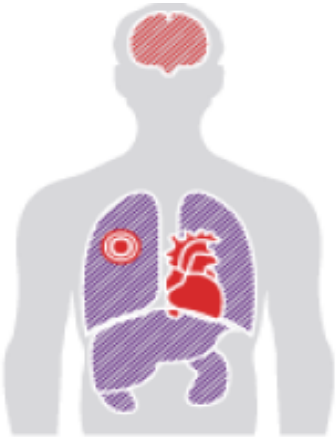
Poca utilidad

Incertidumbre → Mejora juicio clinico

Código Sepsis





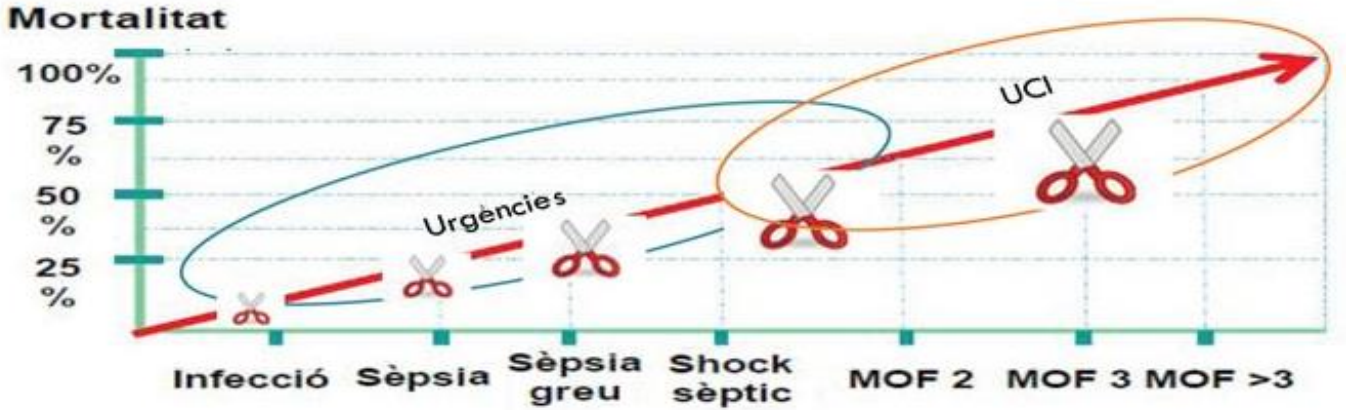


INFECCIÓ → SIRS (SÈPSIA) → SÈPSIA GREU → XOC SÈPTIC → MORT

TEMPS DEPENENT

Diagnosticable

Reversible



Brun-Buisson C. Intensive Care Med 2000; 26 (S 1):S64-74.

Código Sepsis

	AMI	STROKE	TRAUMA	SEPSIS
Clinical Recognition	Easy	Easy	Easy	Complex
Population	Homogeneous	Homogeneous	Heterogeneous	Heterogeneous
Biomarker	YES	NO	NO	YES/NO
Complex Treatment Algorithms	++	++	+++	+++
Multidisciplinary Approach	+	++	+++	+++
Well established guidelines	+++	+++	+++	++
Code	Yes	Yes	Yes	+/-

Código Sepsis

El objetivo del Código Sepsis es revertir la progresión de la disfunción multiorgánica generada por la evolución de la infección que se presenta como sépsis grave coordinando los recursos que sean necesarios.

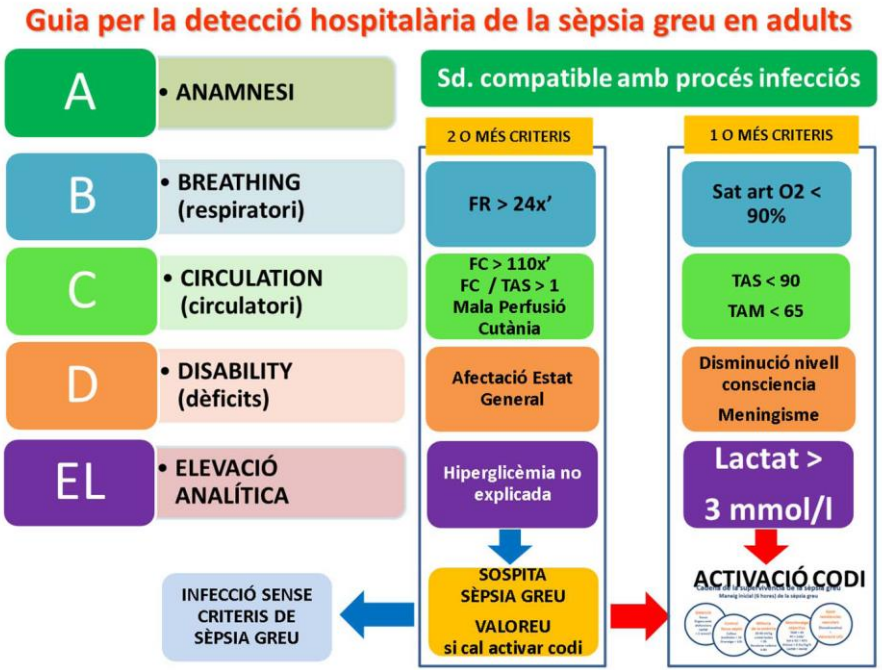
Código Sepsis

	AMI	STROKE	TRAUMA	SEPSIS
Clinical Recognition	Easy	Easy	Easy	Complex
Population	Homogeneous	Homogeneous	Heterogeneous	Heterogeneous
Biomarker	YES	NO	NO	YES/NO
Complex Treatment Algorithms	++	++	+++	+++
Multidisciplinary Approach	+	++	+++	+++
Well established guidelines	+++	+++	+++	++
Code	Yes	Yes	Yes	+/-

Código Sépsis

CODI IAM	CODI SÈPSIA
• **PACIENT:** Dolor toràcic	• **PACIENT:** Anamnesi infecció aguda
• **CRITERI:** Elevació ST (ECG <10')	• **CRITERI:** Hipoperfusió o disfunció de òrgan
• **OBJECTIU:** Perfusió miocàrdica	• **OBJECTIU:** Perfusió sistèmica + control infecció
• **MANEIG:** – O2 /AAP /VDC – TRASLLAT: Angioplastia <120' – Fibrinolisis in situ	• **MANEIG:** – HC / ATB <1h / drenatge <12h – Volèmia / O2 – Ubicació UCI: tècniques suport òrgans

Código Sepsis



Código Sepsis

Estado actual

Nuevos tratamientos

Reconocimiento precoç
Identificación de fenotipos sepsis

Proceso assistencial de la sepsis
Pauta antibiòtica para Microrganismos resistentes

To take home....

- La sepsis sigue teniendo elevada incidència y mortalidad.
- La detección y manejo precoz de la sepsis determina el pronóstico y la mortalidad.
- El criterio clínico sigue prevaleciendo delante del nivel de los diferentes Biomarcadores que cobran importancia en aquellos casos de incertidumbre.
- Importáncia de la activación del Código sepsis.
- Inicio del tratamiento antibiótico empírico lo mas precozmente posible 1h en caso de Dx claro o situación de shock séptico y 3h en incertidumbre

- Determinación de niveles de Ácido láctico para control evolutivo.
- Importáncia de extracción de hemocultivos +/- cultivos adicionales segun foco, adecuación del tratamiento y desescalar con garantía.
- El control del foco y la resucitación hemodinámica precoz son indispensables para la buena evolución del paciente.
- Manejo del paciente a pie de cama e importancia del trabajo en equipo.

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MOLTES GRÀCIES

XIV curso

Gestión Integral de los Medicamentos en los servicios de URgencias

GIMUR

Fisiopatología, diagnóstico y manejo del paciente séptico: CóDIGO SEPSIS

Berta Cisteró Roig. Consorci Corporació Sanitària Parc Taulí.

Jesús Ruiz Ramos. Hospital Santa Creu i Sant Pau

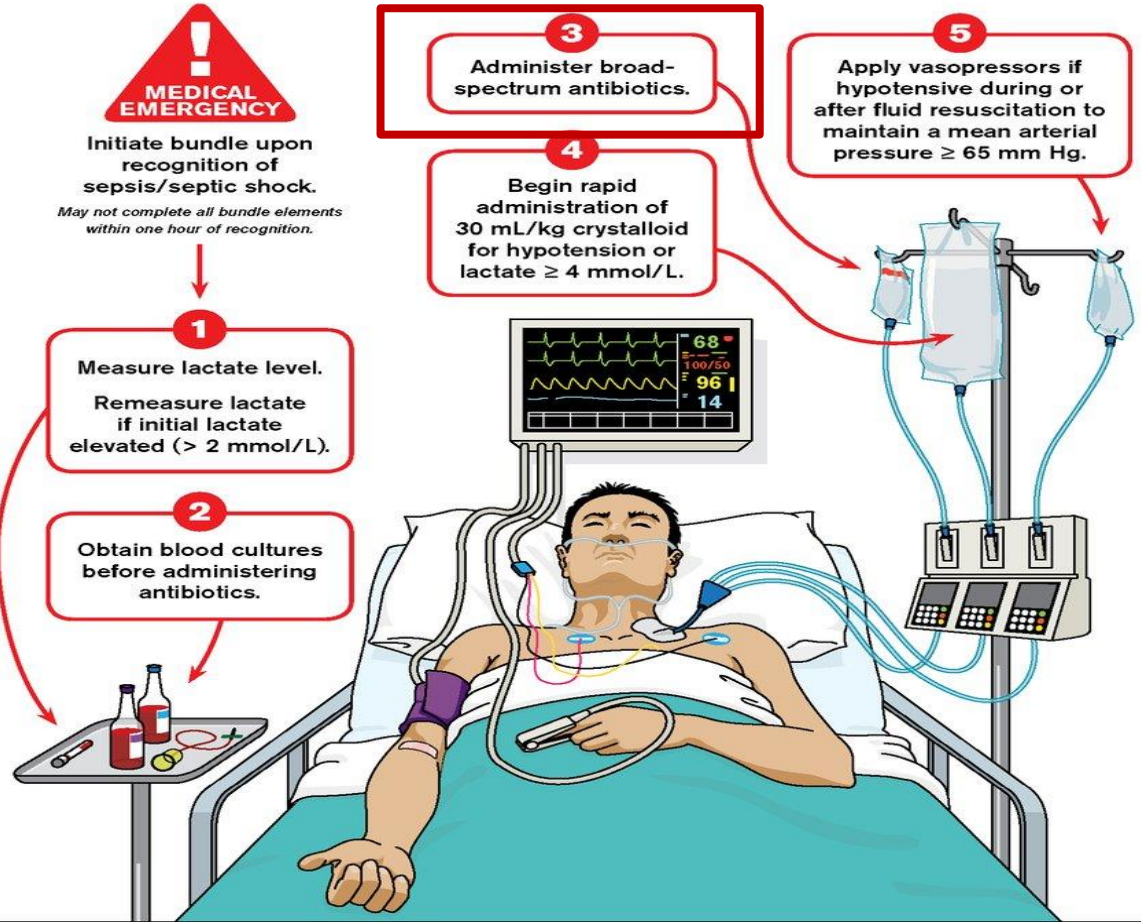
ORGANIZA:

sefh Sociedad Española de Farmacia Hospitalaria · fefh Fundación Española de Farmacia Hospitalaria · redfaster Grupo de trabajo de Atención Farmacéutica en Urgencias de la sefh · Parc Taulí Hospital Universitari

Hour-1 Bundle

Initial Resuscitation for Sepsis and Septic Shock

Surviving Sepsis Campaign



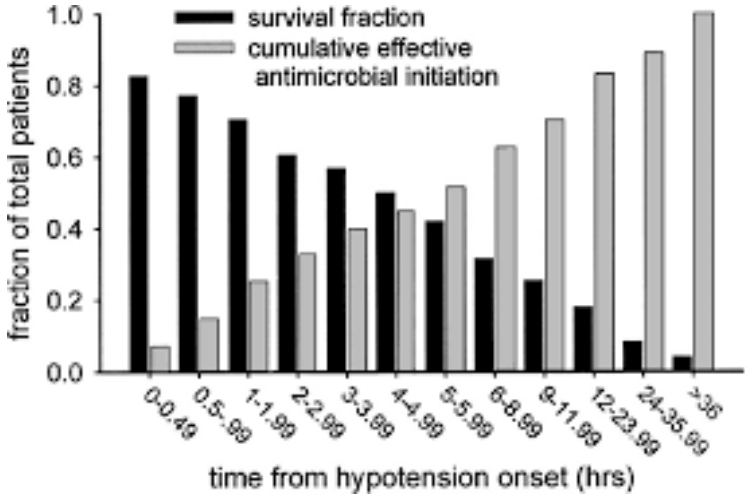
ANTIBIOTERAPIA EN SEPSIS

1. Tiempo
2. Cobertura adecuada
3. Dosificación pK/pD
4. Shock séptico
5. Desescalada/Duración


SEPSIS™
IT'S ABOUT TIME

TIEMPO INICIO ANTIBIOTERAPIA

Tiempo de hipotensión previo a la administración de antibióticos



Kumar A, Crit Care Med. 2006

Tiempo hasta primera dosis de antibióticos

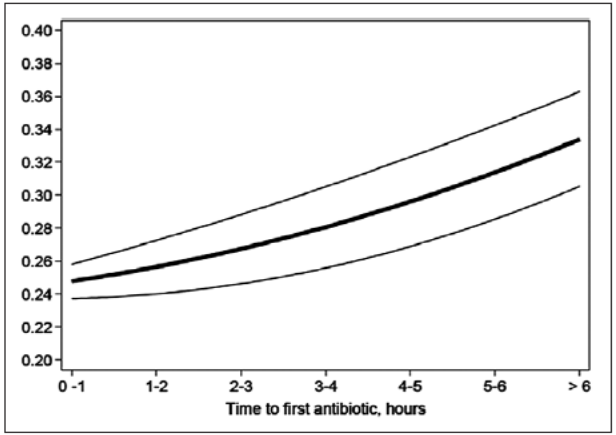


Figure 2. Predicted hospital mortality and the associated 95% CIs for

Ferrer R. Crit Care Med. 2014

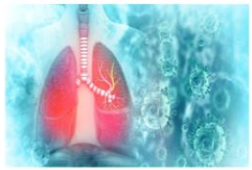
TIEMPO INICIO ANTIBIOTERAPIA

:isk factors for the development of acute lung injury in patients
/ith septic shock: An observational cohort study*

:mzi Iscimen, MD; Rodrigo Cartin-Ceba, MD; Murat Yilmaz, MD; Hasrat Khan, MD; Rolf D. Hubmayr, MD
:kele Afessa, MD; Ognjen Gajic, MD, MSc

Table 2. Risk factors for development of ALI in patients with septic shock: multiple logistic regression analysis

	Odds Ratio	95% CI	p Value
Delayed goal-directed resuscitation	3.55	1.52–8.63	.004
Delayed antibiotics	2.39	1.06–5.59	.039
Respiratory rate (per 5/)	2.03	1.38–3.08	<.001
Chemotherapy	6.47	1.99–24.9	.003
Chronic alcohol use	2.09	.88–5.10	.098
Transfusion	2.75	1.22–6.37	.016
Aspiration	3.48	1.22–10.78	.024
Diabetes mellitus	.44	.17–1.07	.070

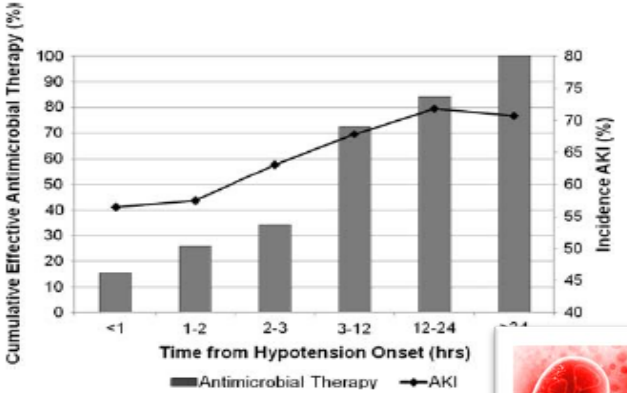


Research

Open Access

Early acute kidney injury and sepsis: a multicentre evaluation

Sean M Bagshaw[1,2], Carol George[3], Rinaldo Bellomo[2,4] for the ANZICS Database Management Committee



TIEMPO INICIO ANTIBIOTERAPIA

Surviving Sepsis Campaign

"Para los adultos con **posible shock o una alta probabilidad de sepsis**, recomendamos la administración de antimicrobianos inmediatamente, idealmente **dentro de 1 hora** después del reconocimiento."

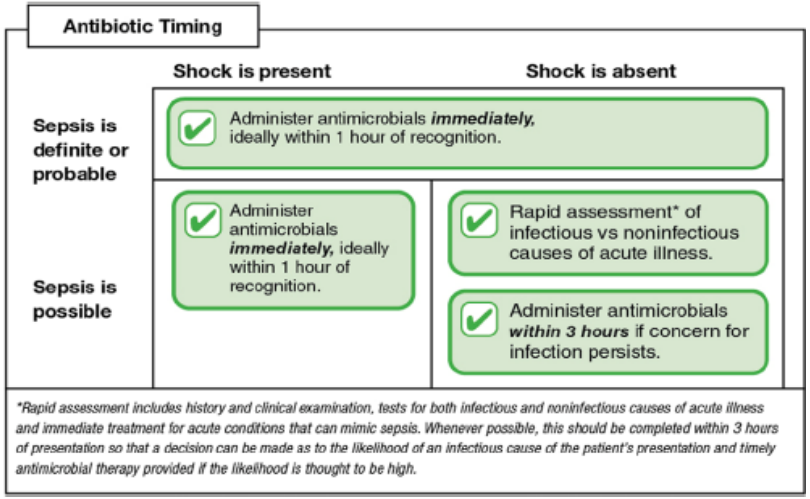
Best practice statement

"Para adultos con **posible sepsis sin shock**, sugerimos un curso de investigación rápida por tiempo limitado y si persiste la preocupación, la administración de antimicrobianos **en las 3 h** desde el momento en que se reconoció la sepsis."

Best practice statement

"Para los adultos con **baja probabilidad de infección y sin shock**, sugerimos **diferir los antimicrobianos** mientras se monitoriza de cerca al paciente"

Best practice statement



TIEMPO INICIO ANTIBIOTERAPIA

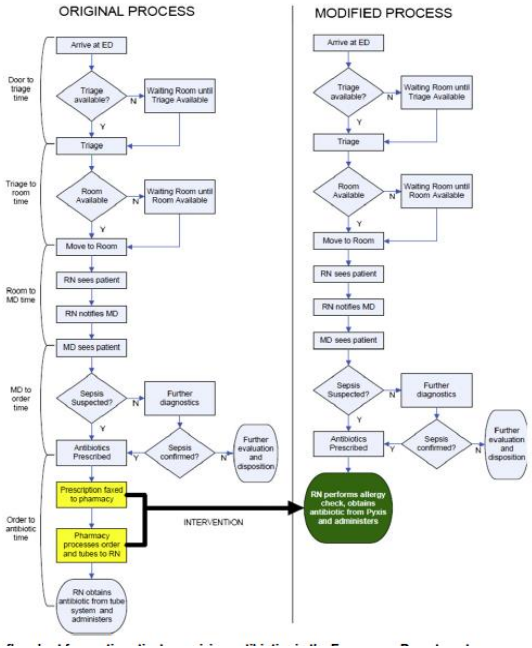
Indicadores a utilizar

- ✗ % Pacientes con antibioterapia en **primera hora**
- ✗ Tiempo puerta – administración de antibiótico

- ✓ Rápida disponibilidad de antibióticos en box
- ✓ Sistemas de alerta automatizada
- ✓ Educación/compartir indicadores
- ✓ Discusión de casos retrasado: mejora de circuitos

IMPROVING DOOR-TO-ANTIBIOTIC TIME IN SEVERELY SEPTIC EMERGENCY DEPARTMENT PATIENTS

Eveline A. Hitti, MD,* John J. Lewin III, PHARMD, BCPS,† Jose Lopez, MD,‡ Jonathan Hansen, MD,‡



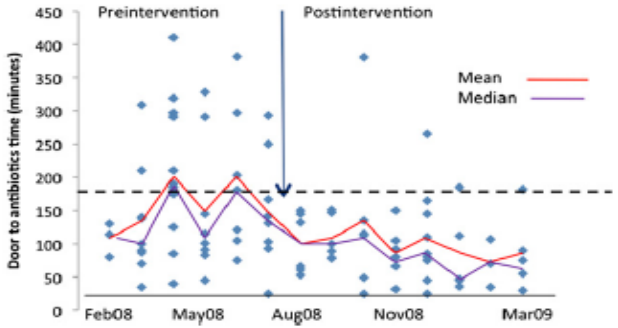


Figure 4. Door-to-antibiotics time (minutes) by month and intervention.

*"Eliminating the process steps involved in obtaining these medications from a central pharmacy led to a **29-min reduction** in mean order-to-antibiotic time and a 70-min reduction in mean door-to-antibiotic time."*

Delayed Second Dose Antibiotics for Patients Admitted From the Emergency Department With Sepsis: Prevalence, Risk Factors, and Outcomes

Daniel Leisman, BS[1,2]; Victor Huang, MD[1]; Qiuping Zhou, DO[1]; Jeanie Gribben, BS[1]; Andrea Bianculli, BS[1];

TABLE 1. Observed Prevalence and Magnitude of Delays in Second Administration of Antibiotics

Cohort	Measure	Precision
Entire cohort		
n	828	–
Patients with major delay (≥ 25% of recommended time)[a]	272 (32.9%)	CI: 29.6–36.2%
Median administration-to-recommendation ratio[a]	0.98	IQR: 0.67–1.14

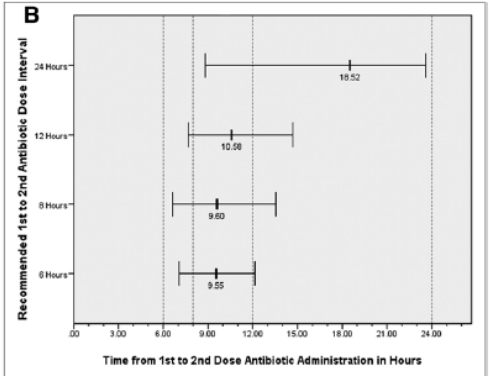


TABLE 3. Summary of Adjusted Regression (Exploratory) Analyses Evaluating Major Delay in Second Antibiotic Administration as a Predictor of Patient Outcomes

Parameter	Regression Type	Model Fit	Model Output	Effect Size	95% CI	*p*
Primary outcome						
Mortality[a]	Logistic	$\chi^2 = 5.9$; $p = 0.65$	OR	1.61	1.01–2.57	0.046
Secondary outcomes						
Hospital length of stay[b]	Cox	–	Inverse hazard ratio	1.16	0.97–1.39	0.11
ICU admission[c]	Logistic	$\chi^2 = 5.9$; $p = 0.66$	OR	1.49	0.92–2.40	0.103
Mechanical ventilation after second antibiotic dose[d]	Logistic	$\chi^2 = 4.2$; $p = 0.84$	OR	2.44	1.27–4.69	0.007

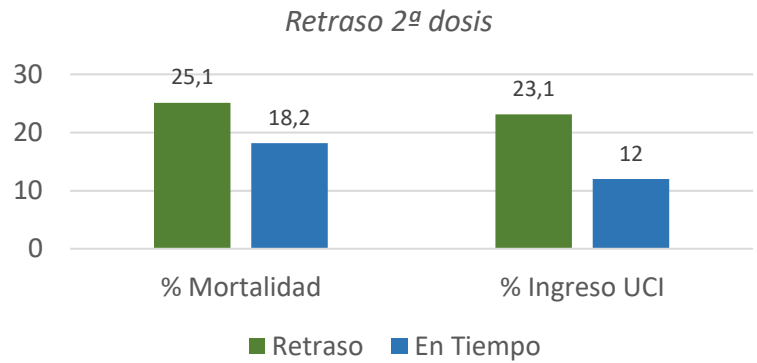
TIEMPO INICIO ANTIBIOTERAPIA

Retraso administración b-lactámicos urgencias

54
Pacientes

Servicio de Urgencias
Hospital Sant Pau.
Ene-Mar 2022

- 40 (74,1%) pacientes con hemocultivos positivos
- 2ª dosis: Retraso >20% en 13 **(24,1%)** pacientes
- 3ª dosis: Retraso >20% 22 **(47,8%)** pacientes



1

Paciente 83 años EPOC con descompensaciones frecuentes que consulta de residencia con código sepsis de origen respiratorio

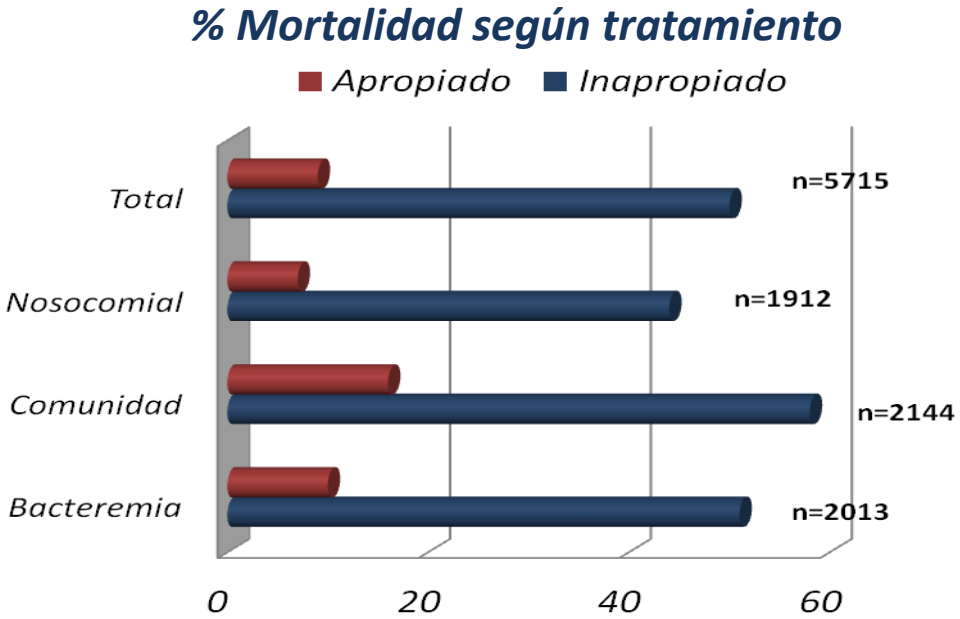
a) Ceftriaxona + Azitrimicina

b) Levofloxacino

c) Meropenem + Amikacina

d) Piperazilina/Tazobactam

TRATAMIENTO ANTIBIÓTICO



Chest. 2009 Nov;136(5):1237-48

- Foco infeccioso
- Hospitalización 30 días previos
- Antibióticos Previos
- Inmunosupresión/DM/ EPOC

TRATAMIENTO ANTIBIÓTICO

S pneumoniae

H influenzae

Abs

Hospital

MRSA

EPOC

Bronquiectasia

P aeruginosa

Enterobacterias

Enterococcus spp

Candida spp

Enterobacterias

Abs

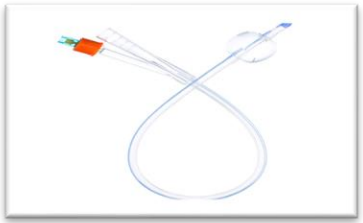
Sonda

Residencia

BLEEs

Enterococcus spp

Candida spp



2/3 Gram (+)

2/3 *S aureus*

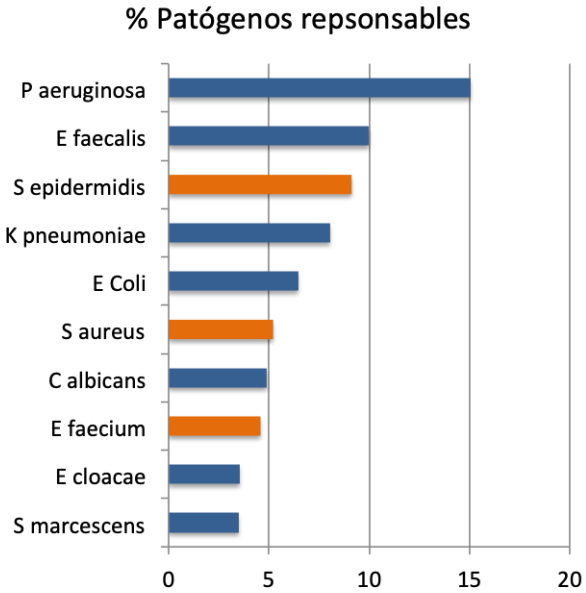
Críticos

+ Gram (-)

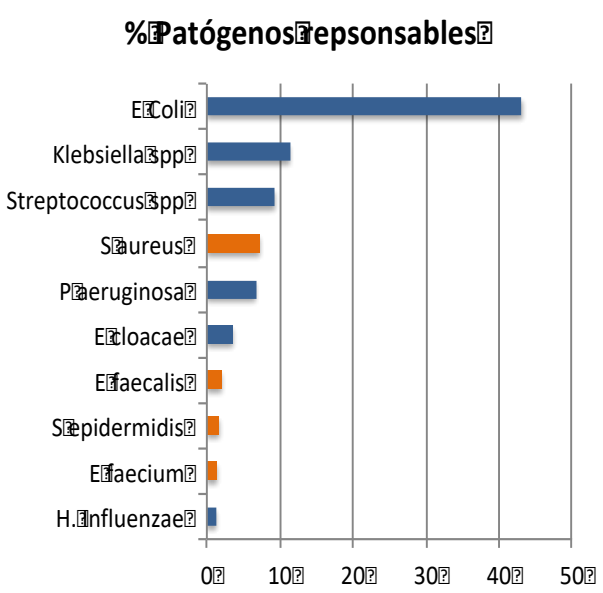
+ Cándida spp

TRATAMIENTO ANTIBIÓTICO

Datos Infecciones UCI ENVIN 2021



Datos Bacteremias Urgencias HSP 2021



TRATAMIENTO ANTIBIÓTICO

European Journal of Clinical Microbiology & Infectious Diseases
https://doi.org/10.1007/s10096-019-03727-4

ORIGINAL ARTICLE

A multidrug-resistant microorganism infection risk prediction model: development and validation in an emergency medicine population

54 *Servicios de Urgencias Españoles*

Derivation	OR (CI 95%)	*p*	*β*	Weight
Model				
Age ≥ 80 years	1.34 (1.10–1.64)	0.0034	0.2960	2
Congestive heart failure	1.46 (1.10–1.93)	0.0088	0.3768	3
End-organ damage diabetes mellitus	1.50 (1.10–2.03)	0.0095	0.4038	3
Indwelling urinary catheter	2.04 (1.51–2.75)	< 0.0001	0.7108	6
Recurrent urinary tract infections	1.38 (1.01–1.88)	0.0434	0.3211	3
Institutionalisation	2.64 (1.99–3.52)	< 0.0001	0.9718	8
> 3 cycles of antibiotics in the previous year	1.70 (1.20–2.42)	0.0030	0.5330	4
Colonisationa	5.77 (4.04–8.23)	< 0.0001	1.7523	15
Antibiotic treatment in < 3 months	1.66 (1.36–2.03)	< 0.0001	0.5089	4
Hospital admission in < 3 months	1.38 (1.12–1.70)	0.0027	0.3203	3
Functional status				
Mild dependence	Ref.	–		0
Moderate dependence	1.27 (1.01–1.60)	0.0431	0.2396	2
Severe dependence	1.79 (1.35–2.36)	< 0.0001	0.5792	5
Skin and soft tissue infection	1.63 (1.29–2.07)	< 0.0001	0.4878	4
Hosmer-Lemeshow, *p* value	0.0584			
AUC (CI95%) model	0.76 (0.74–0.78)			
Range				0–60

Cut-offs of the risk groups in the model	Derivation			
	S	Sp	PPV	NPV
≥ 3 vs. < 3	91.47	35.77	32.20	92.63
≥ 6 vs. < 6	78.92	57.15	38.05	89.05
≥ 10 vs. < 10	58.59	78.08	47.12	84.97
≥ 15 vs. < 15	40.15	90.50	58.50	81.93
≥ 22 vs. < 22	22.58	96.99	71.43	78.98
Optimal cut-off ≥ 9 vs. < 9	62.61	74.27	44.79	85.62

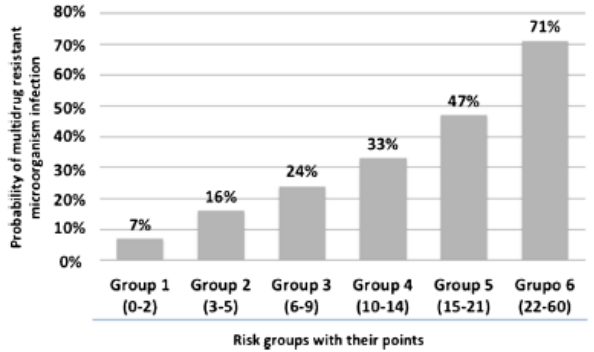


Fig. 4 Risk of multidrug-resistant microorganisms infection based on the score

TRATAMIENTO ANTIBIÓTICO

Weak, very low quality of evidence

"Para adultos con sepsis o shock séptico y **alto riesgo de microorganismos resistentes a múltiples fármacos (MDR)**, sugerimos el uso de **dos antimicrobianos con cobertura gramnegativa** para el tratamiento empírico."

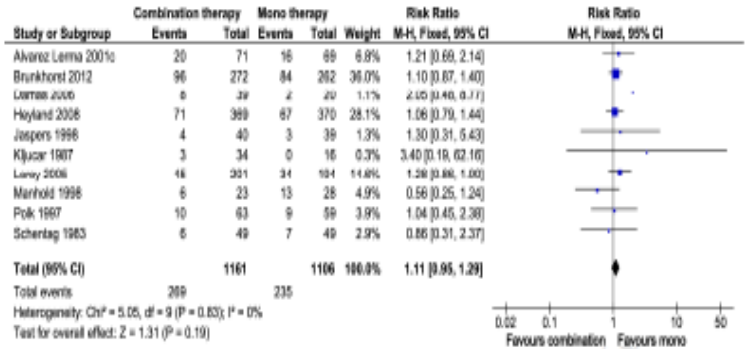
"Para adultos con sepsis o shock séptico y **bajo riesgo de organismos multirresistentes (MDR),** sugerimos **no usar dos agentes frente a gramnegativos**."

"Sugerimos **no utilizar una cobertura doble** contra gramnegativos **una vez que se conocen el patógeno causante** y las susceptibilidades."

Empirical mono- versus combination antibiotic therapy in adult intensive care patients with severe sepsis - A systematic review with meta-analysis and trial sequential analysis

Review J Infect. 2017 Apr;74(4):331-344.

No diferencias en mortalidad (RR: 1.11 (0.95-1.29)) u otras medidas de resultado importantes para el paciente entre el uso de la terapia antibiótica empírica mono o combinada en pacientes adultos de UCI con sepsis grave.



Siempre que el fármaco elegido para la monoterapia **tenga una cobertura adecuada** en el entorno utilizado, es poco probable que la adición de un segundo antibiótico añada un beneficio adicional.

La **información local sobre los patrones de resistencia** de los agentes causantes de sepsis más comunes es fundamental para elegir la antibioticoterapia empírica más adecuada

TRATAMIENTO ANTIBIÓTICO

"Para los adultos con sepsis o shock séptico con **alto riesgo de MRSA**, recomendamos el uso de **antimicrobianos empíricos** con cobertura de MRSA en lugar del uso de antimicrobianos sin cobertura de MRSA."

"Para los adultos con sepsis o shock séptico con **bajo riesgo de MRSA**, sugerimos **no usar** antimicrobianos empíricos con **cobertura de MRSA**, en comparación con el uso de antimicrobianos sin cobertura de MRSA."

Factores de riesgo MRSA

- ✗ Prevalencia región/unidad
  - 2% Europa Este - 10% USA
- ✗ Antecedentes de infección o colonización
- ✗ Antibióticos intravenosos recientes
- ✗ Antecedentes de infecciones cutáneas recurrentes o heridas crónicas
- ✗ Presencia de dispositivos invasivos
- ✗ Hemodiálisis
- ✗ Ingresos hospitalarios recientes
- ✗ Gravedad de la enfermedad

Best practice statement

TRATAMIENTO ANTIBIÓTICO

"Para los adultos con sepsis o shock séptico con **alto riesgo de infección fúngica**, sugerimos usar **terapia antifúngica** empírica en lugar de ninguna terapia antifúngica."

"Para los adultos con sepsis o shock séptico con **bajo riesgo de infección fúngica**, sugerimos **contra el uso empírico** de la terapia antifúngica."

Weak recommendation, low quality of evidence.

Factores de riesgo Candida

Cándida score	
Colonización multifocal	**1**
Cirugía	**1**
Nutrición Parenteral	**1**
Sepsis severa/Shock	**2**
>2 Predictor candidiasis invasiva	

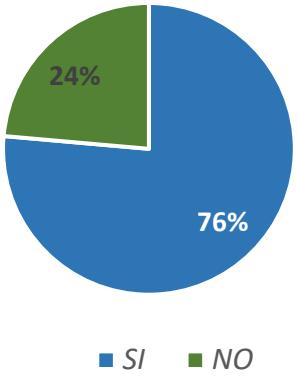
- ✗ Shock séptico
- ✗ Antifúngicos previos
- ✗ Sospecha Candidas R-fluconazol

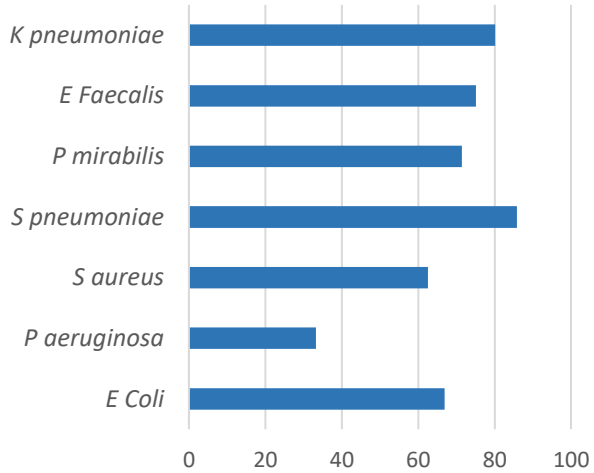
→ Fluconazol

→ Equinocandinas

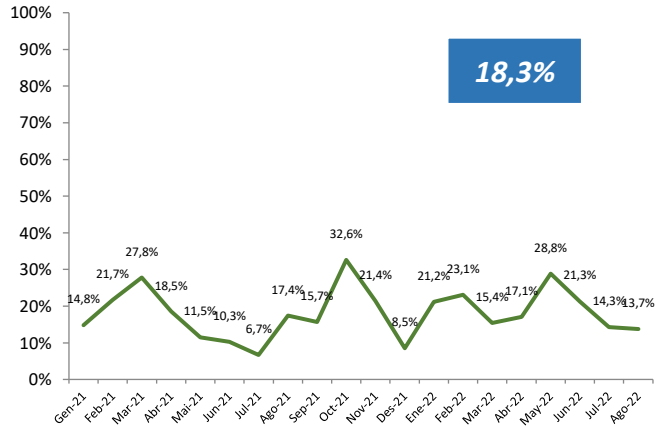
TRATAMIENTO ANTIBIÓTICO

% Adecuación Tratamiento Sepsis con bactermeia 2020





% Multirresistencia



Datos Hospital Santa Creu i Sant Pau. 2021

TRATAMIENTO ANTIBIÓTICO

Guías Clínicas Disponibles y Actualizadas

Consulta equipos SEPSIS/PROA

Alertas sistemas de prescripción

Análisis retrospectivo de casos

TRATAMIENTO ANTIBIÓTICO

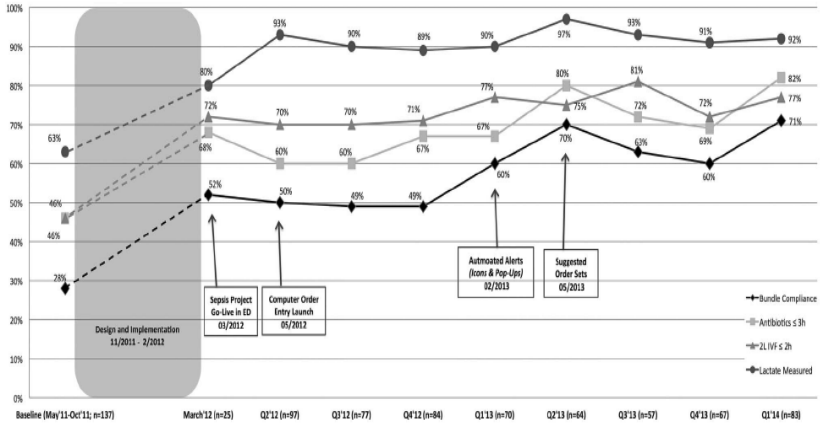
A quality improvement project to improve early sepsis care in the emergency department

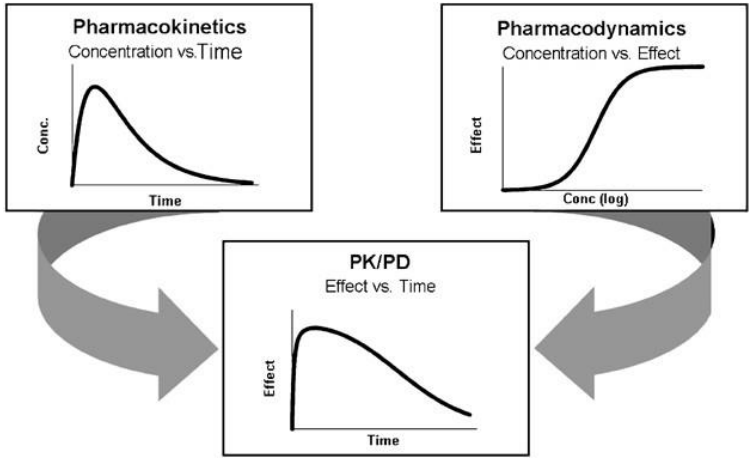
Medley O'Keefe Gatewood,[1] Matthew Wemple,[2] Sheryl Greco,[3] Patricia A Kritek,[4] Raghu Durvasula[5]

1- *Herramienta de detección* dirigida por enfermeras y protocolo de gestión para identificar e iniciar un tratamiento temprano

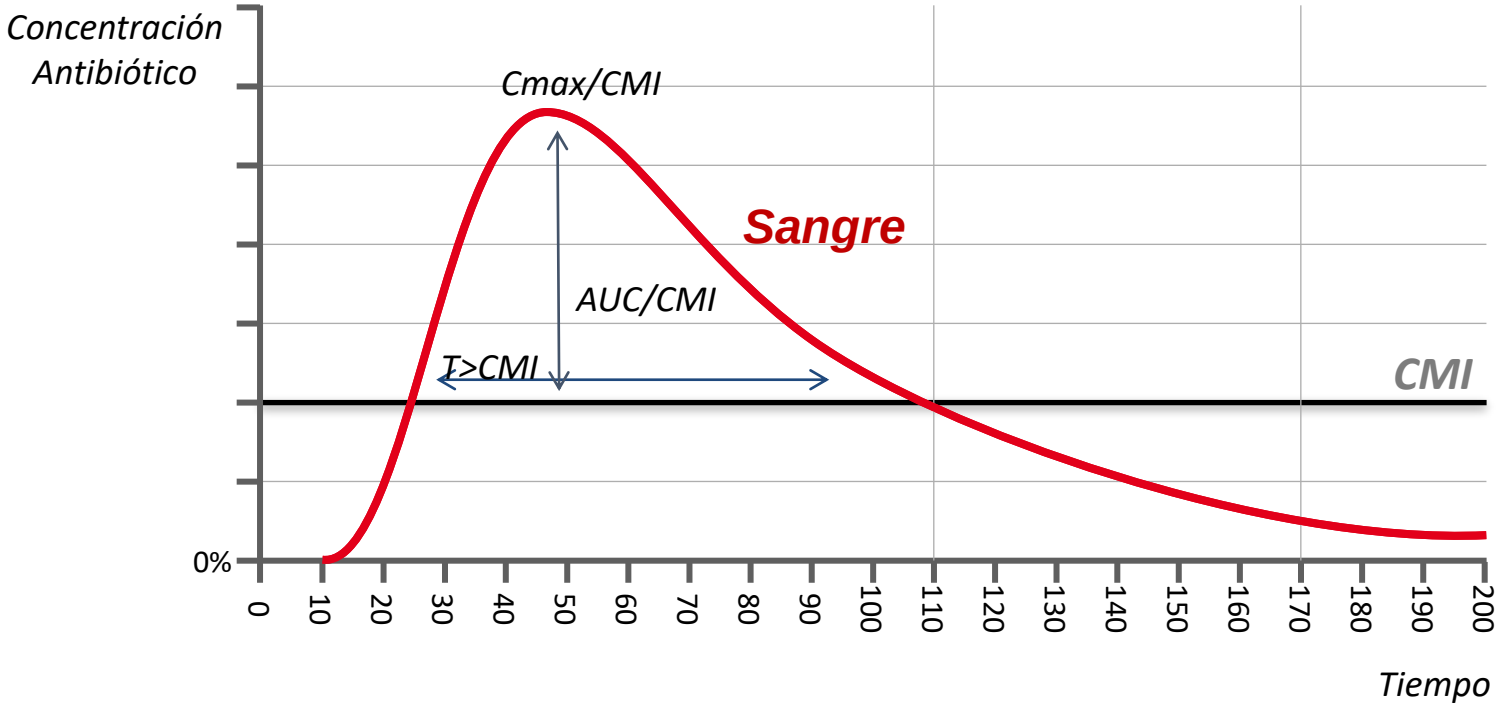
2- Algoritmo de detección asistido por ordenador que genera una ventana emergente de *"Alerta de sepsis"* en el programa de historia clínica electrónica

3- Conjuntos de órdenes sugeridas específicas para la sepsis para el diagnóstico inicial y la reanimación, la selección de antibióticos y la terapia dirigida por objetivos.

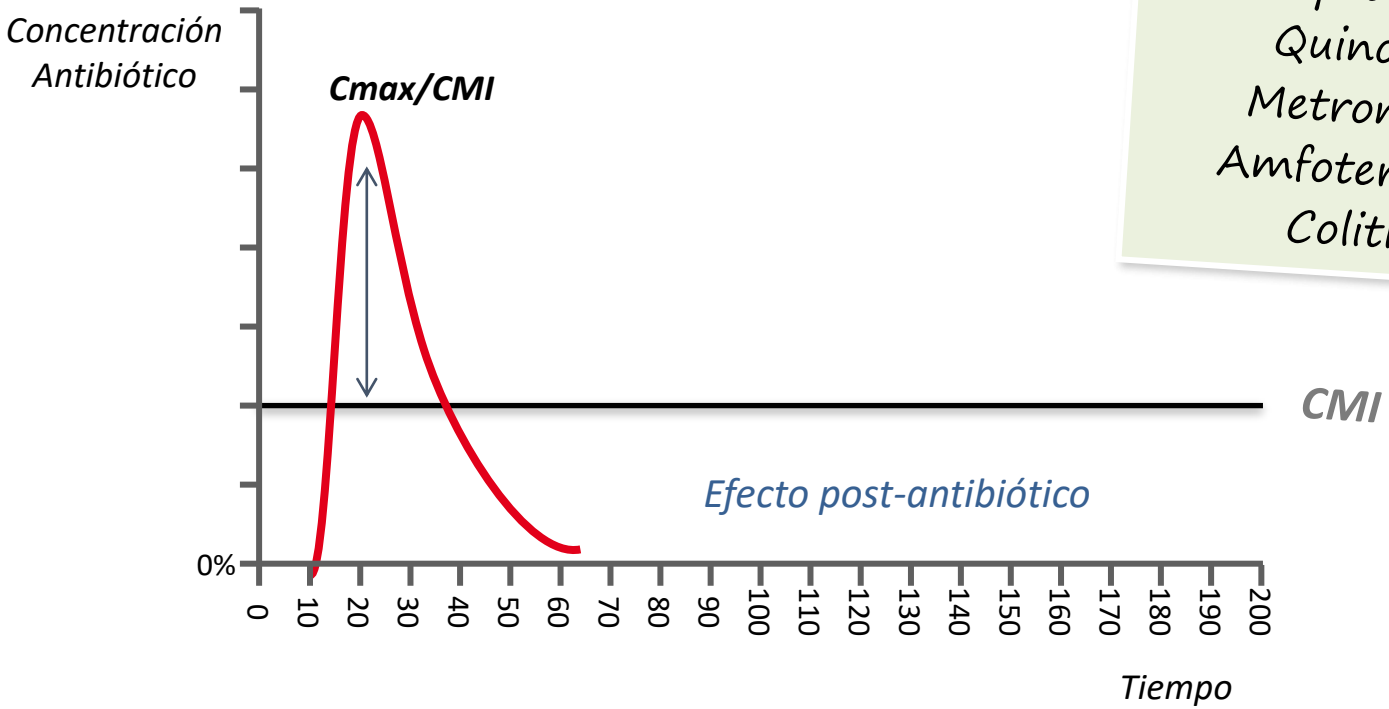



Pharmacokinetics
Concentration vs.Time
Conc.
Time
Pharmacodynamics
Concentration vs. Effect
Effect
Conc (log)
PK/PD
Effect vs. Time
Effect
Time

DOSIFICACIÓN



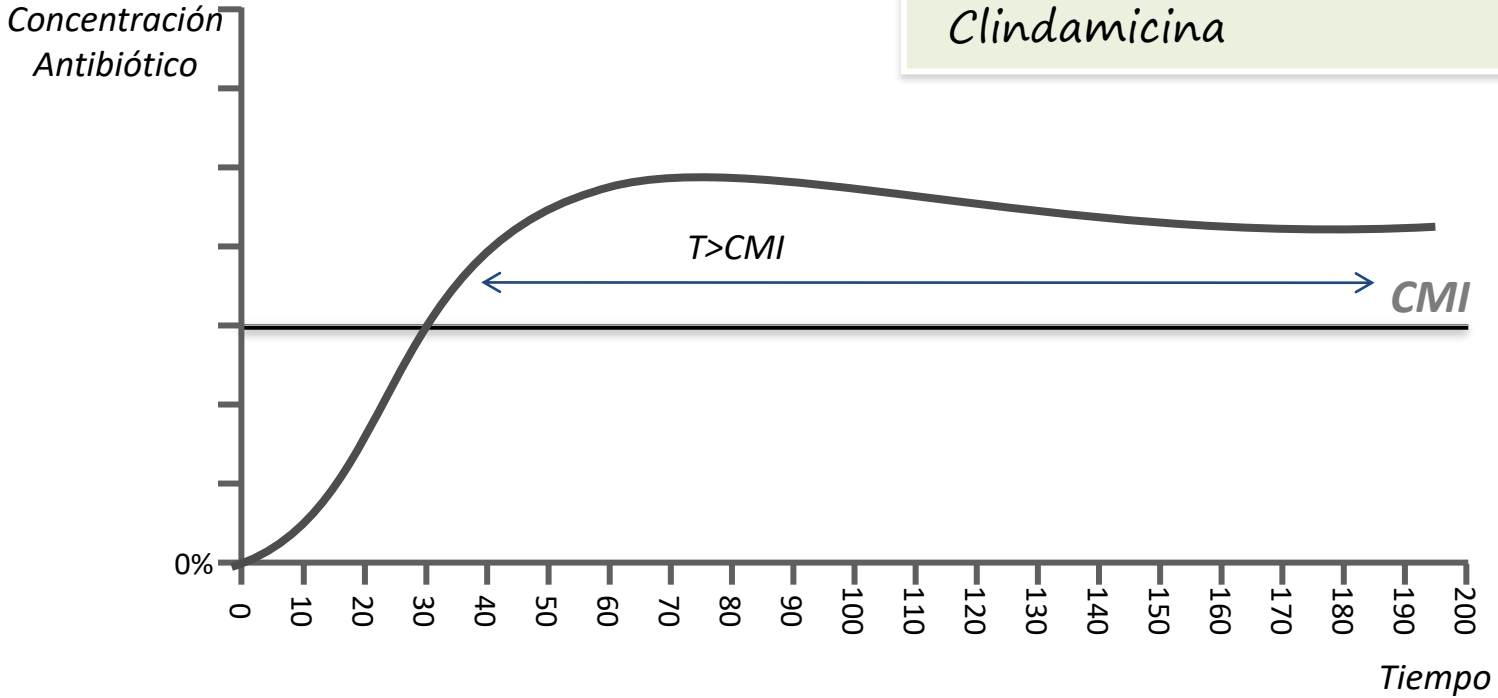
DOSIFICACIÓN



Amikacina
Daptomicina
Quinolonas
Metronidazol
Amfotericina B
Colitina*

DOSIFICACIÓN

Carbapenems > 40-50%
Penicilinas, Cefalosporinas > 80%
Linezolid: 80%
Claritromicina, Fosfomicina, Clindamicina



DOSIFICACIÓN

Endotoxina bacteriana

↓

Respuesta inflamatoria

Aporte de Fluidos (30 mL/kg)

↓

Extravasación

Tercer espacio

↓

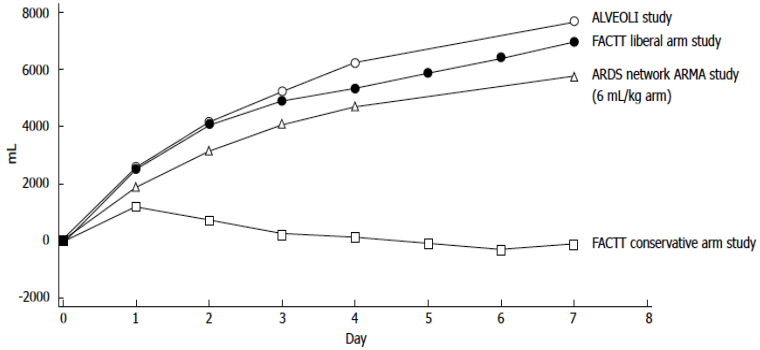
Aumento Vd de F hidrofílicos

Reducción de C plasmática

↓

Reducción eficacia fármacos Cmax dependientes

Balance hídrico



World J Crit Care Med 2015; 4(2): 116-129

HIPERFILTRACIÓN

Inflamación Sistémica

↓

Noradrenalina

Incremento Gasto Cardiaco

Fluidoterapia

↓

Hiperfiltrado

CL ≥ 130 mL/min/1.73 m2

ARC Score Hyperfiltration

Factores de Riesgo	Puntuación
Edad <50 años	6
Trauma	3
SOFA mod <5	1

Alto riesgo = 7-10 puntos

Intermedio riesgo = 4-6 puntos

Bajo riesgo = 0-3 puntos

AUC: 0,89 (IC95%: 0,80-0,97)

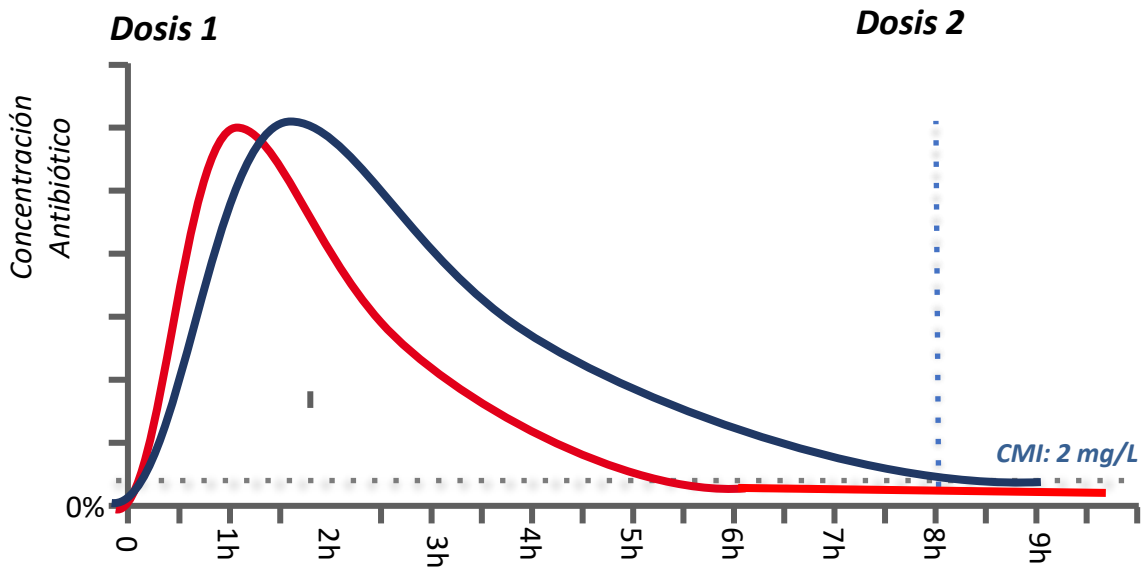
100% Sensibilidad

71,4/ especificidad

Hobbs et al, Pharmacotherapy. 2015

HIPERFILTRACIÓN

Simulación Ceftolozano



Modelo Monocompartimal

Vd:13.8 L; fu: 18%

FG=80 mL/min

- T>CMI Ceftoloz: 109,4%
- T> 0,25 Tazob: 97,3%

FG=150 mL/min

- T>CMI Ceftoloz: 65,6%
- T> 0,25 Tazob: 58,9%

International Journal of Antimicrobial Agents 36 (2010) 332–339

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International Journal of Antimicrobial Agents

journal homepage: http://www.elsevier.com/locate/ijantimicag

Therapeutic drug monitoring of β-lactams in critically ill patients: proof of concept

Jason A. Roberts[a,b,c,*], Marta Ulldemolins[a,d], Michael S. Roberts[e,f], Brett McWhinney[g], Jacobus Ungerer[g], David L. Paterson[h,i], Jeffrey Lipman[a,c]

Primera monitorización: **74,0%** requiere ajuste

Table 4
Effect of antibiotic prescribed on the need for β-lactam antibiotic dose adjustment at the first therapeutic drug monitoring (TDM) level.

Antibiotic	Standard initiation dose[a]	Patients	Dose maintained	Dose increased[b]	Dose decreased
PIP/TAZ[c]	4.5 g q6h	116	27 (23%)	57 (49%)	32 (28%)
Ampicillin	2 g q6h	4	0 (0%)	1 (25%)	3 (75%)
Meropenem	1 g q8h	51	8 (16%)	29 (57%)	14 (27%)
Penicillin G	2.4 g q4h	9	3 (33%)	3 (33%)	3 (33%)
Flucloxacillin	2 g q4h	16	1 (6%)	15 (94%)	0 (0%)
Cefazolin	1 g q8h	6	0 (0%)	6 (100%)	0 (0%)
Ceftriaxone	1 g q12h	33	22 (67%)	7 (21%)	4 (12%)
Cefalothin	1 g q6h	1	0 (0%)	1 (100%)	0 (0%)
Total		236	61 (25.8%)	119 (50.4%)	56 (23.7%)

Media: 53.5 (18.3) años

Objetivo: 4 x CMI

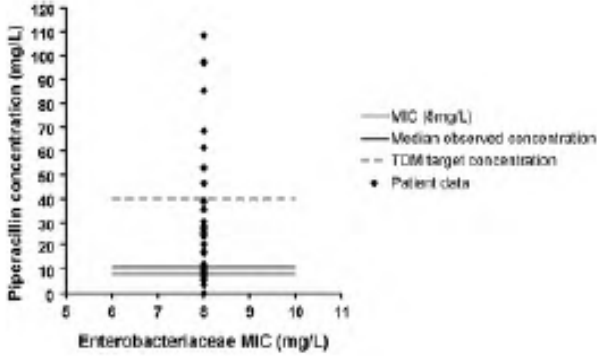


Fig. 1. Comparison of unbound piperacillin concentrations with pharmacodynamic target concentrations for therapy in patients (n = 49) with known or suspected Enterobacteriaceae infection. MIC, minimum inhibitory concentration; TDM, therapeutic drug monitoring.

DOSIFICACIÓN

Journal of Antimicrobial Chemotherapy (2008) **61**, 173–176
doi: 10.1093/jac/dkm431
Advance Access publication 13 November 2007

JAC

Effect of severity of sepsis on tissue concentrations of linezolid

Christiane Thallinger[1,2], Cornelia Buerger[3], Nele Plock[3], Sascha Kljucar[4], Sonja Wuenscher[1], Robert Sauermann[1], Charlotte Kloft[3] and Christian Joukhadar[5]*

Table 1. Pharmacokinetic data of linezolid in plasma, muscle and subcutaneous adipose tissue after a single intravenous dose of 600 mg linezolid in healthy subjects and patients presenting with sepsis or septic shock

	AUC_{0-8} (mg·h/L)	AUC_{0-24} (mg·h/L)[a]	AUC_{0-24} (mg·h/L)[b]	$C_{av(ss)}$ (mg/L)	C_{max} (mg/L)	T_{max} (h)	$t_{1/2\beta}$ (h)	CL (L/h)	V_{ss} (L)
Healthy ($n = 10$)									
plasma free	52.98 ± 11.78	78.30 ± 24.97	159.84 ± 60.42	13.32 ± 5.03	12.84 ± 2.57	0.84 ± 0.1	4.73 ± 2.08	8.59 ± 3.38	51.47 ± 9.51
subcutis	77.43 ± 25.73	129.76 ± 46.18	272.87 ± 113.54	22.74 ± 9.46	18.72 ± 5.43	0.77 ± 0.2	5.72 ± 2.67	ND	ND
muscle	60.28 ± 12.7	92.89 ± 23.33	194.46 ± 61.06	16.21 ± 5.09	13.18 ± 2.85	0.97 ± 0.1	5.39 ± 2.86	ND	ND
Septic shock ($n = 16$)									
plasma free	47.17 ± 13.59	70.78 ± 28.12	146.55 ± 66.54	12.21 ± 5.55	14.23 ± 3.45	0.52 ± 0.4	4.92 ± 2.08	9.81 ± 4.32	60.37 ± 13.92
subcutis	44.61 ± 19.38	65.76 ± 32.61	132.41 ± 68.64	11.03 ± 5.72	11.02 ± 4.80	0.86 ± 0.6	4.50 ± 1.82	ND	ND
muscle	42.76 ± 15.64	68.74 ± 32.84	146.31 ± 86.60	12.19 ± 7.22	9.33 ± 3.08	0.95 ± 0.6	5.41 ± 2.70	ND	ND
Severe sepsis ($n = 8$)									
plasma free	39.85 ± 14.49	50.91 ± 23.13	100.41 ± 46.68	8.37 ± 3.89	14.23 ± 4.13	0.49 ± 0.0	3.14 ± 1.53	14.83 ± 7.55	57.15 ± 17.8
subcutis	48.43 ± 22.80	67.70 ± 45.23	135.00 ± 96.97	11.25 ± 8.08	11.09 ± 4.35	1.67 ± 0.8	3.25 ± 1.70	ND	ND
muscle	40.04 ± 14.93	52.67 ± 26.00	101.95 ± 50.64	8.50 ± 4.22	10.12 ± 4.47	1.49 ± 1.2	2.99 ± 0.98	ND	ND

AUC_{0-8}, AUC from 0 to 8 h; AUC_{0-24}, AUC from 0 to 24 h; $t_{1/2\beta}$, elimination half-life at the β-phase; $C_{av(ss)}$, average concentration at steady state calculated from single-dose measurements; C_{max}, maximum concentration; T_{max}, time to C_{max}; CL, apparent total body clearance; V_{ss}, apparent volume of distribution at steady state; ND, not determined.
Data are expressed as means ± SD.

DOSIFICACIÓN

Para los adultos con sepsis o shock séptico, sugerimos utilizar una **infusión prolongada de betalactámicos** para el mantenimiento (después de un bolo inicial) en lugar de la infusión de un bolo convencional.

Weak, moderate quality of evidence.

Para adultos con sepsis o shock séptico, recomendamos **optimizar las estrategias** de dosificación de antimicrobianos según los principios farmacocinéticos/farmacodinámicos **(PK / PD)** aceptados y las propiedades específicas de los medicamentos.

Best practice statement

TABLE 3.
Guidance for PK/PD-Based Dosing for Specific Drug Classes

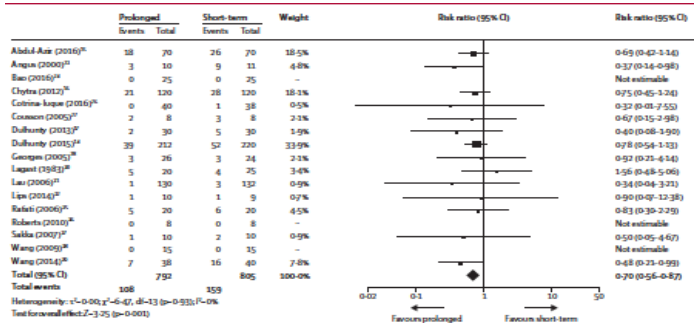
Drug or Drug Class	PK/PD Index Associated With Bacterial Killing or Efficacy	Drug Concentration Target	Considerations for Optimized Dosing*	Reference Number
Antibacterials				
Aminoglycosides	$AUC_{0\text{-}24}$/MIC; C_{max}/MIC	AUC 70–100 C_{max}/MIC 8–10	Use extended interval dosing with patient weight and kidney function	237
Beta-lactams	$fT_{>MIC}$	C_{min} > MIC	Use prolonged infusions, consider patient weight and kidney function	253
Colistin	$AUC_{0\text{-}24}$/MIC	Unspecified	Use patient weight and kidney function	259
Daptomycin	$AUC_{0\text{-}24}$/MIC; C_{max}/MIC	$AUC_{0\text{-}24}$/MIC > 200	Use patient weight and kidney function	237
Fluoroquinolones	$AUC_{0\text{-}24}$/MIC; C_{max}/MIC	$AUC_{0\text{-}24}$/MIC 80–125	Use kidney function	237
Vancomycin	$AUC_{0\text{-}24}$/MIC	$AUC_{0\text{-}24}$/MIC 400	Use patient weight and kidney function	260
Antifungals				
Fluconazole	$AUC_{0\text{-}24}$/MIC	$AUC_{0\text{-}24}$/MIC 100	Use patient weight and kidney function	261
Posaconazole	$AUC_{0\text{-}24}$/MIC	C_{min} 1–4 mg/L	Use formulation-specific dose	261
Voriconazole	$AUC_{0\text{-}24}$/MIC	C_{min} 2–6 mg/L	Use patient weight	261

DOSIFICACIÓN

Prolonged versus short-term intravenous infusion of antipseudomonal β-lactams for patients with sepsis: a systematic review and meta-analysis of randomised trials

Konstantinos Z Vardakas, Georgios L Voulgaris, Athanasios Maliaros, George Samonis, Matthew E Falagas

- ✗ 22 E. Clínicos (1876 pacientes)
- ✗ B-lactámicos antipseudomonas
- ✗ 14 en pacientes UCI
- ✗ 1 en >65 años



RR mortalidad: 0.70 (0.56–0.87)

Prolonged infusion versus intermittent boluses of β-lactam antibiotics for treatment of acute infections: a meta-analysis

Jocelyn Teo, Yixin Liew, Winnie Lee, Andrea Lay-Hoon Kwa*

- ✗ **19** E. Clínicos (1620 pacientes)
- ✗ B-lactámicos

Table 3
Subgroup analyses of included studies.

Study subgroup	Mortality				Clinical success			
	No. of studies	No. of patients	Summary risk ratio (95% CI)	I^2 (%)	No. of studies	No. of patients	Summary risk ratio (95% CI)	I^2 (%)
RCTs	10	779	0.83 (0.57–1.21)	0	14	1125	1.05 (0.99–1.12)	0
Non-RCTs	9	841	**0.57 (0.43–0.76)**	0	5	421	**1.34 (1.02–1.76)**	90
Penicillins	8	974	**0.60 (0.45–0.82)**	0	6	491	1.08 (0.94–1.25)	60
Cephalosporins	5	191	0.92 (0.52–1.63)	33	9	662	1.11 (0.98–1.25)	65
Carbapenems	4	274	0.74 (0.42–1.28)	28	3	333	1.16 (0.93–1.46)	83
Equivalent daily dose	10	813	0.82 (0.56–1.20)	0	10	934	**1.22 (1.05–1.43)**	75
APACHE II score ≥15	10	861	**0.63 (0.48–0.81)**	9	8	663	**1.26 (1.06–1.50)**	83
All studies	19	1620	**0.66 (0.53–0.83)**	0	19	1546	**1.12 (1.03–1.21)**	63

CI, confidence interval; RCT, randomised controlled trial; APACHE, Acute Physiology and Chronic Health Evaluation.
Numbers in bold denote statistically significant results.

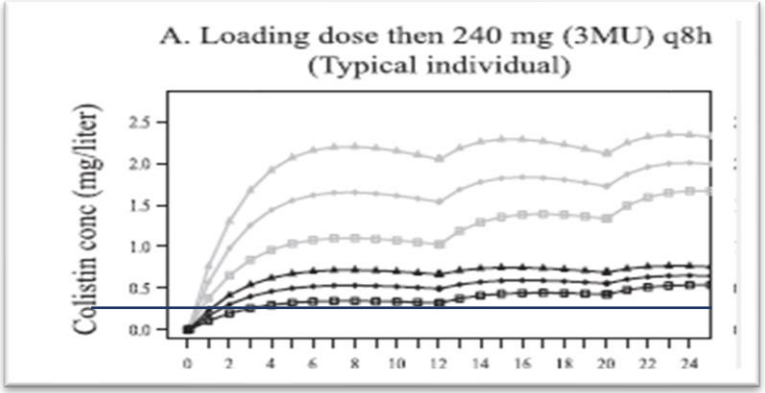
DOSIFICACIÓN

DOSIS DE CARGA

Fármacos hidrofílicos/ CMI alta
Alto Vd

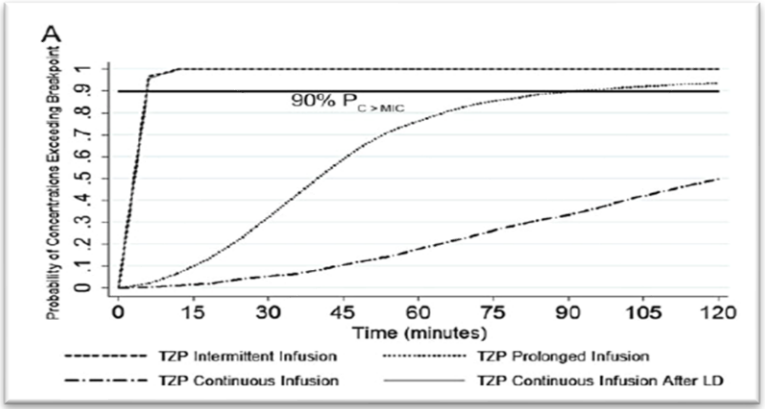
- ✗ *Tigeciclina=200 mg*
- ✗ *Colistina: 4,5 -9 MU*
- ✗ *Vancomicina: 25-30 mg/Kg*
- ✗ *Caspofungina: 70 mg*
- ✗ ***B-Lactámicos perfusión extendida***
- ✗ *Azoles*
- ✗ *Aminoglucósidos: 30mg/kg*

Colistina



AAC. 2014;58(12):7324–30.

Piperazilina/Tazobactam



Clin Infect Dis. 2014;59(6):905-7.

Research Report

A Randomized Trial of Loading Vancomycin in the Emergency Department

Annals of Pharmacotherapy
1–8

DOI: 10.1177/1060028014556813
aop.sagepub.com
SAGE

Jamie M. Rosini, PharmD[1], Julie Laughner, MD[1], Brian J. Levine, MD[1,2], Mia A. Papas, PhD[3], John F. Reinhardt, MD[1], and Neil B. Jasani, MD[1,2]

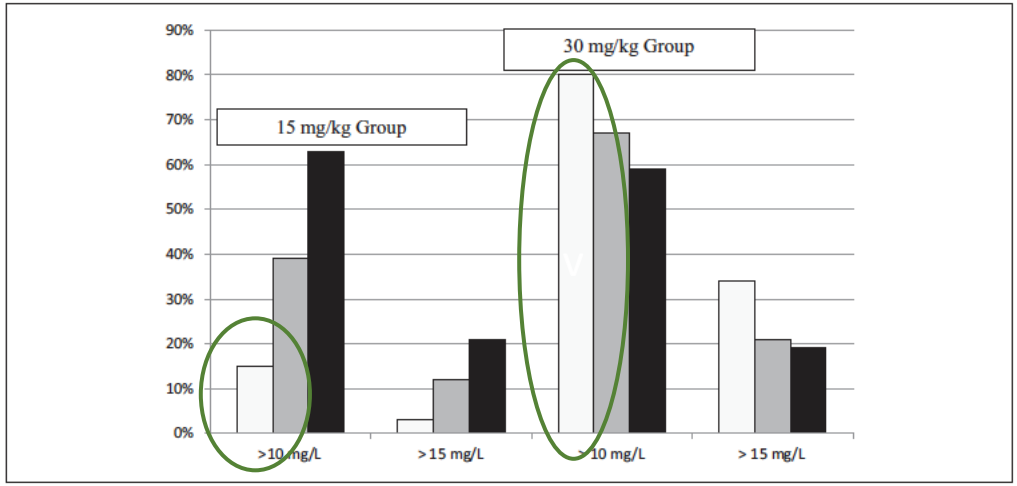
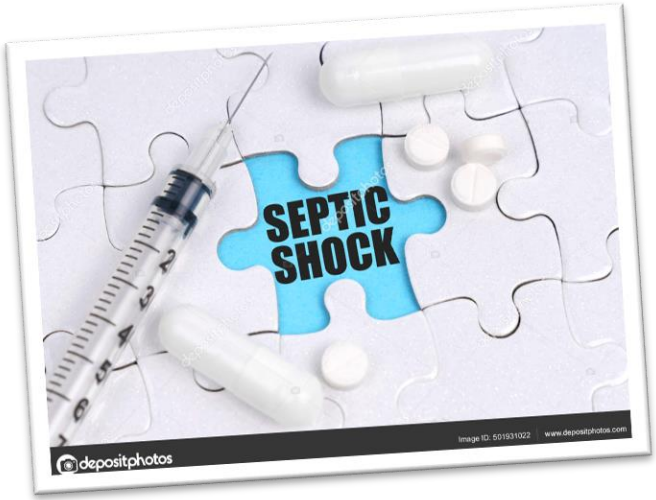


Figure 2. Percentage of troughs >10 mg/L and >15 mg/L at times 12, 24, and 36 hours after initial dose.

- *There was **no** statistically significant **difference in hospital length of stay** (traditional dose, 6.33 days [SD = 5.6]; loading dose, 5.84 days [SD = 4.8]) **or mortality** between the 2 groups.*

- ***Nephrotoxicity** occurred overall in 5.1% of study patients, with 3 (6.1%) in the traditional- and 2 (4%) in the loadingdose groups (P non significant).*


SEPTIC
SHOCK
depositphotos
Image ID: 501931022
www.depositphotos.com

SHOCK SÉPTICO

NORADRENALINA: 1º Elección

PAM: 65 mmHg

- Dosis inicial: 0,01-0,3 mcg/kg/min
- Dosis máxima: 90 mcg/min
- **Estandarizar diluciones**: 4 ampollas/250 mL S. Fisológico/Glucosa 5%

Surviving Sepsis Campaign

✗ ***"No recomendamos*** el uso de dosis bajas de **dopamina** para la protección renal (recomendación sólida, evidencia de alta calidad)."

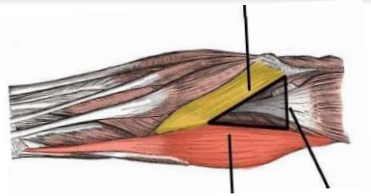
✗ "**Dobutamina** en pacientes que muestren evidencia de hipoperfusión persistente a pesar de sobrecarga de líquidos adecuada y uso de vasopresores **(recomendación débil, evidencia de baja calidad)."**

SHOCK SÉPTICO

Para los adultos con shock séptico, **sugerimos iniciar vasopresores vía periférica** para restaurar la presión arterial media **en lugar de retrasar el inicio** hasta que se asegure un acceso venoso central.

Cuando se usan vasopresores de manera periférica, deben administrarse solo durante un **período corto de tiempo** y en una vena en la **fosa antecubital** o próxima a ella.

- ✗ Frecuencia extravasación: 3.4%
- ✗ No episodios de necrosis/isquemia
- ✗ No secuelas a largo plazo
- ✗ Mayor frecuencia si infusión distal



Tian DH et al: Safety of peripheral administration of vasopressor medications: A systematic review. Emerg Med Australas 2020; 32:220–227

SHOCK SÉPTICO

ACTUACIÓN EXTRAVASACIÓN NORADRENALINA

pH of 3.0 to 4.0
Riesgo de necrosis

Medidas generales

1.Parar la infusión y aspirar a través de la vía 5-10 ml de sangre
2.Evitar la presión manual.
3.Retirar la vía o la aguja si no hay que administrar antídoto por vía intravenosa.
4.Aplicar las medidas específicas descritas para cada fármaco.
5.Elevar la extremidad a nivel superior del corazón.
6.Evitar fotoexposición de la zona afectada.

Medidas específicas

•Elevación y calor
•Fentolamina 5-10 mg en 10-20 mL SF Intradérmico

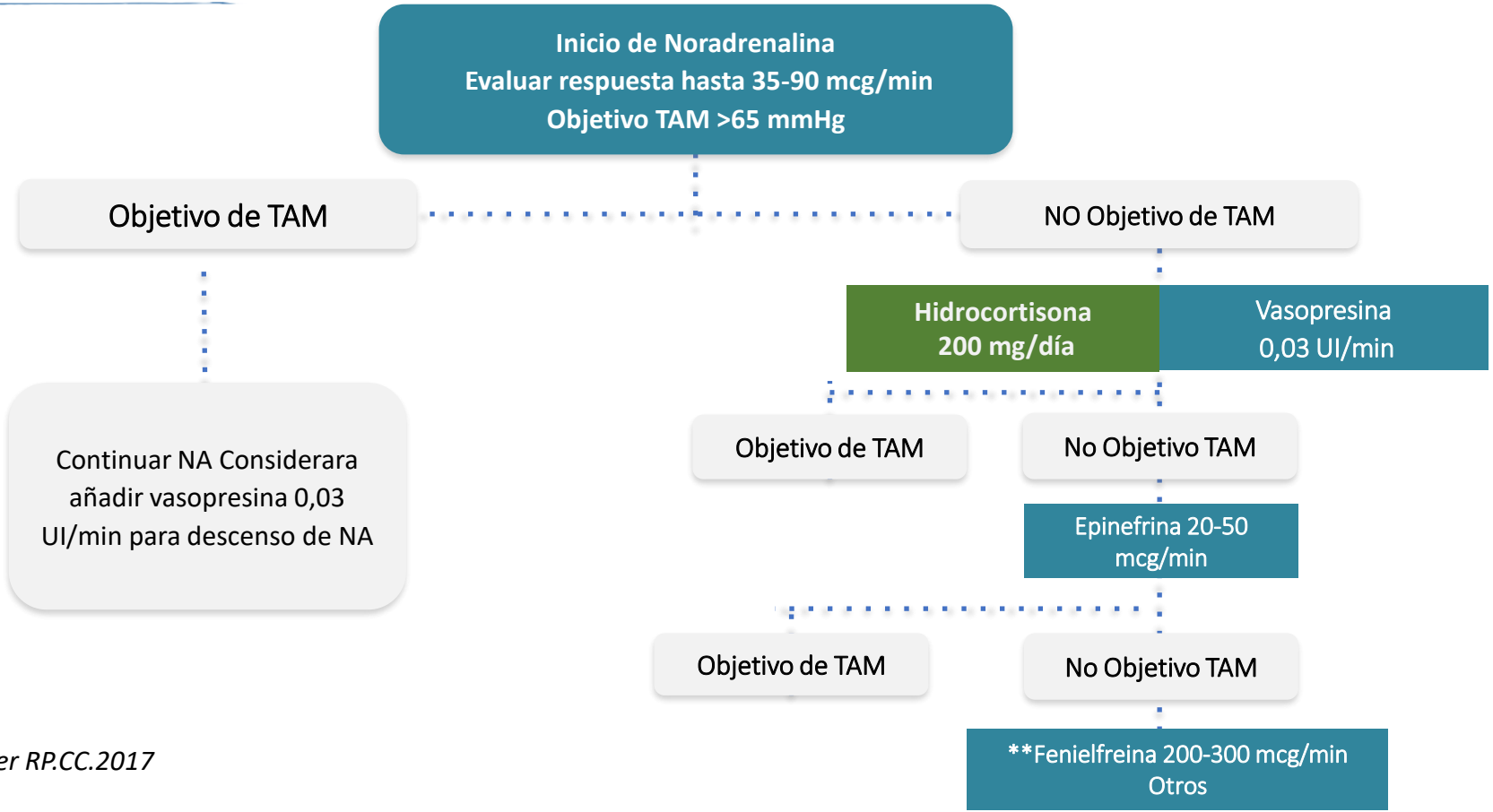
Alternativas:

•Nitroglicerina 2% tópica c/8h
•Terbutalina 1mg/10mL SF Intradérmico
•Sulfadiazina argéntica

Evitar: Frio local (puede empeorar la ulceración del tejido), hialuronidasa

Extravasation of Noncytotoxic Drugs: A Review of the Literature
Ann Pharmacother . 2014 Jul;48(7):870-886

SHOCK SÉPTICO



Dellinger RP.CC.2017

SHOCK SÉPTICO

"Para los adultos con shock séptico con noradrenalina con niveles inadecuados de presión arterial media, sugerimos agregar **vasopresina** en lugar de aumentar la dosis de norepinefrina."

Moderate-quality evidence

"Para los adultos con shock séptico y niveles de presión arterial promedio inadecuados a pesar de la noradrenalina y la vasopresina, sugerimos **agregar epinefrina**."

Low-quality evidence

"Para adultos con shock séptico, sugerimos contra el uso de terlipresina."

Low-quality evidence

TERLIPRESSIN

- ✗ Más específica para los receptores V1
- ✗ 9 Ensayos clínicos 950 pacientes en total.
  - No diferencias en la mortalidad RR: 0,89 [IC95%: 0,70-1,13])
  - Aumento en los eventos adversos (isquemia digital, diarrea)

Liu ZM, et al. Intensive Care Med 2018; 44:1816–1825

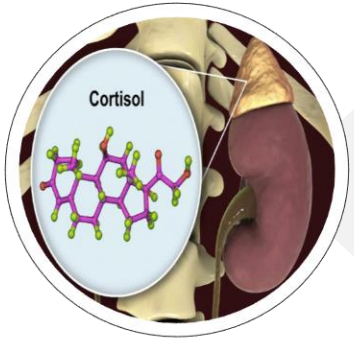
SHOCK SÉPTICO

"Para los adultos con shock séptico y un requerimiento continuo de terapia con vasopresores, sugerimos el uso de **corticosteroides intravenosos**."

Moderate-quality evidence

El corticosteroide típico que se usa en adultos con choque séptico es la **hidrocortisona** intravenosa a una dosis de 200 mg / día administrada como **50 mg por vía intravenosa cada 6 horas** o como una infusión continua. Se sugiere que se inicie con una dosis de noradrenalina ≥ **0,25 mcg / kg / min** al menos 4 horas después del inicio.

SHOCK SÉPTICO

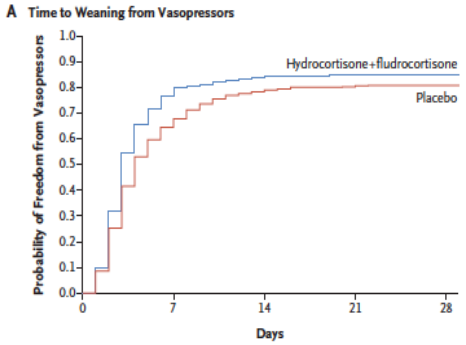


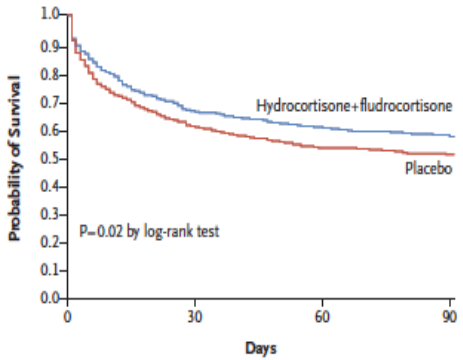
- ✗ Restaura el volumen plasmático (mineralocorticoide) y tono vascular (receptores endoteliales)
- ✗ Atenúa inflamación vía NF-KB
- ✗ Sepsis: Receptores mineralocorticodes atenuados
- ✗ Reduce duración de shock y ventilación mecánica (CORTICUS, ADREANAL)
- ✗ Posible reducción de mortalidad a 90 días (APROCCHSS)

APROCCHSS Study

1241 patients

Hidrocortisona iv 50 mg/6h + Fludrocortisona iv 50-mcg/24h iv 7 días






Shorter is Smarter
Appropriate antibiotic use means prescribing the right antibiotic for the infection, in the right dose, for the right duration—every time.

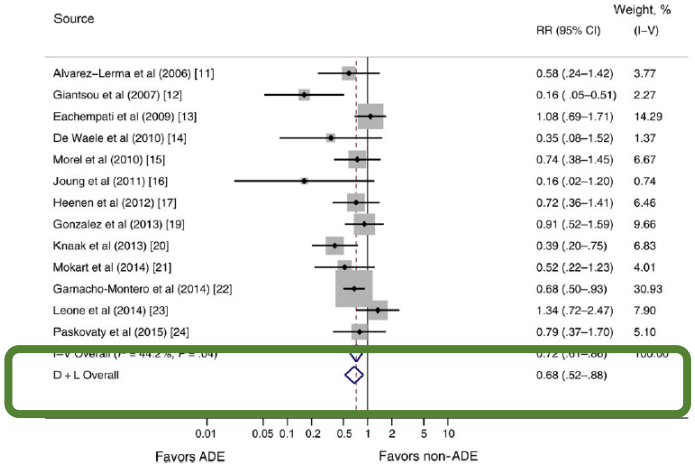
DESECALADA ANTIBIÓTICA

Clinical Infectious Diseases

REVIEW ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

A Systematic Review of the Definitions, Determinants, and Clinical Outcomes of Antimicrobial De-escalation in the Intensive Care Unit



Diferencias en mortalidad

- Desescalada asociada a **menor mortalidad** (RR: 0.68 (0.52-0.88)
- Las **escala de gravedad mejoraron** con la desescalada antibiótica (P = 0,04 a <0,001)
- Reducción riesgo reinfección por Multirresistentes

Intensive Care Med (2020) 46:1039–1042
https://doi.org/10.1007/s00134-020-05951-5

EDITORIAL

Antimicrobial de-escalation is part of appropriate antibiotic usage in ICU

Jean-Francois Timsit[1,2*], Jeffrey Lipman[3,4,5] and Matteo Bassetti[6]

Clinical features suggesting potential new infection

Bloodcultures and adequate microbiology and morphologic exams oriented on clinical exam
Other diseases mimicking infection: non-infective inflammatory processes

1. Direct examination
2. Rapid tests
3. Results of other exams

Microorganism present in the suspected infected site — No → Organ failures, increased need of vasopressor agents — No → Positive results of significant sample cultures — No → **Observe and look for other causes for the observed signs**

Yes

Key elements of AB choice
1. Underlying illness, immune status
2. Local epidemiology (MDRB)
3. Possible source of infection
4. Previous colonization
5. Previous AB used
6. Microbiology

Day 0

Start antimicrobial based on available data *(see left boxes)*
→ Favor narrow spectrum antimicrobials based on previous available data
Combination therapy not needed for sinergy purpose

Start antimicrobial based on available guidelines and local epidemiology
→ Combination AB therapy based on available guidelines adapted to local AB policies and previous available data*

Start targeted antimicrobial therapy with optimized regimen considering PK
→ Favor narrow spectrum antimicrobials adapted to lab results and PK

Seek source control where possible

Key elements of dose choice
1. Start with loading doses
2. Estimate the risk of glomerular hyperfiltration
3. Adapt AB doses within 24h based on estimated clearance, or RRT use.
4. TDM to assess the efficacy

Day 1-3

Consider early stop with multidisciplinary rounds
Early switch of inadequate therapy
Select the most appropriate agents according to MICs, PK, tissue diffusion, toxicities
Deescalate to monotherapy unless absolutely necessary
Favor narrow spectrum AB
Anticipate the duration of therapy

Key elements of the Follow-up
1. Clinical examination and improvement or stabilization of organ failures
2. Microbiological samples if clinically indicated
3. TDM to avoid overdosage and toxicities
4. Adapt AB doses within 24h based on estimated clearance, or renal replacement therapy use.
5. The situation must be stabilized; if not, start again the process.

Day 2-7

Consider early stop with multidisciplinary rounds
Daily reevaluation of the dose used according to clearance, TDM if available
Consider early stop based on recommendations and/or clinical status
If no improvement, start again the process

EOT

Stop therapy usually after 7 days
If not, report the reason to continue and the planned duration of therapy

Potential process quality indicators

Availability of unit AB consumption, nosocomial infection rate, and MDR bacteria epidemiology

Day 0
1. Sampling for cultures and other exams performed before AB start
2. Reason for AB start and precise reasoning described in the report file
3. Source control: assessed, and, if possible, performed.

Day 1-2
1. Report the names of the persons involved in the discussion
2. Report the choice of AB
3. If combination, report the reason of continuation
4. Report the discussion on the choice of the AB
5. AB dose and TDM if any
6. Interaction with pharmacists (PK interactions, AEs, etc.)
7. Planned duration of AB reported in the formulary

Day 3-4
1. Planned date of AB stop reported

Day 5-7
1. Reason for continuation reported
2. Planned date AB stop reported

DURACIÓN DE TRATAMIENTO

"Para los adultos con un diagnóstico de sepsis o shock séptico y **un control adecuado de la fuente**, sugerimos usar una **terapia antimicrobiana más corta sobre una más larga**."

RCT/Systemic Review	Days of treatment	Outcomes
Neumonía		
Capellier 2012	8 days vs 15 days	No difference
Chastre 2003	8 days vs 15 days	No difference
El Moussaoui 2006	3 days vs 8 days	No difference
Fekih Hassen 2009	7 days vs 10 days	No difference
File 2007	5 days vs 7 days	No difference
Kollef 2012	7 days vs 10 days	No difference
Leophonte 2002	5 days vs 10 days	No difference
Medina 2007	8 days vs 12 days	No difference
Siegel 1999	7 days vs 10 days	No difference
Tellier 2004	5 days vs 7 days	No difference
Bacteremia		
Chaudhry 2000	5 days vs 10 days	No difference
Runyon 1991	6 days vs 10 days	No difference
Yahav 2018	7 days vs 14 days	No difference
Intra-abdominal		
Montravers 2018	8 days vs 15 days	No difference
Sawyer 2015	Max 5 days vs Max.10 days	No difference
Urinary tract infection		
Peterson 2008	5 days vs 7 days	No difference

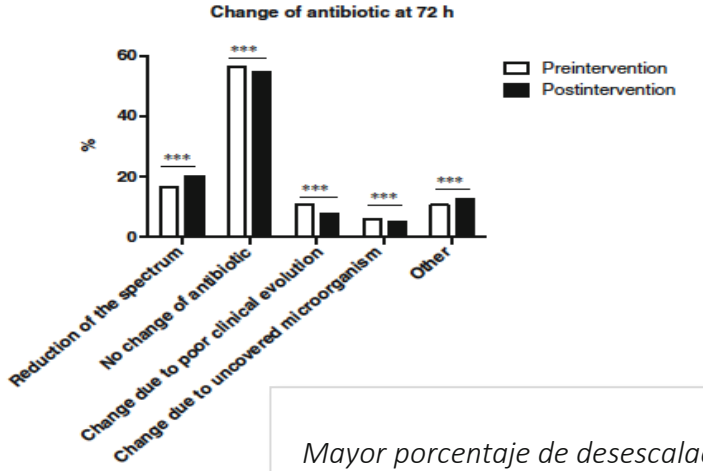
Ferrer et al. Critical Care (2018) 22:167
https://doi.org/10.1186/s13054-018-2091-0

Critical Care

RESEARCH Open Access

Improved empirical antibiotic treatment of sepsis after an educational intervention: the ABISS-Edusepsis study

- 2628 pacientes (64.1 (SD:15.2) años)
- Pacientes admitidos en UCIs Españolas (3 meses)
- Programa educativo multifacético
  - Sesiones educativas
  - Recordatorios periódicos
  - Auditoría y feedback
  - Videojuego

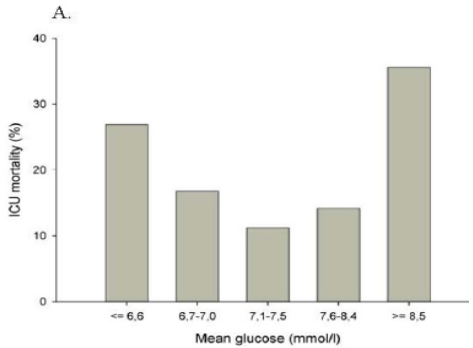


Mayor porcentaje de desescalada (20.1% vs. 16.3%; p = 0.004)

OTRAS COSAS

Tromboprofilaxis

- **Profilaxis farmacológica** en ausencia de contraindicación.
- Recomendación de HBPM sobre Heparina Na.
- Profilaxis mecánica si la farmacológica contraindicada.



Siegelaar *et al. Critical Care* 2010, **14**:R224

Control Glucemia

- Mantener niveles **≤180 mg/dL**
- Insulina (Protocolo) si 2 medidas >180 mg/dL
- Medidas cada 1-2h hasta estabilización
- No recomendado control estricto <110 mg/dL
- Precaución glicemia capilar

Importance of Pharmacy Involvement in the Treatment of Sepsis

Joseph B. Cavanaugh Jr, PharmD*; Jesse B. Sullivan, PharmD, BCPS, BCCCP†;

Beardsley et al 2016	Ordered new abx for 18% of patients Order verification Expedite preparation and delivery process	• Mean abx delivery time: 14.1 ± 13.5 minutes • Decreased administration from 396 to 51 min in non-ICUs • Decreased administration from 427 to 31 minutes in ICUs
Flynn et al 2014	Order abx based on order set Assess patient and abx appropriateness Facilitate vasopressor preparation	• 22-fold increase in appropriate abx within the first hour (OR, 22.4; 95% CI:7.5-69)
Weant et al 2013	Dose recommendations Appropriate empiric abx recommendations Medication preparation Drug information resource	• 130 patients with 585 recommendations • 53% of consults: dosing recommendations • 22% of consults: addition of empiric ab • 19% of consults: medication preparation
Moussavi et al 2016	Appropriate empiric abx recommendations Abx procurement and delivery from pharmacy	• Decrease in median time to abx (0.61 hours [IQR 0.37- 0.95] vs 0.88 hours [IQR 0.525-1.231]; P=0.001) • Increase in abx within 3 hours (100% vs 95%; P=0.025) • Increase in appropriate initial abx (97% VS 81%; p=0.0008)
MacClaren et al 2008	ICU pharmacist on daily patient care rounds	No ICU pharmacist • Increased mortality from sepsis by 4.8% (OR, 1.06; p=0.008) • $224,694,784 extra billing costs (p<0.001) • $3,344,802 extra drug charges (p=0.04) • $23,295,004 extra laboratory charges (p<0.001)
Sarani et al 2008	Pharmacist added to medical response team – Bedside response – Order verification from pharmacy	Pharmacy involvement reduced administration time by 103 minutes (157 min vs 54 min; p<0.01)

Conclusiones

1. **Selecciona el antibiótico a administrar**

   Sigue las guías del centro y piensa en el riesgo de multirresistencia

2. **Ajusta dosis antibióticos (pK/pD)**

   Piensa en dosis de carga, CMI y busca hiperfiltración

3. **Shock Séptico: Noradrenalina**

   Vía periférica, estandarizar diluciones, monitorizar TAM

4. **Desescalada y duración del tratamiento**

   Evaluación precoz de cultivos, Terapias cortas

5. **Indicadores y Acciones de mejora**

   Ayuda a monitorizar resultados y propón alternativas

Berta Cisteró Roig. Consorci Corporació Sanitària Parc Taulí.

Jesús Ruiz Ramos. Hospital Santa Creu i Sant Pau