SOCIEDAD CHILENA DE INFECTOLOGÍA

III CURSO
INFECCIONES NEONATALES
9 y 10 de junio 2017

VANCOMICINA VS CLOXACILINA EN SEPSIS NEONATAL TARDÍA

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Clínica Alemana
Comité Consultivo de Infecciones Neonatales

INMIGRANTES

TÓPICOS DE LA PRESENTACIÓN:

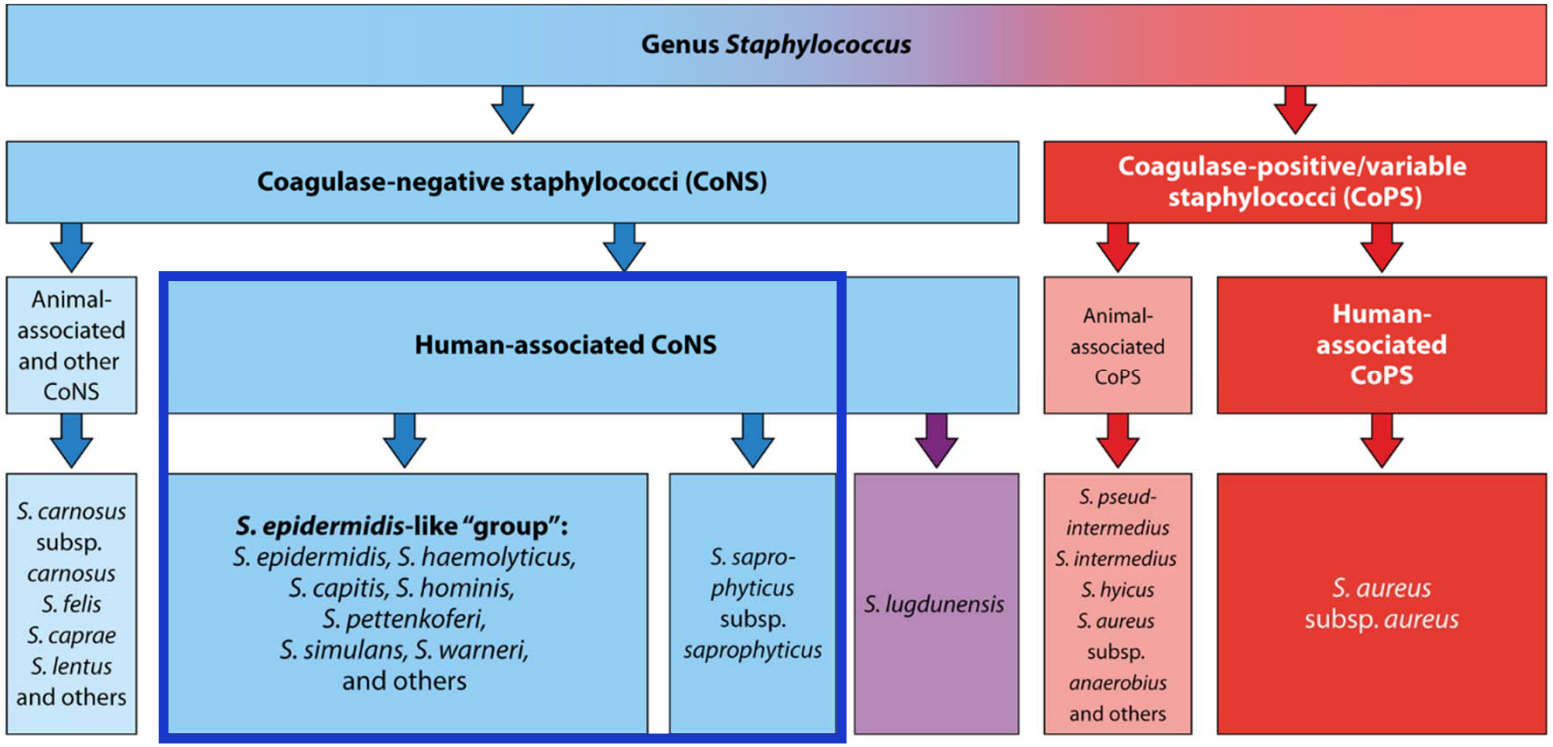
GENERALIDADES *Staphylococcus* coagulasa negativo.

ROL de la vancomicina en infecciones por *Staphylococcus* coagulasa negativo.

VANCOMICINA y microbiota intestinal.

CONCLUSIONES.

Staphylococcus coagulasa negativo



Becker K...Peters G. Clin Microbiol Rev. 2014 Oct;27(4):870-926.

Staphylococcus coagulasa negativo

2,5/1.000 ingresos hospitalarios.
Causa más común de ITS en NICU (30-60%).

Infecciones más frecuentemente asociadas con <1.500g, menor edad gestacional, CVC y NPTP.

Morbilidad sustancial: RDSM (PC), DBP, ROP, HIV y retraso del crecimiento.

Mortalidad rara (1-2%). Infecciones mayoría no graves.

Shane AL, Sánchez PJ, Stoll BJ. Lancet. 2017 Apr 20.
Becker K…Peters G. Clin Microbiol Rev. 2014 Oct;27(4):870-926.
Dong Y, Speer CP. Int J Med Microbiol. 2014 Jul;304(5-6):513-20.
Chong J…Quach C. PLoS One. 2016 Oct 7;11(10):e0164136.
Ericson JE…Smith PB; Antibacterial Resistance Leadership Group. Pediatr Infect Dis J. 2015 Apr;34(4):371-5.
Romanelli RM…Clemente WT. J Pediatr (Rio J). 2016 Sep-Oct;92(5):472-8.

MAJOR ARTICLE

Makhoul IR…Reichman B; Israel Neonatal Network. Clin Infect Dis. 2005 Jan 15;40(2):218-24.

Pathogen-Specific Early Mortality in Very Low Birth Weight Infants with Late-Onset Sepsis: A National Survey

Table 2. Univariate analysis of risk factors associated with early mortality after late-onset sepsis (LOS) among very low birth weight infants.

Risk factor	No. of LOS events	No. (%) of LOS events associated with early mortality	*P*
Total	3462	179 (5.2)	
Type of pathogen			
CoNS	1736	31 (1.8)	<.001
Staphylococcus aureus	115	4 (3.5)	
Enterococcus species	109	2 (1.8)	
Klebsiella species	448	45 (10.0)	
Enterobacter species	132	7 (5.3)	
Pseudomonas species	133	30 (22.6)	
Escherichia species	97	6 (6.2)	
Acinetobacter species	74	4 (5.4)	
Serratia species	42	4 (9.5)	
Candida species	377	27 (7.2)	
Other	199	19 (10.0)	

Table 3. Crude and adjusted logistic regression of risk factors for early mortality after late-onset sepsis among very low birth weight infants.

Risk factor	Crude[a] OR (95% CI)	Adjusted OR (95% CI)
Type of pathogen		
CoNS[b]	1.0	1.0
Staphylococcus aureus	2.0 (0.7–5.6)	3.0 (0.9–7.9)
Enterococcus species	1.1 (0.3–4.6)	1.1 (0.2–4.0)
Klebsiella species	6.3 (3.9–10.1)	6.3 (3.9–10.4)
Enterobacter species	3.2 (1.4–7.5)	4.1 (1.6–9.3)
Pseudomonas species	17.2 (10.0–29.6)	12.3 (6.9–22.0)
Escherichia species	3.8 (1.5–9.3)	4.3 (1.5–10.1)
Acinetobacter species	3.1 (1.1–9.0)	2.6 (0.7–7.0)
Serratia species	6.2 (2.1–18.6)	6.2 (1.7–17.7)
Candida species	4.7 (2.7–7.9)	3.2 (1.8–5.5)
Other	6.1 (3.3–10.9)	5.6 (3.0–10.4)

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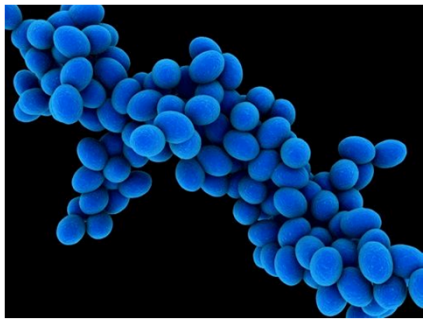
Journals.ASM.org

Coagulase-Negative Staphylococci



Lactantes a los 4 ddv 83% colonizados.
2 semanas de vida aumenta a casi 100%.

FUNDAMENTAL EN EL MICROBIOMA
IMPORTANCIA EVOLUTIVA PARA EL HUÉSPED HUMANO

las barreras (piel y mucosas), procedimientos invasivos.

Baja capacidad invasiva. Progresión insidiosa.

Clin Microbiol Rev. 2014 Oct;27(4):870-926.
Blanchard AC, Quach C, Autmizguine J. Clin Perinatol. 2015 Mar;42(1):119-32.
Dong Y, Speer CP. Int J Med Microbiol. 2014 Jul;304(5-6):513-20.

Staphylococcus coagulasa negativo

Más del 90% tienen el gen mecA: asociado a resistencia a meticilina.

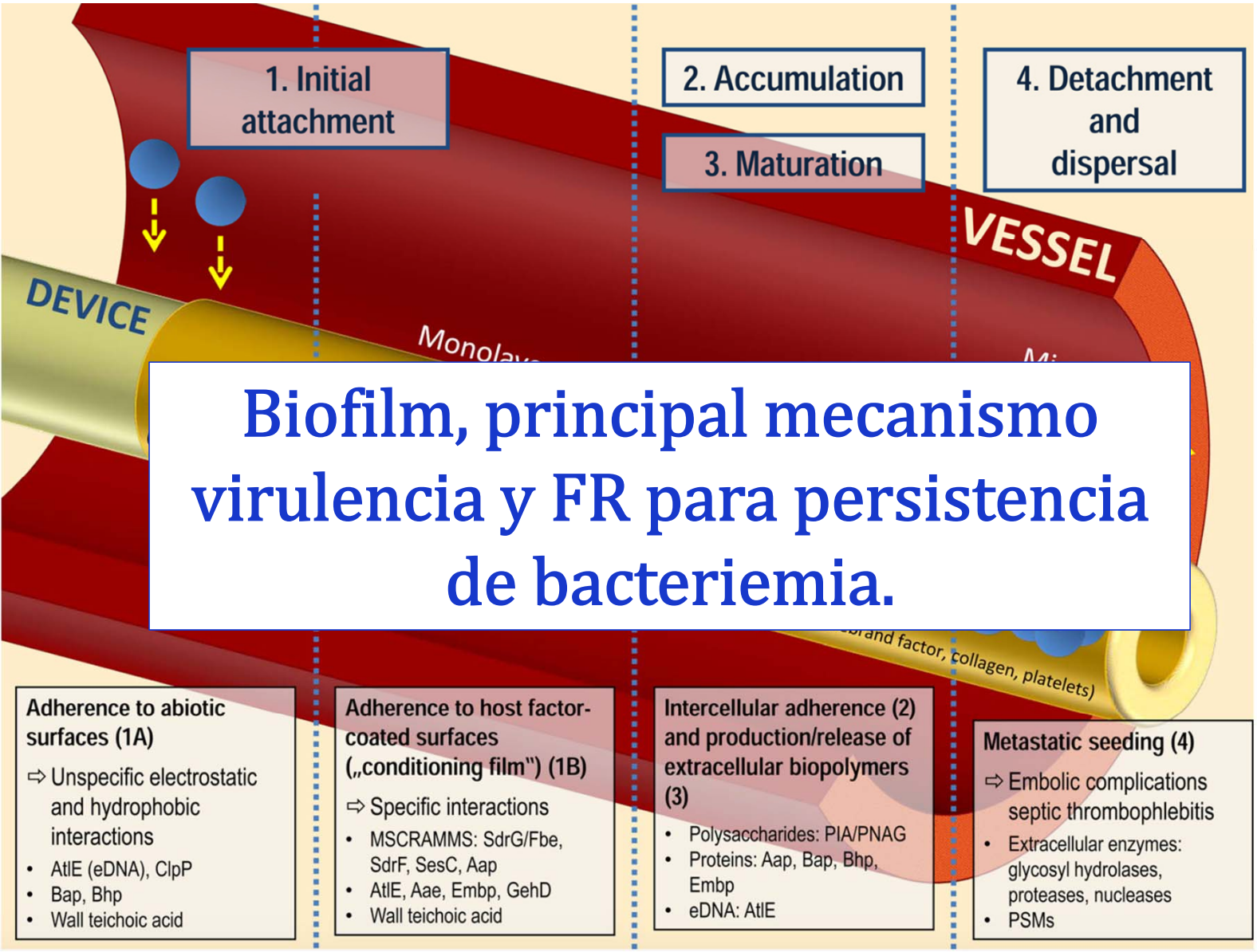
VANCOMICINA

Problemas epidemiológicos:

Mayores tasas de uso de antibióticos amplio espectro.

Mayores costos de la atención sanitaria.

Chong J...Quach C. PLoS One. 2016 Oct 7;11(10):e0164136.



Biofilm, principal mecanismo virulencia y FR para persistencia de bacteriemia.

CMR
Journals.ASM.org

Coagulase-Negative Staphylococci

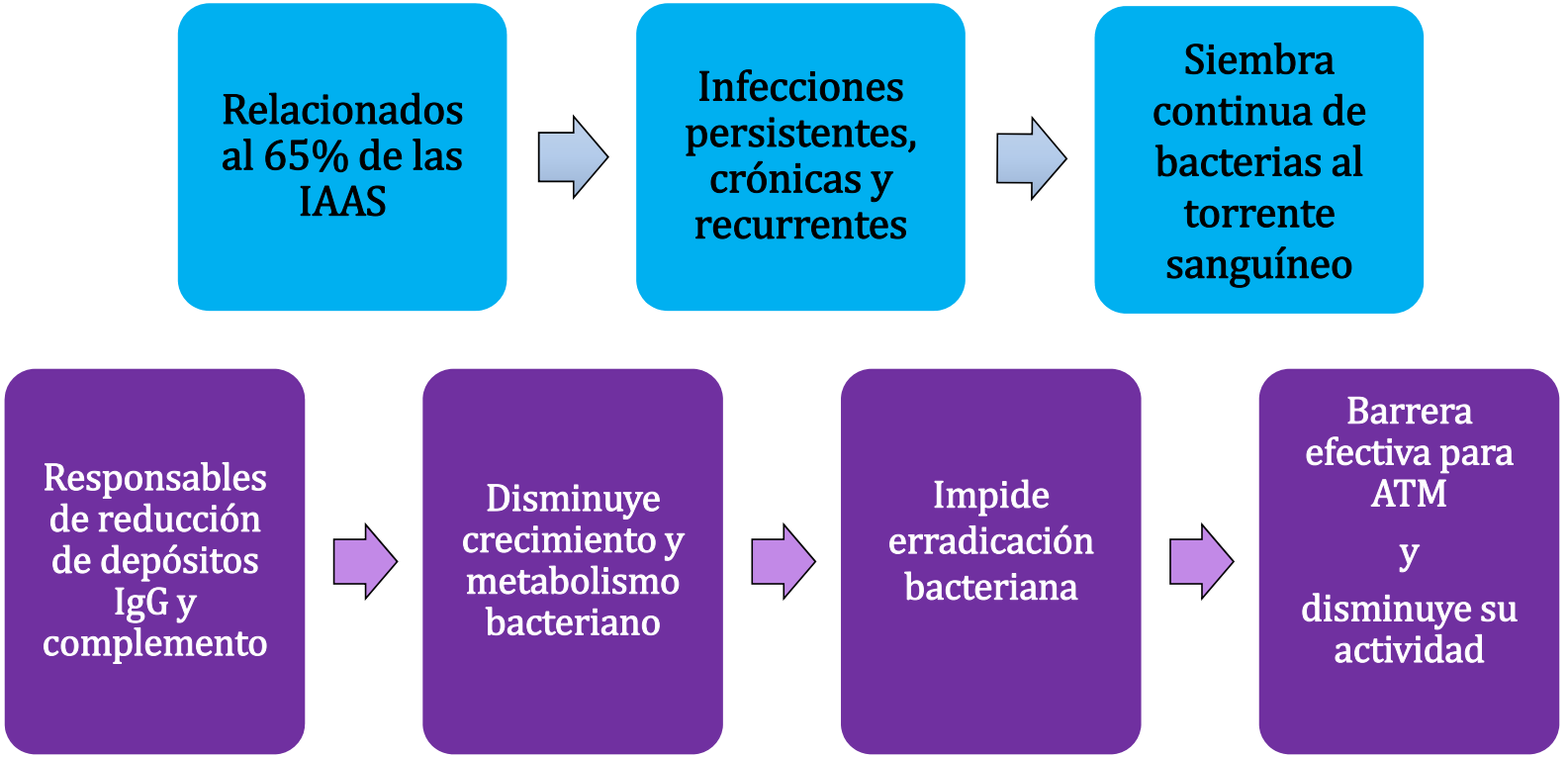
Karsten Becker, Christine Heilmann, Georg Peters
Institute of Medical Microbiology, University Hospital Münster, Münster, Germany

Understanding the significance of *Staphylococcus epidermidis* bacteremia in babies and children

Gordon Y.C. Cheung and Michael Otto

Curr Opin Infect Dis. 2010 Jun;23(3):208-16.

Biofilms



Vancomicina:
es segura? ocasiona problemas en las NICU ?

Box 1
Vancomycin reduction guideline

For infants more than 3 days of age with suspected late-onset sepsis, provided that they are not known or suspected to be colonized with methicillin-resistant *Staphylococcus aureus*

1. Obtain blood cultures and consider obtaining cerebrospinal fluid (CSF) culture; obtain adjunctive diagnostic markers (complete blood count with differential, C-reactive protein) at provider discretion
2. Begin therapy with oxacillin (or nafcillin) and gentamicin
3. If the initial cultures are sterile at 48 hours
   a. Consider discontinuing antibiotic therapy.
   b. If the infant is clinically improved and the provider thinks that continued therapy is warranted, continue the current therapy.
   c. If the infant is deteriorating, obtain a second set of blood cultures and consider changing to vancomycin and gentamicin empirically.
   d. If the second set of blood cultures is sterile at 48 hours, again consider discontinuing antibiotic therapy.
4. If the initial cultures grow oxacillin-resistant coagulase-negative *Staphylococcus*
   a. Draw a second set of blood cultures, obtain CSF culture if not already collected, and change antibiotic therapy to vancomycin alone. The clinical scenario should guide the duration of therapy.
   b. If the second set of cultures is sterile at 48 hours, consider discontinuing all antibiotics on the basis that initial cultures may represent contamination.
   c. If the second set of cultures also grow oxacillin-resistant coagulase-negative *Staphylococcus*
      i. Verify with microbiology that they are the same species.
      ii. Continue therapy with vancomycin.
      iii. Consider removing indwelling catheters.

Adapted from Chiu CH, Michelow IC, Cronin J, et al. Effectiveness of a guideline to reduce vancomycin use in the neonatal intensive care unit. Pediatr Infect Dis J 2011;30:275; with permission.

Desde 1997 protocolos reducción vancomicina

Cantey JB. Pediatr Infect Dis J. 2015 Mar;34(3):267-72
Cantey JB. Infect Dis Clin North Am. 2014 Jun;28(2):247-61

No Survival Benefit With Empirical Vancomycin Therapy for Coagulase-negative Staphylococcal Bloodstream Infections in Infants

Pediatr Infect Dis J. 2015 Apr;34(4):371-5. *Ericson JE⋯ Smith PB; Antibacterial Resistance Leadership Group.*

Problemas del uso de vancomicina:

1.- Toxicidad: disfunción renal, pérdida de audición.
2.- Microbiológico y ecología hospitalaria: VRE, SAMR, infecciones invasivas por *Candida* y colonización más frecuente por Gram negativos resistentes (*Pseudomonas*).
3.- Aumenta mortalidad y secuelas.

CDC: uso injustificado hasta 32-50%, continuación con cultivos negativos.

CDC y AAP: principal FR para aparición de infecciones por VRE y SAMR.

Somily AM…Murray TS. Am J Infect Control. 2014 Mar;42(3):277-82.

Fulminant Late-Onset Sepsis in a Neonatal Intensive Care Unit, 1988–1997, and the Impact of Avoiding Empiric Vancomycin Therapy

Karlowicz MG, Buescher ES, Surka AE. Pediatrics. 2000 Dec;106(6):1387-90.

Gram (+): 57%

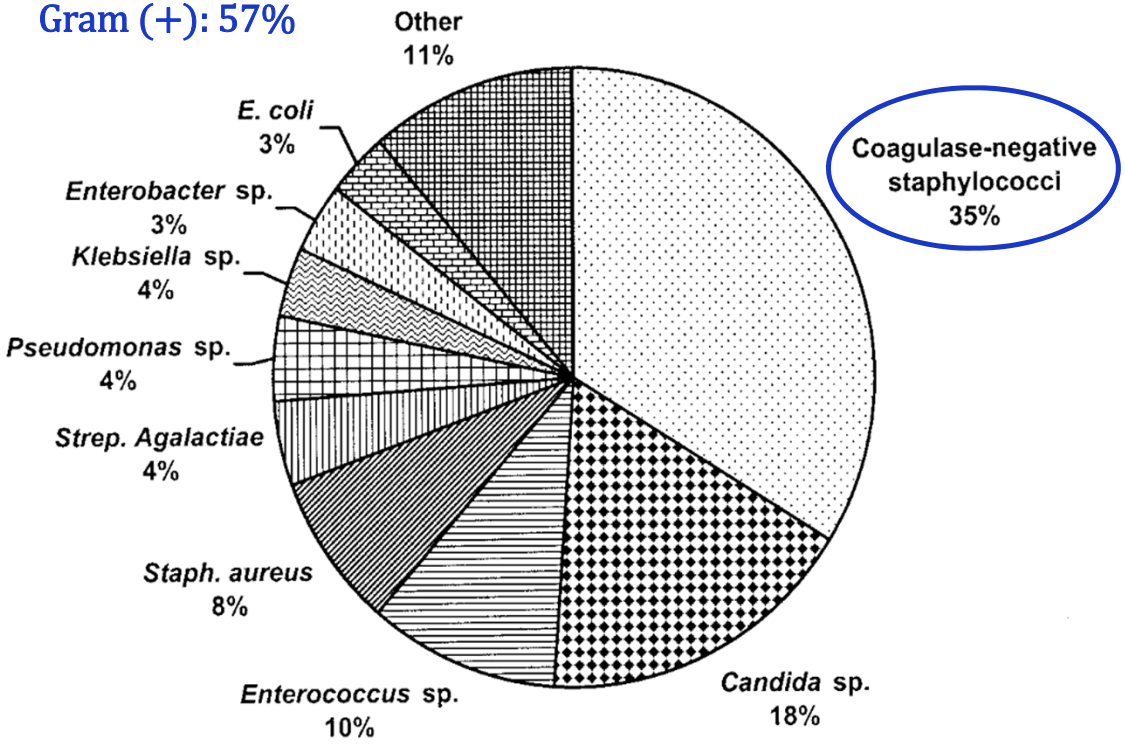


Fig 1. Distribution of pathogens causing late-onset sepsis in neonates (n = 825).

Gram (-): 70%

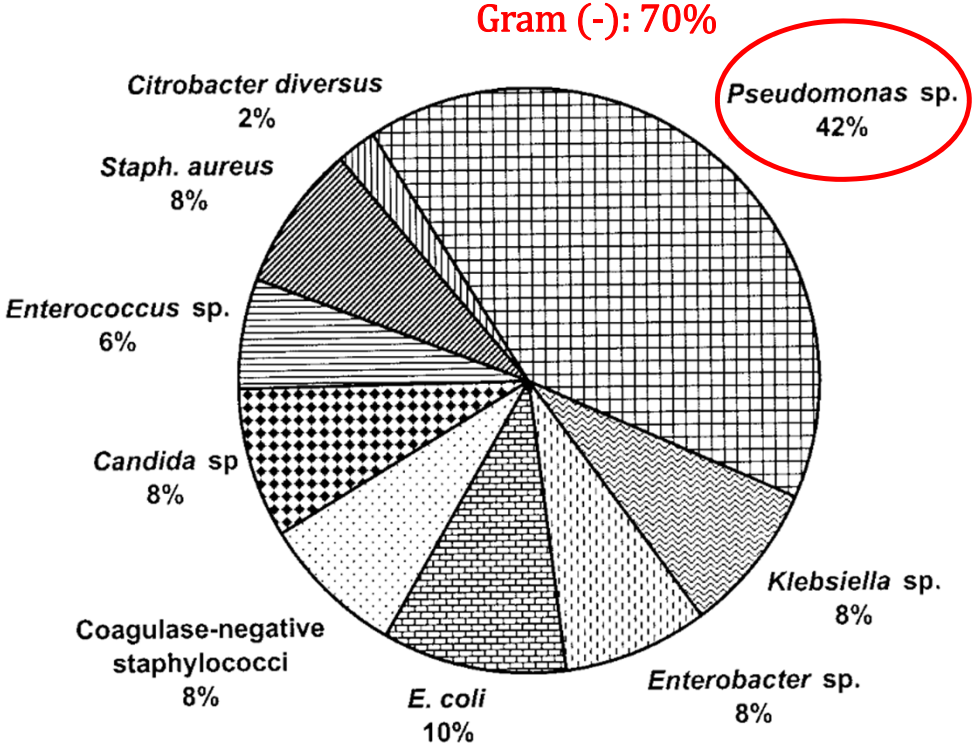


Fig 2. Distribution of pathogens causing fulminant late-onset sepsis in neonates (n = 49).

Fulminant Late-Onset Sepsis in a Neonatal Intensive Care Unit, 1988–1997, and the Impact of Avoiding Empiric Vancomycin Therapy

Karlowicz MG, Buescher ES, Surka AE. Pediatrics. 2000 Dec;106(6):1387-90.

TABLE 1. Frequencies of Fulminant Late-Onset Sepsis for the Most Common Pathogens in the NICU, 1988–1997

Organism	Case Ratio	Frequency (%)
Pseudomonas sp.	20/36	56
Escherichia coli	5/27	19
Enterobacter sp.	4/28	14
Klebsiella sp.	4/31	13
Staphylococcus aureus	4/67	6
Enterococcus sp.	3/83	4
Candida sp.	4/143	3
Coagulase-negative staphylococci	4/277	1

TABLE 2. Coagulase-Negative Staphylococcal Sepsis in the NICU from 1988–1997

Date of sepsis	1/88–9/94	10/94–12/97
Empiric antibiotics	Vancomycin and cefotaxime	Oxacillin and gentamicin
Cases of fulminant sepsis	2	2
Total sepsis cases	141	136
Frequency of fulminant sepsis (%)	1	1
Median duration of sepsis (range)	2 days (1–13)	2 days (1–11)

Ambos períodos la R a oxacilina del SCN fue 85%

Fulminant Late-Onset Sepsis in a Neonatal Intensive Care Unit, 1988–1997, and the Impact of Avoiding Empiric Vancomycin Therapy

Karlowicz MG, Buescher ES, Surka AE. Pediatrics. 2000 Dec;106(6):1387-90.

CONCLUSIONES:

Selección ATB empíricos para sepsis tardía:
- preocupación por sepsis fulminante (Gram negativos: *Pseudomonas*).
- lactantes mueren en <48 horas (antes de identificar patógenos y antibiograma).

El inicio de vancomicina más tardía no prolongó la duración de sepsis por SCN.

La reducción de vancomicina no tuvo impacto en la incidencia de sepsis fulminante.

No Survival Benefit With Empirical Vancomycin Therapy for Coagulase-negative Staphylococcal Bloodstream Infections in Infants

Jessica E. Ericson, MD,† Joshua Thaden, MD, PhD,‡ Heather R. Cross, DPhil,†*
Reese H. Clark, MD,§ Vance G. Fowler Jr., MD, MHS,†‡ Daniel K. Benjamin Jr., MD, PhD,†*
Michael Cohen-Wolkowiez, MD, PhD,† Christoph P. Hornik, MD, MPH,*† P. Brian Smith, MD, MPH, MHS*†*
for the Antibacterial Resistance Leadership Group

La vancomicina empírica no mejoró la mortalidad ni días estadía hospitalaria.

El uso empírico de vancomicina debe limitarse a los casos en los que se sospecha SAMR.

entre

7 days of 1st culture			
Death before hospital discharge	100 (8)	236 (9)	1.06 (0.81, 1.39)

Pediatr Infect Dis J 2015;34:371–375

Effectiveness of a Guideline to Reduce Vancomycin Use in the Neonatal Intensive Care Unit

TABLE 2. Incidence and Complications of Hospital-acquired Infection

	BWH*		MGH*	
	Before	After	Before	After
Incidence of LOS (per 1000 patient-days)	2.15 (95% CI: 1.45–2.86)	2.65	5.26 (95% CI: 2.40–9.20)	3.89
No. cases with meningitis (% total cases)	10 (4.2)	3 (5.8)	1 (3.1)	0
No. deaths due to LOS (% total cases)	19 (8.1)	3 (5.8)	2 (6.3)	0

The data refer to all newborns cared for during the study period. The overall proportion of all births with BW <1500 g; the relative proportion of births with BW <1500 g versus 1000 g; and mortality rate for all infants with BW <1500 g were not significantly different between 2005 and 2007 at either site (data not shown). Among infants born with BW <1500 g and surviving >72 hours, the mean incidence of LOS was 20.5% (annual range: 12.2%–27.5%) during the "before" period; the incidence was 26% during the "after" period (data available for BWH site only).

*P values for all comparisons, nonsignificant.

BWH indicates Brigham and Women's Hospital; MGH, Massachusetts General Hospital; LOS, late-onset sepsis.

Uso vancomicina disminuyó a 62% ($p<0,05$).

Aumentaron las infecciones por SCN.

Chiu CH...Puopolo KM. Pediatr Infect Dis J. 2011 Apr;30(4):273-8

Jornal de Pediatria
www.jped.com.br

Romanelli RM...Clemente WT. J Pediatr (Rio J). 2016 Sep-Oct;92(5):472-8.

ORIGINAL ARTICLE

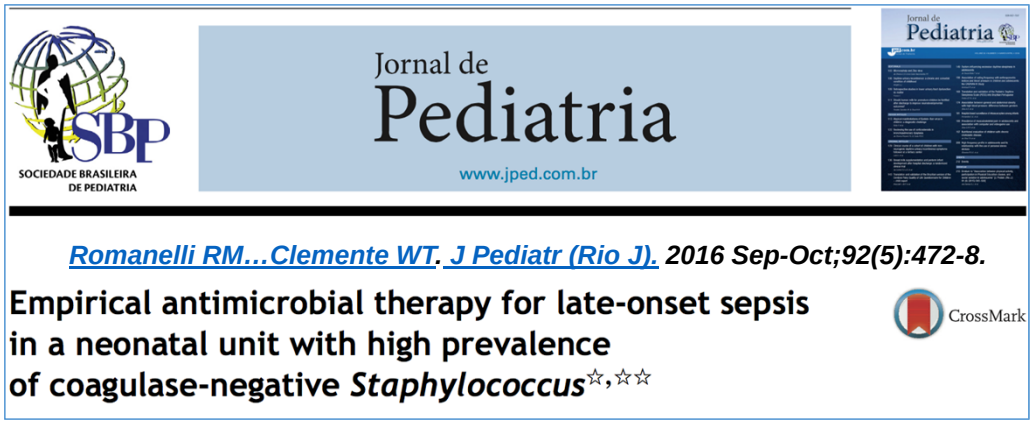
Empirical antimicrobial therapy for late-onset sepsis in a neonatal unit with high prevalence of coagulase-negative *Staphylococcus*☆,☆☆

Tasas de mortalidad y morbilidad infecciones SNC no aumentaron.

Mejoría infecciones a *S. aureus*.

Table 4 Mortality and lethality of patients with *Staphylococcus* spp. hospital-associated infections, Neonatal Intensive Care Unit, HC/UFMG, 2011–2014.

Mortality/lethality	Total 2011–2014 *n* (%)	Period 1 2011–2012 *n* (%)	Period 2 2013–2014 *n* (%)	*p*	OR	95% CI
General mortality						
Coagulase negative *Staphylococcus*/patient at risk	3 (0.24)	1 (0.18)	2 (0.29)	0.63	0.63	0.06–6.95
Staphylococcus aureus/patient at risk	6 (0.49)	5 (0.92)	1 (0.15)	0.08	6.32	0.74–53.91
Lethality associated to coagulase negative Staphylococcus						
Coagulase negative *Staphylococcus*/total of infections	3 (0.82)	1 (0.56)	2 (1.07)	1	0.52	0.02–7.32
S. coagulase negative/total of infections by agent	3 (2.56)	1 (2.5)	2 (2.6)	1	0.96	0–14.16
Lethality associated to Staphylococcus aureus						
S. *aureus*/total of infections	6 (1.63)	5 (2.78)	1 (0.53)	0.116	5.31	0.6–20.0
S. *aureus*/total of infections by agent	6 (14.29)	5 (18.52)	1 (6.67)	0.395	3.18	0.3–30.0



USO CLOXACILINA

NO s negativas y
hong

No h

Se lo

Menor número de infecciones está directamente relacionado con un menor uso de agentes antimicrobianos (vanco y CBP).

Adicionar gentamicina puede dar efecto sinérgico in vitro sobre SCN.

Lawrence SL... Lemyre B. BMC Pediatr. 2005 Dec 23;5:49.
Brilene T... Lutsar I. APMIS. 2013 Sep;121(9):859-64.

SOCIEDADE BRASILEIRA DE PEDIATRIA

Jornal de Pediatria

www.jped.com.br

EDITORIAL

Empiric therapy with vancomycin in the neonatal intensive care unit: let's ''get smart'' globally!☆,☆☆

J Pediatr (Rio J). 2016 Sep-Oct;92(5):432-5. *Sánchez P…Michelow IC*.

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Brief report Holzmann-Pazgal G...Eichenwald EC. Am J Infect Control. 2015 Nov;43(11):1255-7.

Decreasing vancomycin utilization in a neonatal intensive care unit

1.- Sólo se aislan un 7% de MOR con necesidad de vancomicina.

2.- Sólo el 21% de los pacientes hemocultivos positivos documentados.

Scope of Topic

This guideline will address the choice of empiric antibiotics for infants >3 days old being treated for possible sepsis or NEC.

Target Population

Infants in the NICUs at Children's Memorial Hermann

Empiric Treatment of Late Onset Sepsis

Obtain at least 2 blood cultures prior to antibiotics. Consider CSF culture as indicated.

Begin therapy with Nafcillin and Gentamicin (exception: For infants known to be MRSA colonized, begin Vancomycin and Gentamicin).

After 48 hours and negative blood cultures, consider discontinuing antibiotics. If clinical course is consistent with clinical sepsis and the patient improves after initiation of antibiotics, continue with Nafcillin and Gentamicin for 7-10 days.

Antibiotic coverage may be expanded if the patient's clinical condition does not improve or is deemed severe enough to warrant broader antibiotic coverage.

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Brief report

Decreasing vancomycin utilization in a neonatal intensive care unit

Characteristics and outcomes by study period

basal — Educación y guía — vigilancia y feedback

Characteristics	Period 1	Period 2	Period 3	*P* value
Death*	10 (12.8)	12 (12.8)	15 (13.5)	.99
Death and any positive culture	6 (7.7)	6 (6.4)	9 (8.1)	.88
Death and any positive CONS culture	1 (1.3)	0	2 (1.8)	.29
Death and ≥2 blood cultures CONS	0	0	0	N/A
Death and any positive culture MRSA	0	0	0	N/A
Episode characteristics by study period (N = 500)				
Antibiotic administration episodes	146 (29.2)	172 (34.4)	182 (36.4)	.13
No. of antibiotic episodes per patient	1.9 ± 1.4	1.9 ± 1.4	1.6 ± 1.0	.13
No. of antibiotic starts per episode	2.8 ± 1.9	2.9 ± 1.5	2.8 ± 1.1	.75
Vancomycin†	118 (80.8)	35 (20.4)	42 (23.1)	<.001
No. of vancomycin episodes per patient	1.5 ± 1.2	0.4 ± 0.7	0.4 ± 0.8	<.001
Vancomycin >3 d	42 (28.8)	17 (9.9)	18 (9.9)	<.001
Judicious vancomycin >3 d	8 (19.1)	10 (58.8)	12 (66.7)	<.01
≥1 CONS-positive culture any site	12 (8.6)	18 (10.9)	18 (10.1)	.79
≥2 blood cultures with CONS	4 (2.7)	9 (5.2)	9 (5.0)	.45
≥1 MRSA-positive culture any site	3 (2.1)	2 (1.2)	3 (1.7)	.85
≥1 blood culture with MRSA	1 (0.7)	0	2 (1.1)	.26
No. of antibiotic episodes with negative blood cultures (N = 459)	108 (81.8)	125 (79.6)	133 (78.2)	.74
No. of antibiotic episodes without any positive culture any site (N = 483)	80 (57.1)	90 (54.6)	98 (55.1)	.89

Holzmann-Pazgal G…Eichenwald EC. Am J Infect Control. 2015 Nov;43(11):1255-7.

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Somily AM...Murray TS. Am J Infect Control. 2014 Mar;42(3):277-82.

Extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* in the neonatal intensive care unit: Does vancomycin play a role?

Table 1
Characteristics of patients at the time of admission and univariate analysis for risk factors for infection or colonization with extended-spectrum β-lactamase-producing *Klebsiella pneumoniae*

Variables	Number of neonates	Infected neonates	Colonized neonates	Person-days	IDR (95% CI)
Mechanical ventilation					
Yes	27	4	5	1,191	2.69 (0.73-9.95)†
No	90	0	3	1,069	Reference
N/A	1	0	0	5	
Parenteral nutrition					
Yes	32	4	6	1,331	3.22 (0.70-14.68)†
No	80	0	2	856	Reference
N/A	6	0	0	78	
Ampicillin + gentamicin					
Yes	58	0	5	1,132	0.71 (0.23-2.25)
No	60	4	3	1,133	Reference
Cefotaxime					
Yes	6	1	2	330	1.95 (0.53-7.22)
No	112	3	6	1,935	Reference
Vancomycin					
Yes	14	3	6	941	4.22 (1.14-15.59)
No	104	1	2	1,324	Reference

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* in the neonatal intensive care unit: Does vancomycin play a role?

3 o 10 días de tratamiento, es factor de riesgo *p* sig para la colonización GI con cepas *Klebsiella* productoras de BLEE en RNPT.

La exposición a la vancomicina efecto más dramático sobre la colonización (EG, PNAC y estancia hospitalaria).

Somily AM...Murray TS. Am J Infect Control. 2014 Mar;42(3):277-82.

ARTICLE

Gastrointestinal colonization with ESBL-producing *Klebsiella* in preterm babies—is vancomycin to blame?

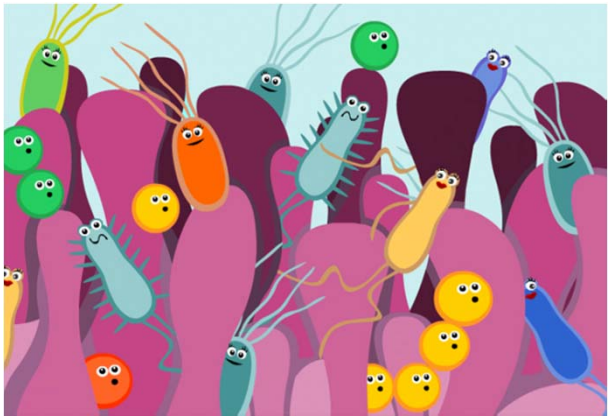
Table 1 Demographic and clinical description of colonized and non-colonized babies

	Non-colonized babies	Colonized babies	*p*-value
Gestational age, weeks (range)	32 (24–42)	30 (24–40)	0.001
Birth weight, g (range)	1,781 (759–1,657)	1,418 (500–3,270)	0.025
Male gender, % (*n*)	53.9 (153)	54.5 (30)	0.523
Days to isolation/discharge, days (range)	34 (1–145)	39 (6–182)	0.241
Vancomycin treatment, % (*n*)	47 (147)	70.9 (39)	0.001
CoNS infection, % (*n*)	21.5 (61)	50.9 (28)	<0.001

CoNS, coagulase-negative *Staphylococcus*

Ofek-Shlomai N…Bar-Oz B. Eur J Clin Microbiol Infect Dis. 2012 Apr;31(4):567-70.

VANCOMICINA
Y
MICROBIOTA INTESTINAL



Cell Host & Microbe

Perspective

Vangay P……..Knights D. Cell Host Microbe. 2015 May 13;17(5):553-64.

Antibiotics, Pediatric Dysbiosis, and Disease

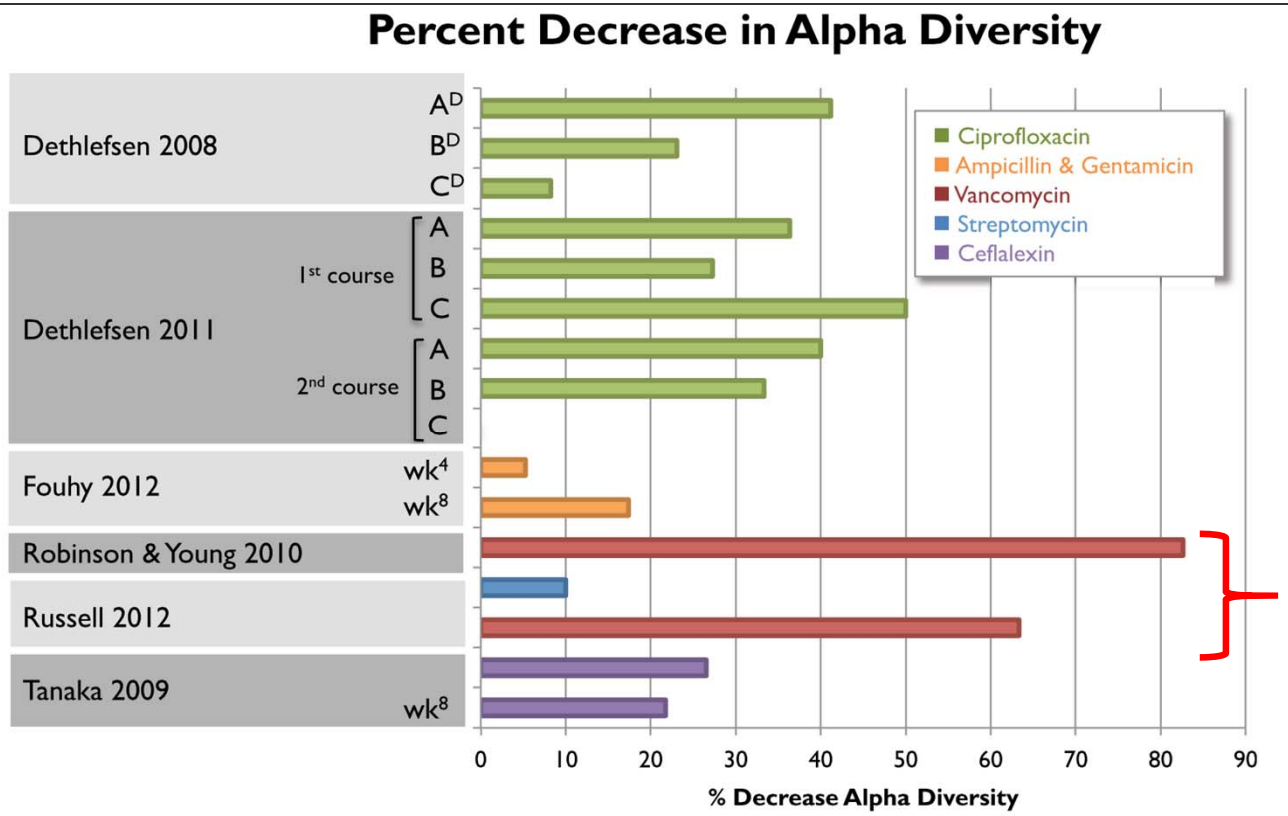


Table 2 | **Antibiotic-associated changes in immunity**

Antibiotic	Effects on the microbiota	Effects on immunity	Refs
Vancomycin, neomycin and metronidazole	• Reduced total bacteria	• Reduced expression of REG3γ (recovered with LPS treatment)	5
Streptomycin	• Reduced total bacteria	• Reduced expression of REG3β (recovered with a TLR2 agonist)	37
Amoxycillin	• Change in the microbial composition • Depletion of lactobacilli	• Reduced antimicrobial defence • Reduced expression of MHCmolecules • Increased mast cell proteases	63
Polymyxin B	• Unknown	• Increased mast cell numbers	65
Vancomycin or ampicillin	• Depleted Gram-positive bacteria • Depleted SFB	• Depletion of T helper 17 cells	4,6
Ampicillin, gentamicin, metronidazole, neomycin and vancomycin	• Reduced total bacteria	• Reduced expression of IFNγ and IL-17A by $CD4^+$ T cells • Reduced production of RELMβ	69
Streptomycin and cefotaxime	• Reduced total bacteria	• Reduced expression of TLR2 and TLR4 in peritoneal macrophages • Macrophages less able to respond to LPS induction	70
Metronidazole	• Changes in the composition • More *Bifidobacterium* spp.	• Disrupted mucus layer • Increased colonization of intestinal crypts	75
Ampicillin, vancomycin, neomycin and metronidazole	• Reduced bacterial ligand CpG DNA	• Suppressed immune response to oral vaccination and infection	84
Amoxicillin and clavulanic acid	• Undetermined change in the microbiota	• Reduced systemic IgG	85
Ampicillin, neomycin sulphate, metrondiazole and vancomycin	• Reduced total bacteria	• Reduced bacteriocidal activity of bone marrow-derived neutrophils	3

IFNγ, interferon-γ; IgG, immunoglobulin G; IL-17A, interleukin-17A; LPS, lipopolysaccharide; MHC, major histocompatibility complex; RELMβ, resistin-like molecule-β; SFB, segmented filamentous bacteria; TLR, Toll-like receptor.

Willing BP……..Finlay BB. Nat Rev Microbiol. 2011 Apr;9(4):233-43.

FOCUS ON MUCOSAL MICROBIOLOGY

REVIEWS

Willing BP, Russell SL, Finlay BB. Nat Rev Microbiol. 2011 Apr;9(4):233-43

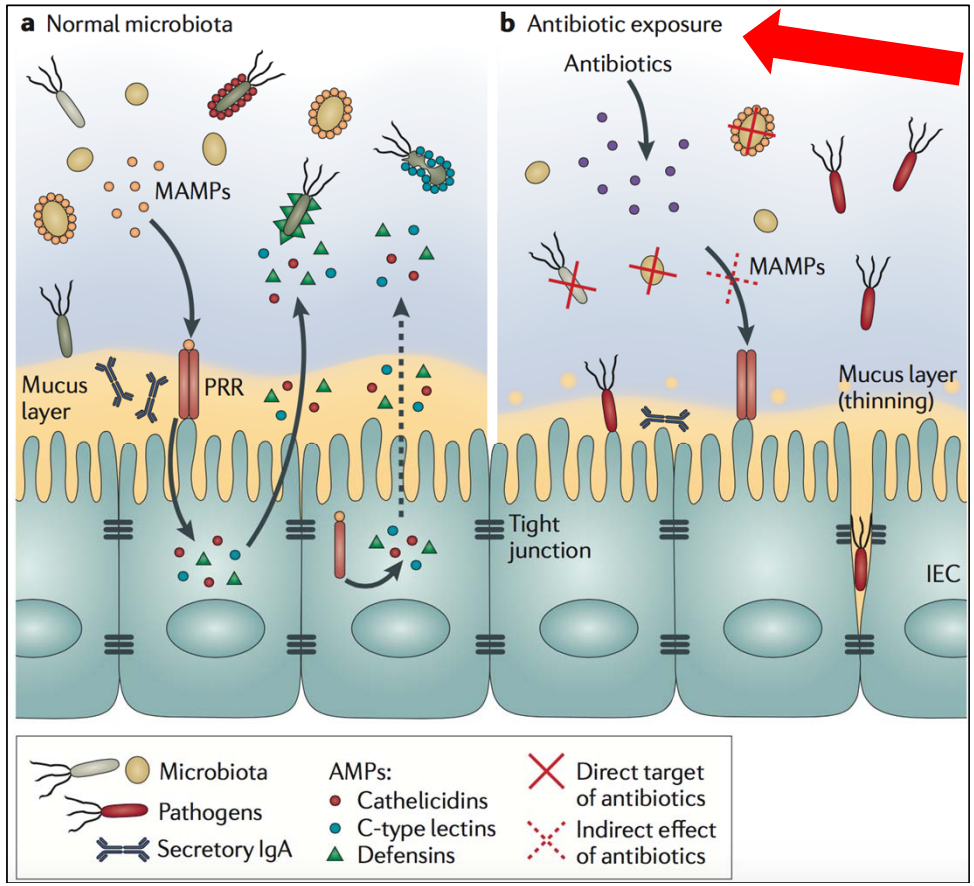
Shifting the balance: antibiotic effects on host–microbiota mutualism

Inmediato:

Adquisición de bacterias R desde nacimiento

Cambios en la ecología de la UCIN

Quiebre óptimo desarrollo de sistema inmune innato y adquirido

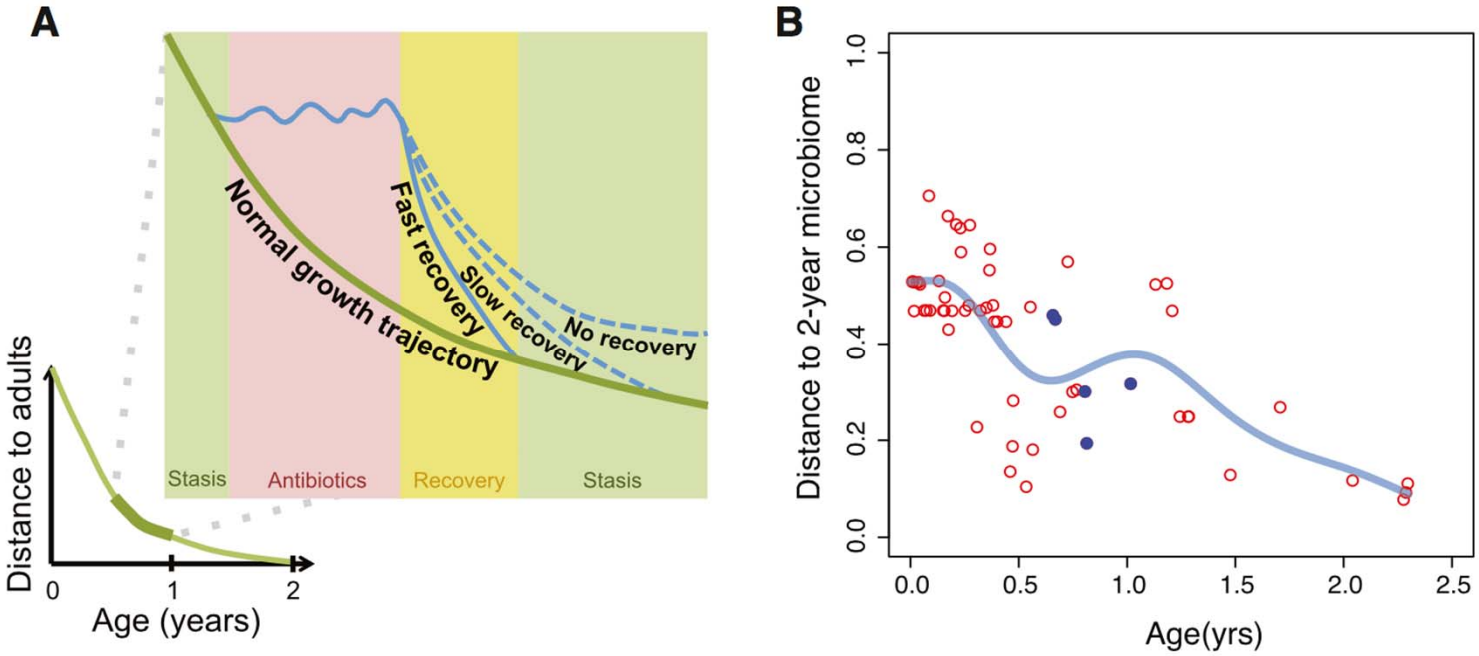


VANCOMICINA

Cell Host & Microbe

Perspective

Largo plazo:
Recuperabilidad hasta un año.

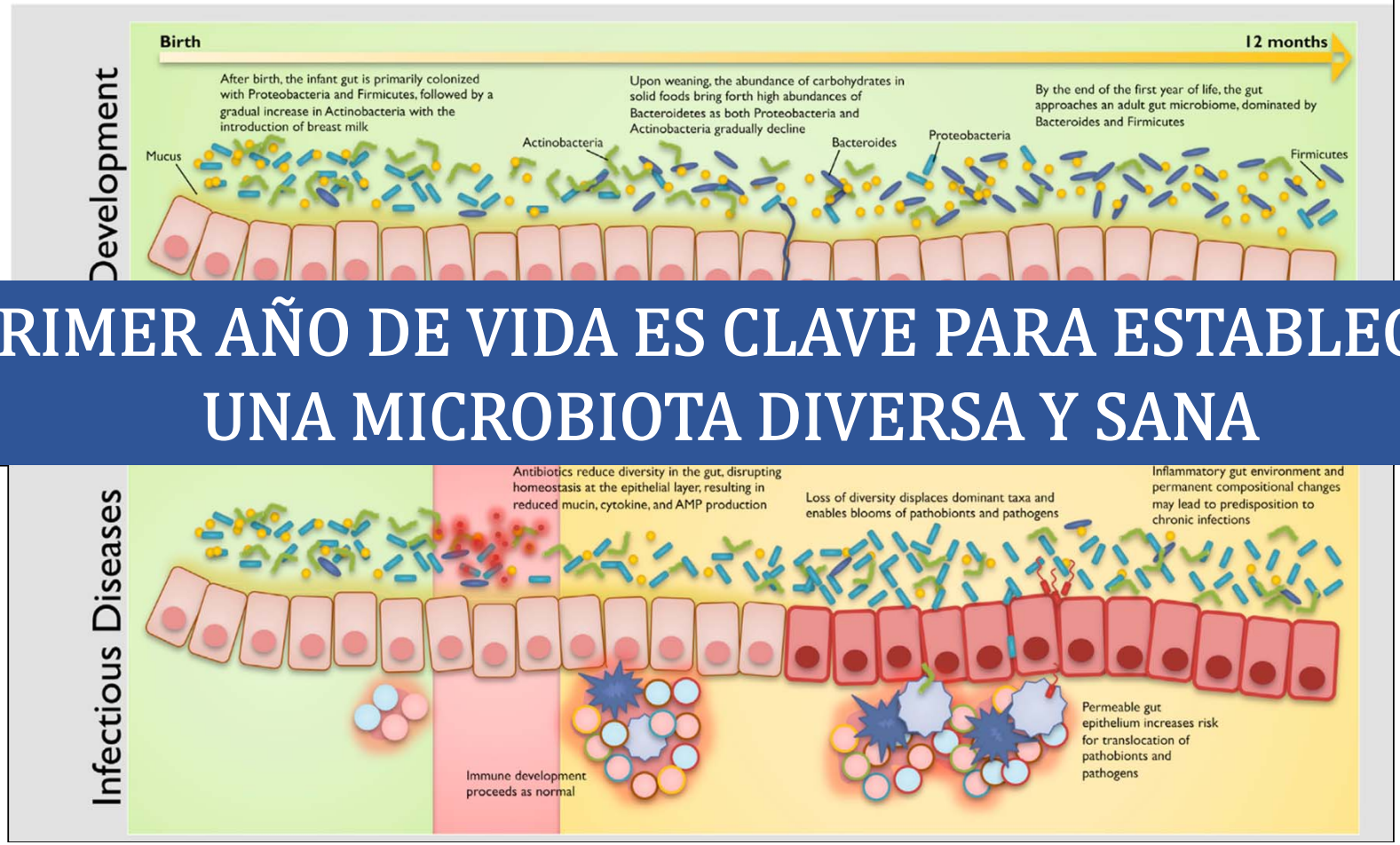


Vangay P……..Knights D. Cell Host Microbe. 2015 May 13;17(5):553-64.

Cell Host & Microbe

Perspective

Vangay P……..Knights D. Cell Host Microbe. 2015 May 13;17(5):553-64.



PRIMER AÑO DE VIDA ES CLAVE PARA ESTABLECER UNA MICROBIOTA DIVERSA Y SANA

Infectología al Día

Rev Chilena Infectol 2015; 32 (2): 182-189

Reposicionando la cloxacilina como antibioticoterapia empírica inicial de la sepsis tardía neonatal

Alejandra Sandoval, Fernanda Cofré, Luis Delpiano, Giannina Izquierdo, Yenis Labraña y Alejandra Reyes

Vancomicina:

- Dificultad en titular dosis → NIVELES¡¡¡
  - Concentraciones séricas subterapéuticas.
  - Eventual fracaso terapéutico.
- *S. warnerii* y *S. capitis* mayores CIM a vancomicina (heterorresistencia). Presión selectiva por concentraciones subterapéuticas en superficies mucosas y CVC (biopelículas).

Padari *et al. BMC Pediatrics*
DOI 10.1186/s12887-016-0753-0

BMC Pediatrics

Padari H... Lutsar I. BMC Pediatr. 2016 Dec 8;16(1):206

RESEARCH ARTICLE Open Access

Coagulase negative staphylococcal sepsis in neonates: do we need to adapt vancomycin dose or target?

AUC/CIM> 400 se asocia con la eficacia del tratamiento neumonía por SAMR para adultos.

Con administración vancomicina actual + CIM actual de SCN, el AUC/CIM se logra en menos de la mitad de RN.

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

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

Original Article

Kato H... Yamagishi Y. J Infect Chemother. 2017 Mar;23(3):154-160.

Assessment of optimal initial dosing regimen with vancomycin pharmacokinetics model in very low birth weight neonates

Estudio retrospectivo, 1 centro.

≤1500 g, hasta 30 días= 10 pacientes.

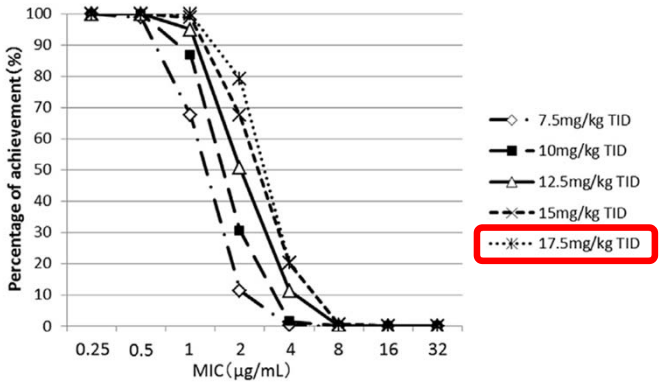


Fig. 3. Probability to achieve the pharmacokinetic target (AUC/MIC ≥ 400) according to the dosing regimen of three times a day (TID) and the theoretical minimum inhibitory concentration of the strain in the Monte Carlo simulation. ◇: vancomycin 7.5 mg/kg TID, ■: vancomycin 10 mg/kg TID, △: vancomycin 12.5 mg/kg TID, ×: vancomycin 15 mg/kg TID, *: vancomycin 17.5 mg/kg TID. MIC; minimal inhibitory concentration.

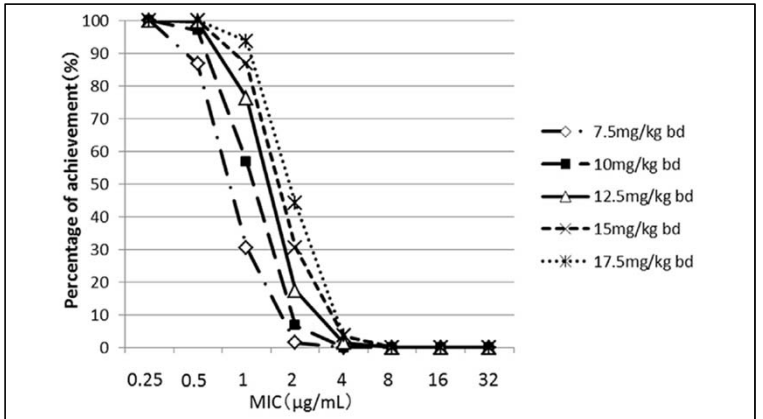


Fig. 4. Probability to achieve the pharmacokinetic target (AUC/MIC ≥ 400) according to the dosing regimen of twice a day (bd) and the theoretical minimum inhibitory concentration of the strain in the Monte Carlo simulation. ◇: vancomycin 7.5 mg/kg bd, ■: vancomycin 10 mg/kg bd, △: vancomycin 12.5 mg/kg bd, ×: vancomycin 15 mg/kg bd, *: vancomycin 17.5 mg/kg bd. MIC; minimal inhibitory concentration.

CONCLUSIONES

SCN:

1.- Baja mortalidad: reservar vancomicina en pacientes graves, sin retiro de CVC y sin respuesta clínica, microbiológica y de laboratorio.

2.- Sin evidencia que sugiere aumento de mortalidad por falta de cobertura precoz.

3.- Eliminación del CVC es crucial y la medida terapéutica más eficaz.

Vancomicina

1.- Trae consigo infecciones por MR (VRE, SAMR, BLEE,) e infecciones por *Candida*.

2.- Limitar uso con infección severa y/o UCIN con alto SAMR. NO a tratamiento empírico inicial.

3.- Importante interferencia en el microbioma.

CONCLUSIONES

Respuesta a oxacilina a pesar de la resistencia por:

- baja virulencia de SCN.
- Heterorresistencia (a la oxa): eliminando susceptibles y resistentes puede ser erradicada por la respuesta inmune.

Cloxacilina + aminoglicósido alternativa empírica de sepsis tardía y excelente estrategia para reducir el uso de vancomicina.