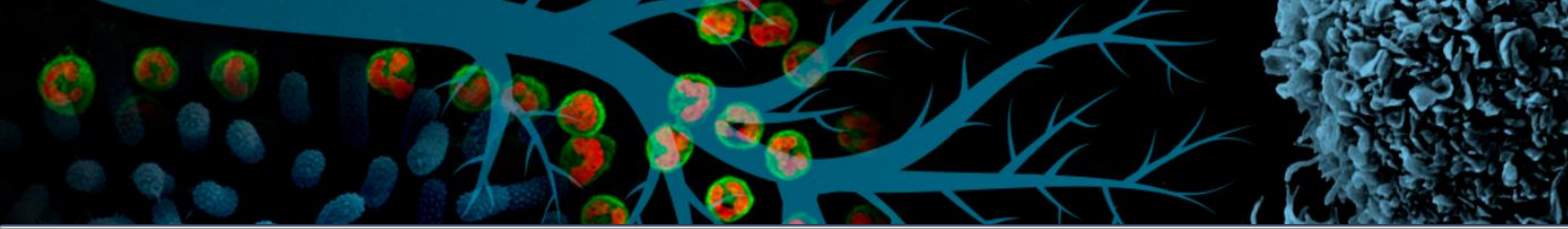


DESMIR A1 – Module Infectiologie – Paris, mercredi 7 décembre 2022

Réévaluation de l'antibiothérapie probabiliste

Cas clinique

François Barbier, MD PhD

Médecine Intensive Réanimation – Centre Hospitalier Régional d'Orléans

UFR de Médecine & CEPR/INSERM U1100 – Université de Tours

francois.barbier@chr-orleans.fr

CHR ORLÉANS

université de TOURS

eMIR COLLÈGE DES ENSEIGNANTS DE MÉDECINE INTENSIVE RÉANIMATION

Conflits d’intérêt potentiels (2019-2022)

MSD

BioMérieux

Cas clinique

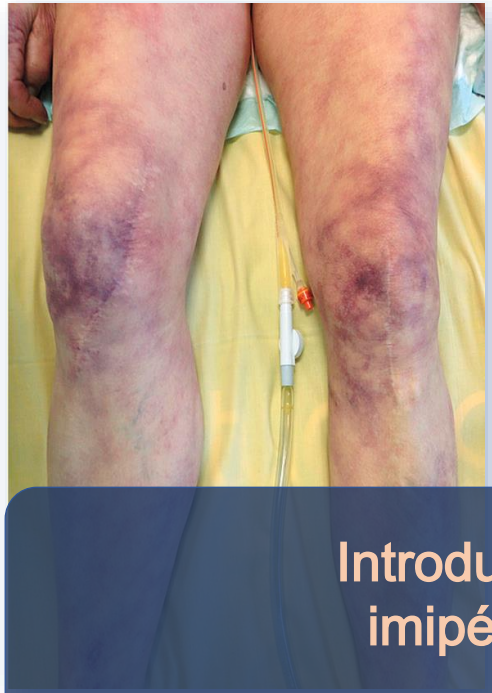
- Patiente de 32 ans, IMC 25,8 kg/m^2, pas d'antécédent notable hormis 2 IU basses d'évolution simple (2018 et 2021)
- **J-15 :** retour d'un voyage touristique de 3 semaines en Inde (Radjasthan), milieux urbain et rural, restaurants de rue, épisode de diarrhée aqueuse (auto-médication par ofloxacine pendant 4 jours)
- **J-2 :** lombalgies gauches fluctuantes, pollakiurie, fébricule
- **H-12 :** recrudescence des lombalgies, vomissements, fièvre, frissons
- Admission au SAU pour prise en charge

Cas clinique

Au SAU :

- Hyperalgique, agitation, score de Glasgow 14 (E4V4M6)
- Empâtement douloureux de la fosse lombaire gauche, abdomen sensible sans défense, vomissements
- FC 130/min, PA 80/40/55 mmHg, marbrures des MI
- FR 28/min, SpO_2 94% en AA
- Température 40,1°C
- BU : GB+++, GR+++, nitrites++
- **Biologie :**
  - GDS (AA) : pH 7,32, PaO_2 64 mmHg, $PaCO_2$ 23 mmHg
  - Lactates 4,5 mmol/L
  - HyperPNN, thrombopénie modérée, AKI KDIGO 1

Cas clinique



Après 2500 ml d'expansion volémique (NaCl 0,9%) :

- PA 88/45/59 mmHg (noradrénaline)
- Lactatémie 4,2 mmol/l
- Oligurie

Choc septique sur pyélonéphrite aiguë communautaire

Introduction d'une antibiothérapie probabiliste par imipénème 1 gr IVL et amikacine 25 mg/kg IVL

Appel du réanimateur : transfert en MIR à H3 de l'admission au SAU

Question #1

Quelle antibiothérapie probabiliste auriez-vous initiée au SAU ? Sur quels arguments ?

1. Ceftriaxone en monothérapie
2. Ceftriaxone + gentamicine
3. Ceftriaxone + amikacine
4. Imipénème ou méropénème en monothérapie
5. Imipénème ou méropénème + amikacine

Question #1

Quelle antibiothérapie probabiliste auriez-vous initiée au SAU ? Sur quels arguments ?

1. Ceftriaxone en monothérapie
2. Ceftriaxone + gentamicine
3. Ceftriaxone + amikacine
4. Imipénème ou méropénème en monothérapie
5. **Imipénème ou méropénème + amikacine**

Bacterial epidemiology of acute pyelonephritis

Data from recent RCT on new β-lactams in UTI

	ASPECT-UTI [1] (n = 731 isolates)	RECAPTURE [2] (n = 819 isolates)	S-649266 [3] (n = 386 GNB isolates)
Enterobacterales	**709 (97.0)**	**772 (94.3)**	**362 (93.8)**
Escherichia coli	594 (81.2)	598 (73.0)	231 (59.8)
Klebsiella pneumoniae	55 (7.5)	100 (12.2)	73 (18.9)
Proteus spp	23 (3.1)	30 (3.7)	19 (4.9)
Others	37 (5.1)	44 (5.4)	39 (10.1)
Pseudomonas aeruginosa	20 (2.7)	38 (4.6)	23 (5.9)
Enterococcus faecalis	35 (4.8)	<10 (<1.2)	-

[1] Wagenlehner et al. *Clin Infect Dis* 2016; 63(6): 754-762

[2] Portsmouth et al. *Lancet Infect Dis* 2018;18(12):1319-1328

[3] Wagenlehner et al. *Lancet* 2015;385(9981):1949-56

SURVEILLANCE DE LA RÉSISTANCE BACTÉRIENNE AUX ANTIBIOTIQUES EN SOINS DE VILLE ET EN ÉTABLISSEMENTS POUR PERSONNES ÂGÉES DÉPENDANTES

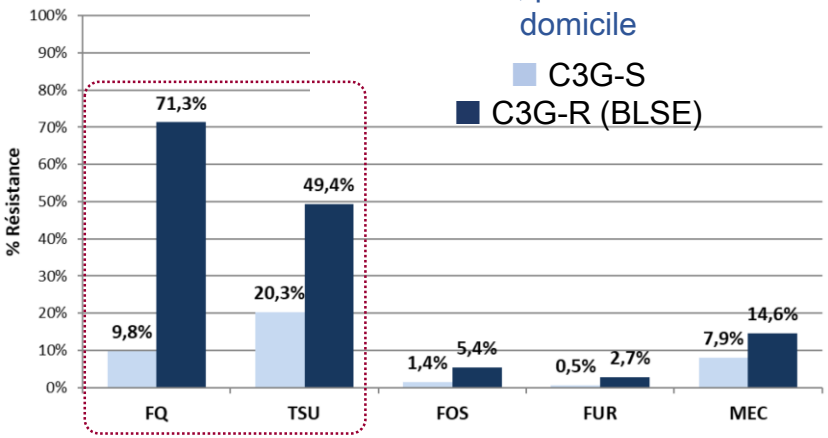
Données 2020 (publication : mars 2022)

Souches d'*Escherichia coli* isolées de prélèvements urinaires

Souches urinaires de *E. coli* Année 2020	Patients vivant à domicile[1]		
Antibiotiques testés	**n**	**%R**	**IC 95%**
Amoxicilline	443272	42,6%	[42,5% - 42,8%]
Amoxicilline + acide clavulanique (cystite)	246577	17,7%	[17,5% - 17,8%]
Mecillinam	436701	8,2%	[8,1% - 8,3%]
Cefixime	416544	4,6%	[4,5% - 4,7%]
Céphalosporines de 3ème génération[3]	454340	3,3%	[3,3% - 3,4%]
Ertapénème	448777	0,020%	[0,016% - 0,024%]
Acide nalidixique	451136	13,7%	[13,6% - 13,9%]
Fluoroquinolones[4]	452660	11,8%	[11,7% - 11,9%]
Triméthoprime	452660	21,2%	[21,1% - 21,4%]
Fosfomycine	452660	1,6%	[1,5% - 1,6%]
Nitrofurantoïne	450661	0,6%	[0,6% - 0,6%]

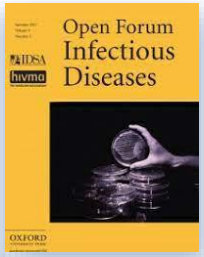
Prévalence des souches BLSE stable sur 2012-2020 (~3,5%)

Co-résistances selon sensibilité aux C3G, patients vivant à domicile



Risk Factors for Community-Acquired Extended-Spectrum Beta-Lactamase–Producing *Enterobacteriaceae* Infections—A Retrospective Study of Symptomatic Urinary Tract Infections

Dheeraj Goyal,[1,a] Nathan Dean,[2] Sarah Neill,[3] Peter Jones,[4] and Kristin Dascomb[4]



Open Forum Infectious Diseases, Volume 6, Issue 2, February 2019

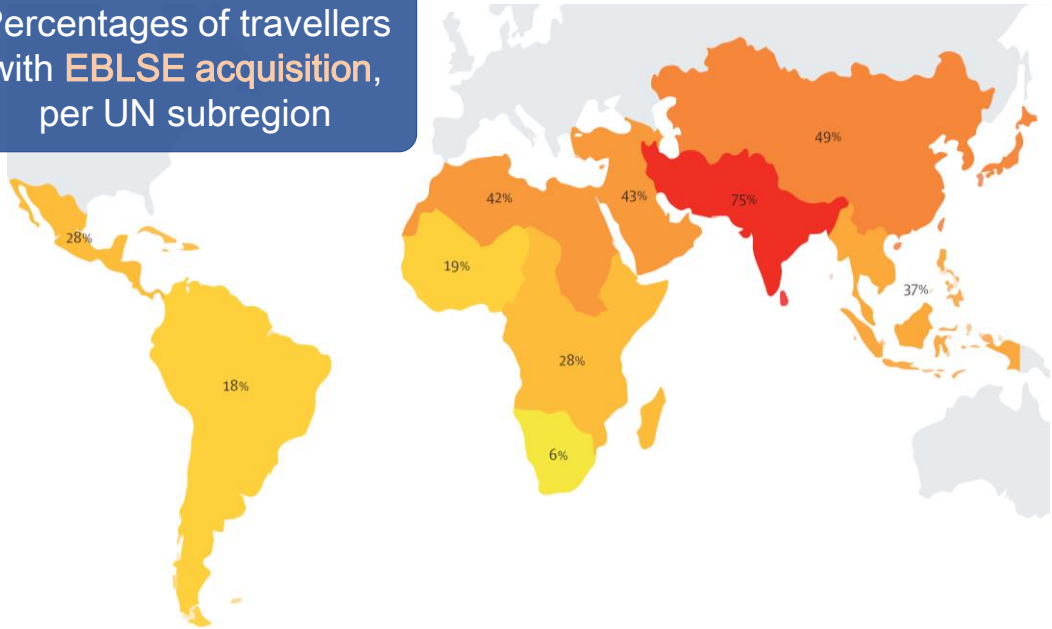
- 22 hôpitaux (Utah), 2001-2016
- 251 patients hospitalisés pour IU communautaires à EBLSE (matching 1:1 avec patients avec IU communautaires à entérobactéries non BLSE)
- **Facteurs de risque d'IU à EBLSE :**
  - Cathéter urinaire à l'admission : aOR 2,36, IC 95% 1,15-4,98, *P* <0,05
  - Antécédent d'IU à répétition : aOR 6,40, IC 95% 3,42-12,66, *P* <0,001
  - Antibiothérapie dans les 3 mois (C3G, fluoroquinolones) : aOR 7,98,

Import and spread of extended-spectrum β-lactamase-producing Enterobacteriaceae by international travellers (COMBAT study): a prospective, multicentre cohort study

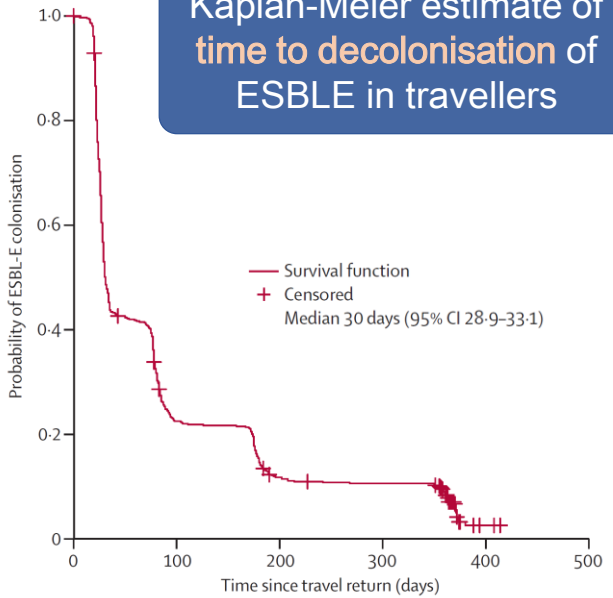
Maris S Arcilla, Jarne M van Hattem*, Manon R Haverkate, Martin C J Bootsma, Perry J J van Genderen, Abraham Goorhuis, Martin P Grobusch, Astrid M Oude Lashof, Nicky Molhoek, Constance Schultsz, Ellen E Stobberingh, Henri A Verbrugh, Menno D de Jong, Damian C Melles, John Penders*

Lancet Infect Dis 2017; 17: 78–85

Percentages of travellers with EBLSE acquisition, per UN subregion



Kaplan-Meier estimate of time to decolonisation of ESBLE in travellers



Risk Factors for Community-Acquired Urinary Tract Infections Caused by ESBL-Producing *Enterobacteriaceae* –A Case–Control Study in a Low Prevalence Country

Arne Søraas[1]*, Arnfinn Sundsfjord[2,3], Irene Sandven[4], Cathrine Brunborg[4], Pål A. Jenum[1]

PLOS ONE

July 2013 | Volume 8 | Issue 7 | e69581

Table 4. Independent risk factors of ESBL positive community acquired urinary tract infection identified using multivariate logistic regression analysis.

Variable	Level	Adjusted OR	95% CI	P
Travelling to Asia, Middle East or Africa[a]				
- During the past 6 weeks	yes/no	21	4.5–97	<0.001
- Between the previous 6 weeks to 24 months	yes/no	2.3	1.2–4.4	0.017
Use of fluoroquinolones the past 90 days	yes/no	16	3.2–80	<0.001
Use of β-lactams except mecillinam in the past 90 days	yes/no	5.0	2.1–12	<0.001
Diabetes mellitus	yes/no	3.2	1.0–11	0.051
Recreational freshwater swim past year	yes/no	2.1	1.0–4.3	0.040
Age	5 year increase	0.89	0.82–0.97	0.014
Number of fish meals per week	1 meal increase	0.68	0.51–0.90	0.008

Travel >24 months : NS

Antibiothérapie probabiliste des IU communautaires graves (pyélonéphrite aiguë, prostatite aiguë)

Guidelines SPILF 2015

C3G (ceftriaxone ou céfotaxime)
+ amikacine

Antécédent <6 mois d'ECBU positif à EBLSE

Choc septique avec ≥ 1 facteur de risque d'IU à EBLSE *

Carbapénème (imipénème, méropénème)
+ amikacine

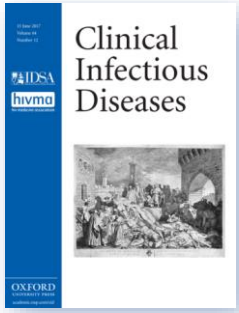
Si allergie aux C3G ou aux carbapénèmes : aztréonam + amikacine

* Colonisation urinaire ou IU à EBLSE <6 mois, antibiothérapie (BL/IBL, C3G/C3G, FQ) <6 mois, voyage récent en zone d'endémie d'EBLSE, hospitalisation < 3 mois, SLD/EPHAD

Short-Course Adjunctive Gentamicin as Empirical Therapy in Patients With Severe Sepsis and Septic Shock: A Prospective Observational Cohort Study

David S. Y. Ong,[1,2] Jos F. Frencken,[2,3] Peter M. C. Klein Klouwenberg,[1,2] Nicole Juffermans,[4] Tom van der Poll,[5] Marc J. M. Bonten,[1,3] and Olaf L. Cremer[2]; for the MARS consortium[a]

Clinical Infectious Diseases® 2017;64(12):1731–6



Pays-Bas, 2 réanimations, 2011-2015

Antibiothérapie probabiliste protocolisée

ICU A : β-lactamine (C3G 84%) + gentamicine (5 mg/kg/24h, 24h-72h)

ICU B : β-lactamine seule (C3G 82%) (ICU B)

N = 648 patients

Infections intra-abdominales 49%, infections urinaires 16%

Short-Course Adjunctive Gentamicin as Empirical Therapy in Patients With Severe Sepsis and Septic Shock: A Prospective Observational Cohort Study

David S. Y. Ong,[1,2] Jos F. Frencken,[2,3] Peter M. C. Klein Klouwenberg,[1,2] Nicole Juffermans,[4] Tom van der Poll,[5] Marc J. M. Bonten,[1,3] and Olaf L. Cremer[2]; for the MARS consortium[a]

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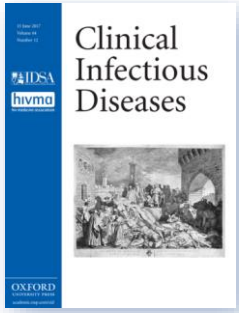


Traitement empirique inadéquate :

5% (A) vs 4% (B), *P* = 0,66

Table 4. Associations of Gentamicin Use With Renal Failure–Free Days, Shock-Free Days, and Death Before Day 14

	Primary Outcome	Secondary Outcome	
Model	Renal Failure–Free Days	Shock-Free Days	Death Before Day 14
Per protocol (primary) analysis			
Crude	1.35 (1.00–1.82)	1.30 (0.96–1.77)	1.41 (0.98 – 2.02)
Adjusted[a]	1.39 (1.00–1.94)	1.34 (0.96–1.86)	1.41 (0.94 – 2.12)
Intention-to-treat (sensitivity) analysis			
Crude	1.39 (1.04–1.86)	1.17 (0.87–1.57)	1.47 (1.03 – 2.10)
Adjusted[a]	1.70 (1.22–2.36)	1.28 (0.93–1.77)	1.76 (1.17 – 2.64)

Original Investigation | Infectious Diseases

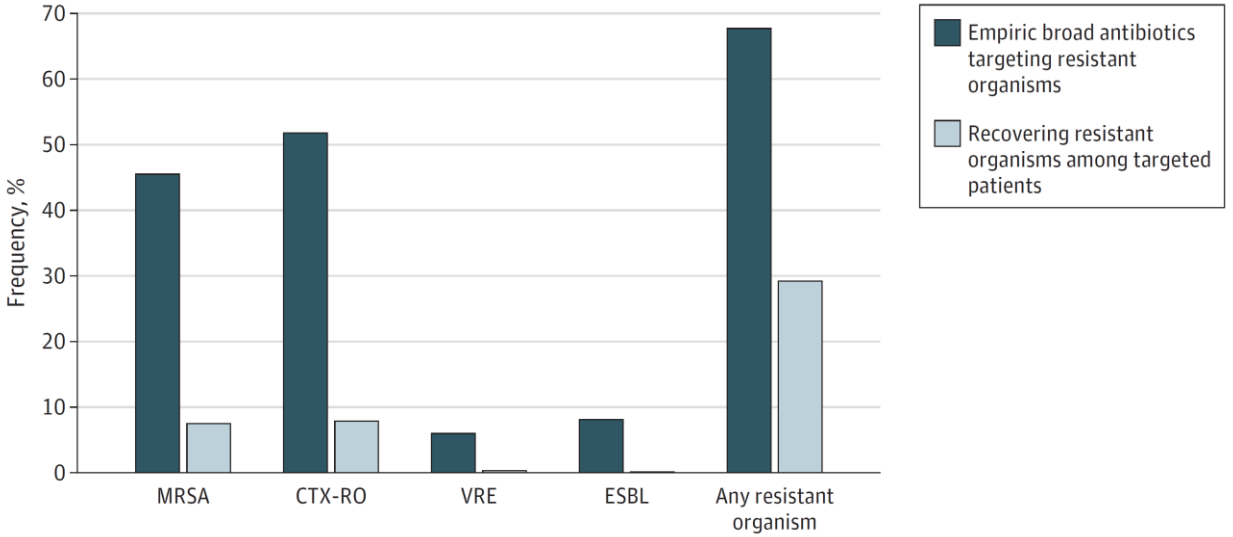
Prevalence of Antibiotic-Resistant Pathogens in Culture-Proven Sepsis and Outcomes Associated With Inadequate and Broad-Spectrum Empiric Antibiotic Use

Chanu Rhee, MD, MPH; Sameer S. Kadri, MD, MSc; John P. Dekker, MD, PhD; Robert L. Danner, MD; Huai-Chun Chen, PhD; David Fram, BA; Fang Zhang, PhD; Rui Wang, PhD; Michael Klompas, MD, MPH; for the CDC Prevention Epicenters Program

JAMA Network Open

JAMA Network Open. 2020;3(4):e202899.

Figure 3. Proportion of Culture-Positive Sepsis Patients Treated With Broad-Spectrum Antibiotics in Whom Targeted Resistant Organisms Were Subsequently Recovered



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JAMA Network Open

JAMA Network Open. 2020;3(4):e202899.

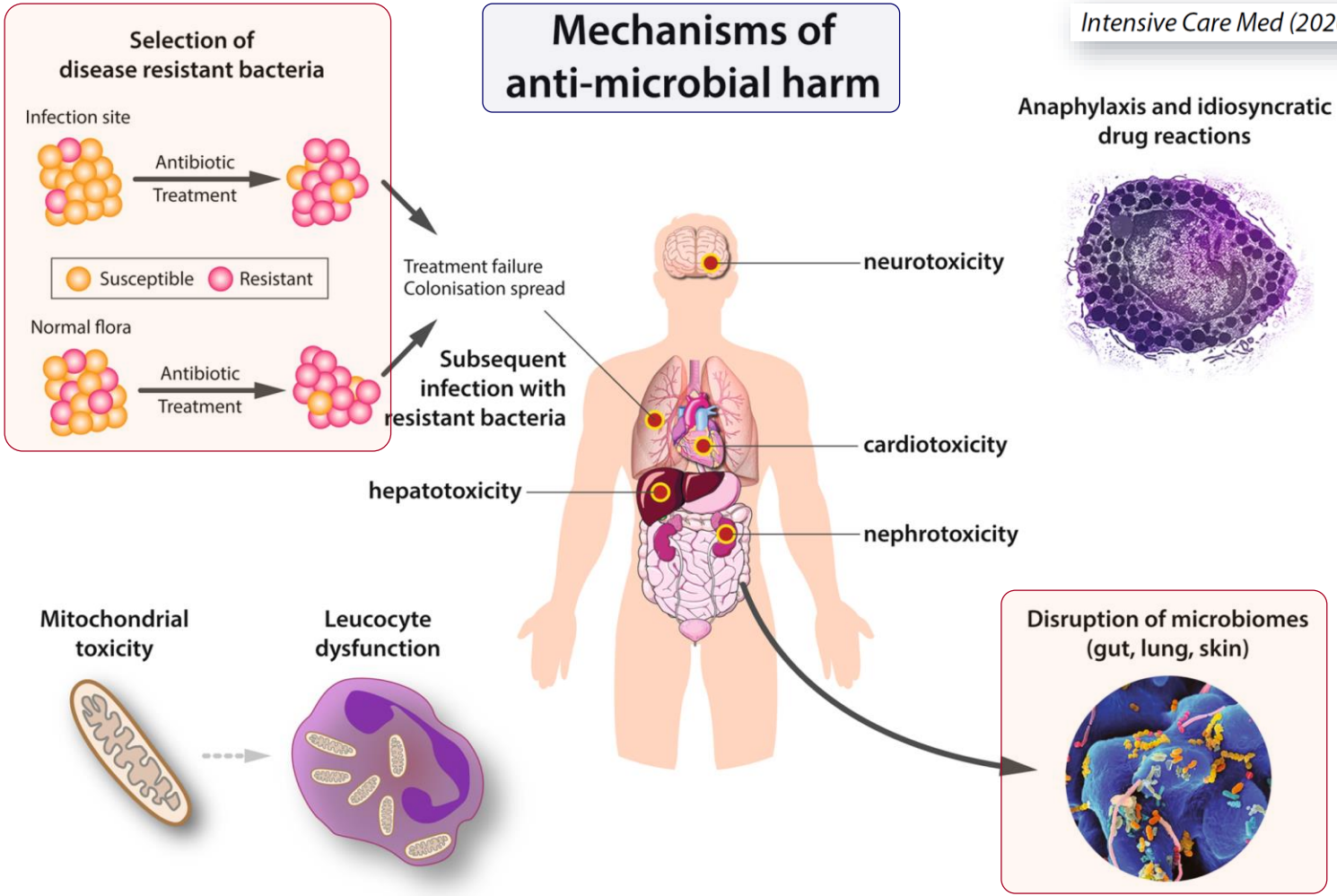
Both inadequate (AOR 1.19, 95% CI 1.03-1.37) and unnecessarily broad empiric antibiotics (aOR 1.22, 95% CI 1.06-1.40) were associated with hospital mortality.

Table 2. Outcomes Associated With Inadequate and Unnecessarily Broad Empiric Antibiotic Therapy[a]

	Inadequate vs adequate empiric therapy						Unnecessarily broad vs not unnecessarily broad empiric therapy[b]					
	No./total No. (%)						No./total No. (%)					
Outcome	Inadequate	Adequate empiric therapy	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value	Unnecessarily broad	Not unnecessarily broad	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
In-hospital death	488/2785 (17.5)	2011/12 388 (16.3)	1.10 (0.98-1.22)	.09	1.19 (1.03-1.37)	.02	1575/8405 (18.7)	436/3993 (10.9)	1.88 (1.68-2.11)	<.001	1.22 (1.06-1.40)	.007
Hospital-onset acute kidney injury	486/2785 (17.5)	2196/12 398 (17.7)	0.98 (0.88-1.09)	.74	1.02 (0.90-1.16)	.72	1641/8405 (19.5)	555/3993 (13.9)	1.50 (1.35-1.67)	<.001	1.12 (1.00-1.26)	.05
Clostridioides difficile	207/2785 (7.4)	498/12 398 (4.0)	1.92 (1.63-2.27)	<.001	1.19 (0.98-1.45)	.09	367/8405 (4.4)	131/3993 (3.3)	1.34 (1.10-1.65)	.004	1.26 (1.01-1.57)	.04

Mechanisms of anti-microbial harm

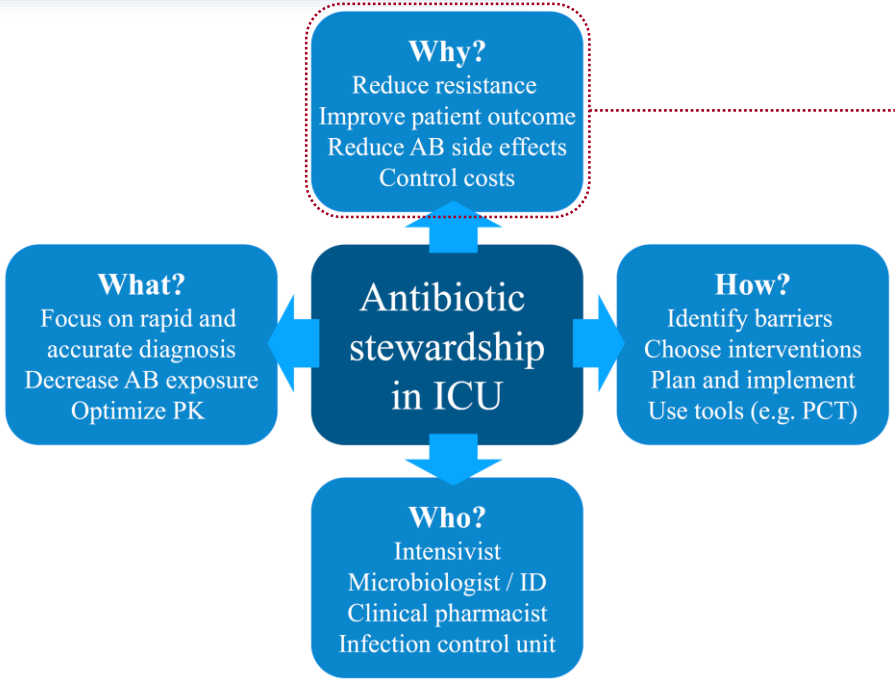
Intensive Care Med (2020) 46:225–235



Understanding antibiotic stewardship for the critically ill

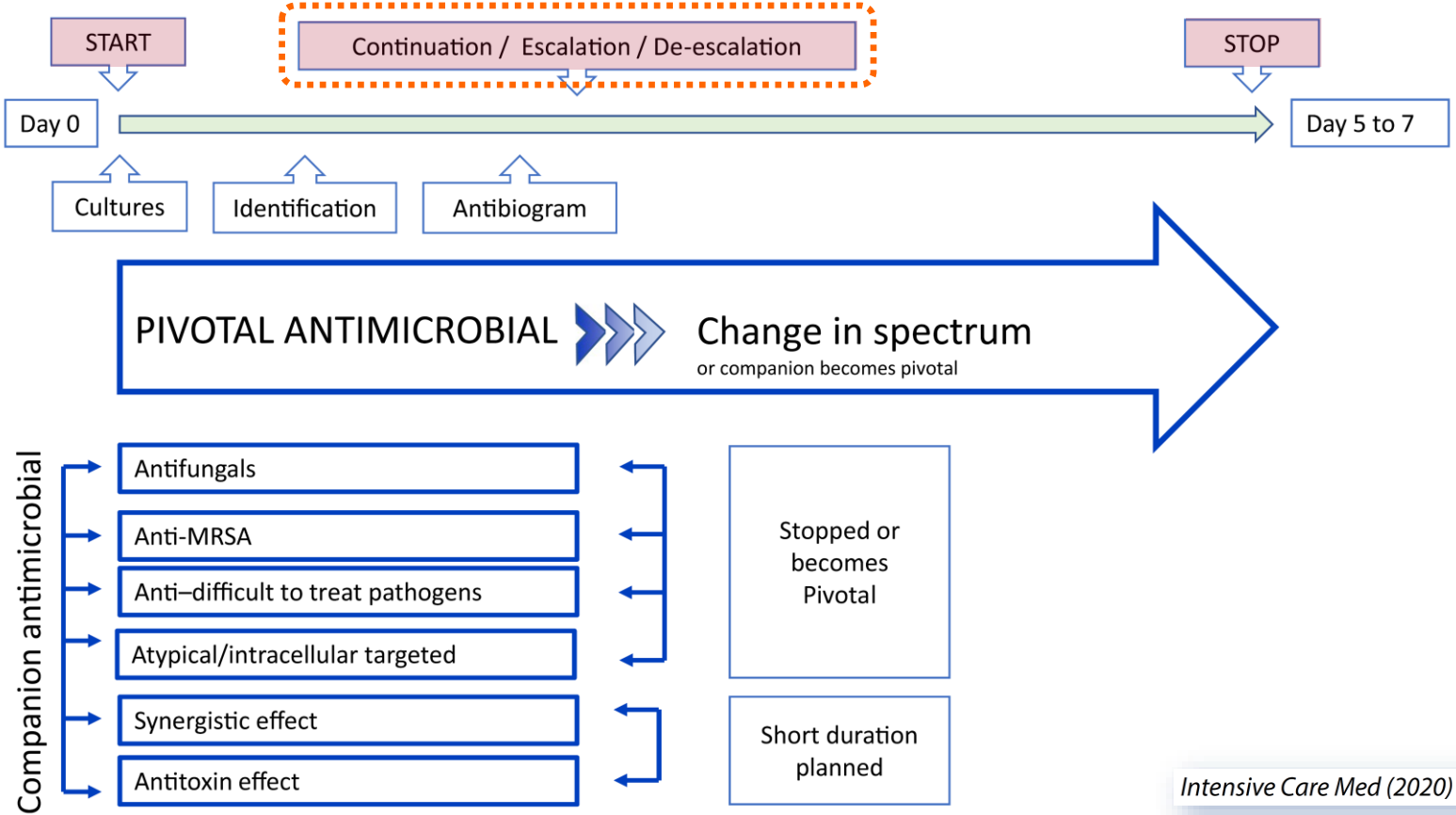
J. J. De Waele
J. Schouten
G. Dimopoulos

Intensive Care Med (2016) 42:2063–2065



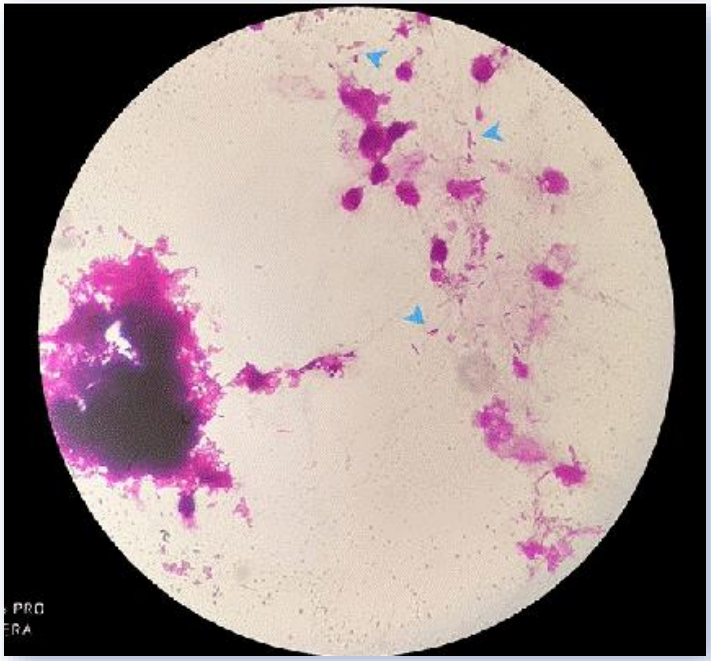
Control multidrug resistance and optimize patient outcomes through optimized antibiotic use and reduced overall antibiotic consumption

Time-line of antibiotic stewardship in ICU patient



Intensive Care Med (2020) 46:236–244

Cas clinique



H6 admission MIR :

- VAC FiO_2 50% PEEP 8 cmH_2O
- Noradrénaline 2,2 mg/h
- Marbrures MI stade 3
- Lactatémie 3,2 mmol/L

Examen direct de l'ECBU :

nombreux bacilles à Gram négatif

Question #2

À partir de cet ECBU positif à BGN à l'examen direct, existe-t-il un moyen rapide d'infirmer l'implication d'une souche productrice de BLSE ?

1. Oui
2. Non

Question #2

À partir de cet ECBU positif à BGN à l'examen direct, existe-t-il un moyen rapide d'infirmer l'implication d'une souche productrice de BLSE ?

1. **Oui** (??? – très peu de données cliniques sur tests phénotypiques)
2. Non

Comparison of Three Biochemical Tests for Rapid Detection of Extended-Spectrum-β-Lactamase-Producing *Enterobacteriaceae*

Laurent Poirel,[a] Javier Fernández,[a,b,c] Patrice Nordmann[a,d]

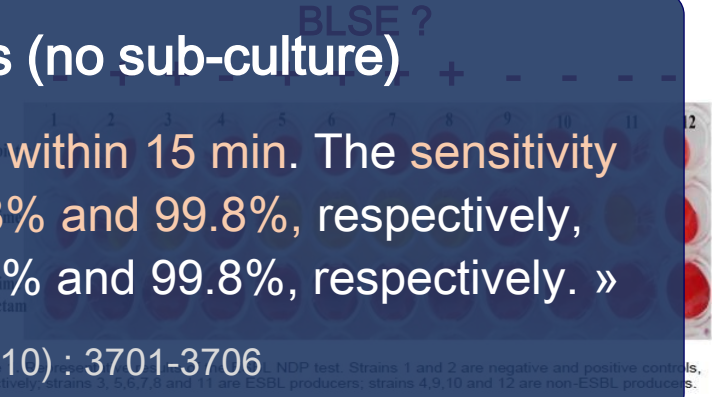
February 2016 Volume 54 Number 2

Détection <2h des souches productrices de BLSE sur cultures H12-H24

sans attendre l'antibiogramme (tests biochimiques/chromogéniques)

TABLE 3 Diagnostic parameters of the different tests

Diagnostic test parameter	Performance (%) by test			
	NDP	β-Lacta	Rapid ESBL Screen kit 30 min	Rapid ESBL Screen kit 2 h
Sensitivity for CTX-M-type ESBL	100	91.4	82.8	94.3
Sensitivity for non-CTX-M-type ESBL	88	84	72	88.0
Global sensitivity for ESBL	95.0	88.0	80	91.7
Global specificity	100	70.8	87	83



NDP test. Strains 1 and 2 are negative and positive controls, respectively; strains 3, 5,6,7,8 and 11 are ESBL producers; strains 4,9,10 and 12 are non-ESBL producers.

Ex : Rapid NDP test

Phenotypic test directly on urines (no sub-culture)

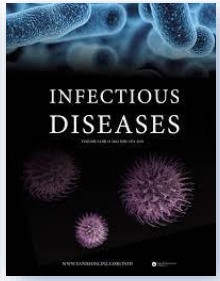
« Results of the ESBL NDP test were obtained within 15 min. The sensitivity and specificity of the ESBL NDP test were 98% and 99.8%, respectively, whereas the PPV and NPV of this test were 98% and 99.8%, respectively. »

Dortet et al. *J Clin Microbiol* 2014; 52 (10) : 3701-3706

Impact of the beta-lacta test on the management of urinary tract infections at the emergency department

Mizrahi A, Naouri D, Hobson D, Amzalag J, Pilmis B, Couzigou C, Ganansia O, Le Monnier A

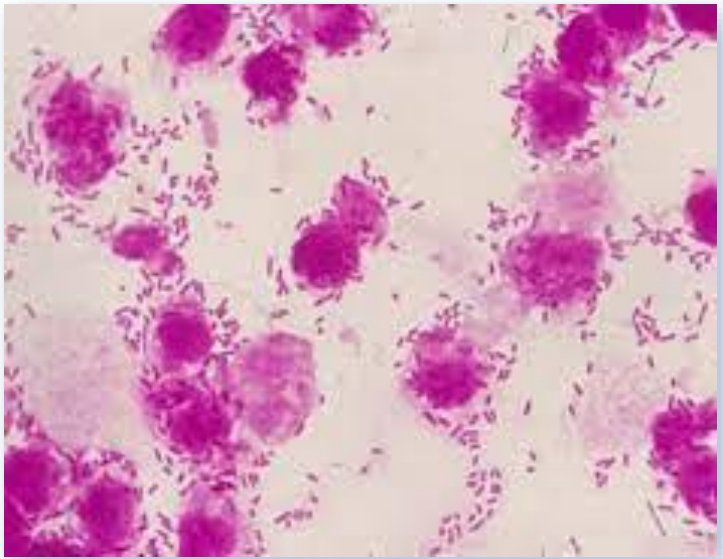
Infect Dis (Lond) 2021;53(1):52-60



Patients and methods: We included prospectively all the patients admitted to the ED for clinical suspicion of UTI. Compared with physician's decision, we analysed the potential impact of β-lacta test on the initial antibiotic therapy and on the implementation of hygiene measures.

Results: We included 203 patients, 43% with acute pyelonephritis and 21% with acute prostatitis. The β-lacta test had a 95.2% sensitivity and a 99.5% specificity to detect ESBL. **Taking the β-lacta test results into account would have decreased significantly both the time to appropriate therapy from 54 hours to 2.7 hours**.

Cas clinique



H8 de l'admission en MIR :

Hémocultures prélevées au SAU positives à bacilles à Gram négatif

H10 / MALDI-TOF : *Escherichia coli*

Question #5

À partir de ces hémocultures positives à *E. coli*, existe-t-il un moyen rapide d'infirmer l'implication d'une souche productrice de BLSE ?

1. Oui
2. Non

Question #5

À partir de ces hémocultures positives à *E. coli*, existe-t-il un moyen rapide d'infirmer l'implication d'une souche productrice de BLSE ?

1. **Oui** (?? – très peu de données en réanimation)
2. Non

BioFire® Blood Culture Identification 2 (BCID2) Panel

1 test. 43 cibles. ~1 heure.

BACTÉRIES À GRAM NÉGATIF

Complexe *Acinetobacter calcoaceticus-baumannii*
Bacteroides fragilis
Enterobacterales
- Complexe *Enterobacter cloacae*
- *Escherichia coli*
- *Klebsiella aerogenes*
- *Klebsiella oxytoca*
- Groupe *Klebsiella pneumoniae*
- *Proteus*
- *Salmonella*
- *Serratia marcescens*

Haemophilus influenzae
Neisseria meningitidis
Pseudomonas aeruginosa
Stenotrophomonas maltophilia

BACTÉRIES À GRAM POSITIF

Enterococcus faecalis
Enterococcus faecium
Listeria monocytogenes
Staphylococcus
- *Staphylococcus aureus*
- *Staphylococcus epidermidis*
- *Staphylococcus lugdunensis*

Streptococcus
- *Streptococcus agalactiae*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*

LEVURES

Candida albicans
Candida auris
Candida glabrata
Candida krusei
Candida parapsilosis
Candida tropicalis
Cryptococcus neoformans/gattii

GÈNES DE RÉSISTANCE AUX ANTIBIOTIQUES

Carbapénémases
IMP
KPC
OXA-48-like
NDM
VIM

Résistance à la colistine
mcr-1

BLSE
CTX-M

Résistance à la méticilline
mecA/C
mecA/C et MREJ (SARM)

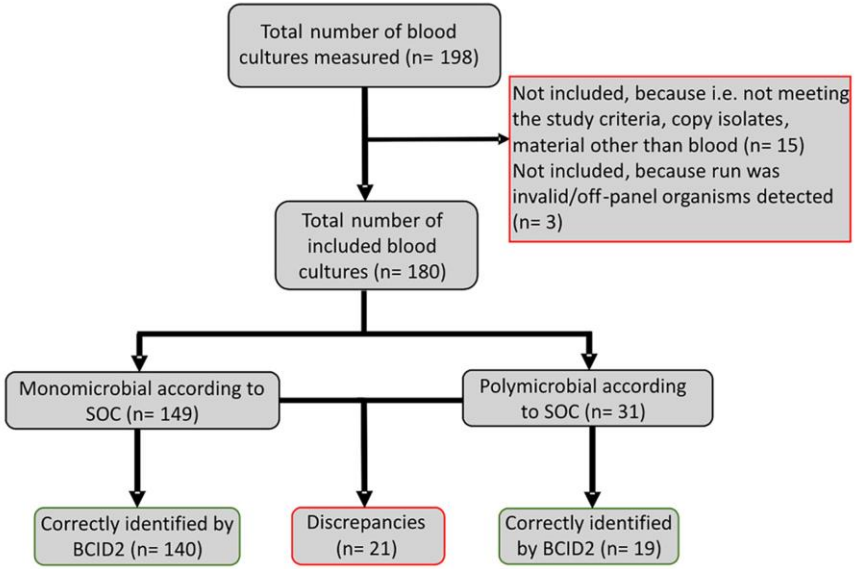
Résistance à la vancomycine
vanA/B

Usefulness of BioFire FilmArray BCID2 for Blood Culture Processing in Clinical Practice

Benjamin Berinson,[a] Anna Both,[a] Laura Berneking,[a] Martin Christner,[a] Marc Lütgehetmann,[a] Martin Aepfelbacher,[a] Holger Rohde[a]

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology®

August 2021 Volume 59 Issue 8 e00543-21



94%

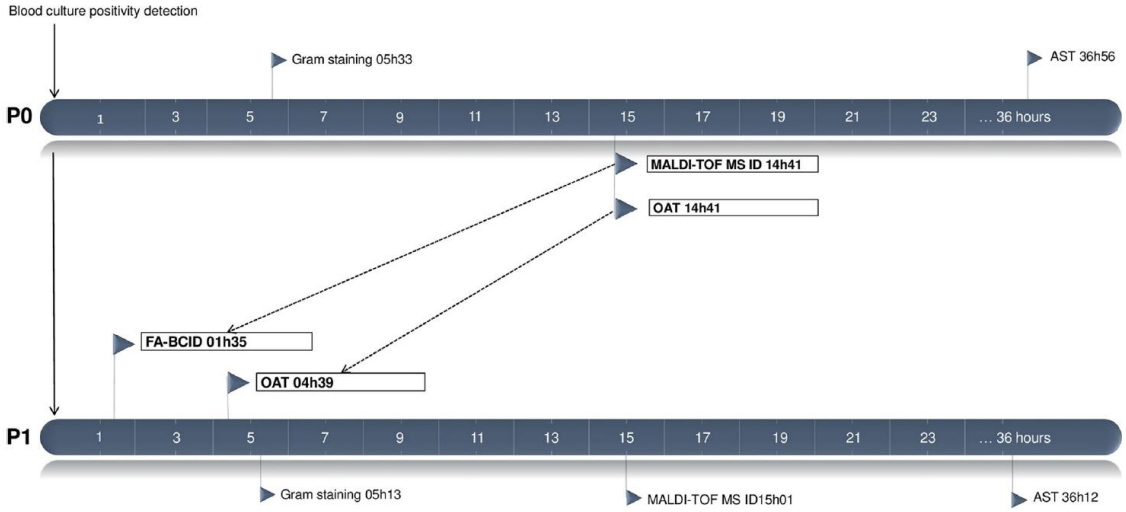
TABLE 2 Distribution of resistance markers detected by BCID2

Isolate	Resistance marker detected by BCID2 (*n*)			
	bla$_{CTX-M}$	*bla*$_{OXA-48}$-like	*bla*$_{VIM}$	None detected
Phenotypic third-generation cephalosporin resistance				
E. coli (*n* = 12)	11	0	0	1[a]
K. pneumoniae group (*n* = 3)	1	0	0	2[b]
K. oxytoca (*n*= 1)	0	0	0	1[c]
Carbapenem-resistant isolates				
P. aeruginosa (*n* = 1)	0	0	1	0
K. pneumoniae group (*n* = 1)	1	1	0	0

The impact of a rapid molecular identification test on positive blood cultures from critically ill with bacteremia: A pre-post intervention study

Alexia Verroken[1]*, Noémie Despas[1], Hector Rodriguez-Villalobos[1], Pierre-François Laterre[2]

PLOS ONE | https://doi.org/10.1371/journal.pone.0223122 September 26, 2019



- Étude monocentrique
- P0 : hémoculture conventionnelle + identification MALDI-TOF
  P1 : FilmArray panel BC
- Effectifs : 110 patients x 2
- Délai entre positivité de l'hémoculture et antibiothérapie optimale : 4h39 (P1) vs 14h41 (P0), P <0,0001

Cas clinique

H36 de l'admission en MIR :

- RASS 0, sevrage ventilatoire en cours
- Noradrénaline 0,6 mg/h
- Lactatémie 1,2 mmol/L
- Normalisation de la fonction rénale
- Thrombopénie stable
- Résiduelle amikacinémie 2,2 mg/L
- Antibiogramme du colibacille en attente

Question #6

Faut-il réinjecter une dose d'amikacine ?

1. Oui
2. Non

Question #6

Faut-il réinjecter une dose d'amikacine ?

1. Oui
2. **Non**

Cas clinique

H48 de l'admission en MIR :

Escherichia coli **multi-sensible**

(souche sauvage)

Antibiothérapie définitive des IU communautaires graves (pyélonéphrite aiguë, prostatite aiguë*)

Guidelines SPILF 2015

Entérobactérie non BLSE	Entérobactérie BLSE
Amoxicilline Amoxicilline-clavulanate Fluoroquinolone* Cotrimoxazole*	Si FQ-S : fluoroquinolone Si FQ-R et SXT-S : cotrimoxazole Si FQ-R et SXT-R : Amoxicilline-clavulanate si CMI <8 mg/l Pipéracilline-tazobactam si CMI <8 mg/l C3G si CMI <1 mg/l Céfoxitine Aminoside (monothérapie) Carbapénèmes

Antibiothérapie définitive des IU communautaires graves (pyélonéphrite aiguë, prostatite aiguë*)

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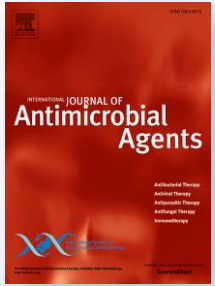
Très peu de données chez les patients de réanimation

Non-carbapenem β-lactam/β-lactamase inhibitors versus carbapenems for urinary tract infections caused by extended-spectrum β-lactamase-producing Enterobacteriaceae: a systematic review

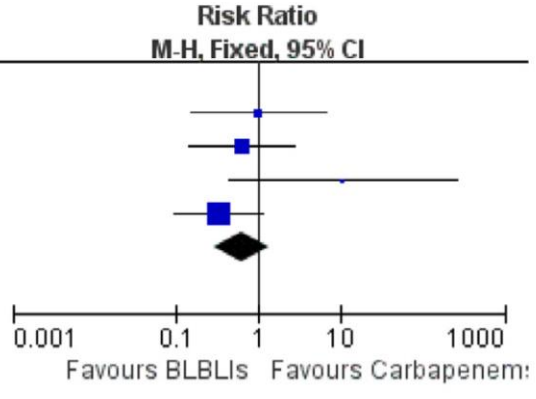
Huan Zhang[a,b,1], Beibei Liang[a,1], Jin Wang[a], Yun Cai[a,*]

International Journal of Antimicrobial Agents 58 (2021) 106410



Study or Subgroup	BLBLIs Events	Total	Carbapenems Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 PTZ						
Seo 2017	2	33	2	33	11.7%	1.00 [0.15, 6.68]
Sharara 2020	2	45	10	141	28.4%	0.63 [0.14, 2.75]
Tullos 2020	1	39	0	141	1.3%	10.65 [0.44, 256.44]
Yoon 2017	3	68	11	82	58.6%	0.33 [0.10, 1.13]
Subtotal (95% CI)		**185**		**397**	**100.0%**	**0.63 [0.30, 1.32]**
Total events	8		23			

Heterogeneity: Chi² = 4.32, df = 3 (P = 0.23); I² = 31%
Test for overall effect: Z = 1.23 (P = 0.22)
Test for subgroup differences: Not applicable



Patients de réanimation ?

JAMA | Original Investigation

Effect of Piperacillin-Tazobactam vs Meropenem on 30-Day Mortality for Patients With *E coli* or *Klebsiella pneumoniae* Bloodstream Infection and Ceftriaxone Resistance

A Randomized Clinical Trial

JAMA. 2018;320(10):984-994.

Table 2. Primary Analysis and Subgroup Analyses

	30-d Mortality, No./Total No. (%)		Risk Difference, % (1-Sided 97.5% CI)[a]	*P* Value for Noninferiority
	Piperacillin-Tazobactam	Meropenem		
Primary analysis	23/187 (12.3)	7/191 (3.7)	8.6 (−∞ to 14.5)	.90
Per-protocol analysis	18/170 (10.6)	7/186 (3.8)	6.8 (−∞ to 12.8)	.76
UT vs non-UT source				
UT	7/102 (6.9)	4/128 (3.1)	3.7 (−∞ to 10.7)	.44
Non-UT	16/85 (18.8)	3/63 (4.8)	14.1 (−∞ to 24.5)	

HAS
HAUTE AUTORITÉ DE SANTÉ

Antibiothérapie des infections à entérobactéries et à *Pseudomonas aeruginosa* chez l'adulte : place des carbapénèmes et de leurs alternatives

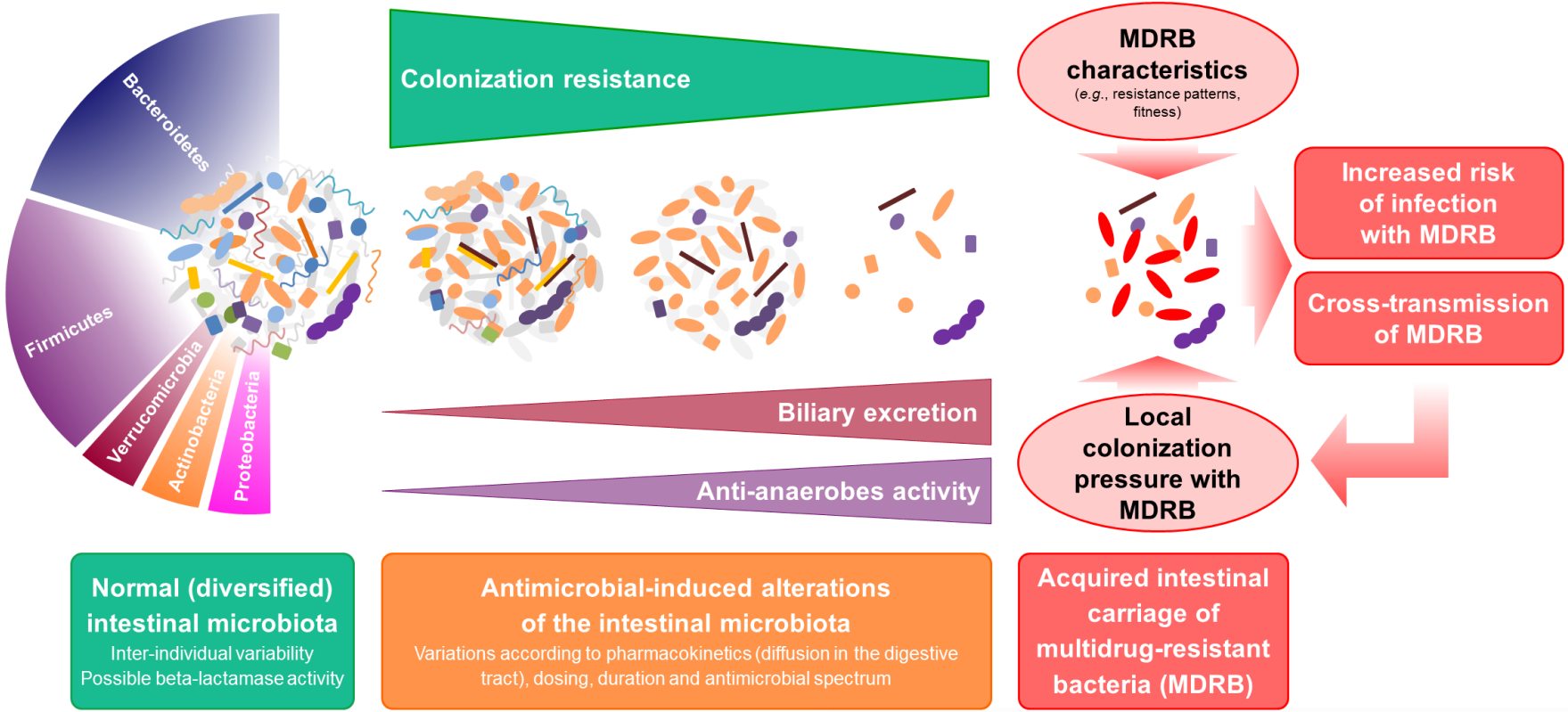
Mai 2019

Tableau 2. Proposition de classement des molécules antibiotiques pouvant être utilisées en désescalade thérapeutique des infections à entérobactérie résistante aux C3G, en fonction de leur impact potentiel sur le microbiote digestif

Impact écologique potentiellement croissant	Molécules
Rang 1	Aminosides (mais risque de toxicité)*
Rang 2	Témocilline, cotrimoxazole**
Rang 3	Céfoxitine, amoxicilline-clavulanate
Rang 4	Pipéracilline-tazobactam, céfépime, fluoroquinolones**
Rang 5	Carbapénèmes (incluant l'ertapénème), ceftazidime-avibactam, ceftolozane-tazobactam

???

Impact des antibiotiques sur la résistance à la colonisation



Woerther, Ruppé, Barbier. *Int J Antimicrob Agents* 2018; 52: 762-770

Antibiotics with activity against intestinal anaerobes and the hazard of acquired colonization with ceftriaxone-resistant Gram-negative pathogens in ICU patients: a propensity score-based analysis

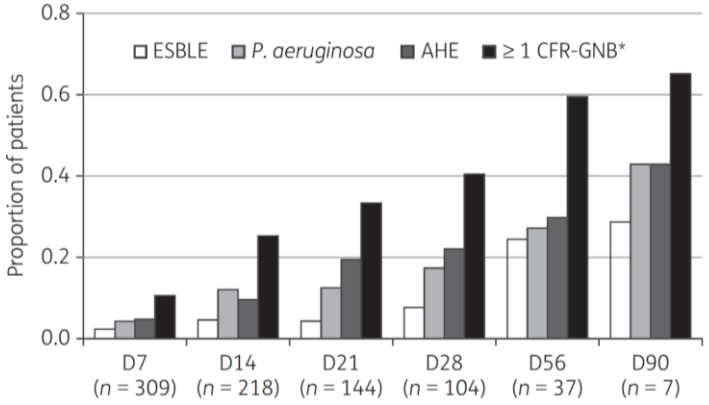
Maxime Boutrot[1], Khalid Azougagh[1], Jérôme Guinard[2], Thierry Boulain[3] and François Barbier[3]*

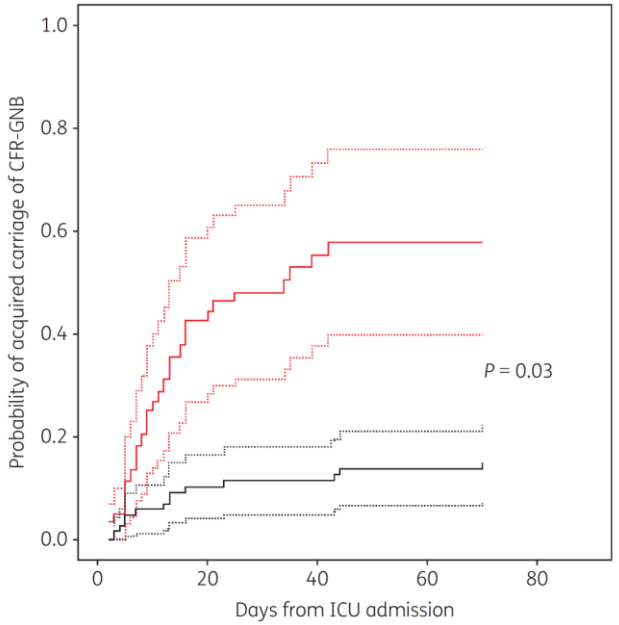
J Antimicrob Chemother 2019; **74**: 3095–3103

Exposition aux antibiotiques anti-anaérobies hors carbapénèmes (AAC, PTZ, métronidazole) : FdR indépendant d'acquisition d'un portage intestinal de BGN C3G-R (aHR 3,92, IC 95% 1,12-13,7)

Autres classes (dont **IMI/MER** et C3G) : pas d'impact indépendant

Portage intestinal de BGN C3G-R, %
(n = 309)





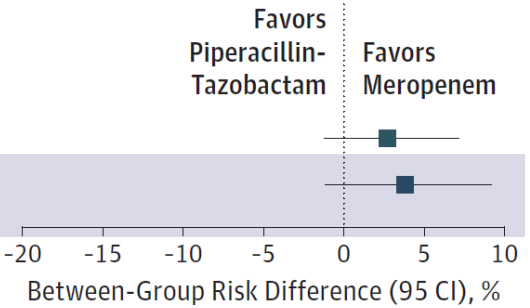
Effect of Piperacillin-Tazobactam vs Meropenem on 30-Day Mortality for Patients With *E coli* or *Klebsiella pneumoniae* Bloodstream Infection and Ceftriaxone Resistance

A Randomized Clinical Trial

JAMA. 2018;320(10):984-994.

JAMA®
The Journal of the American Medical Association

Measure of Failure	Patients Meeting End Point, No./Total No. (%)		Between-Group Difference (95% CI)
	Piperacillin-Tazobactam	Meropenem	
Microbiological relapse	9/187 (4.8)	4/191 (2.1)	2.7 (-1.1 to 7.1)
Secondary infection with multiresistant organism or *Clostridium difficile*	15/187 (8.0)[b]	8/191 (4.2)[c]	3.8 (-1.1 to 9.1)



MERINO trial - NCT02176122

Ventilator-associated pneumonia due to *Stenotrophomonas maltophilia*: Risk factors and outcome ☆

Wafa Ibn Saied[a,1], Sybille Merceron[b,1], Carole Schwebel[c], Alban Le Monnier[d], Johana Oziel[e], Maité Garrouste-Orgeas[b,f,h], Guillaume Marcotte[g], Stéphane Ruckly[h], Bertrand Souweine[i], Michael Darmon[j,o], Lila Bouadma[a,p], Etienne de Montmollin[p], Bruno Mourvillier[k,p], Jean Reignier[l], Laurent Papazian[m], Shidasp Siami[n], Elie Azoulay[o], Jean-Pierre Bédos[b], Jean-Francois Timsit[a,h,p,*]

J Infect 2020; 80(3): 279-285

102 patients with VAP due to *S. maltophilia* (6.2% of all VAP patients)

matched with 237 patients with *P. aeruginosa* VAP and 375 patients with other VAP

Independent predictor of *S. maltophilia* VAP :

Variables[a]	OR IC 95%	*P**
SOFA score 2 days before VAP		
Respiratory systems score > 2	1.73 [1.02–2.92]	0.04
Coagulation system score > 2	2.93 [1.33–6.48]	<0.01
Antibiotic 1 week before VAP occurrence		
Ureido/carboxypenicillin*	2.08 [1.22–3.55]	<0.01
Carbapenems (Imipenem/meropenem)	3.20 [1.77–5.79]	<0.001

* Mostly piperacillin-tazobactam

AAC
Journals.ASM.org

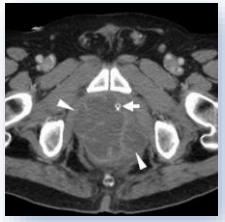
August 2015 Volume 59 Number 8

A Simulation Study Reveals Lack of Pharmacokinetic/Pharmacodynamic Target Attainment in De-escalated Antibiotic Therapy in Critically Ill Patients

Mieke Carlier,[a,b] Jason A. Roberts,[c,d,e] Veronique Stove,[a,f] Alain G. Verstraete,[a,f] Jeffrey Lipman,[c,d] Jan J. De Waele[b]

« **The probability that therapeutic exposure will be achieved was lower for the narrower-spectrum antibiotics with conventional dosing** than for the broad-spectrum alternatives and could drastically be improved with higher dosages and different modes of administrations. »

Diffusion prostatique des antibiotiques



Antibiotiques	Ratio prostate/sérum (%)	Doses utilisées pour les IUM fébriles
Ciprofloxacine *(9)*	200	500 mg/12 h p.o.
TMP-SMX *(1)*	100/30	800/160 mg/12 h p.o.
Céfotaxime *(1)*	50	1 g/8 h i.v.
Méropénème *(9)*	15	1 g/8 h i.v.
Témocilline *(1)*	75	2 g/8-12 h i.v.
Amikacine *(1, 9)*	25	20-30 mg/kg/24 h i.v.
Amoxicilline *(1, 9)*	60 à 75	NR en dehors des IUM à *Enterococcus faecalis*
Fosfomycine *(1, 9)*	50 à 75	NR
Nitrofurantoïne *(9)*	< 10	NR

Colombier & Lafaurie. La Lettre de l'Infectiologue • Tome XXXIII - n° 4 - juillet-août 2018

Antimicrobial de-escalation in the critically ill patient and assessment of clinical cure: the DIANA study

Intensive Care Med (2020) 46:1404–1417

Prospective study (2016-2018), 1495 patients, 152 ICUs, 28 countries

	Total $n = 1495$	No change $n = 934$; 62.5%	ADE $n = 240$; 16.1%	Other change $n = 321$; 21.5%	ADE vs no change p value		Other change vs no change p value		% of available data
					p value	Relative risk (95% CI)	p value	Relative risk (95% CI)	
Clinical cure on day 7 [g]	650 (43.5%)	399 (42.7%)	139 (57.9%)	112 (34.9%)	< 0.001	1.34 (1.18–1.52)	0.03	0.83 (0.71–0.98)	95.9
Infection relapse[(c)]	103 (6.9%)	61 (6.5%)	22 (9.2%)	20 (6.2%)	0.24	1.37 (0.86–2.18)	0.96	0.96 (0.59–1.56)	96.5
Infections other than the infection under study or a relapse infection[c]	184 (12.3%)	109 (11.7%)	38 (15.8%)	37 (11.5%)	0.12	1.34 (0.95–1.89)	1	0.99 (0.69–1.40)	95.5
Emergence of MDR pathogens between day 2 and day 28 [h]	192 (12.8%)	111 (11.9%)	18 (7.5%)	63 (19.6%)	0.06	0.63 (0.39–1.01)	0.001	1.63 (1.23–2.16)	98.7
28-day mortality	296 (19.8%)	181 (19.4%)	38 (15.8%)	77 (24%)	0.27	0.83 (0.60–1.14)	0.07	1.26 (0.99–1.59)	97.8
ICU mortality	243 (16.3%)	145 (15.5%)	28 (11.7%)	70 (21.8%)	0.18	0.76 (0.52–1.11)	0.009	1.42 (1.10–1.84)	97.8

Safety and clinical outcomes of carbapenem de-escalation as part of an antimicrobial stewardship programme in an ESBL-endemic setting

Kaung Yuan Lew[1], Tat Ming Ng[2], Michelle Tan[2], Sock Hoon Tan[2], Ee Ling Lew[2], Li Min Ling[3], Brenda Ang[3], David Lye[3,4] and Christine B. Teng[1,2]*

J Antimicrob Chemother 2015; **70**: 1219–1225

Table 2. Primary and secondary outcomes

Outcomes	De-escalated ($n=204$)	Not de-escalated ($n=96$)	*P*	Absolute risk difference (95% CI)
Clinical success, *n* (%)	183 (89.7)	85 (88.5)	0.84	1.2 (−5.8 to 9.8)
Survival at discharge, *n* (%)	173 (84.8)	79 (82.3)	0.58	2.5 (−5.9 to 12.3)
Duration of carbapenem use (days), median (IQR)	6 (4–8)	8 (7–11)	<0.001	−2 (−3 to −2)
Incidence of MDR organisms at 30 days, *n* (%)				
carbapenem-resistant *A. baumannii*	4 (2.0)	7 (7.3)	0.042	−5.3 (−12.4 to −0.6)
other carbapenem-resistant Gram-negative bacteria[b]	6 (2.9)	1 (1.0)	0.44	1.9 (−3.0 to 5.3)
CDAD	2 (1.0)	4 (4.2)	0.081	−3.2 (−9.3 to 0.4)
Candida sp. in sterile sites	1 (0.5)	0	>0.99	0.5 (−3.4 to 2.7)

Conclusions: ASP-guided de-escalation of carbapenems led to comparable clinical success, fewer adverse effects and a lower incidence of the development of resistance.

Duration of Exposure to Antipseudomonal β-Lactam Antibiotics in the Critically Ill and Development of New Resistance

(Pharmacotherapy 2019;39(3):261–268)

Besu F. Teshome,[1,2] Scott Martin Vouri,[3,4] Nicholas Hampton,[5] Marin H. Kollef,[6] and Scott T. Micek[1,7,*]

Development of new resistance per day of exposure to anti-pseudomonal β-lactam

	Adjusted hazard ratio (95% confidence interval)			
	Any antipseudomonal β-lactam	Cefepime	Meropenem	Piperacillin-tazobactam
Each additional day of exposure	1.04 (1.04–1.05)[a]	1.08 (1.07–1.09)[b]	1.02 (1.01–1.03)[c]	1.08 (1.06–1.09)[d]
Sensitivity analyses (each additional day of exposure)[e]				
Among patients with multiple follow-up cultures[f]	1.01 (1.01–1.02)[g]	1.07 (1.06–1.08)[h]	1.00 (0.99–1.01)[i]	1.05 (1.04–1.06)[i]
Among patients with ≥ 1 negative culture for antipseudomonal β-lactam resistance 60 days prior to cohort entry	1.01 (1.00–1.02)	1.22 (1.14–1.31)	1.02 (1.01–1.04)	1.10 (1.08–1.12)

Top emergening MDRB

Meropenem group (103/3625): *Pseudomonas aeruginosa* (65.0%)

PTZ group (108/2463): *Enterobacter spp* (42.7%) / Cefepime group (61/5274): *Escherichia coli* (23.0%)

Evaluation of a ceiling effect on the association of new resistance development to antipseudomonal beta-lactam exposure in the critically ill

Besu F. Teshome PharmD[1,2], Scott Martin Vouri PharmD, PhD[3,4], Nicholas B. Hampton PharmD[5], Marin H. Kollef MD[6] and Scott T. Micek PharmD[1,7]

Infection Control & Hospital Epidemiology (2020), **41**, 484–491

Table 1. Cumulative Days of Antipseudomonal β-Lactam Antibiotic Exposure and New Resistance Development

Cumulative Days of Antipseudomonal Exposure	No. of Patients	New Resistance Events, No. (%)	Hazard Ratio (95% Confidence Interval)
1–3	1,816	38 (2.09)	1.00 (reference)
4–6	1,632	85 (5.21)	1.01 (0.93–1.10)
7–9	1,249	98 (7.85)	1.85 (1.69–2.02)
10–12	709	66 (9.31)	2.93 (2.66–3.24)
13–15	474	44 (9.28)	3.94 (3.54–4.39)
16–18	326	30 (9.20)	6.29 (5.62–7.04)
19–21	234	27 (11.5)	7.05 (6.19–8.02)
≥22	678	56 (8.3)	8.52 (7.62–9.53)

Antimicrobial de-escalation in critically ill patients

A position statement from a task force of the European Society of Intensive Care Medicine (ESICM) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Critically Ill Patients Study Group (ESGCIP)

Q3: In critically ill patients receiving antimicrobials for an infection, what are the effects of antimicrobial de-escalation compared to no de-escalation on mortality and length of stay?

The ADE strategy is likely safe with regard to patients' outcomes. (Statement of fact; moderate quality of evidence.)

Q4: In critically ill patients receiving antimicrobials for an infection, what are the effects of antimicrobial de-escalation compared to no de-escalation on the total duration of antimicrobial therapy?

ADE is associated with a risk of increase in total duration of antimicrobial therapy. We recommend that ADE and duration of antimicrobial therapy are assessed separately but as part of the global stewardship strategy. (Statement of fact; low quality of evidence.)

Q5: In critically ill patients receiving antimicrobials for an infection, what are the effects of antimicrobial de-escalation compared to no de-escalation on the development of resistance to antimicrobials?

No recommendation can be made

Intensive Care Med (2020) 46:245–265

Antimicrobial de-escalation in critically ill patients

A position statement from a task force of the European Society of Intensive Care Medicine (ESICM) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Critically Ill Patients Study Group (ESGCIP)

Q6: In critically ill patients receiving antimicrobials for an infection, when is it recommended to perform de-escalation of the empirical antimicrobial regimen?

We recommend ADE is performed within 24 h of definitive culture results and antibiograms availability. (Strong recommendation; low quality of evidence.)

Q7: In critically ill patients receiving antimicrobials for an infection, are recommendations for or against antimicrobial de-escalation different for certain bacterial pathogens? For which?

Recommendations for or against ADE are similar for all bacterial pathogens except for difficult-to-treat pathogens in patients with a high risk of death. (Moderate recommendation, low quality of evidence.)

Intensive Care Med (2020) 46:245–265

Antibiothérapie définitive des IU communautaires graves (pyélonéphrite aiguë, prostatite aiguë)

Guidelines SPILF 2015

Durée de traitement :

Pyélonéphrite aiguë grave : 10 à 14 jours – y compris si EBLSE
(durée >21 jours si abcès rénal)

Prostatite aiguë : 14 jours si évolution favorable sous FQ ou cotrimoxazole
(21 jours si autres antibiotiques, immunodépression, uropathie sous-jacente)

Pas d'ECBU de contrôle systématique (sauf grossesse) si évolution favorable

Procalcitonin-Guided Antibiotic Discontinuation and Mortality in Critically Ill Adults

A Systematic Review and Meta-analysis

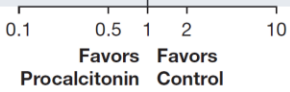
Dominique J. Pepper, MD; Junfeng Sun, PhD; Chanu Rhee, MD; Judith Welsh, MLS; John H. Powers III, MD; Robert L. Danner, MD; and Sameer S. Kadri, MD

CHEST 2019; 155(6):1109-1118

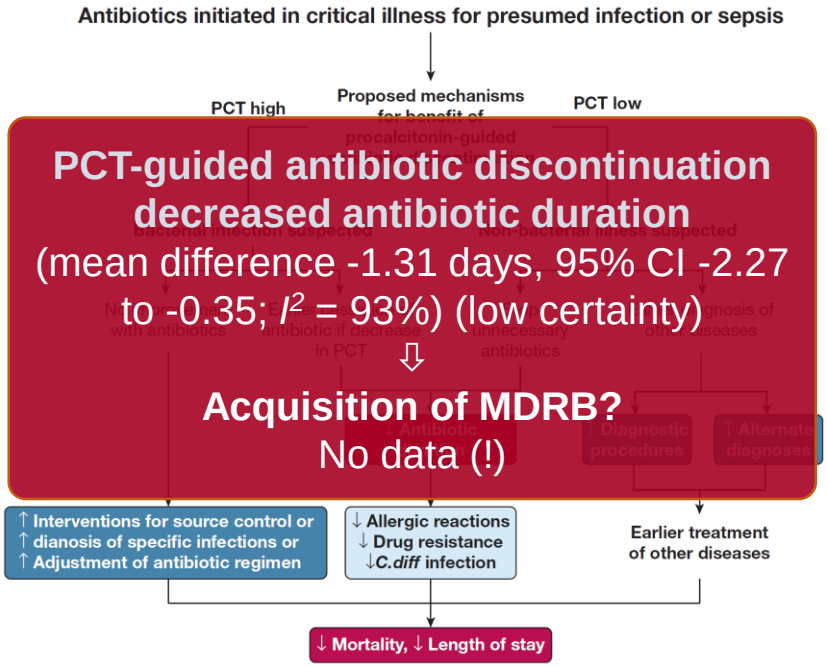
PROSPERO N° CRD42016049715

Study	Procalcitonin Events	Procalcitonin Total	Control Events	Control Total	RR	95%-CI	Weight
Nobre	9	39	9	40	1.03	(0.46-2.31)	1.7%
Hochreiter	15	57	14	53	1.00	(0.53-1.86)	2.9%
Schroeder	3	14	3	13	0.93	(0.23-3.81)	0.6%
Stolz	10	51	14	50	0.70	(0.34-1.43)	2.2%
Bouadma	65	307	64	314	1.04	(0.76-1.41)	12.0%
Maravic	3	99	3	100	1.01	(0.21-4.88)	0.5%
Qu	7	35	8	36	0.90	(0.37-2.22)	1.4%
Annane	7	31	10	30	0.68	(0.30-1.55)	1.7%
Deliberato	2	42	4	39	0.46	(0.09-2.39)	0.4%
Liu	6	42	5	40	1.14	(0.38-3.45)	0.9%
Oliveira	21	49	21	45	0.92	(0.59-1.44)	5.6%
Shehabi	30	196	26	198	1.17	(0.72-1.90)	4.8%
Bloos	140	547	149	529	0.91	(0.75-1.11)	29.0%
deJong	149	761	196	785	0.78	(0.65-0.95)	31.9%
Xu	10	79	9	77	1.08	(0.47-2.52)	1.6%
Daubin	19	151	17	151	1.12	(0.60-2.07)	3.0%
Random effects model		**2,500**		**2,500**	**0.89**	**(0.83-0.97)**	**100.0%**

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $P = .97$



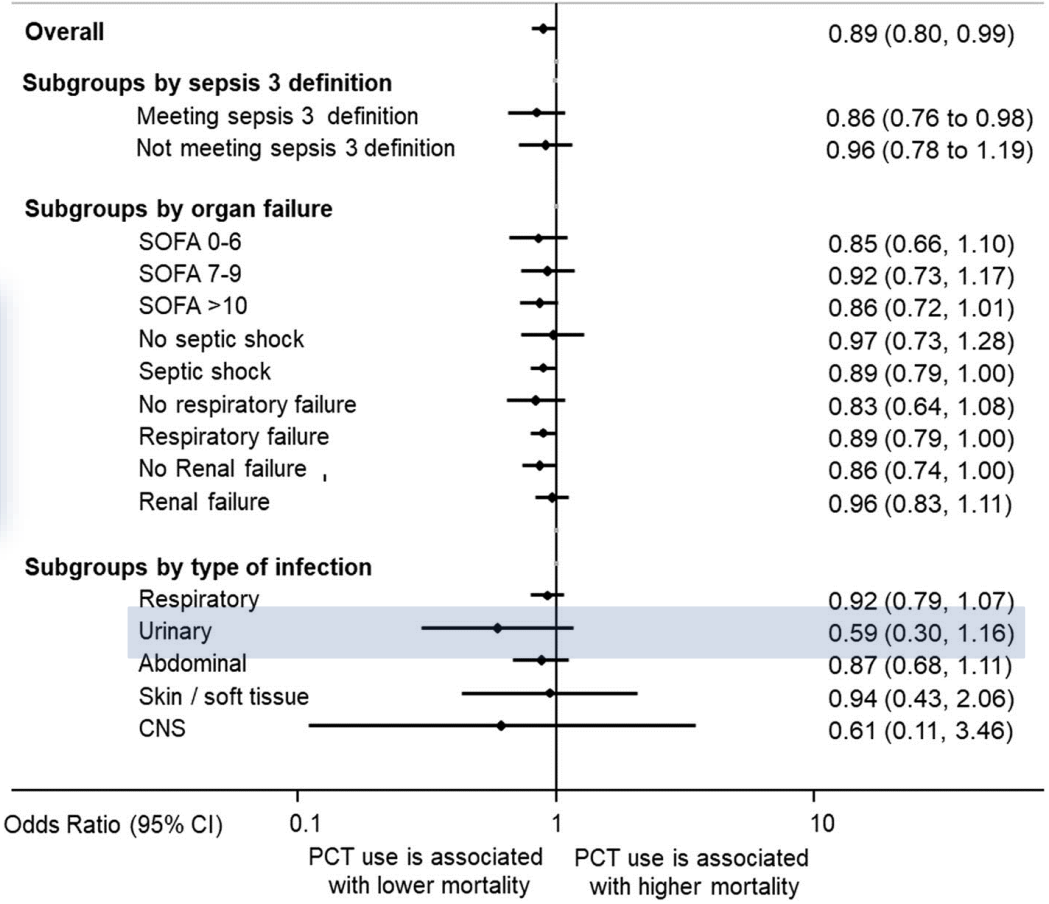
$P = .007$



CRITICAL CARE

Effect of procalcitonin-guided antibiotic treatment on clinical outcomes in intensive care unit patients with infection and sepsis patients: a patient-level meta-analysis of randomized trials

Wirz *et al. Critical Care* (2018) 22:191



Désescalade de l'antibiothérapie en réanimation

Points essentiels

1. **Aspect essentiel du bon usage des antibiotiques** – objectif : réduction du risque d'effets indésirables écologiques / non-écologiques de l'antibiothérapie
2. **Documenter (prélever) pour réévaluer** – données nécessaires sur TDR +++
3. **Raisonner sur impact écologique global** (microbiotes commensaux) et pas uniquement sur spectre « clinique » - mais données parcellaires
4. **Optimiser la pharmacocinétique** de l'antibiotique utilisé en relais (diffusion, schéma d'administration)
5. **L'arrêt d'une antibiothérapie** (ex : aminoside si bithérapie probabiliste, durée de traitement la plus courte possible) est une modalité de désescalade