Journée OutcomeRéa

Paris - Jeudi 17 mai 2018

Prédiction des infections à BGN multi-résistants et choix de l'antibiothérapie probabiliste chez les patients de réanimation

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Hôpital de la Source – Centre Hospitalier Régional d'Orléans
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COI potentiels : MSD, Pfizer

Taux de résistance aux antibiotiques chez les BGN responsables d'IN en réanimation, France, 2016

Réseau de surveillance Réa-RAISIN

www.invs.sante.fr

Enterobacteriaceae

C3G : 28,4% (BLSE : 16,8% / AmpC : 11,6%)

Carbapénèmes : 1,8%

Pseudomonas aeruginosa

Ceftazidime : 19,4%

Imipénème/méropénème : 23,3%

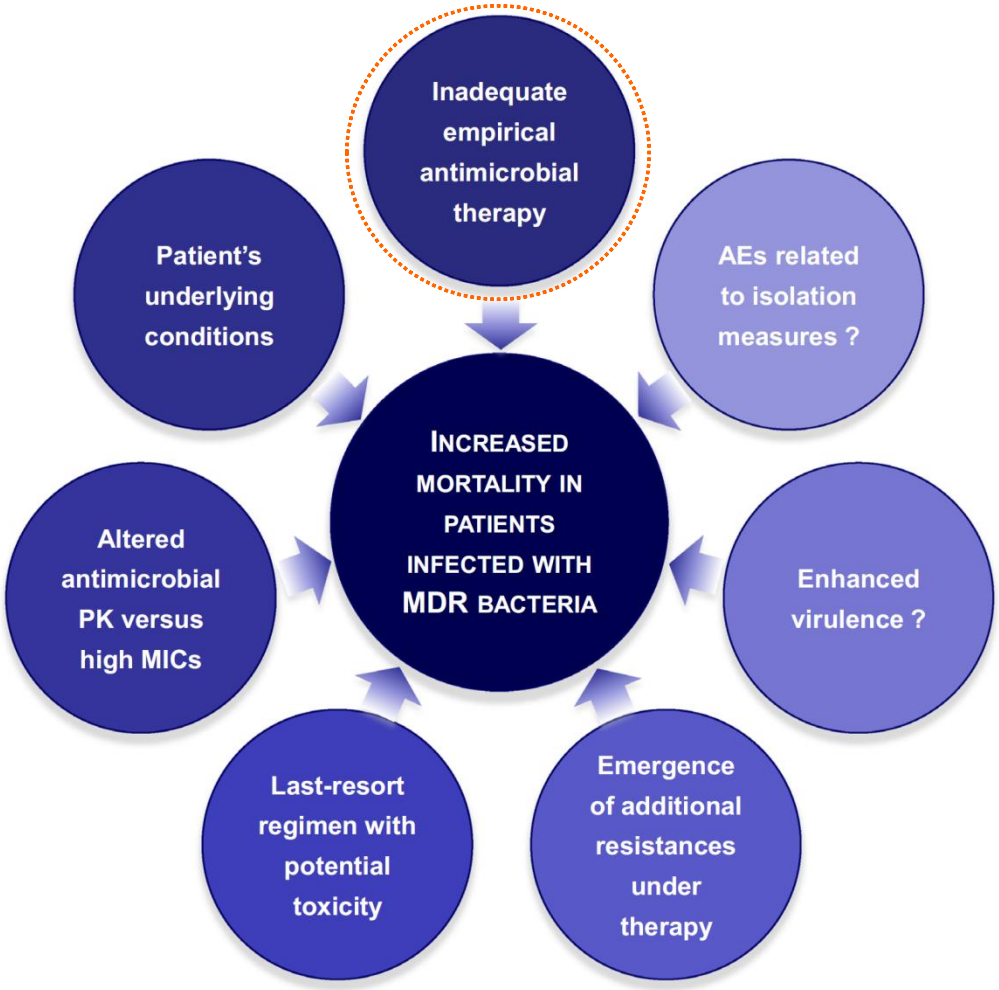
Acinetobacter baumannii

Ceftazidime : 44,3%

Imipénème/méropénème : 29,3%

Understanding why resistant bacteria are associated with higher mortality in ICU patients

François Barbier, Thiago Lisboa, Saad Nseir. *Intensive Care Med* 2016; 42: 2066-2069



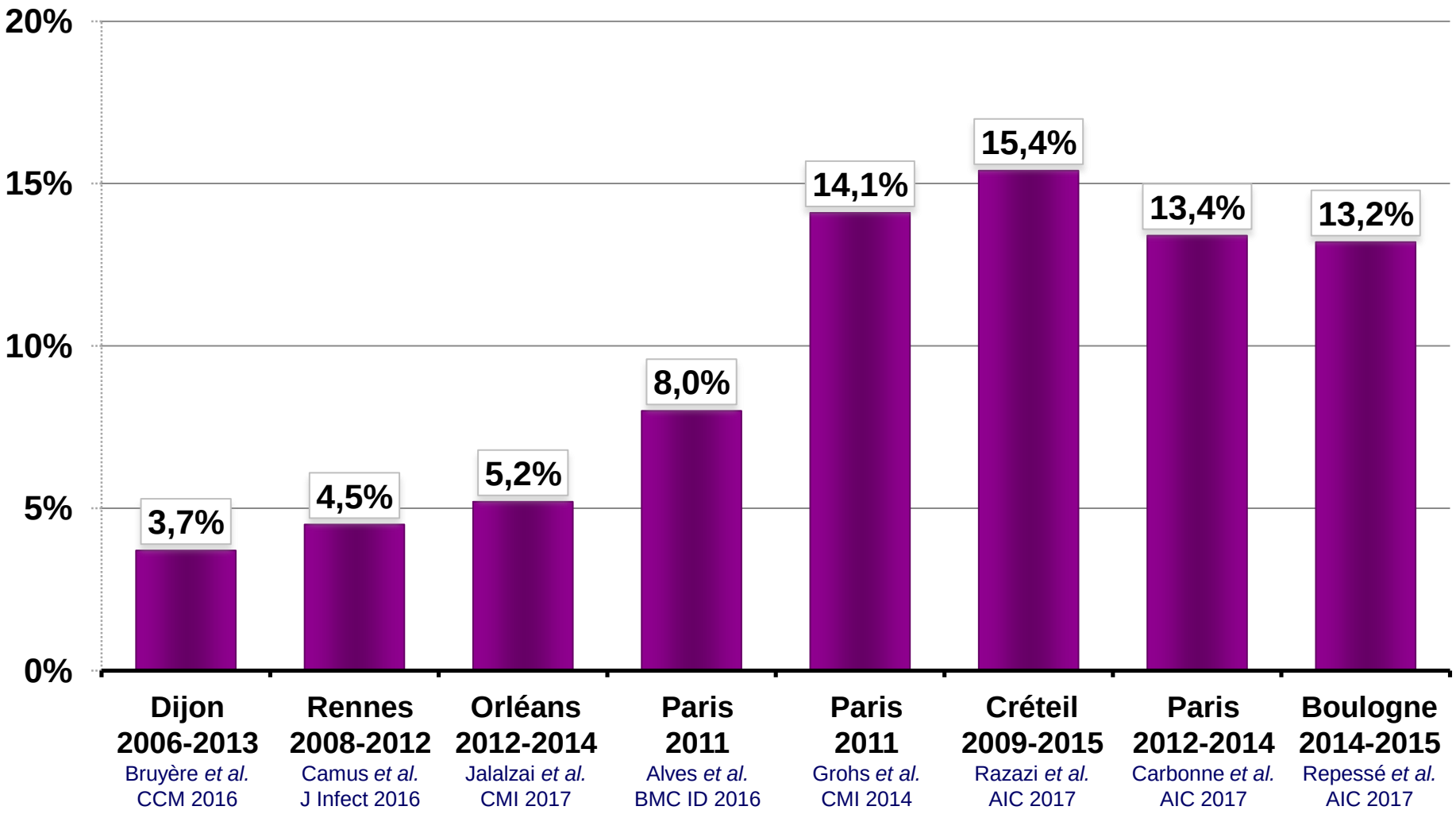
Comment optimiser l'antibiothérapie probabiliste chez les patients de réanimation à risque de BGN-MR ?

1. Dépistage systématique de la colonisation à BGN-MR
2. Épidémiologie locale et épisodes épidémiques
3. Nouveaux outils prédictifs et diagnostiques
4. Nouveaux antibiotiques

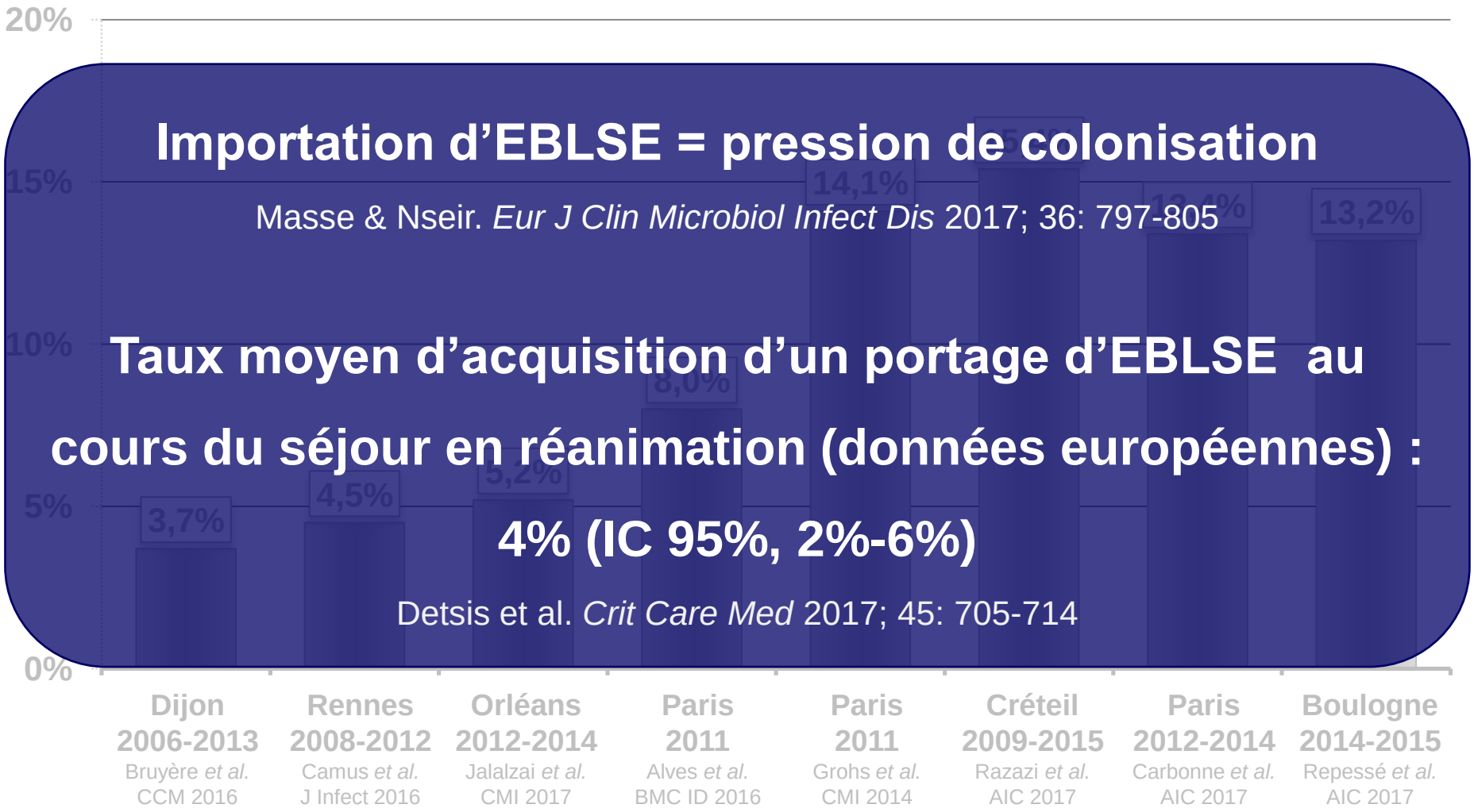
Comment optimiser l'antibiothérapie probabiliste chez les patients de réanimation à risque de BGN-MR ?

1. **Dépistage systématique de la colonisation à BGN-MR**
2. Épidémiologie locale et épisodes épidémiques
3. Nouveaux outils prédictifs et diagnostiques
4. Nouveaux antibiotiques

Portage d'EBLSE à l'admission en réanimation, France



Portage d'EBLSE à l'admission en réanimation, France



Importation d'EBLSE = pression de colonisation

Masse & Nseir. *Eur J Clin Microbiol Infect Dis* 2017; 36: 797-805

Taux moyen d'acquisition d'un portage d'EBLSE au cours du séjour en réanimation (données européennes) : 4% (IC 95%, 2%-6%)

Detsis et al. *Crit Care Med* 2017; 45: 705-714

ICU Acquisition Rate, Risk Factors, and Clinical Significance of Digestive Tract Colonization With Extended-Spectrum Beta-Lactamase–Producing Enterobacteriaceae: A Systematic Review and Meta-Analysis*

Marios Detsis, MD, MPH; Styliani Karanika, MD; Eleftherios Mylonakis, MD, PhD

(*Crit Care Med* 2017; 45:705–714)

Prior colonization as Risk Factor for Infection

Study ID	RR (95% CI)	Events, colonized	Events, noncolonized	% Weight
Martins (2006)	50.22 (5.92, 426.04)	4/18	1/226	17.25
Overall	49.62 (20.42, 120.58)	29/173	5/1199	100.00

NOTE: Weights are from random effects analysis

1 49.6

tau-square<0.001

Microbiote intestinal = principal réservoir de souches invasives d'EBLSE

⇩

Portage intestinal = facteur de risque d'infection à EBLSE

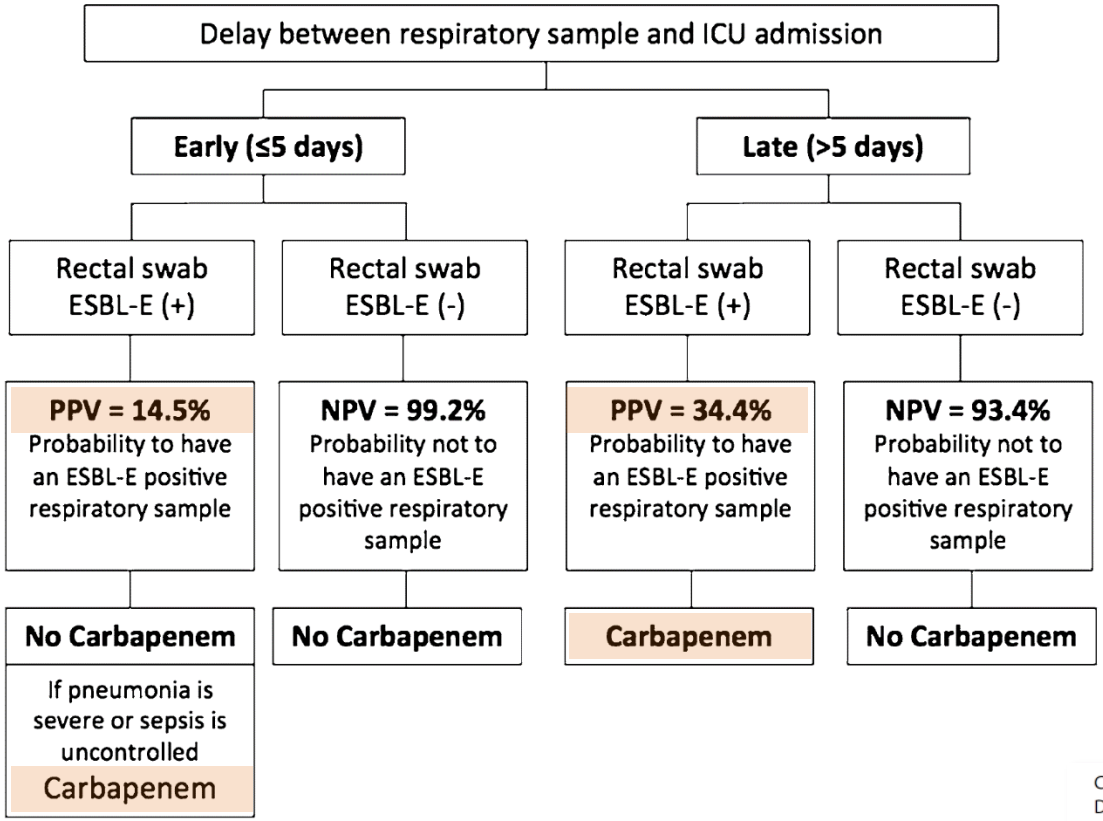
Infections à EBLSE acquises en réanimation : quelle fréquence chez les patients avec portage documenté?

Données récentes, France

Population	Patients colonisés, n	Infection si portage, %	Référence
Multicentrique (OutcomeRéa)	594 (4%, n = 16734)	**16%**	Barbier et al. *JAC* 2016
Monocentrique	161 (3%, n = 5059)	**23%**	Vodovar et al. *Infection* 2014
Monocentrique	95 (25%, n = 383)	**10%**	Razazi et al. *ICM* 2012
Monocentrique	28 (5%, n = 524)	**14%**	Jalalzaï et al. *CMI* 2017
Monocentrique	40 (7%, n = 587 avec VAP)	**42% des VAP**	Bruyère et al. *CCM* 2016

Relation between presence of extended-spectrum β-lactamase-producing *Enterobacteriaceae* in systematic rectal swabs and respiratory tract specimens in ICU patients

Hélène Carbonne[1,4*†], Matthieu Le Dorze[1*†], Anne-Sophie Bourrel[2], Hélène Poupet[2], Claire Poyart[2], Emmanuelle Cambau[3], Jean-Paul Mira[4], Julien Charpentier[4] and Rishma Amarsy[3,5]



Carbonne *et al. Ann. Intensive Care (2017) 7:13*
DOI 10.1186/s13613-017-0237-x

J Antimicrob Chemother 2016; **71**: 1088–1097
doi:10.1093/jac/dkv423 Advance Access publication 10 January 2016

Journal of Antimicrobial Chemotherapy

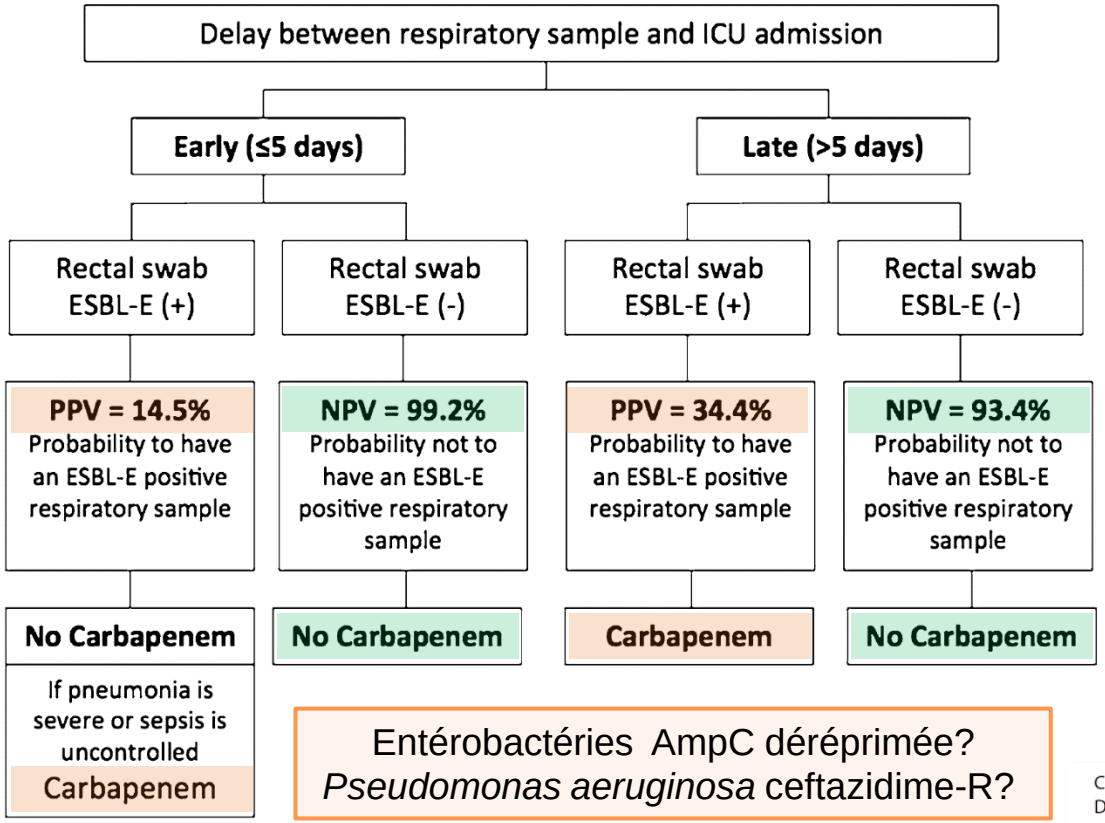
Colonization and infection with extended-spectrum β-lactamase-producing Enterobacteriaceae in ICU patients: what impact on outcomes and carbapenem exposure?

François Barbier[1], Cécile Pommier[2], Wafa Essaied[2], Maïté Garrouste-Orgeas[3], Carole Schwebel[4], Stéphane Ruckly[5], Anne-Sylvie Dumenil[6], Virginie Lemiale[7], Bruno Mourvillier[8], Christophe Clec'h[9], Michaël Darmon[10], Virginie Laurent[11], Guillaume Marcotte[12], Jean-Christophe Lucet[2,13], Bertrand Souweine[14], Jean-Ralph Zahar[15] and Jean-François Timsit[2,8]* on behalf of the OUTCOMEREA Study Group†

Classe d'antibiotiques	Nb de jours de traitement pour 1000 jours-patient			
	Pas de colonisation	Colonisation sans infection	Infection	*p*
BL-IBL	220	103	123	<0,0001
Fluoroquinolones	114	87	108	0,89
Carbapénèmes	69	241	627	<0,0001

Relation between presence of extended-spectrum β-lactamase-producing *Enterobacteriaceae* in systematic rectal swabs and respiratory tract specimens in ICU patients

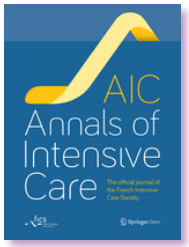
Hélène Carbonne[1,4*†], Matthieu Le Dorze[1*†], Anne-Sophie Bourrel[2], Hélène Poupet[2], Claire Poyart[2], Emmanuelle Cambau[3], Jean-Paul Mira[4], Julien Charpentier[4] and Rishma Amarsy[3,5]



Entérobactéries AmpC déréprimée?
Pseudomonas aeruginosa ceftazidime-R?

Carbonne *et al. Ann. Intensive Care* (2017) 7:13
DOI 10.1186/s13613-017-0237-x

Frequency, associated factors and outcome of multi-drug-resistant intensive care unit-acquired pneumonia among patients colonized with extended-spectrum β-lactamase-producing Enterobacteriaceae



Razazi *et al. Ann. Intensive Care (2017) 7:61*

Single ICU, 2009-2015

6303 admitted patients

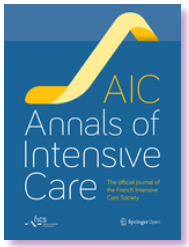
843 ESBLE carriers (13%)

111 ESBLE carriers with ICU-acquired pneumonia (VAP / non-VAP) (13%)

48 ESBLE carriers with ESBLE pneumonia (43%)

63 ESBLE carriers with non-ESBLE pneumonia (57%)

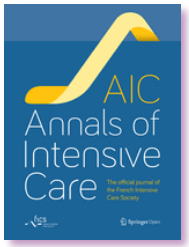
Frequency, associated factors and outcome of multi-drug-resistant intensive care unit-acquired pneumonia among patients colonized with extended-spectrum β-lactamase-producing Enterobacteriaceae



Razazi *et al. Ann. Intensive Care (2017) 7:61*

Microorganisms responsible for ICU-acquired pneumonia in ESBLE carriers (n = 111)	**ESBL - (n=63)**	**ESBL + (n=48)**
Enterobacteriaceae alone	17 (27%)	31 (65%)
ESBL *Enterobacter* spp and/or *Klebsiella pneumoniae*	-	25 (52%)
ESBL *Escherichia coli*	-	4 (8%)
Non-fermenting GNB and Enterobacteriaceae	6 (10%)	17 (35%)
Polymicrobial with ESBL *Enterobacter* or *K. pneumoniae* and NF-GNB	**0 (0%)**	**17 (35%)**
Polymicrobial with ESBL *E. coli* and NF-GNB	0 (0%)	0 (0%)
NF-GNB alone	**37 (59%)**	**0 (0%)**
Carbapenem-resistant NF-GNB	**17 (27%)**	**6 (12%)**
Gram-positive bacteria	3 (5%)	0 (0%)

Frequency, associated factors and outcome of multi-drug-resistant intensive care unit-acquired pneumonia among patients colonized with extended-spectrum β-lactamase-producing Enterobacteriaceae



Razazi *et al. Ann. Intensive Care (2017) 7:61*

Facteurs de risque de pneumonie nosocomiale à EBLSE chez les patients colonisés :

Colonisation à *Enterobacter* spp ou *Klebsiella pneumoniae* BLSE [OR 10,96 (2,93-41,0)]

SAPS II à l'admission en réanimation > 43 points : [OR 2,81 (1,16–6,79)]

Traitement par amoxicilline-clavulanate > 2 jours en réanimation : [OR 0.24 (0,08–0,71)]

Developing a New, National Approach to Surveillance for Ventilator-Associated Events: Executive Summary

Shelley S. Magill,[1] Michael Klompas,[2,3,4] Robert Balk,[5,6] Suzanne M. Burns,[6,7] Clifford S. Deutschman,[6,8] Daniel Diekema,[9,10] Scott Fridkin,[1] Linda Greene,[11,12] Alice Guh,[1] David Gutterman,[6,13] Beth Hammer,[6,14] David Henderson,[15] Dean Hess,[16,17,18] Nicholas S. Hill,[6,19] Teresa Horan,[1] Marin Kollef,[6,20] Mitchell Levy,[6,21] Edward Septimus,[22,23] Carole VanAntwerpen,[24,25] Don Wright,[26] and Pamela Lipsett[6,27]

Clinical Infectious Diseases 2013;57(12):1742–6

Ventilator-associated condition (VAC)

Increase in the level of PEEP ≥ 3 cmH_2O AND/OR increase in FiO_2 ≥ 20%
after a period of stability or improvement of oxygenation ≥ 2 calendar days

Infection-related ventilator-associated complication (iVAC)

VAC PLUS fever/hypothermia OR WBC ≥ 12000/mm3 or ≤ 4000/mm3
AND start of a new antimicrobial for ≥ 4 days

Possible VAP

Purulent respiratory secretions
OR positive culture of a respiratory sample (sputum, ETA, PDS, BAL)

Chest X-ray not considered

Probable VAP

Purulent respiratory secretions AND positive culture of a respiratory sample (sputum, ETA, PDS, BAL) above the significance thresholds

Chest X-ray not considered

ORIGINAL

Infection-related ventilator-associated complications in ICU patients colonised with extended-spectrum β-lactamase-producing Enterobacteriaceae

François Barbier[1], Sébastien Bailly[2], Carole Schwebel[3], Laurent Papazian[4], Élie Azoulay[5], Hatem Kallel[6], Shidasp Siami[7], Laurent Argaud[8], Guillaume Marcotte[9], Benoît Misset[10], Jean Reignier[11], Michaël Darmon[5], Jean-Ralph Zahar[12], Dany Goldgran-Toledano[13], Étienne de Montmollin[14], Bertrand Souweine[15], Bruno Mourvillier[16] and Jean-François Timsit[2,16*] for the OUTCOMEREA Study Group

***Intensive Care Medicine* 2018 (e-pub)**

318 ESBLE carriers / MV >2 days
576 episodes of IVAC

A carbapenem exposure within the preceding 3 days was the sole independent predictor of ESBLE infection as the causative event of IVAC, with a protective effect (aOR 0.2, 95% CI 0.05-0.6, *P* < 0.01).

No predicting role for :

Episode rank

Recent exposure to non-carbapenem antimicrobials (including BL-BLI, 3GC and fluoroquinolones)

Colonization with ESBL-producing *E. coli* versus other ESBLE

Imported versus ICU-acquired carriage

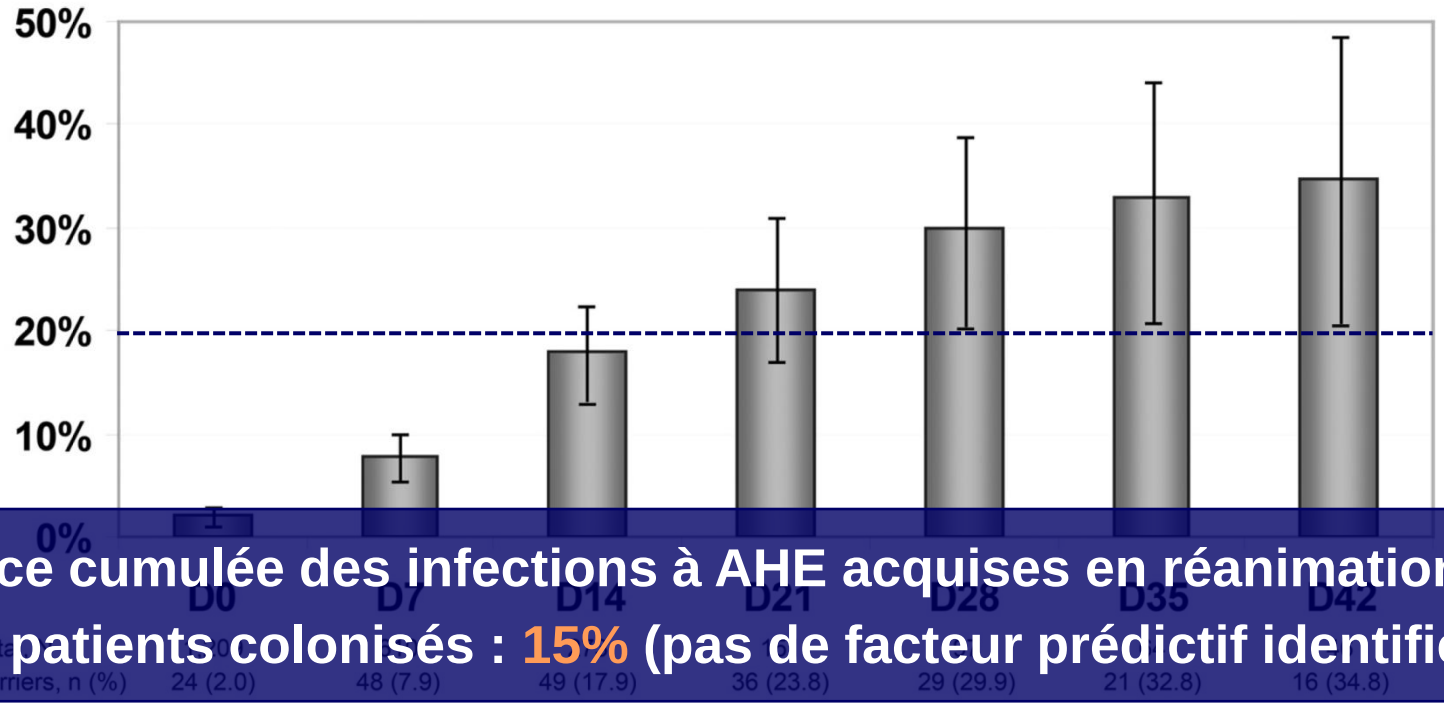
AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy

Risk Factors and Outcomes for Intestinal Carriage of AmpC-Hyperproducing *Enterobacteriaceae* in Intensive Care Unit Patients

Simon Poignant,[a] Jérôme Guinard,[b] Aurélie Guigon,[b] Laurent Bret,[b] Didier-Marc Poisson,[b] Thierry Boulain,[a] François Barbier[a]

Medical Intensive Care Unit[a] and Department of Microbiology,[b] La Source Hospital, CHR Orléans, Orléans, France

FIG 1 Observed rates of intestinal carriage of high-level AmpC cephalosporinase-producing *Enterobacteriaceae* isolates in critically ill patients according to their length of stay in the intensive care unit (days). *P* value for trend was <0.0001 (chi-square test). Bars indicate 95% confidence intervals.



Incidence cumulée des infections à AHE acquises en réanimation chez les patients colonisés : 15% (pas de facteur prédictif identifié)

Risk factors for colonization and infection by *Pseudomonas aeruginosa* in patients hospitalized in intensive care units in France

S. Hoang[1,2,3¤], A. Georget[3], J. Asselineau[3], A-G. Venier[1,4,5], C. Leroyer[1,4], A. M. Rogues[1,4], R. Thiébaut[1,3]*

PLOS ONE | https://doi.org/10.1371/journal.pone.0193300 March 9, 2018

Étude prospective, 10 réanimations, France, 2009

↓

1314 patients non porteurs de *P. aeruginosa* à l'admission

Dépistage hebdomadaire : rectal, trachéal, oropharyngé

↓

201 patients (15,3%) avec acquisition d'un portage en réanimation

16,9 acquisitions pour 1000 jours-patient (IC 95%, 14,6-19,2)

↓

87 porteurs (43,3%) avec infection à *P. aeruginosa* en réanimation

6,9 infections pour 1000 jours-porteur (IC 95%, 5,5-8,3)

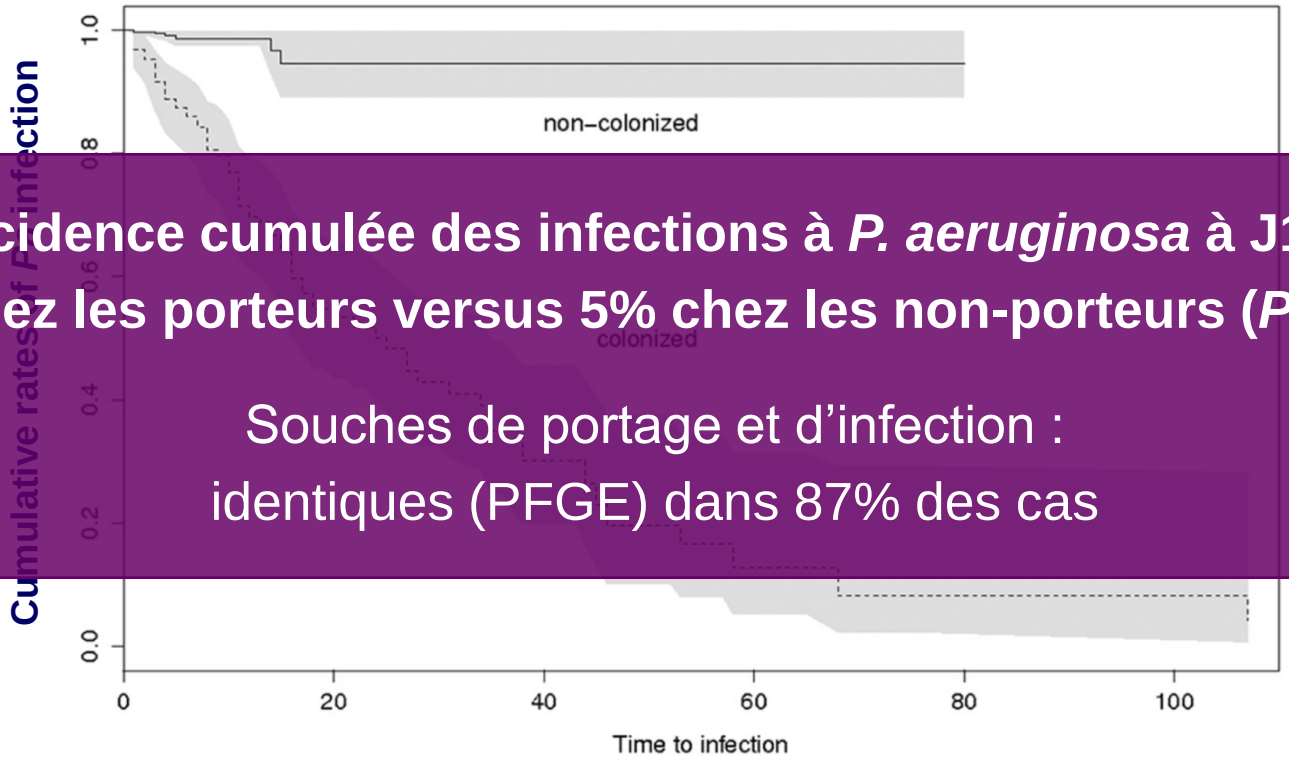
Prospective Observational Study of Prior Rectal Colonization Status as a Predictor for Subsequent Development of *Pseudomonas aeruginosa* Clinical Infections

Silvia Gómez-Zorrilla,[a] Mariana Camoez,[b] Fe Tubau,[b] Rosario Cañizares,[c] Elisabet Periche,[c] M. Angeles Dominguez,[b] Javier Ariza,[a] Carmen Peña[a]

AAC Journals.ASM.org

Étude prospective mono-centrique (Barcelone, 2012-2013), 414 patients

Portage digestif de *P. aeruginosa* au cours du séjour : 43% (importé, 63%)



Incidence cumulée des infections à *P. aeruginosa* à J14 :
26% chez les porteurs versus 5% chez les non-porteurs (*P* <0.001)

Souches de portage et d'infection :
identiques (PFGE) dans 87% des cas

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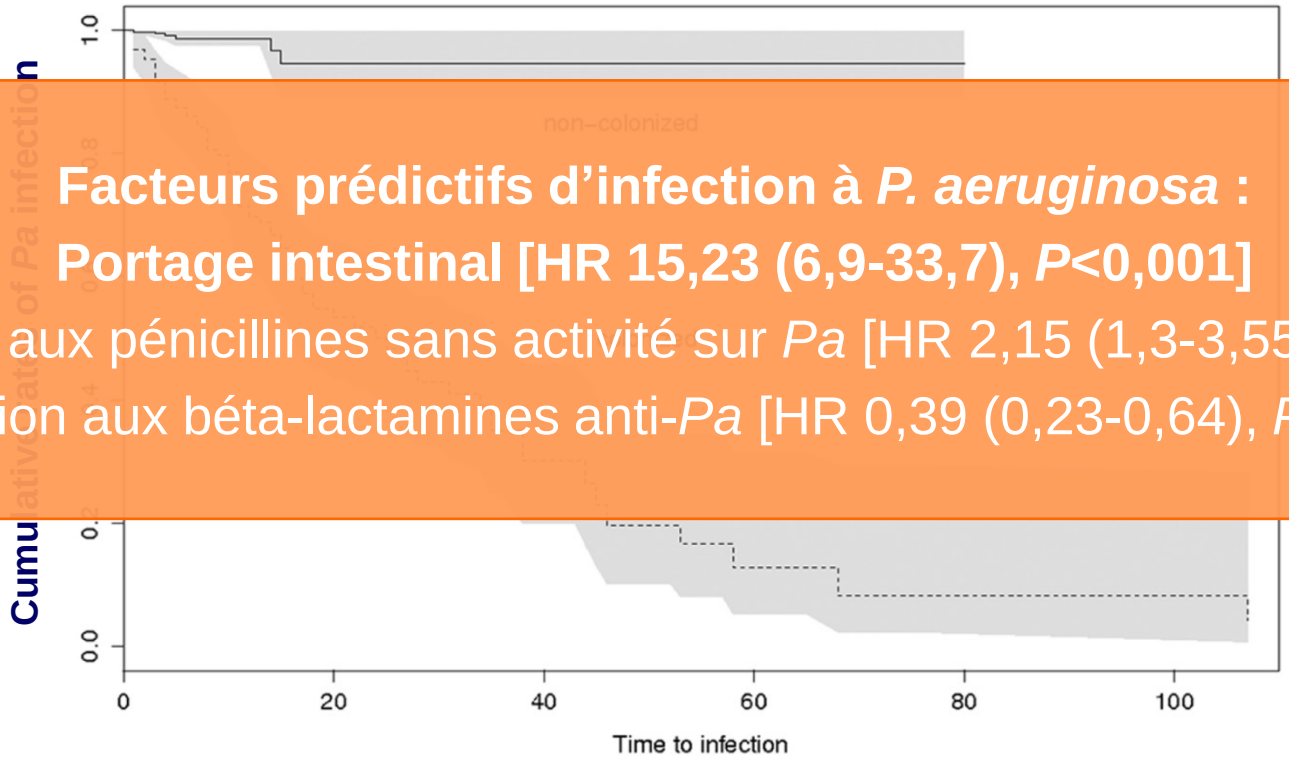
AAC Journals.ASM.org

Single-ICU prospective study (Barcelona, 2012-2013), 414 patients

Overall rate of *P. aeruginosa* carriage : 43% (imported carriage, 63%)



Facteurs prédictifs d'infection à *P. aeruginosa* :

Portage intestinal [HR 15,23 (6,9-33,7), *P*<0,001]

Exposition aux pénicillines sans activité sur *Pa* [HR 2,15 (1,3-3,55), *P*=0,003]

Exposition aux béta-lactamines anti-*Pa* [HR 0,39 (0,23-0,64), *P*<0,001]

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

Merceron S., Ibn Saied W., Schwebel C., Le Monnier A., Garrouste-Orgeas M., Marcotte G., Ruckly S., Souweine B., Darmon M., De Montmollin E., Mourvillier B., Reignier J., Papazian L., Siami S., Azoulay É., Bédos J.-P., Timsit J.-F., OutcomeRea Study Group

réanimation 2018
PARIS 24-26 JANVIER

Annals of Intensive Care 2018, **8 (Suppl 1):** F-37

	VAP-other N= 380 *(control)*	VAP-SM N=93 *(case)*	Univariate analysis		Multivariate analysis	
			OR	p	OR	p
Patients characteristics baseline						
Age N (%)	66 [54.5 ; 75]	62 [53 ; 76]	0.99 [0.98 ; 1.01]	0.47		
Male N (%)	274 (72.1)	57 (61.3)	0.60 [0.37 ; 0.97]	0.04		
SAPS II Median [IQR]	52 [41 ; 66]	50 [40 ; 65]	1.02 [0.97 ; 1.08]	0.41		
Chronic heart failure N (%)	61 (16.1)	8 (8.6)	0.499 [0.22; 1.13]	0.09		
Immunosuppression N (%)	82 (21.6)	19 (20.4)	0.86 [0.47; 1.57]	0.63		
Haematological malignancy N (%)	34 (8.9)	10 (10.8)	1.13 [0.52 ; 2.42]	0.76		
Scores and procedures Two days before VAP						
Central catheter	265 (69.7)	70 (75.3)	1.68 [0.93 ; 3.01]	0.08		
Accidental extubation	29 (7.6)	13 (14)	2.36 [1.07 ; 5.2]	0.03		
SOFA Resp Day1-2 Median [IQR]	94(24.7]	37(39.8]	2.11 [1.29; 3.46]	<.0.01	1.93[1.15; 3.25]	<.0128
SOFA Coag Day1-2 Median [IQR]	19(5)	16(17.2)	4.47 [2.12; 9.43]	<. 0.01	3.31[1.52; 7.2]	<.0025
SOFA cardio Day1-2 Median [IQR]	96 (25.3)	31 (33.3)	1.59 [0.94; 2.72]	0.09		
Antibiotics use and procedures during the week before VAP						
Large spectrum antibiotics N (%)	141 (37.1)	54 (58.1)	2.51 [1.54 ; 4.09]	<.01		
Antifungal therapy N (%)	49 (12.9)	19 (20.4)	1.77 [0.94 ; 3.34]	0.08		
Ureido-carboxypenicillin N (%)	97 (25.5)	34 (36.6)	1.86 [1.12 ; 3.34]	0.02		
Ciprofloxacin N (%)	50 (13.2)	18 (19.4)	1.77 [0.92; 3.39]	0.09		
Tazobactam N (%)	83 (21.8)	29 (31.2)	1.75 [1.04; 2.94]	0.04		
Glycopeptides N (%)	56 (14.7)	21 (22.6)	1.66 [0.95; 2.89]	0.08		
Imipenem-Meropenem N (%)	52 (13.7)	31 (33.3)	3.16 [1.82 ; 5.49]	<.01	2.68 [1.51;4.75]	<.0007
Parenteral nutrition N (%)	111 (29.2)	35 (37.6)	1.67 [0.99 ; 2.82]	0.05		
Corticosteroid therapy N (%)	160 (42.1)	47 (50.5)	1.41 [0.88 ; 2.25]	0.15		
Dialysis/catecholamines N (%)	245 (64.5)	70 (75.3)	1.84 [1.04 ; 3.24]	0.04		
Duration of ICU stay before VAP Median [IQR]	11 [7 ; 18]	13 [7 ; 19]	1.18 [0.96 ; 1.44]	0.12		
Number of antibiotics per day before VAP	1.8 [1.1 ; 2.4]	2 [1.3 ; 3]	1.33 [1.07 ; 1.64]	<.01		

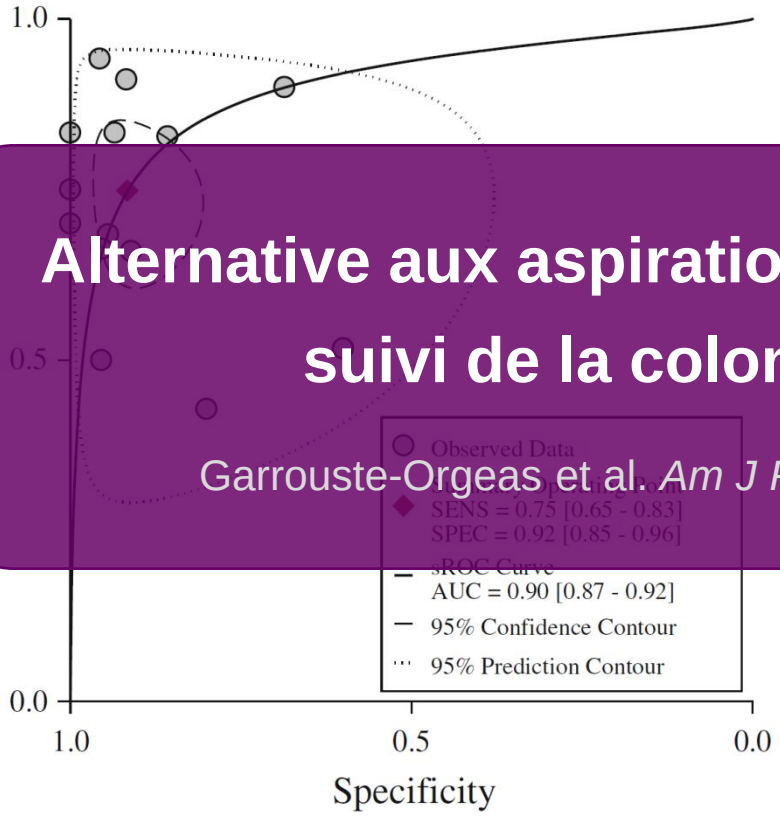
- **PAVM-*Sm* : 6% des PAVM**
- **Traitement empirique inadéquate :** 44% (PAVM-*Sm*) vs 30% (autres PAVM), *P* = 0,01
- **Principal facteur de risque de PAVM-*Sm* :** exposition aux carbapénèmes dans les 7 jours précédents

Intensive Care Med (2013) 39:365–375
DOI 10.1007/s00134-012-2759-x

REVIEW

Nele Brusselaers
Sonia Labeau
Dirk Vogelaers
Stijn Blot

Value of lower respiratory tract surveillance cultures to predict bacterial pathogens in ventilator-associated pneumonia: systematic review and diagnostic test accuracy meta-analysis



- 14 études, 791 PAVM chez 688 patients
- **Performance globale :**
  - ✓ Se 75% [65%-83%]
  - ✓ Sp 92% [85%-96%]
  - ✓ AUROC 0,90 [0,87-0,92]
- **AT ≥ 2/semaine versus 1/semaine :**
  - ✓ Se 78% [73%-83%] vs 61% [52%-69%]
  - ✓ Sp 96% [94%-98%] vs 87% [82%-93%]
- BGN-NF-MR : peu de données
- Hétérogénéité des études

Alternative aux aspirations trachéales de surveillance : suivi de la colonisation oropharyngée

Garrouste-Orgeas et al. *Am J Respir Crit Care Med* 1997; 156: 1647-55

Comment optimiser l'antibiothérapie probabiliste chez les patients de réanimation à risque de BGN-MR ?

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3. **Nouveaux outils prédictifs et diagnostiques**

4. **Nouveaux antibiotiques**

frontiers in
MICROBIOLOGY

REVIEW ARTICLE
published: 28 May 2013
doi: 10.3389/fmicb.2013.00129

Causes, consequences, and perspectives in the variations of intestinal density of colonization of multidrug-resistant enterobacteria

Etienne Ruppé* and Antoine Andremont

Laboratoire de Bactériologie, AP-HP, Hôpitaux Paris Nord Val de Seine, site Bichat-Claude Bernard, Paris, France

Relation entre risque d'infection à BMR et densité de colonisation intestinale (abondance relative)

- **Dans les IU communautaires à *E. coli* BLSE**

  Ruppé et al. *Antimicrob Agents Chemother* 2013; 57: 4512-7

- **Chez les patients avec hémopathie maligne**

  Woerther et al. *J Med Microbiol* 2015; 64: 676-681

- **Chez les patients avec allogreffe de MO**

  Taur et al. *Clin Infect Dis* 2012; 55: 905-914

ORIGINAL ARTICLE BACTERIOLOGY

Performance and impact of a rapid method combining mass spectrometry and direct antimicrobial susceptibility testing on treatment adequacy of patients with ventilator-associated pneumonia

M. Le Dorze[1], N. Gault[2,3,4], A. Foucrier[1], E. Ruppé[5,6], B. Mourvillier[1,6], P. L. Woerther[5], G. Birgand[6,7], P. Montravers[8], M. P. Dilly[9], F. Tubach[2,3,4], A. Andremont[5,6], J. F. Timsit[1,6], M. Wolff[1,6] and L. Armand-Lefèvre[5,6]

« **The sensitivity and negative predictive values of Direct AST were 100% for all antibiotics tested**, except gentamicin (97.1% and 97.4%) and amikacin (88.9% and 96.4%), compared with Conventional AST."

TABLE 3. Potential antibiotic changes after direct antimicrobial susceptibility testing (DAST) results

Initial antibiotic therapy	*n*	Change for inadequacy (*n*)	De-escalation (*n*)	No change (*n*)
Amoxicillin/clavulanate acid ± aminoglycoside	6	0	0	6
Piperacillin/tazobactam ± aminoglycoside	17	1	8	8
Third-generation cephalosporin ± aminoglycoside	9	2	1	6
Carbapanem ± aminoglycoside	32	5	14	13
Carbapenem + others[a]	11	1	3	7
Others[b]	9	0	0	9
No treatment	1	0	0	1
Total (%)	85 (100%)	9 (10.6%)	26 (30.6%)	50 (58.8%)

Adaptation plus précoce d'un ttt initial inefficace : 11 % des patients
Désescalade plus précoce (carbapénèmes +++) : 31% des patients

RCT en cours (NCT02897466)

Clin Microbiol Infect 2015; **21**: 468.e1–468.e6

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology

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]

Détection rapide (< 2h) des souches productrices de BLSE à partir des cultures H12-H24, sans attendre l'antibiogramme (tests biochimiques/chromogéniques)

TABLE 3 Diagnostic parameters of the different tests

Diagnostic test parameter	Performance (%) by test			
	Rapid ESBL 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

BLSE ?

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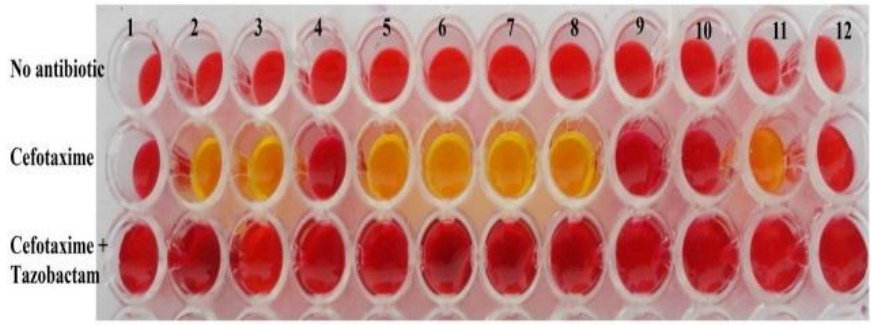

Figure 1. Representative results of the ESBL NDP test. Strains 1 and 2 are negative and positive controls, respectively; strains 3, 5,6,7,8 and 11 are ESBL producers; strains 4,9,10 and 12 are non-ESBL producers.

Ex : Rapid NDP test

β LACTA test performance for detection of extended-spectrum β-lactamase-producing Gram-negative bacilli directly on bronchial aspirates samples: a validation study☆

S. Gallah [1], Y. Benzerara [1], J. Tankovic [1], P.-L. Woerther [2], H. Bensekri [3], J.-L. Mainardi [3, 4], G. Arlet [1, 5, 6], S. Vimont [1, 5, 7], M. Garnier [5, 8, 9, *]

Clinical Microbiology and Infection 24 (2018) 402–408

Objectives: Incidence of extended-spectrum β-lactamase-producing Gram-negative bacilli (ESBL-PE-GNB)-related infections is worryingly increasing worldwide. ESBL-PE-GNB detection directly on bronchial aspirate samples (BAS) performed for suspected pneumonia may help save empirical carbapenems. Our objectives were to optimize β-LACTA™ test (BLT) realization and evaluate BLT performance for ESBL-

The β-LACTA test detected ESBL-PE-GNB directly on bronchial aspirates positive for GNB on MGSE and/or growing with 10^4 CFU/mL with 100% sensitivity, specificity, and positive and negative predictive values.

validation cohort, 21 (17%) gave positive BLT (ten in BAS positive and 11 in BAS negative on MGSE). All BLT-positive BAS grew with ESBL-PE-GNB, including five hyper-L2-producing *Stenotrophomonas maltophilia* strains. BLT detected ESBL-PE-GNB directly on clinical BAS positive for GNB on MGSE and/or growing with $\geq 10^4$ CFU/mL with 100% sensitivity, specificity, and positive and negative predictive values. *Conclusions:* BLT is an accurate tool for ESBL-PE-GNB detection directly on BAS. Further studies are needed to evaluate the impact of BLT-guided early antimicrobial de-escalation strategies. **S. Gallah, Clin Microbiol Infect 2018;24:402**

RCT en cours (NCT03147807)

Comercially available systems for the identification of pathogens from positive blood cultures

System (Manufacturer)	Methods	Time to result	Microorganism coverage	Resistance and virulence markers	Sensitivity Specificity Correlation with conventional methods (%)
PNA FISH and QuickFISH (AdvanDx, Woburn, MA, USA)	FISH	<1–3 hours	4 Gram positive 4 Gram negative 5 Fungi	0	97–100 90–100 96–99
AccuProbe (Gen-Probe, San Diego, CA, USA)	FISH	<1 hour	*Staphylococcus aureus* *Enterococcus* spp. *Streptococcus pneumoniae* *Streptococcus* group A *Streptococcus* group B	0	80.8–100 98.7–100 nr
Verigene (Nanosphere, Northbrook, IL, USA)	Microarray	2.5 hours	12 Gram positive 9 Gram negative	*mecA*, *van*A/B, KPC, NDM, CTX-M,VIM, IMP,OXA12	81–100 98–100 nr
Prove-it Sepsis (Mobidiag, Esbo, Finland)	Microarray	3.5 hours	60 bacteria 13 fungi	*mecA*	95% 99% nr
FilmArray (Idaho Technology, Salt Lake City, UT, USA)	Multiplex PCR	1 hour	8 Gram positive 11 Gram negative 5 Fungi	*mecA*, *van*A/B, KPC	97–95 91–98 nr
Xpert MRSA/SA BC (Cepheid, Sunnyvale, CA, USA)	Real-time PCR	1 hour	*S. aureus*	*mecA*	100 99–100 nr
StaphSR assay (BD GeneOhm, San Diego, CA, USA)	Multiplex PCR	1–2 hours	*S. aureus*	*mecA*	96–100 95–98 nr
StaphPlex (Genaco Biomedical Products, Huntsville, AL, USA)	Multiplex PCR + Microarray	5 hours	*S. aureus*	*mecA* (+ PVL)	100 95–100 92
MALDI-TOF MS Brucker Daltonics (Bremen, Germany) bioMérieux (Marcy l'Etoile, France)	Mass-spectrometry	<1 hour	<1000[a]	not in routine	– – 76–99

Opota et al. *Clin Microbiol Infect* 2015; 21: 313–322

Usefulness of the multiplex-PCR Unyvero system to decrease broad-spectrum antibiotics consumption in patients with VAP

Luyt C.-E., Bréchot N., Hékimian G., Aubry A., Lafeuille E., Schmidt M., Franchineau G., Besset S., Nieszkowska A., Bourcier S., Coutrot M., Combes A.

réanimation 2018 PARIS 24-26 JANVIER

Annals of Intensive Care 2018, **8 (Suppl 1):** CO-25

Unyvero « hospitalized pneumonia » (HPN) cartridge

Gram-positive bacteria	*Enterobacteriaceae*	Non-fermenting bacteria	Others / Fungi	Resistance	Gene
Staphylococcus aureus	*Citrobacter freundii*	*Moraxella catarrhalis*	*Pneumocystis jirovecii*	Macrolide/ Lincosamide	*ermB*
Streptococcus pneumoniae	*Escherichia coli*	*Pseudomonas aeruginosa*	*Haemophilus influenzae*	Oxacillin	*mecA*
	Enterobacter cloacae complex	*Acinetobacter baumannii* complex	*Mycoplasma pneumoniae*		*mecC*
	Enterobacter aerogenes	*Stenotrophomonas maltophilia*	*Chlamydophila pneumoniae*	Penicillin	*tem*
	Proteus spp.	*Legionella pneumophila*			*shv*
	Klebsiella pneumoniae			3rd generation Cephalosporins	*ctx-M*
	Klebsiella oxytoca			Carbapenem	*kpc*
	Klebsiella variicola				*imp*
	Serratia marcescens				*ndm*
	Morganella morganii				*oxa-23*
					oxa-24/40
					oxa-48
					oxa-58
					vim
				Sulfonamide	*sul1*
				Fluoroquinolone	*gyrA83*
					gyrA87

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réanimation 2018 PARIS 24-26 JANVIER

Annals of Intensive Care 2018, **8 (Suppl 1):** CO-25

- Étude prospective mono-centrique
- Suspicion de PAVM avec LBA positif à l'examen direct (n = 44 patients)
- **PAVM :** *P. aeruginosa* 43%, entérobactéries 48%, polymicrobien 30%
- **Identification bactérienne : correcte dans 80% des cas** (10% faux-négatifs, 10% discordance avec culture conventionnelle)
- **Détection de la résistance : échec dans 43% des cas** (défaut/excès), essentiellement dans les PAVM à *P. aeruginosa*

Review

New agents for the treatment of infections with Gram-negative bacteria: restoring the miracle or false dawn?

H. Wright [1], R.A. Bonomo [2], D.L. Paterson [1,*]

Clinical Microbiology and Infection 23 (2017) 704–712

Ceftolozane-tazobactam

Ceftazidime-avibactam

Céfidérocol

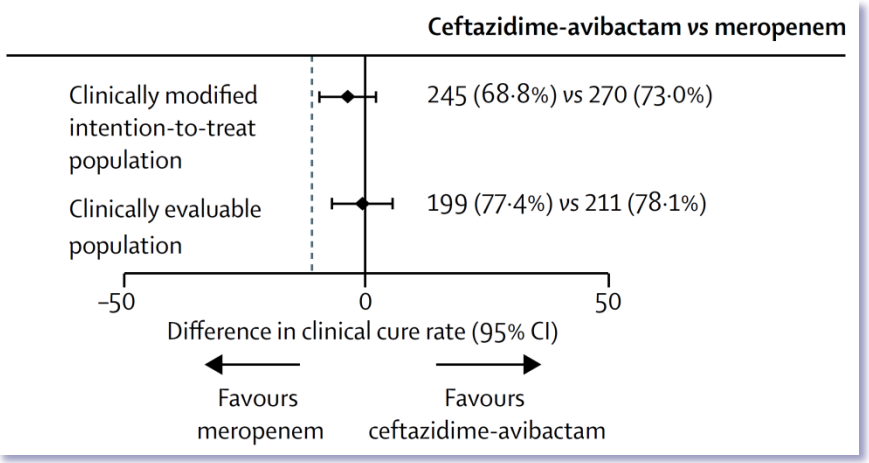
Implications: The development of new agents with activity against multidrug-resistant Gram-negative pathogens has provided important therapeutic options for clinicians. Polymyxins appear to have been supplanted by new agents as first-line therapy for *Klebsiella pneumoniae* carbapenemase producers. Cefiderocol and ceftazidime/avibactam/aztreonam are promising options for metallo-β-lactamase producers, and cefiderocol and ceftolozane/tazobactam for multiply resistant *Pseudomonas aeruginosa*, but definitive data showing clinical efficacy is as yet lacking. Reports of the development of resistance early after the release and use of new agents is of concern. Orally administered options and agents active effective against *Acinetobacter baumannii* are under-represented in clinical development. **H. Wright, Clin Microbiol Infect 2017;23:704**

Ceftazidime-avibactam versus meropenem in nosocomial pneumonia, including ventilator-associated pneumonia (REPROVE): a randomised, double-blind, phase 3 non-inferiority trial

Antoni Torres, Nanshan Zhong, Jan Pachl, Jean-François Timsit, Marin Kollef, Zhangjing Chen, Jie Song, Dianna Taylor, Peter J Laud, Gregory G Stone, Joseph W Chow

Lancet Infect Dis 2018; 18: 285–95

	Patients with clinical cure (clinically evaluable population)		
	Ceftazidime-avibactam (n=257)	Meropenem (n=270)	% difference (95% CI)
Enterobacteriaceae			
Klebsiella pneumoniae	31/37 (83·8%)	39/49 (79·6%)	4·2 (–13·49 to 20·50)
Enterobacter cloacae	20/21 (95·2%)	7/11 (63·6%)	31·6 (4·79 to 61·30)
Escherichia coli	8/11 (72·7%)	14/18 (77·8%)	–5·1 (–39·26 to 25·79)
Proteus mirabilis	11/11 (100·0%)	7/8 (87·5%)	12·5 (–16·54 to 48·07)
Serratia marcescens	10/12 (83·3%)	8/8 (100·0%)	–16·7 (–45·58 to 19·48)
Enterobacter aerogenes	4/6 (66·7%)	2/5 (40·0%)	26·7 (–31·92 to 70·73)
Gram-negative pathogens other than Enterobacteriaceae			
Pseudomonas aeruginosa	27/42 (64·3%)	27/35 (77·1%)	–12·8 (–32·25 to 8·01)
Haemophilus influenzae	10/11 (90·9%)	11/13 (84·6%)	6·3 (–26·19 to 36·09)



Interpretation Ceftazidime-avibactam was non-inferior to meropenem in the treatment of nosocomial pneumonia. These results support a role for ceftazidime-avibactam as a potential alternative to carbapenems in patients with nosocomial pneumonia (including ventilator-associated pneumonia) caused by Gram-negative pathogens.

Prédiction des infections à BGN-MR en réanimation

- Take-home messages -

- **Épidémiologie locale (endémie / épidémie)**
- **Dépistage qualitatif du portage rectal :** excellente VPN mais VPP médiocre (*P. aeruginosa* > Enterobacteriaceae) ⇨ sur-consommation probabiliste de molécules à large spectre, notamment carbapénèmes
- **Dépistage qualitatif d'un portage oro-pharyngé (PAVM)?**
- **Dépistage quantitatif du portage rectal (abondance relative)?**
- **Nouveaux outils pour détecter rapidement la résistance dans les prélèvements cliniques :** l'avenir de l'*antibiotic stewardship* en réanimation?
- Études écologiques nécessaires (carbapénèmes vs alternatives)