Université de Paris

HÔPITAUX UNIVERSITAIRES PARIS NORD VAL DE SEINE
Bichat - Claude Bernard

MI² Medical Infectious diseases Intensive care unit

Stratégie d'optimisation de l'utilisation des antibiotiques en réanimation

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Infection • Antimicrobiens • Modélisation • Evolution

JARCA, Bordeaux 15 Nov 2019

Liens d'intérêt

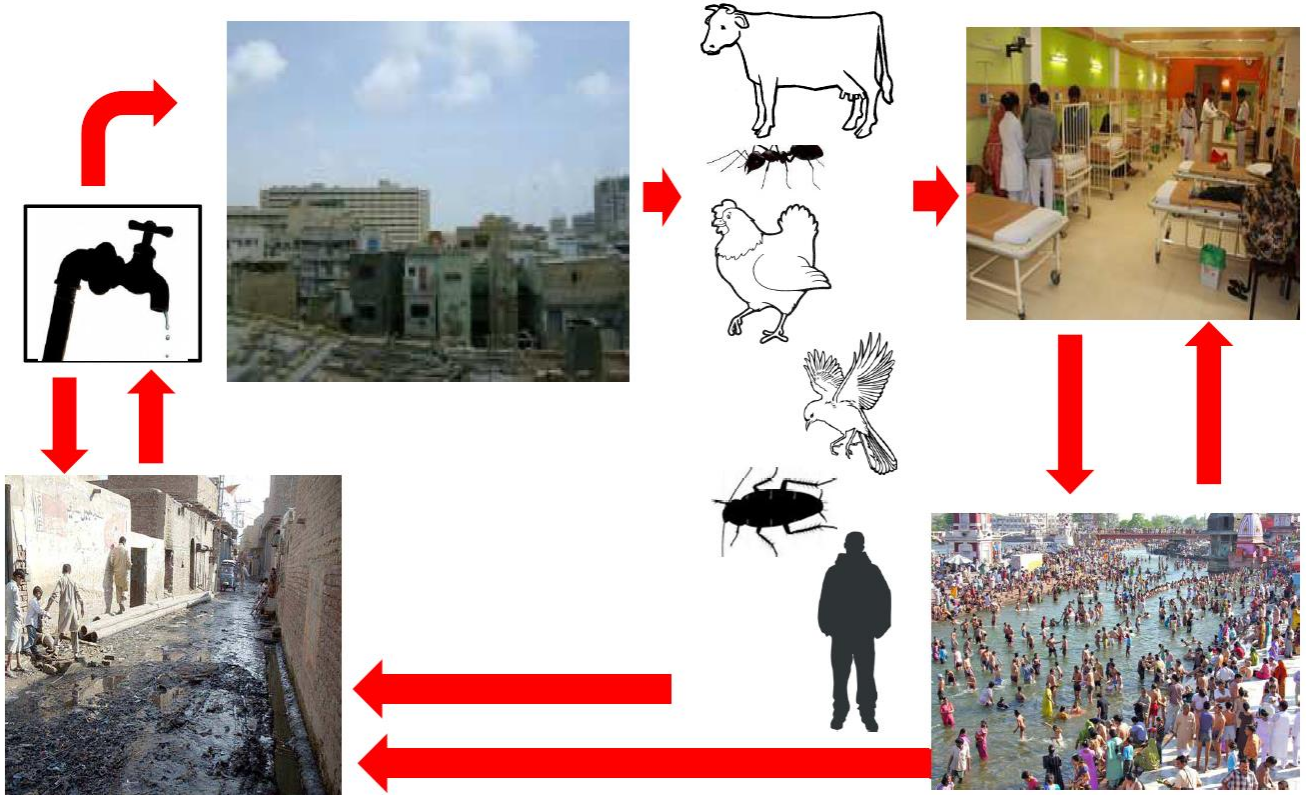
- Scientific Board: Bayer, Paratek, MSD, Nabriva, Gilead, Medimune
- Grants: MSD, Astelas, 3M, Pfizer
- Lectures: Pfizer, MSD, Astelas, Gilead, Biomerieux

Deux objectifs

- Traiter les patients infectés
  - Pas de recettes magiques
  - Eviter de traiter les malades seulement colonisés
  - Contrôler la source de l'infection

- Protéger les autres patients
  - Programme de lutte contre l'infection nosocomiale
  - Prévention de la transmission croisée (précautions contact → « search and isolate+++ » si XDR)
  - Ne pas irriter les bactéries du microbiote (politique globale de bonne utilisation des antibiotiques, arrêt précoce, ré-evaluation, durée de traitement courte)

Il n’y a plus de vrais obstacles entre l’hôpital et la communauté



Carbapenemases
Winter is coming

L'histoire se répète: Carbapenemases, BLSE

- On en trouve :
  - Chez 6% des voyageurs
  - Dans les égouts et les eaux de traitement
  - Dans la nature : *Salmonelle sp, E. Coli*
  - Sur les animaux de companie, oiseaux
  - Sur les animaux de ferme
  - Dans la nourriture et la nourriture animale
  - Dans les eaux de baignade
  - …

Asie du sud est
Amérique latine
Moyen orient
Europe centrale

Ruppe E Eurosurv 2016
Feasey NA PLoS Negl Trop Dis. 2015
Day MR JAC 2015
Guerra B Vet Micobiology 2014
Fischer J JAC 2013
Montezzi LF Int J Antimicob Agents 2015

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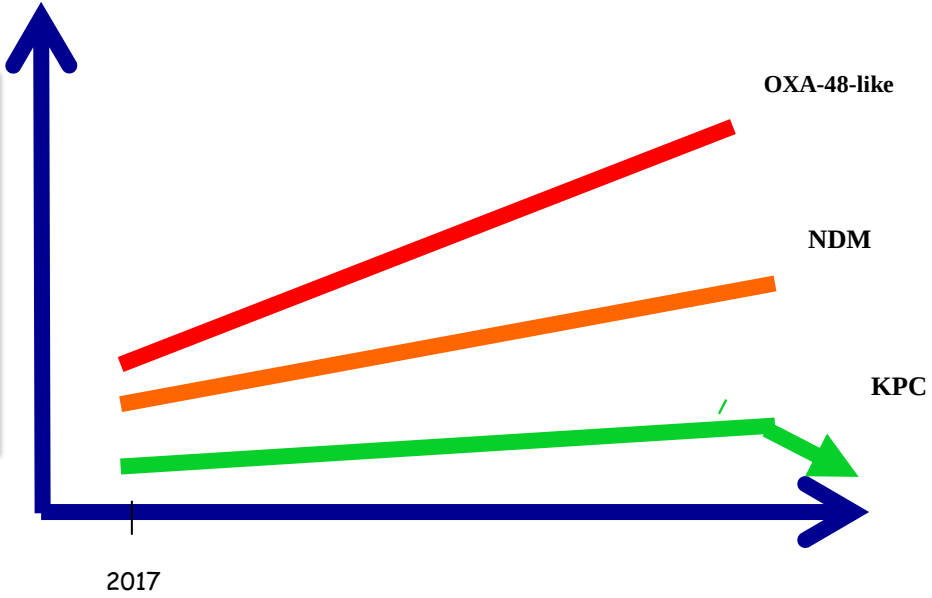
842 millions de billets d’avion
Usage non raisonné des antibiotiques
Diffusion clonale
Adaptabilité

Diffusion attendue des entérobactéries productrices de carbapenemases

- Adaptabilité
- Diffusion clonale
- Pression de sélection AB
- Transmission familiale



OXA-48: *E. coli* ++, community-acquired, highly transferable plasmid
NDM: *Enterobacteriaceae*, community- and hospital-acquired
KPC; *K. pneumoniae*, hospital-acquired

Courstesy of P Nordmann

Agenda

- **Traiter seulement les malades réellement infectés**
- Commencer rapidement: quand suspecter une résistance bactérienne?
- Utiliser la bonne molécule à la bonne dose avec la bonne voie d'administration
- Contrôler la source de l'infection
- Arrêter précocement les antibiotiques inutiles

Ventilator-Associated Events: Prevalence, Outcome, and Relationship With Ventilator-Associated Pneumonia*

Lila Bouadma, MD, PhD[1–3]; Romain Sonneville, MD[3]; Maité Garrouste-Orgeas, MD, PhD[1,4]; Michael Darmon, MD, PhD[5,6]; Bertrand Souweine, MD, PhD[7]; Guillaume Voiriot, MD[2,3]; Hatem Kallel, MD[8]; Carole Schwebel, MD, PhD[9]; Dany Goldgran-Toledano, MD[10]; Anne-Sylvie Dumenil, MD[11]; Laurent Argaud, MD, PhD[12]; Stéphane Ruckly, MSc[13]; Samir Jamali, MD[14]; Benjamin Planquette, MD[15]; Christophe Adrie, MD, PhD[16]; Jean-Christophe Lucet, MD, PhD[1,2,17]; Elie Azoulay, MD, PhD[2,18]; Jean-François Timsit, MD, PhD[1–3]; on behalf of the OUTCOMEREA Study Group

Infection-Related Ventilator-Associated Complication
Two successive sequences:
A ≥ 2 d stable or decreasing range of PEEP (≥ 6, ≥ 10, and ≥ 16 mm Hg) and a stable or improved Pao_2/Fio_2 ratio
A ≥ 2 d rise in range of PEEP or a decreasing Pao_2/Fio_2 ratio by > 50 mm Hg with the same level of PEEP or by > 100 mm Hg whatever the level of PEEP
At least 2 criteria within 2 calendar days before or after the onset of respiratory deterioration:
Body temperature < 36°C or > 38°C
Heart rate > 90 beats/min
WBC count > 12,000 or < 4,000 cells/mm³
At least one new antimicrobial agent prescribed within 2 calendar days before or after the onset of respiratory deterioration and continued for ≥ 4 d or less in case of death, ICU discharge, or withholding or withdrawing life-sustaining medical treatment

Variables[a]	Ventilator-Associated Condition (*n* = 2,331)	Infection-Related Ventilator-Associated Complication (*n* = 869)
Number of etiologies per patient		
0	818 (35.1)	189 (21.78)
1	726 (31.2)	260 (29.9)
2	445 (19.1)	213 (24.5)
3	214 (9.2)	124 (14.3)
≥ 4	128 (5.5)	83 (9.6)
Nosocomial infections	637 (27.3)	381 (43.8)
Ventilator-associated pneumonia	339 (14.5)	240 (27.6)
Tracheobronchitis	23 (1)	12 (1.4)
Bloodstream infection	173 (7.4)	95 (10.9)
Catheter-related infection	81 (3.5)	44 (5.1)
Urinary infection	102 (4.4)	42 (4.8)
Sinusitis	5 (0.2)	4 (0.5)
Viral infection	10 (0.4)	8 (0.9)
Surgical site infections	41 (1.8)	30 (3.5)
Iatrogenic adverse events	322 (13.8)	137 (15.8)
Pneumothorax	37 (1.6)	23 (2.6)
Failure of planned extubation	11 (0.5)	1 (0.1)
Accidental extubation	21 (0.9)	9 (1)
Self-extubation	71 (3)	19 (2.2)
Venous puncture accident	14 (0.6)	9 (1)
Atelectasis	52 (2.2)	20 (2.3)
Peripheral thrombosis	36 (1.5)	18 (2.1)
Pulmonary embolism	9 (0.4)	1 (0.1)
Myocardial infarction	10 (0.4)	4 (0.5)
Cardiac arrest	43 (1.8)	24 (2.8)
Cardioversion	29 (1.2)	17 (2)
Gastrointestinal bleeding	26 (1.1)	11 (1.3)
Acute mesenteric infarction	5 (0.2)	4 (0.5)
Intestinal pseudo-obstruction	2 (0.1)	0
Transport	387 (16.6)	186 (21.4)
Fluid resuscitation	123 (5.3)	58 (6.7)

(*Crit Care Med* 2015; 43:1798–1806)

Aggressive versus conservative initiation of antimicrobial treatment in critically ill surgical patients with suspected intensive-care-unit-acquired infection: a quasi-experimental, before and after observational cohort study

Tjasa Hranjec, Laura H Rosenberger, Brian Swenson, Rosemarie Metzger, Tanya R Flohr, Amani D Politano, Lin M Riccio, Kimberley A Popovsky, Robert G Sawyer

Lancet Infect Dis 2012; 12: 774–80

	Aggressive (n=247)	Conservative (n=237)	p value
Time from blood culture to start of treatment (h)			
Number	189	206	
Median (IQR)	12 (3–30)	22 (7–58)	<0·0001
Time from fever to start of treatment (h)			
Number	103	139	
Median (IQR)	6 (3–14)	24 (9–44)	<0·0001
Duration of antimicrobial treatment (days)			
Median (IQR)	11 (7–8)	10 (7–14)	0·015
Appropriate antimicrobials (number [%])			
Initial*	144 (62%)	158 (74%)	0·0095
Switched	64 (28%)	48 (23·5%)	0·17
Overall	208 (90%)	206 (96%)	0·010

	Aggressive	Conservative	p value
Lowest MAP mm Hg			
All patients	247	237	
Mean (SD)	75·9 (26·6)	68·9 (25·0)	<0·0001
Median (IQR)	65 (56–90)	62 (54–68)	<0·0001
Deceased patients	27 (11%)	13 (5%)	
Mean (SD)	66·2 (25·9)	71·9 (58·0)	<0·0001
Median (IQR)	69 (61–110)	63 (56–90)	<0·0001
Infections associated with MAP <60 mm Hg			
Number	95	110	0·077
APACHE II score			
Mean (SD)	22·0 (6·9)	22·4 (6·4)	0·71
Median (IQR)	21 (17–29)	22 (17–27)	0·79
Time from blood culture to initiation of treatment (h)			
Mean (SD)	9·2 (14·0)	31·8 (37·6)	<0·0001
Median (IQR)	4 (3–12·5)	20 (8–39)	<0·0001
Deaths	63 (66%)	29 (26%)	0·0004

MAP=mean arterial pressure.

Table 8: **Distribution of mean arterial pressures and descriptive statistics and outcomes for infections treated with MAP less than 60 mm Hg**

Agressive treatment increased the risk of death due to infection

OR=2.5 (1.5-4.0), p<0.0001

Even in infected patients with low MAP during the 1st 24h of ABX..

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COMMENTAIRES

Aggressive versus conservative initiation of antimicrobial treatment in critically ill surgical patients with suspected intensive-care-unit-acquired infection: a quasi-experimental, before and after observational cohort study

Tjasa Hranjec, Laura H Rosenberger, Brian Swenson, Rosemarie Metzger, Tanya R Flohr, Amani D Politano, Lin M Riccio, Kimberley A Popovsky, Robert G Sawyer

Lancet Infect Dis 2012; 12: 774–80

- Etude monocentrique, malades peu sévères
- Etude avant/après
- Pas de formation en antibiothérapie: AB rapide mais inappropriés ou inutiles dans la « période agressive »
  - Courbe d'apprentissage ds la période d'intervention
- Augmentation des effets indésirables?
- Masque un diagnostic alternatif

→ **Antimicrobials are not candies**

(Too early, too aggressive antimicrobial policy worsen the prognosis of SICU patients)

Colonisation ou infection?

- Cathéter positif sans signes cliniques
- ECBU positif
- Cultures de drain positive
- Prélèvements bronchiques positifs?

On a souvent « 5 minutes » pour réfléchir
Bonne connaissance du dossier
Examen clinique rigoureux → diagnostics alternatifs
Examens paracliniques nécessaires et possibles
Un coup de fil !!

PRÉLEVER LES MALADES AVANT TOUTE MODIFICATION DU TRAITEMENT ANTIBIOTIQUE (BASELINE PCT LEVEL?)

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Les cliniciens ne désescaladeront pas en l'absence de culture positive

Table 3: Differences in patient characteristics by final antibiotic grouping.

	Deescalation (n = 189)	No change (n = 156)	Escalation (n = 42)	Mixed changes (n = 8)	p value
SAPS II	48 ± 19.5	41 ± 19	47 ± 18.5	44 ± 23.7	0.007
Admission procalcitonin	2.3 (IQR 0.7–7.4)	7.9 (IQR 2–33.6)	4.6 (IQR 1.1–11.1)	11.1 (IQR 7–15.3)	0.007
No growth	86 (45.5%)	102 (65.3%)	12 (28.5%)	0	<0.001
Single site of sepsis	60 (31.7%)	35 (22.4%)	22 (52.3%)	3 (37.5%)	0.002
MDR organism	12 (6.3%)	22 (14.1%)	5 (11.9%)	2 (25%)	0.05
Fungal sepsis	11 (5.8%)	15 (9.6%)	8 (19%)	2 (25%)	0.019
ICU length of stay	6.5 (IQR 4.2–44)	5.5 (IQR 4–17)	5 (IQR 4–36.5)	7.5 (IQR 5–33.2)	0.003
ICU mortality	28 (14.8%)	38 (24.4%)	6 (14.3%)	2 (25%)	0.11

Salahuddin et al - Critical Care Research and Practice 2016

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Early antimicrobial therapy: « as soon as possible »

this can become problematic when guideline recommendations are overly rigid [12]. The Surviving Sepsis Campaign Guidelines recommend "that administration of IV antimicrobials be initiated as soon as possible after recognition and within 1 hour for both sepsis and septic shock (strong recommendation, moderate quality of evidence; grade applies to both conditions)."

IDSA agrees that antimicrobials should be initiated as soon as possible to patients with severe infections. We are fearful,

CID 2018:66 (15 May) • IDSA Sepsis Task Force

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

Daniel Leisman, BS[1,2]; Victor Huang, MD[1]; Qiuping Zhou, DO[1]; Jeanie Gribben, BS[1]; Andrea Bianculli, BS[1]; Michelle Bernshteyn, BS[3]; Mary Frances Ward, RN, MS, ANP[4,5]; Sandra M. Schneider, MD[1,6]

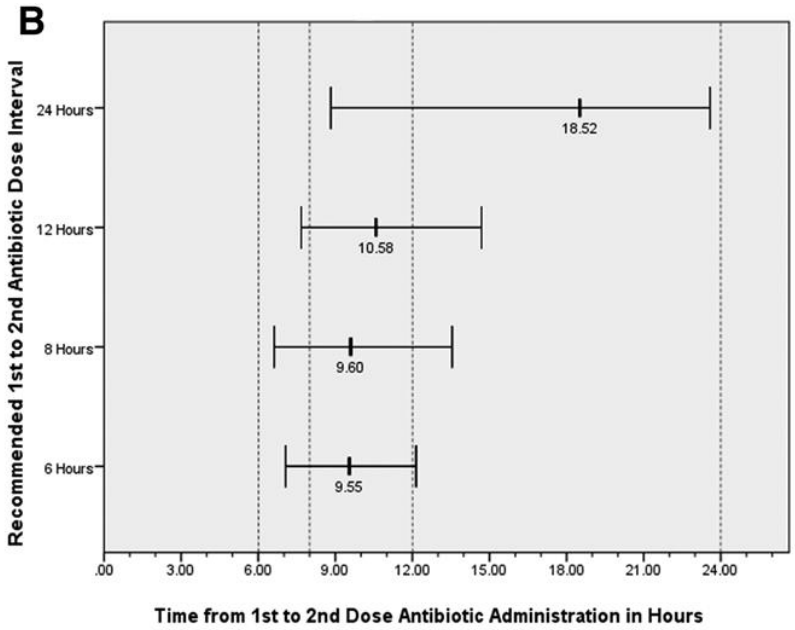
Clinical Investigations

Crit Care Med 2017; 45:956–965

Beware of the 2nd dose++++

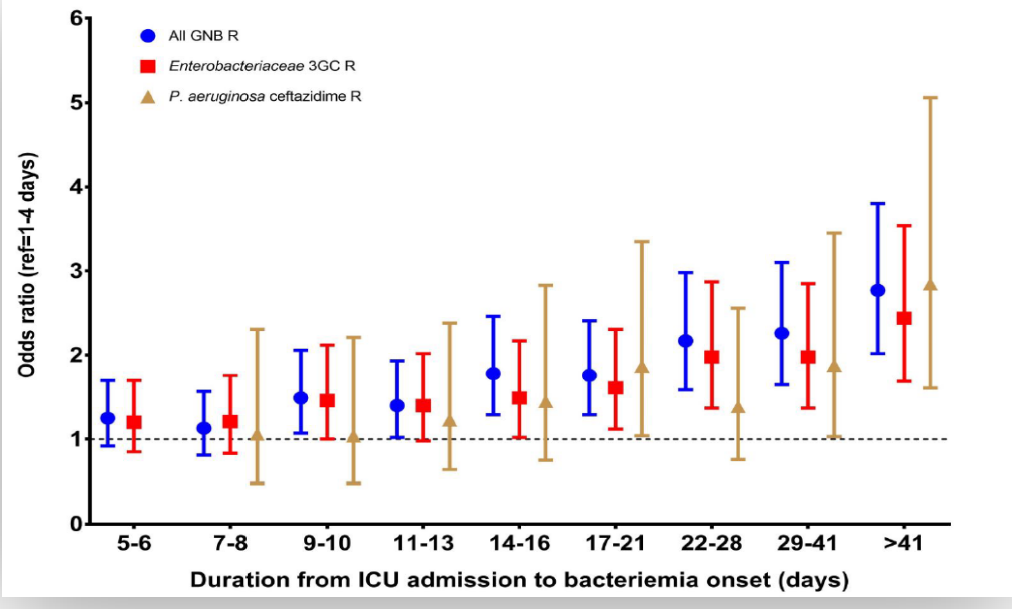
- 828 sepsis or septic shock
- 1 ED/ 10 months
- Delayed= superior to 25% of the recommended interval
- Delays (33% cases) are associated with mortality independently of severity and 3h bundle compliance

(OR 1.61; CI, 1.01–2.57)



Quand doit on penser à une bactérie resistante?

Influence de la durée préalable de séjour en réanimation (4547 episodes)



Bailly S et al (SRLF 2017)

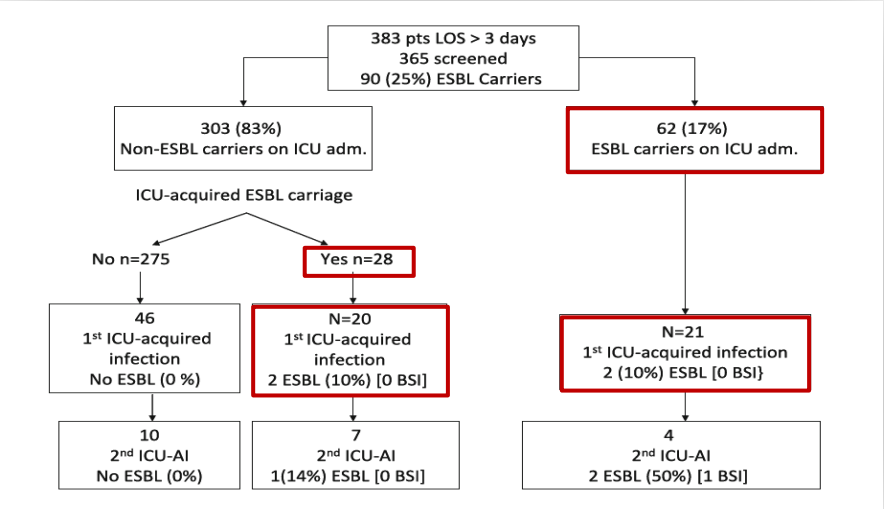
Quand doit on penser à une bactérie resistante?
Colonisation préalable

probablement plus important pour les BGN non fermentant

Pour les BLSE interet si colonisation des voies respiratoires pour les PAVM

Moins bon pour la colonisation digestive

PPV 10%
NPV 100%



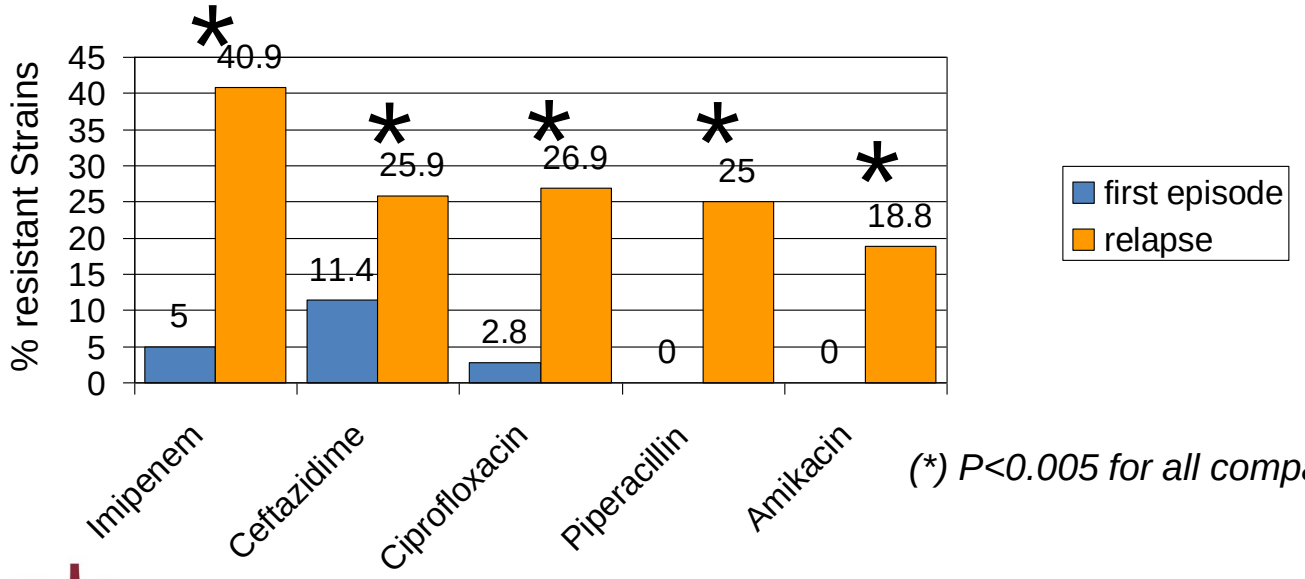
Razazi K et al – Intens care med 2012; 38:1769

Quand doit on penser à une bactérie resistante?

En pratique ne pas utiliser les molecules utilisées précédemment

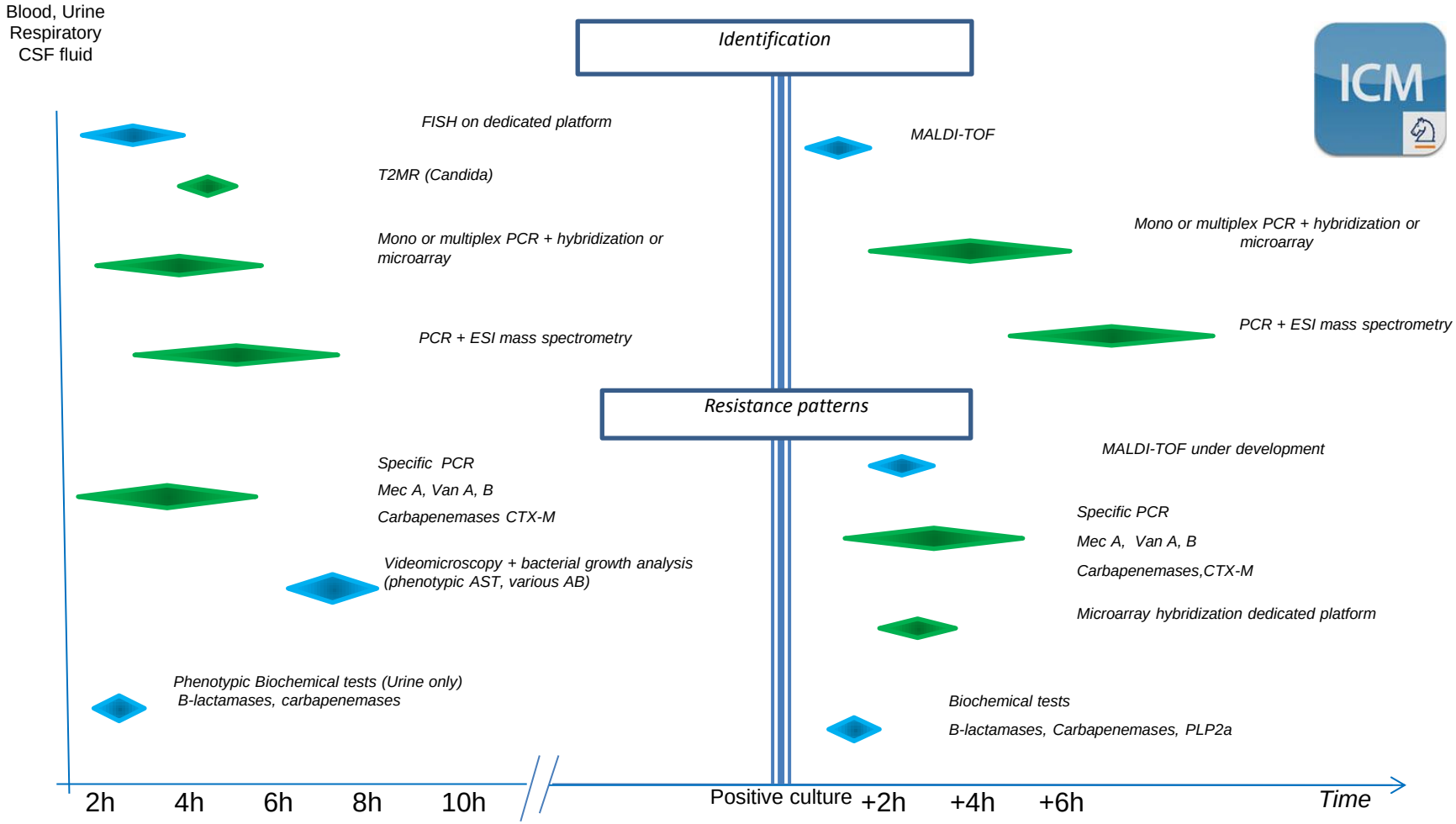
OUTCOMEREA

62 recurrences in 314 patients with *P. aeruginosa* VAP



(*) P<0.005 for all comparisons

Planquette B et al – Am J Respir crit care Med 2012



Laupland K et al – Intensive care Med 2017; May 13

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For MDR EB and *P. aeruginosa*, No magic bullets high MICs for all the traditional antimicrobials

EUCAST breakpoints

	Species related breakpoints (S≤/R>)	
	Enterobacteriaceae	*Pseudomonas*
Piperacillin-tazobactam	8/16	16/16
Ceftazidime	1/8	8/8
Cefepime	1/8	8/8
Meropenem	2/8	2/8
Amikacin	8/16	8/16
Ceftolozane-tazobactam	**1/1**	**4/4**
Ceftazidime-avibactam	**8/8**	**8/8**

Règles de base

1. Association si pari hasardeux
2. Dose de charge
3. Optimisation PK PRECOCE: Temps > CMI ou Cmax/CMI
4. Hyperfiltration glomérulaire
5. Limiter les toxicités
6. Durée de traitement individualisée …courte

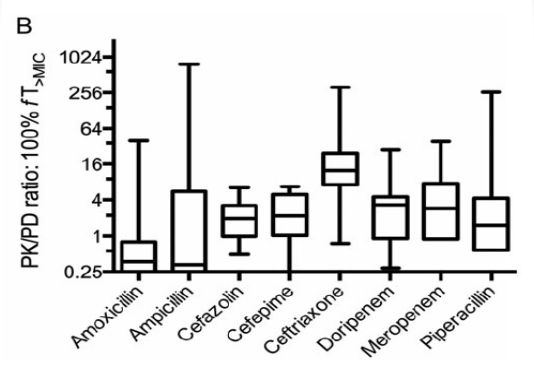
DALI: Defining Antibiotic Levels in Intensive Care Unit Patients: Are Current β-Lactam Antibiotic Doses Sufficient for Critically Ill Patients?

Clinical Infectious Diseases 2014;58(8):1072–83

Jason A. Roberts,[1,2] Sanjoy K. Paul,[3,4] Murat Akova,[5] Matteo Bassetti,[6] Jan J. De Waele,[7] George Dimopoulos,[8] Kirsi-Maija Kaukonen,[9] Despoina Koulenti,[1,8] Claude Martin,[10,11] Philippe Montravers,[12] Jordi Rello,[13] Andrew Rhodes,[14] Therese Starr,[2] Steven C. Wallis,[1] and Jeffrey Lipman[1,2]; for the DALI Study[a]

Dosing and PK/PD Data	Antibiotic (No. of Patients)								
	Amoxicillin (n = 71)	Ampicillin (n = 18)	Cefazolin (n = 14)	Cefepime (n = 14)	Ceftriaxone (n = 33)	Doripenem (n = 13)	Piperacillin (n = 109)	Meropenem (n = 89)	Total (N = 361)
Dosage per 24 h[b], g	6.0 (3.5–6.0)	12.0 (8.3–12.0)	3.0 (3.0–4.0)	6.0 (5.0–6.0)	2.0 (2.0–4.0)	1.75 (1.50–3.0)	12.0 (12.0–16.0)	3.0 (3.0–4.0)	
50% $fT_{>MIC}$ achieved	52.1%	55.6%	100.0%	78.6%	97.0%	100.0%	80.6%	95.0%	78.9%
50% $fT_{>4\times MIC}$ achieved	16.9%	27.8%	50.0%	50.0%	93.9%	69.2%	48.9%	68.8%	48.9%
100% $fT_{>MIC}$ achieved	18.3%	33.3%	78.6%	78.6%	93.9%	76.9%	67.0%	69.7%	60.4%
100% $fT_{>4\times MIC}$ achieved	11.3%	22.2%	14.3%	71.4%	87.9%	30.8%	30.3%	41.6%	35.0%

Median (IQR) MICs allowing to reach 100% time above MIC for a given antimicrobial



Le Vd est indépendant de la clairance++++

Antibiotic	Healthy volonteers (L/kg)	Patients with AKI on RRT (L/kg)
Lipophilic drugs		
Ciprofloxacin	1.98	1.60
Levofloxacin	0.96 / 1.13	1.02 / 1.51
Hydrophilic drugs		
Amikacin	0.18	0.44
Daptomycin	0.10	0.23
Meropenem	0.17	0.26
Piperacillin	0.15	0.14
Vancomycin	0.39 / 0.59 / 0.63	0.57 / 0.65

↑ Vd → loading dose even in case of AKI

Intensive Care Med
DOI 10.1007/s00134-015-4188-0

ORIGINAL

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Beta-Lactam Infusion in Severe Sepsis (BLISS): a prospective, two-centre, open-labelled randomised controlled trial of continuous versus intermittent beta-lactam infusion in critically ill patients with severe sepsis

Table 2 Primary and secondary endpoints by treatment arm in the intention-to-treat population and the subgroups of interest

Primary endpoint	Intervention (n = 70)	Control (n = 70)	Absolute difference (95 % CI)	Significance (p value)[a,b]
Clinical cure for ITT population, n (%)	39 (56)	24 (34)	22 (−0.4 to −0.1)	**0.011**
Clinical cure by antibiotic, n (%)[c]				
Piperacillin/tazobactam	22 (58)	15 (32)	26 (−0.4 to −0.1)	**0.016**
Meropenem	14 (67)	8 (38)	29 (−0.5 to 0.1)	0.064
Cefepime	3 (27)	1 (50)	23 (−0.3 to 0.7)	1.000
Clinical cure by concomitant antibiotic treatment, n (%)[d]				
Yes	14 (42)	13 (39)	3 (−0.3 to 0.2)	0.802
No	25 (68)	11 (30)	38 (−0.6 to −0.2)	**0.001**
Clinical cure by site of infection, n (%)[e]				
Lung	27 (59)	12 (33)	25 (−0.4 to −0.1)	**0.022**
Clinical cure by *A. baumannii* or *P. aeruginosa* infection, n (%)[f]				
Yes	13 (52)	6 (25)	27 (−0.5 to 0.1)	0.052
No	10 (44)	12 (38)	6 (−0.3 to 0.2)	0.655

Secondary endpoints	Intervention (n = 70)	Control (n = 70)	Absolute difference (95 % CI)	Significance (p value)[a,b]
PK/PD target attainment, n (%)[g]				
50 % $fT_{>MIC}$ on day 1	56 (98)	49 (93)	5 (−0.2 to 0.1)	0.194
100 % $fT_{>MIC}$ on day 1	55 (97)	37 (70)	27 (−0.4 to −0.1)	**<0.001**
50 % $fT_{>MIC}$ on day 3	56 (98)	49 (93)	5 (−0.2 to 0.1)	0.194
100 % $fT_{>MIC}$ on day 3	55 (97)	36 (68)	29 (−0.4 to −0.1)	**<0.001**
ICU-free days	20 (12–23)	17 (0–24)	3 (−3 to 9)	0.378
ICU survivors[h]	21 (19–23)	21 (14–24)	0 (−3 to 3)	0.824
Ventilator-free days	22 (0–24)	14 (0–24)	8 (−2 to 18)	**0.043**
ICU survivors[i]	23 (21–25)	21 (0–25)	2 (−3 to 7)	0.076
14-day survival, n (%)	56 (80)	50 (71)	9 (−0.2 to 0.1)	0.237
30-day survival, n (%)	52 (74)	44 (63)	11 (−0.3 to 0.1)	0.145
WCC normalisation days	3 (2–7)	8 (4–15)	5 (1 to 5)	**<0.001**

CI better If :
Monotherapy
Lung infections
MDRO

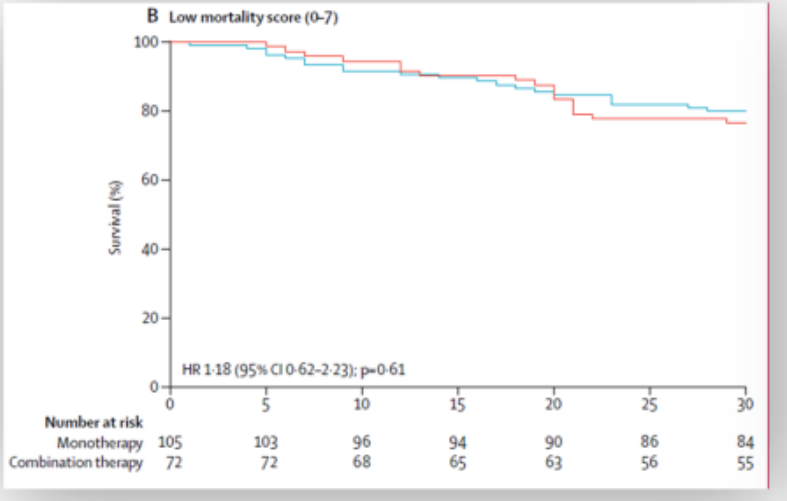
Warning: LOADING DOSE++++/ Glomerular hyperfiltration

Combo (with AG) increases the adequation of initial antibiotic therapy

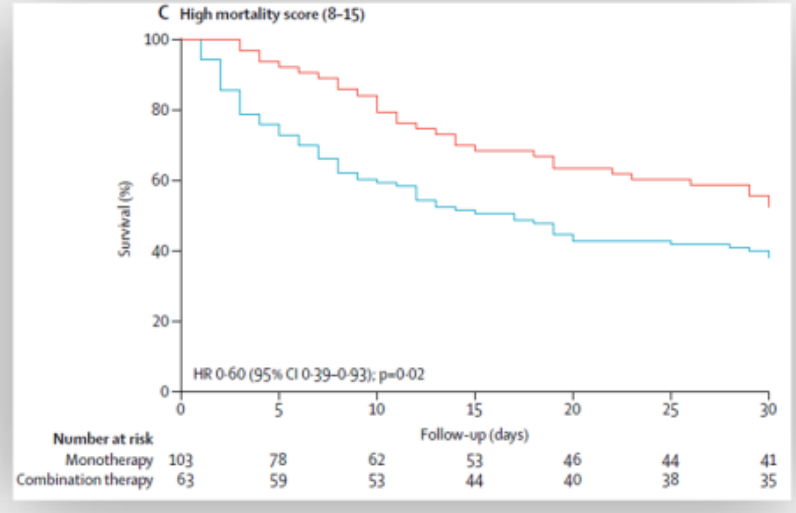
Martinez JA et al., Antimicrob Agents Chemother. 2010 Sep;54(9):3590-6

Microorganism	Combination No./total no. (%)	Beta-lactam No./total no. (%)	OR (95% CI)	P
Non-ESBL *E. coli*	242/248 (98)	2,454/2,489 (99)	0.6 (0.2-1.7)	0.3
ESBL *E. coli*	**21/28 (75)**	**62/122 (51)**	**2.9 (1.1-8.2)**	**0.02**
Non-ESBL *Klebsiella*	62/63 (98)	393/420 (94)	4 (0.7-177)	0.2
ESBL *K. pn.*	**18/20 (90)**	**38/63 (60)**	**2 (1.2-4.2)**	**0.01**
P. mirabilis	10/10 (100)	116/118 (98)		1
Salmonella spp.	15/15 (100)	108/109 (99)		1
AmpC organisms	**78/82 (95)**	**258/326 (79)**	**5.1 (1.8-20)**	**0.001**
P. aeruginosa	**133/143 (93)**	**201/319 (63)**	**7.8 (3.8-16)**	**<.0001**
Other NF-GNB	24/51 (47)	53/105 (51)	0.9 (0.4-1.8)	0.7
Miscellaneous	18/18 (100)	105/114 (92)		0.4

Mono vs Combo for CPE BSIs?
Mortality stratified by the level of increment CPE score



Death: 20 vs 24%



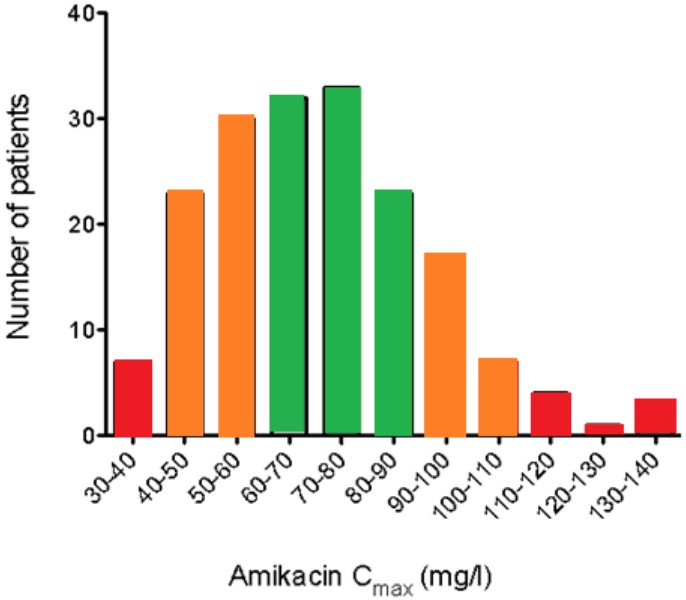
Death: 62 vs 48%

Adjusted HR for combination 0.56 (0.34-0.91), p=0.02

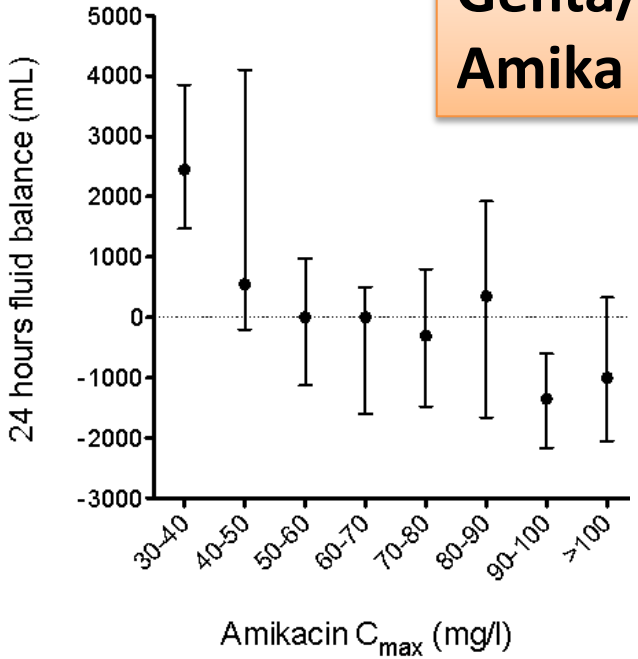
Gutierez-Gutierez et al – Lancet Infect Dis 2017 Apr 21

Aminoglycosides in ICU patients

N=181
Target 8-10 X MIC
Dose 25 mg/kg (1.6 g to 2.25g)

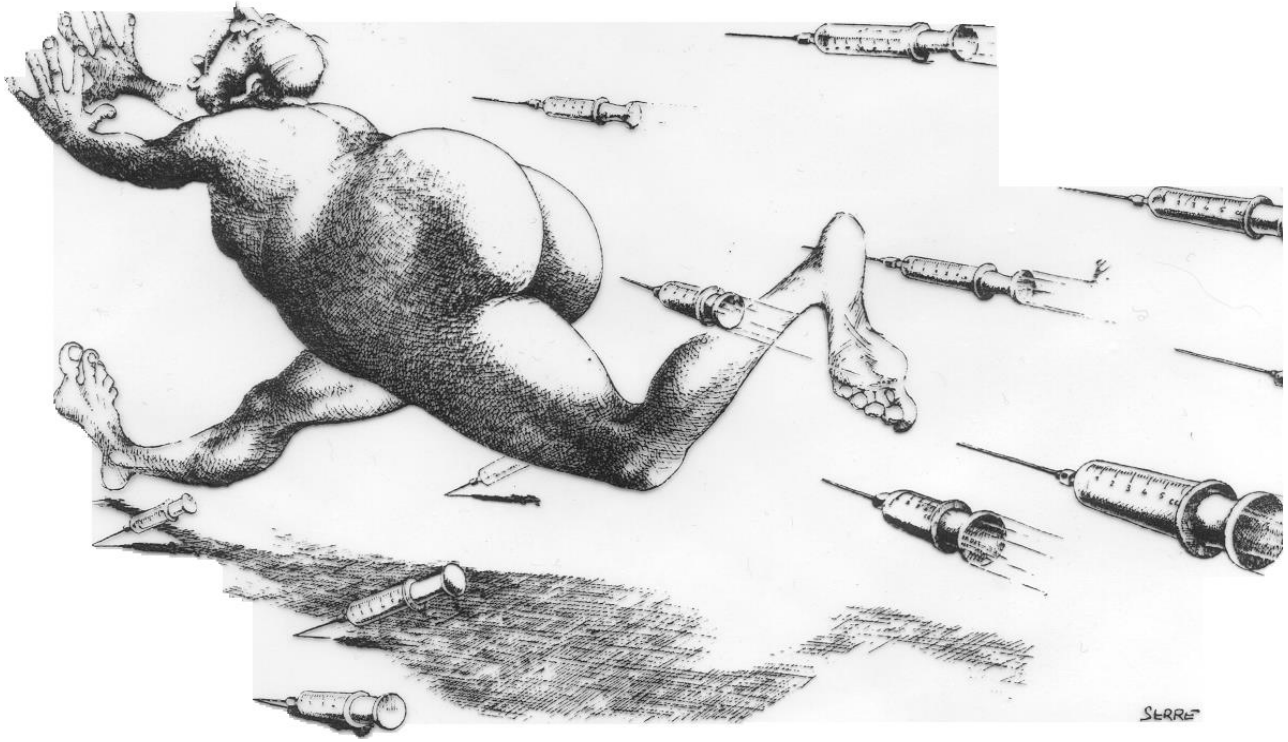


Genta/tobra 7 mg/kg
Amika 25-30 mg/kg



E. De Montmollin et al - Intensive Care Med. 2014 Jul;40(7):998-1005

HighVd → high initial dose and PK optimization
Decreased clairance → secondary toxicity

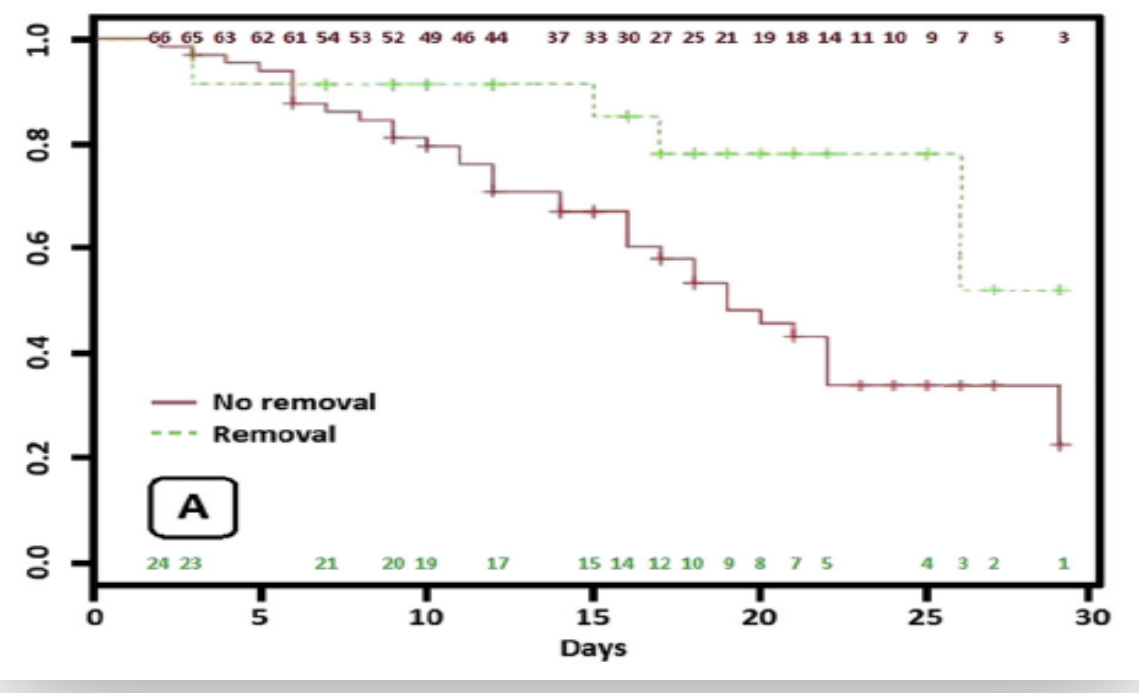


Agenda

- Traiter seulement les malades réellement infectés
- Commencer rapidement: quand suspecter une résistance bactérienne?
- Utiliser la bonne molécule à la bonne dose avec la bonne voie d'administration
- **Contrôler la source de l'infection**
- Arrêter précocement les antibiotiques inutiles

D’autant plus important que votre bactérie est résistante aux antibiotiques

111 KPC septic shock



Falcone et al CMI 2016; 22:444

Agenda

- Traiter seulement les malades réellement infectés
- Commencer rapidement: quand suspecter une résistance bactérienne?
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"Au lieu de s’ ingénier à tuer les microbes dans les plaies, ne serait-il pas plus raisonnable de ne pas en introduire"?

Louis Pasteur

Antibiotic stewardship program is nothing without a good hygiene program

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Dix règles de base

1. Traitez UNIQUEMENT les malades RÉELLEMENT INFECTÉS
2. L'antibiotherapie doit ÊTRE IMMÉDIATEMENT ADÉQUATE surtout en cas de choc septique, et pour les patients neutropéniques
3. Vous devez connaitre votre ÉCOLOGIE
4. La connaissance de la COLONISATION PRÉALABLE des patients peut aider
5. NE JAMAIS débuter des antibiotiques que vous avez précédemment utilisés (Penem, CIP)
6. Les patients les plus sévères sont à haut risque de SOUS DOSAGE (optimisation PK , dosages++)
7. Préférez une ASSOCIATION si vous suspectez une bactérie résistante+++
8. Attention aux SURDOSAGES quand le patient se stabilise
9. LIMITER LA DURÉE de l'antibiothérapie le plus possible (élément essentiel du contrôle de pression de sélection des antibiotiques, requiert un bon contrôle de la source)
10. PROTÉGEZ LES AUTRES patients de la colonisation croisée – hygiène des mains….

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REVIEW

Rationalizing antimicrobial therapy in the ICU: a narrative review

Jean-François Timsit[1,2*], Matteo Bassetti[3], Olaf Cremer[4], George Daikos[5], Jan de Waele[6], Andre Kallil[7], Eric Kipnis[8], Marin Kollef[9], Kevin Laupland[10], Jose-Artur Paiva[11], Jesús Rodríguez-Baño[12], Étienne Ruppé[2,13], Jorge Salluh[14], Fabio Silvio Taccone[15], Emmanuel Weiss[16,17] and François Barbier[18]

Table 1 Determinants of increased risk of MDRB infection at ICU admission and during the ICU stay

Predictors of MDRB infection	At ICU admission	During the ICU stay
Patient features	Co-morbid illness/immunosuppression/recent hospital and/or ICU stay	Higher severity of acute illness/Invasive interventions
Type of infection	Hospital-acquired > healthcare-associated > community-acquired	ICU-acquired > others
Antimicrobial selection pressure	Prior antibiotics*/antifungals	Antibiotics*/antifungals in the ICU
Colonization status	Previously documented colonization with MDRB	In-ICU acquisition of MDRB
Local epidemiology	Epidemiology of MDRB in community/hospital/areas recently traveled to	Local epidemiology of MDRB in the ICU
Infection prevention measures	Poor hygiene practices in hospital	Poor hygiene practices in the ICU

MDRB multidrug-resistant bacteria, *ICU* intensive care unit

*Especially if agents with broad-spectrum and/or potent activity against intestinal anaerobes