

# **Patients à risques. Quand couvrir le Pseudomonas?**

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**-Quels risques pour une infection à Pseudomonas ?**

**-Quels risques de multirésistance?**

**-Que faire de la littérature, à l'heure de la mondialisation?**

# Infections à Pseudomonas

- ~~-Maladies infectieuses nosocomiales~~
- ~~-La multirésistance est un phénomène hospitalier....~~

**UN PARADIGME A OUBLIER!**

# Les risques d'infection à *Pseudomonas* (Schechner et coll, 2009)

Gram-Negative Bacteremia upon Hospital Admission: When Should *Pseudomonas aeruginosa* Be Suspected?

Vered Schechner,<sup>1</sup> Vandack Nobre,<sup>2</sup> Keith S. Kaye,<sup>5</sup> Moshe Leshno,<sup>3</sup> Michael Giladi,<sup>2</sup> Peter Rohner,<sup>4</sup> Stephan Harbarth,<sup>4</sup> Deverick J. Anderson,<sup>5</sup> Adolf W. Karchmer,<sup>6</sup> Mitchell J. Schwaber,<sup>1</sup> and Yehuda Carmeli<sup>1,6</sup>

- Etude rétrospective, sur 4 hôpitaux (Boston, Durham, Genève, Tel-Aviv)
- Comparaison 151 bactériémies à *P aeruginosa* vs 152 bactériémies à entérobactéries
- Régression logistique: paramètres discriminants

# Les risques d'infection à *Pseudomonas* (Schechner et coll, 2009)

## -Résultats:

**Table 2. Independent predictors of *Pseudomonas aeruginosa* bacteremia upon hospital admission among patients without severe immunodeficiency on the basis of multivariate logistic regression analysis.**

Variable	OR (95% CI)	<i>P</i>
Presence of a urinary device <sup>a</sup>	6.80 (2.53–18.26)	<.001
Age >90 years	5.39 (1.91–15.17)	.001
Recent antimicrobial use <sup>b</sup>	3.70 (1.87–7.36)	<.001
Presence of a central venous catheter	2.97 (1.31–6.73)	.009

# Les risques d'infection à Pseudomonas

(Schechner et coll, 2009)

**Table 3. Risk classification for *Pseudomonas aeruginosa* bacteremia among 250 patients without severe immunodeficiency, according to the total number of independent predictors, and the number of patients needed to treat in each group to effectively treat a single case of *P. aeruginosa* bacteremia.**

No. of predictors (risk category)	Occurrence based on data, %	Probability of <i>P. aeruginosa</i> bacteremia, %	No. of patients needed to treat		
			Per risk group <sup>a</sup>	For risk group or higher risk <sup>b</sup>	For risk group or lower risk <sup>c</sup>
0	71.77	2.36	42.4	20.00	42.4
1	24.39	8.84	11.3	8.55	25.0
2	3.75	28.13	3.55	3.35	20.4
3	0.09	100.00	1.00	1.00	20
4	0.00	...	...	...	...

<sup>a</sup> For treatment of only patients with gram-negative bacteremia in the specific risk category.

<sup>b</sup> For treatment of all patients with gram-negative bacteremia in the specific risk category or higher.

<sup>c</sup> For treatment of all patients with gram-negative bacteremia in the specific risk category or lower. This provides an estimate of limiting the overuse of anti-pseudomonal agents per 1 missed case of *P. aeruginosa* bacteremia.

# Les risques d'infection à Pseudomonas

(Schechner et coll, 2009)

## **-Conclusions:**

**-En l'absence d'immunodépression, la bactériémie à *P aeruginosa* est rare**

**-Chez l'immunocompétent, le traitement anti-pseudomonas empirique est justifié en présence de  $\geq 2$  facteurs de risque**

# Epidémiologie des pneumonies: 59 hôpitaux US (Kollef MH, 2005)

**Table 1—Definitions of Pneumonia Categories**

Pneumonia Category <sup>a</sup>	Definition
VAP	Patients receiving mechanical ventilation for at least 24 h with a first positive bacterial† respiratory culture finding after ventilator start date
HAP	Patients with a first positive bacterial† respiratory culture finding > 2 days from admission who do not meet VAP definition
HCAP	Patients with a first positive bacterial† respiratory culture finding within 2 days of admission and any of the following: (1) admission source indicates a transfer from another health-care facility; (2) receiving long-term hemodialysis (ICD-9-CM codes); and (3) prior hospitalization within 30 days who do not meet VAP definition
CAP	Patients with a first positive bacterial† respiratory culture finding who do not meet VAP or HCAP definition



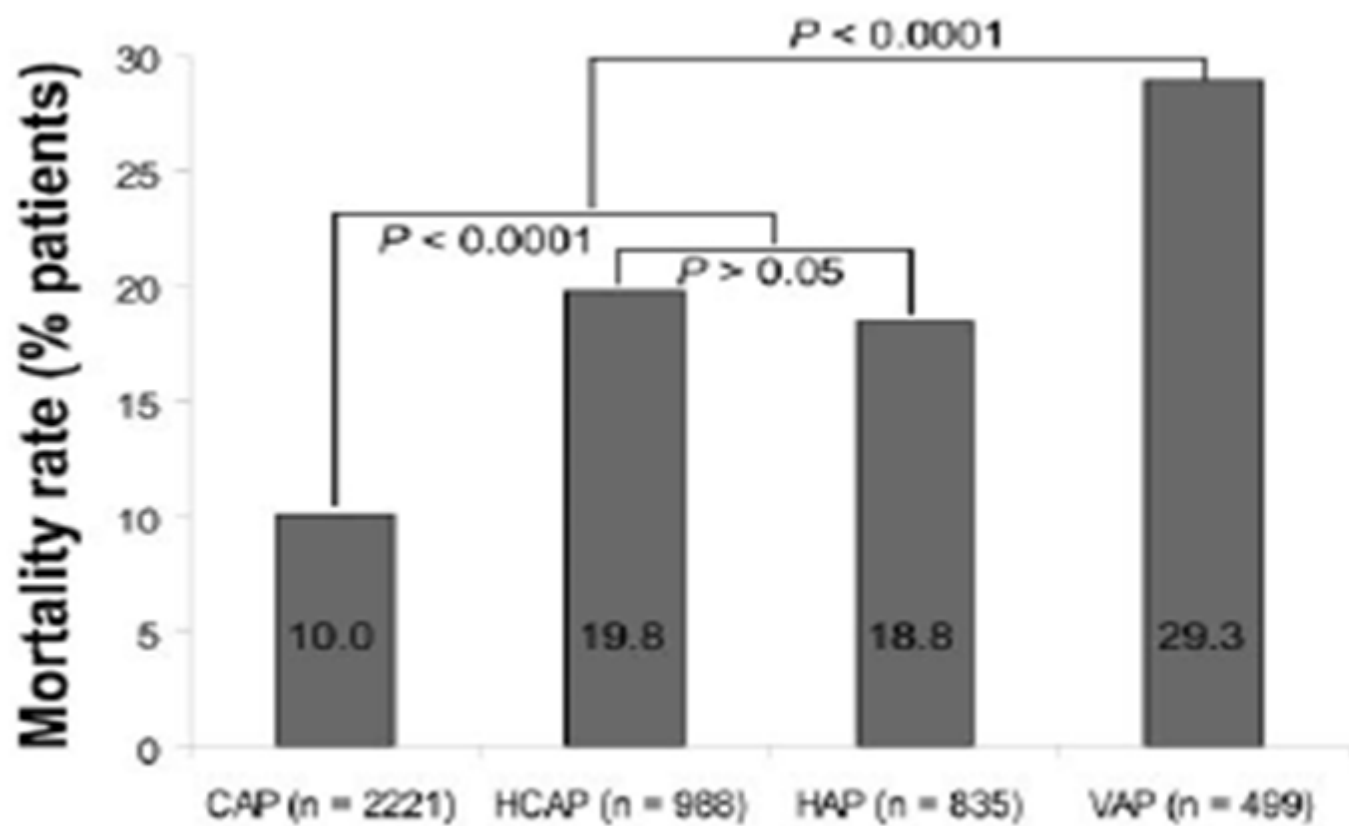


FIGURE 1. Mean mortality rates in patients with CAP, HCAP, HAP, and VAP.

**Table 4—Results of Logistic Regression Analysis for Risk Factors Associated With Mortality in Patients ( $n = 4,543$ ) With Pneumonia**

Predictors	OR	95% CI	p Value
Age	1.02	1.01–1.03	< 0.0001
Coma	1.58	1.32–1.89	< 0.0001
<i>S aureus</i>	1.58	1.32–1.89	< 0.0001
Pneumonia sepsis*	1.77	1.35–2.32	< 0.0001
Albumin < 2.4 g/dL	1.68	1.32–2.14	< 0.0001
pH arterial < 7.3	2.40	1.87–3.08	< 0.0001
Creatinine > 1.5 mg/dL	1.38	1.10–1.73	< 0.0001
WBC < 4.3 or > 19.8 $\times 10^3/\mu\text{L}$	1.50	1.22–1.84	0.0007
Platelets < 115,000/ $\mu\text{L}$	2.10	1.57–2.82	0.0001
Bands > 32%	1.64	1.18–2.27	< 0.0001
BUN > 55 mg/dL	1.54	1.16–2.05	0.0034
BUN 40 to 55 mg/dL	1.47	1.10–1.96	0.0033
Temperature < 35.6°C	1.37	1.09–1.70	0.0092
Respiration > 39 breaths/min	1.55	1.15–2.08	0.0058
Metastatic cancer	3.45	2.41–4.92	0.0039
HCAP	1.65	1.31–2.08	< 0.0001
HAP	2.07	1.63–2.64	< 0.0001
VAP	3.24	2.48–4.25	< 0.0001

\*Same pathogen found in the respiratory culture was also found in the blood culture.

# Les infections en réanimation

(GG Zhanel, 2009)

**-19 ICU canadiennes. Recueil sur 9 mois**

**-4180 isolats (poumons, urines, parties molles, sang...)**

TABLE 1. The 20 most common organisms isolated from ICUs in Canada

Ranking	Organism <sup>a</sup>	No. of isolates	% of total
1	<i>Staphylococcus aureus</i> (MSSA)	687	16.4
2	<i>Escherichia coli</i>	536	12.8
3	<i>Pseudomonas aeruginosa</i>	419	10.0
4	<i>Haemophilus influenzae</i>	329	7.9
5	CoNS/ <i>Staphylococcus epidermidis</i>	273	6.5
6	<i>Enterococcus</i> spp.	255	6.1
7	<i>Streptococcus pneumoniae</i>	244	5.8
8	<i>Klebsiella pneumoniae</i>	224	5.4
9	<i>Staphylococcus aureus</i> (MRSA)	197	4.7
10	<i>Enterobacter cloacae</i>	164	3.9
11	<i>Stenotrophomonas maltophilia</i>	108	2.6
12	<i>Serratia marcescens</i>	100	2.4
13	<i>Moraxella catarrhalis</i>	78	1.9
14	<i>Klebsiella oxytoca</i>	77	1.8
15	<i>Streptococcus pyogenes</i>	49	1.2
16	<i>Enterobacter aerogenes</i>	47	1.1
17	<i>Citrobacter freundii</i>	39	0.9
18	<i>Streptococcus agalactiae</i>	39	0.9
19	<i>Proteus mirabilis</i>	38	0.9
20	<i>Acinetobacter baumannii</i>	28	0.7
	Other <sup>b</sup>	249	6.0
Total		4,180	100.0

<sup>a</sup> CoNS, coagulase-negative staphylococci; MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*.

<sup>b</sup> Includes *Acinetobacter*, *Burkholderia*, *Bacillus*, *Citrobacter*, *Corynebacterium*, *Enterobacter*, *Haemophilus*, *Micrococcus*, *Morganella*, *Neisseria*, *Pseudomonas*, *Salmonella*, *Serratia*, *Staphylococcus*, and *Streptococcus* spp.

TABLE 2. The 10 most common organisms isolated by specimen site in ICUs in Canada

Specimen site and ranking	Organism <sup>a</sup>	No. of isolates	% of total
Respiratory specimens (n = 2,292) (54.8%)			
1	<i>S. aureus</i> (MSSA)	467	20.5
2	<i>H. influenzae</i>	323	14.1
3	<i>P. aeruginosa</i>	289	12.6
4	<i>S. pneumoniae</i>	198	8.6
5	<i>E. coli</i>	122	5.3
6	<i>K. pneumoniae</i>	122	5.3
7	<i>S. aureus</i> (MRSA)	118	5.1
8	<i>E. cloacae</i>	107	4.7
9	<i>S. maltophilia</i>	95	4.1
10	<i>M. catarrhalis</i>	78	3.4
	Other <sup>b</sup>	373	16.3
Total		2,292	100.0

Blood specimens  
(n = 738) (17.7%)

1	CoNS/ <i>S. epidermidis</i>	166	22.5
2	<i>S. aureus</i> (MSSA)	87	11.8
3	<i>Enterococcus</i> spp.	74	10.0
4	<i>E. coli</i>	73	9.9
5	<i>S. aureus</i> (MRSA)	49	6.6
6	<i>S. pneumoniae</i>	40	5.4
7	<i>P. aeruginosa</i>	33	4.5
8	<i>K. pneumoniae</i>	26	3.5
9	<i>E. cloacae</i>	24	3.3
10	<i>S. pyogenes</i>	17	2.3
	Other <sup>b</sup>	149	20.2
Total		738	100.0

Wound/tissue specimens  
(n = 581) (13.9%)

1	<i>S. aureus</i> (MSSA)	113	19.5
2	CoNS/ <i>S. epidermidis</i>	85	14.6
3	<i>Enterococcus</i> spp.	72	12.4
4	<i>E. coli</i>	58	10.0
5	<i>P. aeruginosa</i>	52	9.0
6	<i>S. aureus</i> (MRSA)	27	4.6
7	<i>K. pneumoniae</i>	25	4.3
8	<i>S. pyogenes</i>	24	4.1
9	<i>E. cloacae</i>	17	2.9
10	<i>S. marcescens</i>	15	2.6
	Other <sup>b</sup>	93	16.0
Total		581	100.0

Urine specimens  
(n = 569) (13.6%)

1	<i>E. coli</i>	283	49.7
2	<i>Enterococcus</i> spp.	78	13.7
3	<i>K. pneumoniae</i>	51	9.0
4	<i>P. aeruginosa</i>	45	7.9
5	<i>S. aureus</i> (MSSA)	20	3.5
6	<i>E. cloacae</i>	16	2.8
7	CoNS/ <i>S. epidermidis</i>	14	2.5
8	<i>C. freundii</i>	11	1.9
9	<i>K. oxytoca</i>	8	1.4
10	<i>P. mirabilis</i>	8	1.4
	Other <sup>b</sup>	35	6.2
Total		569	100.0



TABLE 5. Multidrug-resistant phenotypes in Canadian ICUs<sup>a</sup>

Organism	No. of MDR isolates/ total no. of isolates	% of MDR isolates
<i>E. coli</i>	1/536	0.2
<i>P. aeruginosa</i>	53/420	12.6
<i>K. pneumoniae</i>	0/225	0
<i>E. cloacae</i>	1/165	0.6
<i>H. influenzae</i>	0/329	0

<sup>a</sup> Multidrug resistance for gram-negative bacilli was defined as resistance to three or more of the following antimicrobials: cefepime, piperacillin-tazobactam, meropenem, amikacin or gentamicin, and ciprofloxacin.

# Et en Europe?

(Eurosurveillance, Souli M et al,2008 )

- Les facteurs de risque:
  - matériel étranger
  - ventilation mécanique
  - brûlures ou actes chirurgicaux
- Incidence en Europe (EARSS, 2002): 6,8% des hémocultures positives.
- Résistance aux carbapenems TRES VARIABLE selon les pays (EARSS 2007): 10 à 25%

# Les Pneumonies sous Ventilation Assistée: épidémiologie, facteurs de risque et traitement

(J Rello, 2005)

**-importance de la précocité du traitement..mais lequel?**

**Table 1**

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**Risk factors for oropharyngeal colonization by Gram-negative bacilli**

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Life-threatening illness	Pulmonary disease
Prolonged hospitalization/ intensive care unit stay	Smoking
Advanced age	Uraemia
Antibiotic exposure	Alcoholism
Intubation	Coma
Major surgery	Multiple organ failure
Malnutrition	Neutropenia

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# Les Pneumonies sous Ventilation Assistée: épidémiologie, facteurs de risque et traitement

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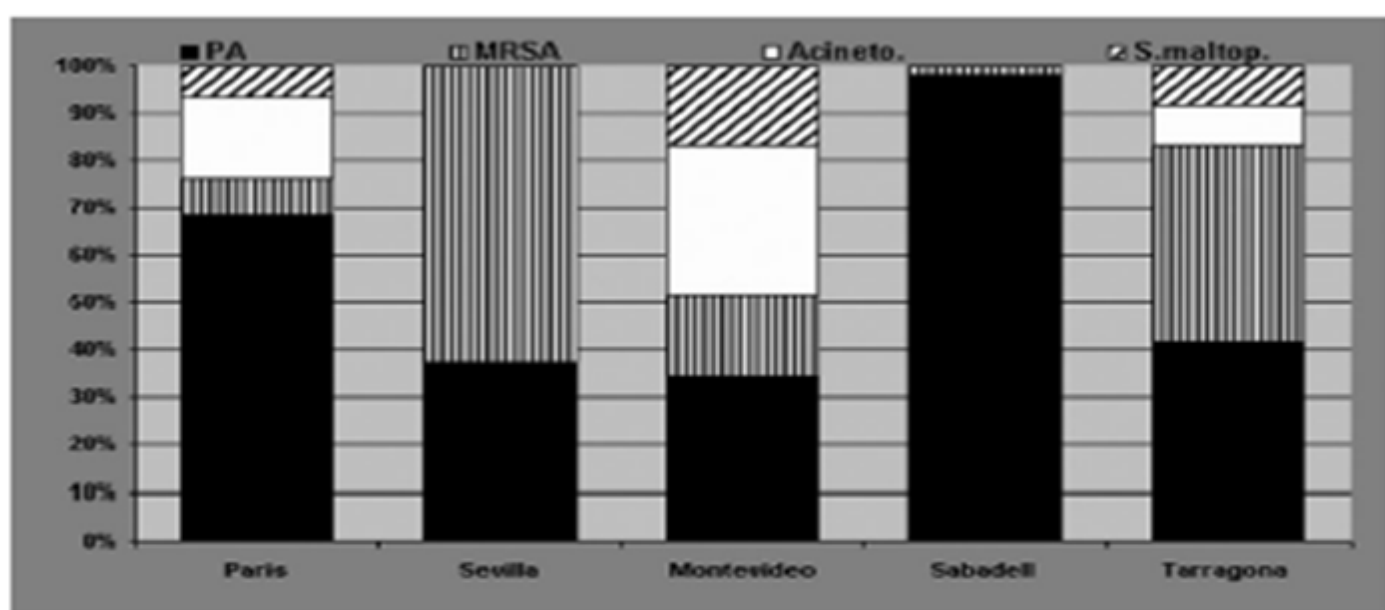
Table 2

Common causative pathogens associated with ventilator-associated pneumonia

Pathogen	Frequency [n (%)]		
	Trouillet [12] (n = 245)	Rello [10,51] (n = 301)	Ibrahim [11] (n = 420)
<i>Pseudomonas aeruginosa</i>	39 (15.9)	102 (33.9)	130 (30.9)
<i>Acinetobacter baumannii</i>	22 (9.0)	38 (12.6)	16 (3.8)
<i>Haemophilus influenzae</i>	15 (6.1)	26 (8.6)	19 (4.5)
<i>Streptococcus pneumoniae</i>	3 (1.2)	25 (8.3)	6 (1.4)
MRSA	20 (8.2)	10 (3.3)	81 (19.3)
MSSA	32 (13.1)	38 (12.6)	62 (14.7)

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.

Figure 1



Different aetiologic patterns for multiresistant pathogens in different institutions among patients who were mechanically ventilated for more than 7 days and had prior antibiotic exposure. Acineto., *Acinetobacter baumannii*; MRSA, methicillin-resistant *Staphylococcus aureus*; PA, *Pseudomonas aeruginosa*; S.maltop., *Stenotrophomonas maltophilia*.

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## The Tarragona strategy

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Point	Details
1	Antibiotic therapy should be started immediately
2	Antibiotic choice can be targeted, in some cases, based on direct staining
3	The prescription should be modified in accordance with microbiologic findings
4	Prolonging antibiotic treatment does not prevent recurrence
5	Patients with chronic obstructive pulmonary disease or 1 week of intubation should receive combination therapy because of the risk for ventilator-associated pneumonia caused by <i>Pseudomonas aeruginosa</i>
6	Methicillin-resistant <i>Staphylococcus aureus</i> is not anticipated in the absence of antibiotic exposure, whereas methicillin-sensitive <i>S aureus</i> should be strongly suspected in comatose patients
7	Therapy against yeast is not required, even in case of colonization with <i>Candida</i> spp.
8	Vancomycin administration for Gram-positive pneumonias is associated with very poor outcome
9	The specific choice of agent should avoid the regimen to which each patient has previously been exposed
10	Guidelines should be updated regularly and customized in accordance with local patterns

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Modified from Sandiumenge and coworkers [41].

**Quels sont les risques de  
résistance?**

# Facteurs de risques de BMR

**N=639 HCAP**

**Bactéries résistantes: 289**

**4 variables indépendantes prédictives:**

**-hospitalisation récente**

**-maison de retraite**

**-hémodialyse**

**-réanimation**

Schorr et coll, 2008



# Variabilité de la résistance

(Giske CG, 2008)

TABLE 3. Prevalence of MDR among *P. aeruginosa* strains in various parts of the world

Region	Period	Setting	Resistance (%)	Reference
North America				
United States	2001	ICU/non-ICU	9.1/7.0	35
United States	2002	ICU	14	35
United States	2003	Nosocomial infections	9.9	36
South America	1997–1999	Nosocomial infections	8.2	24
18 sites				
Europe	1997–1999	Nosocomial infections	4.7	24
12 to 23 sites				
33 ICUs	1997–2000	ICU	3–50	29
Asia/Pacific	1997–1999	Nosocomial infections	1.6	24
17 sites				
Japan	2001	Nosocomial infections	2.8	74
Malaysia	2005	Nosocomial infections	6.9	62

-La multirésistance augmente la mortalité et la durée de séjour

# Conclusion (1)

**Kollef MH, 2005**

**Paramythiotou, 2004**

**-Le traitement anti-pseudomonas précoce doit être administré aux seuls patients présentant des facteurs de risque**

**-La « désescalade » doit être faite chaque fois que possible**

**-L'usage approprié et responsable des antibiotiques en réanimation peut seul permettre de maintenir l'activité des anti-pseudomonas disponibles.**

# Conclusion (2)

**-La littérature sert à alerter**

**-Rien ne remplace:**

**\*l'obstination à documenter une infection  
(intérêt épidémiologique et thérapeutique)**

**\*la connaissance de l'épidémiologie locale, ou  
loco-régionale**

**\*un référentiel local adapté à l'établissement**

**\*un traitement précoce réévalué à 48h**

**Study population.** In the 4 participating centers, a total of 4114 unique patient gram-negative rods (GNRs) were isolated from cultures of blood specimens obtained at admission (i.e.,  $\leq 48$  h after hospital admission). *Escherichia coli* was the most common isolate (51%; range, 41%–63%), followed by *Klebsiella* species (16%; range, 12%–21%), *P. aeruginosa* (6.8%; range, 5.3%–8.4%), *Enterobacter* species (4.9%; range, 2.7%–7.8%), and *Proteus* species (5%; range, 2.7%–6.2%). *Serratia*, *Morganella*, and *Citrobacter* species together contributed 5% of the cases. The incidence of *P. aeruginosa* bacteremia was calculated to be 5 cases per 10,000 hospital admissions.