Réévaluation de l'antibiothérapie à J2-J3

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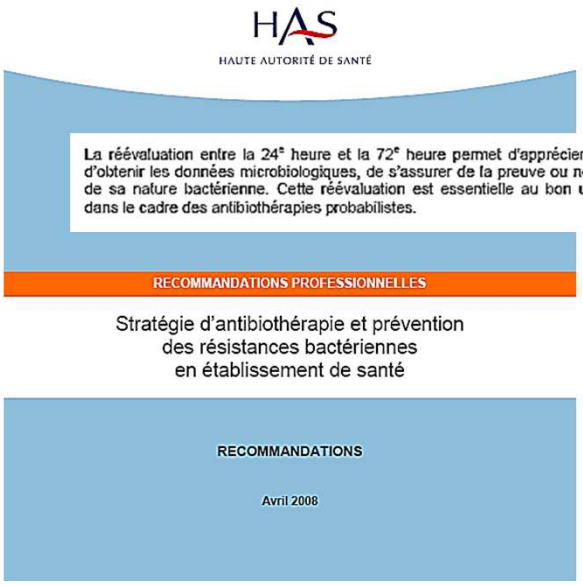
Pourquoi réévaluer à J2-J3 ?

- Recommandations
- Efficacité
- Acceptation
- Bénéfique (ou au moins pas délétère)
- Plus facile

Réévaluation J2-J3 : recommandations



Préserver l'efficacité des antibiotiques à l'hôpital

3 volets, 10 messages clés

2008
10 Vacciner
9 Prévenir la transmission croisée
8 Limiter les dispositifs invasifs

2007
7 Modalités d'administration appropriées
6 Savoir dire non aux associations
5 Bien choisir le traitement initial

2006
4 Savoir arrêter un traitement
3 Ré-évaluer la prescription à 48 heures
2 Traiter l'infection, pas la colonisation
1 Traiter les seules infections bactériennes

Prévenir les infections

Mieux utiliser les antibiotiques

Savoir dire non aux antibiotiques

Core Elements of Hospital Antibiotic Stewardship Programs (CDC)

Table 1. Core Elements of Hospital Antibiotic Stewardship Programs

Leadership commitment	Dedicating necessary human, financial, and information technology resources
Accountability	Appointing a single leader responsible for program outcomes and accountable to an executive-level or patient quality–focused hospital committee. Experience with successful programs shows that a physician or pharmacist leader is effective
Drug expertise	Appointing a single pharmacist leader responsible for working to improve antibiotic use
Action	Implementing at least 1 recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (ie, antibiotic "time-out" after 48 h)
Tracking	Monitoring process measures (eg, adherence to facility-specific guidelines, time to initiation or de-escalation), impact on patients (eg, *Clostridium difficile* infections, antibiotic-related adverse effects and toxicity), antibiotic use and resistance
Reporting	Regular reporting of the above information to doctors, nurses, and relevant staff
Education	Educating clinicians about disease state management, resistance, and optimal prescribing

Source: Centers for Disease Control and Prevention [4].

Pollack LA. et al, Clin Infect Dis 2014

Prescription appropriée

- **Indication**
- **Molécule**
- **Posologie**
- **Modalité d'administration**
- **Durée**
- **Efficacité, tolérance**
- Coût

Table 1. Core Principles of Antimicrobial Prescribing

- Prescribe the correct antimicrobial promptly at the correct dose for the correct duration based on local and national treatment guidelines.
- Order appropriate microbiologic and other diagnostic testing.
- Document the dose, duration, and indication for all antimicrobial prescriptions.
- Conduct periodic review, or antimicrobial "time-out" (eg, ≥48 hours), of antimicrobial prescription(s) and diagnostic studies, with goal of streamlining to most appropriate choice and transitioning any intravenous antimicrobials to oral.
- Remain aware of local antimicrobial resistance patterns.

Adapted from the Centers for Disease Control and Prevention. Core Elements of Hospital Antibiotic Stewardship Programs. 2014. Available at http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html. Accessed 26 January 2015.

Audit and Feedback to Reduce Broad-Spectrum Antibiotic Use among Intensive Care Unit Patients: A Controlled Interrupted Time Series Analysis

- 3 ICU, 48 lits
- Audit : 3 jours d'ATB spectre large (C3G, pénicillines + inhibiteurs, carbapénèmes, quinolones, vancomycine)
- EMA : binôme pharmacien/infectiologue
- Sur 12 mois : 717 prescriptions, modification 34%, compliance 82%
- Modifications : arrêt 56%, changement 26%, autres 8%

Elligsen M. et al, Infect Control Hosp Epidemiol 2012

Audit and Feedback to Reduce Broad-Spectrum Antibiotic Use among Intensive Care Unit Patients: A Controlled Interrupted Time Series Analysis

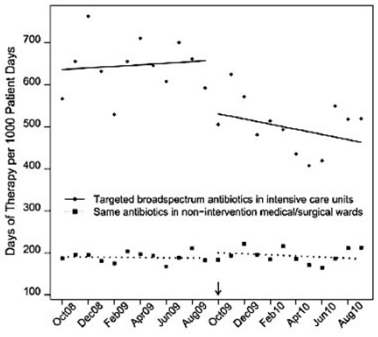


FIGURE 1. Monthly use of broad-spectrum antibiotics in critical care patients and control medical and surgical ward patients. This autoregressive integrated moving average model demonstrated a significant decrease of −119 days of therapy per 1,000 patient-days (standard error, 37.9; $P = .0054$) in the use of targeted antimicrobials immediately after the audit and feedback intervention was implemented in October 2009. The use of these same targeted antimicrobials did not change in those medical and surgical units that did not receive the audit and feedback intervention (dotted line).

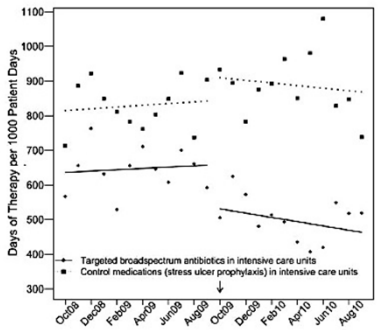


FIGURE 2. Monthly use of broad-spectrum antibiotics and control medications (stress ulcer prophylaxis) in critical care patients. The reduction in targeted antibiotics is once again displayed (solid line), this time in comparison with the use of a control medication. Use of stress ulcer prophylaxis (dotted line) exhibited a nonsignificant immediate increase of 71.0 days of therapy per 1,000 patient-days after the antibiotic stewardship intervention (standard error, 70.3; $P = .32$).

Elligsen M, Infect Control Hosp Epidemiol 2012

Audit and Feedback to Reduce Broad-Spectrum Antibiotic Use among Intensive Care Unit Patients: A Controlled Interrupted Time Series Analysis

Autres effets :

• Consommation globale :
1134 -> 985 j/1000 pts (p=0.003)

• Mortalité :
13.1% -> 14.4% (p=0.20)

• Coût ATB :
- 95 000 $ (-23.7%)

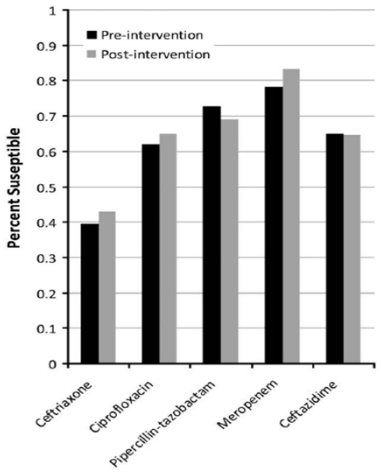


FIGURE 3. Overall susceptibility of gram-negative bacteria isolated from intensive care unit patients during the preintervention period versus during the postintervention period. The increase in meropenem susceptibility (from 78.2% to 83.4% of isolates) was statistically significant ($P = .03$).

Elligsen M. et al, Infect Control Hosp Epidemiol 2012

Implementation of an antimicrobial stewardship program on the medical-surgical service of a 100-bed community hospital

Table 3 Characteristics of 313 AST audits with one or more recommendations

Recommendation category	Number of audits	Implemented recommendations	Implementation rate (%)
All	313	234	75
Discontinue all agent(s)	115	85	74
De-escalate[a]	65	53	82
Limit duration[b]	21	13	62
Consult infectious diseases	19	16	84
Optimize dose	14	7	50
Broaden[c]	5	3	60
Convert parenteral to oral[d]	3	3	100
More than 1 category	71	54	76

1h/twice a week
ATB > 2 days

- DDD/100 admissions - 22% (P = .006)
- Antimicrobial acquisition cost /admission - 32% (P = .013)

Storey *et al. Antimicrobial Resistance and Infection Control* 2012, **1**:32

Pourquoi J2-J3 ?

- La situation clinique s'est le plus souvent éclaircie … et le conseil + facile
- 50% des prescriptions sont associées à une documentation bactériologique
- Rarement disponible avant J2

Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study

Rachida el Moussaoui, Corianne A J M de Borgie, Peterhans van den Broek, Willem N Hustinx, Paul Bresser, Guido E L van den Berk, Jan-Werner Poley, Bob van den Berg, Frans H Krouwels, Marc J M Bonten, Carla Weenink, Patrick M M Bossuyt, Peter Speelman, Brent C Opmeer, Jan M Prins

Contexte

- **Pays-Bas, 2000-2003, 9 CHU**
- **PAC adultes, clinique + radiologique, hospitalisées**
- **Exclusion**
  - **Immunodéprimés (VIH, neutropénie)**
  - **PAC sévères (PSI > 110, réa, détresse respi)**
  - **PNP atypiques, empyèmes, etc.**

Intervention

- **Amoxicilline i.v.**
- Si évolution favorable à 72 h (T < 38°C, relais PO)

Randomisation (J3-J8) => **placebo** ou **amoxicilline** PO, 750 mg x 3/j

El Moussaoui R et al. British Med J 2006

Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study

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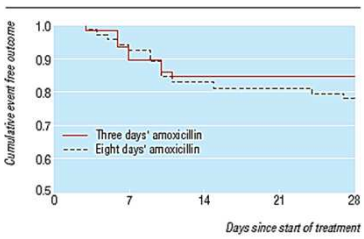


Fig 3 Proportion of patients considered clinical successes in intention to treat population. Day 3=day of randomisation

Table 2 Clinical, bacteriological, and radiological outcomes for adults with community acquired pneumonia randomised to oral placebo or oral amoxicillin for five days after three days' amoxicillin treatment. Values are numbers (percentages) unless stated otherwise

Outcomes	Three day treatment group	Eight day treatment group	Difference (95% CI)
Day 10:			
Clinical cure (per protocol analysis)	50/54 (93)	56/60 (93)	0.1 (−9 to 10)
Clinical cure	50/56 (89)	56/63 (89)	0.4 (−11 to 12)
Bacteriological success	22/25 (88)	19/20 (95)	−7 (−23 to 9)
Radiological success	48/56 (86)	52/63 (83)	3 (−10 to 16)
Day 28:			
Clinical cure (per protocol analysis)	47/52 (90)	49/56 (88)	2 (−9 to 15)
Clinical cure	47/56 (84)	49/63 (78)	6 (−8 to 20)
Bacteriological success	20/25 (80)	15/20 (75)	5 (−20 to 30)
Radiological success	48/56 (86)	50/63 (79)	6 (−7 to 20)

All analyses were by intention to treat, unless indicated otherwise.

bmj.com 2006;332:1355

Effectiveness of early switch from intravenous to oral antibiotics in severe community acquired pneumonia: multicentre randomised trial

Patients were randomised to the intervention group when clinically stable:

- respiratory rate < 25/min,
- oxygen saturation > 90% or arterial oxygen pressure > 55 mm Hg,
- haemodynamically stable,
- > 1° C decrease in temperature in case of fever,
- absence of mental confusion,
- and the ability to take oral drugs

Oosterheert JJ et al, Br Med J 2006

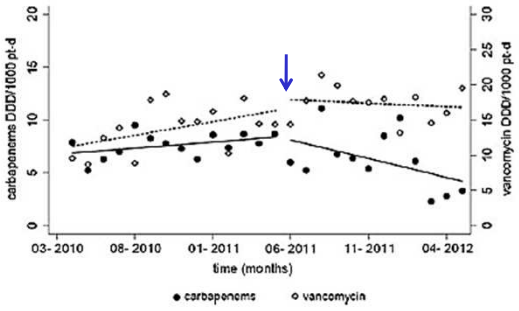
Effectiveness of early switch from intravenous to oral antibiotics in severe community acquired pneumonia: multicentre randomised trial

Table 3 Outcomes in multicentre randomised trial of early switch from intravenous to oral antibiotics in severe community acquired pneumonia. Intention to treat analysis. Values are number of patients (percentage) unless stated otherwise

Clinical outcome	Treatment group		Mean difference (95% CI)
	Intervention (n=132)	Control (n=133)	
Death after day 3	5 (4)	8 (6)	2% (–3% to 8%)
Clinical cure	110 (83)	113 (85)	2% (–7% to 10%)
Clinical failure:	22 (17)	20 (15)	–2% (–10% to 7%)
Clinical cure but still in hospital	9 (7)	6 (5)	–2% (–4% to 8%)
Clinical deterioration	8 (6)	6 (5)	–1% (–4% to 7%)
Death	5 (4)	8 (6)	2% (–3% to 8%)
Clinical deterioration and death	13 (10)	14 (11)	1% (–1% to 8%)
Mean (SD) length of hospital stay (days)	9.6 (5.0)	11.5 (4.9)	1.9 (0.6 to 3.2)
Mean (SD) duration of intravenous treatment (days)	3.6 (1.5)	7.0 (2.0)	3.4 (2.8 to 3.9)

Oosterheert JJ et al, Br Med J 2006

Contrôle de la prescription des carbapénèmes



82% documenté
64% probabiliste

Fig. 1 Intervention effect on carbapenems and vancomycin consumptions. Carbapenems consumption is represented by *filled symbols* and vancomycin consumption is represented by *open symbols*. Consumption trends are represented by *lines*. The diffusion period was from May to July 2011. Only carbapenems consumption was affected by the intervention with a direct and sustained decreasing effect: (1) change in mean (−1.66 DDD/1,000 pt-d, p=0.048) corresponding to the global consumption change between the pre- and intervention periods; (2) change in level (−5.34 DDD/1,000 pt-d, p=0.049) corresponding to the consumption change at the start of the intervention; (3) change in slope (−2.66 DDD/1,000 pt-d, p=0.02) corresponding to the consumption change during the intervention period

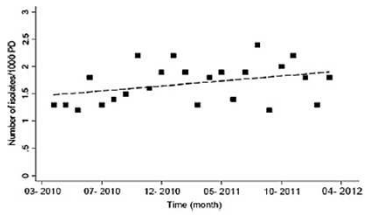


Fig. 2 ESBL-PE evolution among study. Trend (*dashed line*) to a linear increase in the monthly incidence of ESBL-PE (0.02/1,000 pt-d; p=0.093)

Delory T. et al, Eur J Clin Microb Infect Dis 2012

Réévaluation des prescriptions de carbapénèmes

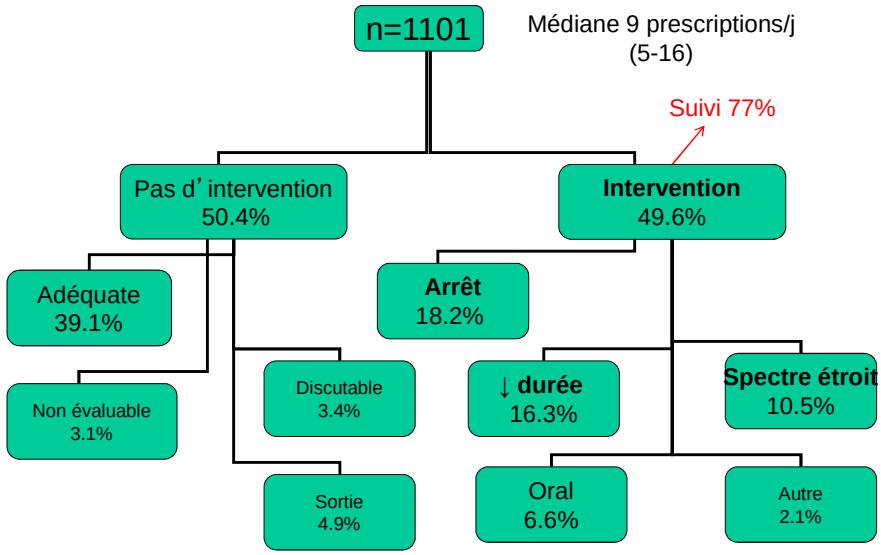
Réévaluation	Globale, nb (%)	Service, nb (%)	Référent, nb (%)
Désescalade*	176 (52.2)	63 (18.7)	113 (33.5)
Réduction durée	24 (7.1)	0 (0)	24 (7.1)
Relai per-os	20 (6.0)	15 (14.5)	5 (1.5)
Arrêt	51 (15.1)	32 (9.5)	19 (5.6)
Autre	7 (2.1)	0 (0)	7 (2.1)
Total	258 (76.6)	95 (28.2)	163 (48.4)

* céfoxitine, céfotaxime/ceftriaxone, céfépime, n=83 (47.2%); pip/taz, n= 48 (27.3%)

76.6% de modifications thérapeutiques, délai médian de 2 jours [1;4]

Delory T, Eur J Clin Microb Infect Dis 2012

Réévaluation des antibiothérapies entre J3 et J5 (médecine et chirurgie)



Lesprit P et al, Eur J Clin Microbiol Infect Dis 2012

Unsolicited post-prescription antibiotic review in surgical and medical wards: factors associated with counselling and physicians' compliance

Table 2 Multivariate analysis of factors associated with an IDP intervention for counselling

	Adjusted odds ratio	95 % confidence interval	*p*-value
Broad-spectrum antibiotics[a]	1.03	0.76–1.39	0.84
Antibiotic combination	5.27	1.80–15.45	**0.002**
No clinically documented infection	4.98	2.81–8.82	**<0.001**
Microbiological documentation	2.04	1.51–2.75	**<0.001**

Lesprit P. et al, Eur J Clin Microbiol Infect Dis 2012

Clinical impact of unsolicited post-prescription antibiotic review in surgical and medical wards: a randomized controlled trial.

TABLE 3. Duration of antibiotic therapy in the two study groups, overall and for the antibiotic regimen subgroups

Median duration, days (IQR)	Control group *N* = 377	Intervention group *N* = 376	p value
Total antibiotic course	7 (5–9)	6 (4–9)	<0.0001
Broad-spectrum antibiotic[a]	4 (0–7)	2 (0–5)	0.0003
Narrow to intermediate-spectrum antibiotic[a]	4 (0–8)	5 (0–7)	0.13
Intravenous administration	4 (0–8)	3 (0–6)	0.004
Oral therapy	4 (0–7)	4 (0–7)	0.84

aAntibiotic spectrum was classified as narrow to intermediate (amoxicillin/clavulanate or aminoglycosides or glycopeptides-linezolid) or broad spectrum (third-generation cephalosporins, piperacillin/tazobactam, imipenem or fluoroquinolones).

TABLE 4. Clinical outcomes of patients in the two study groups

	Control group *N* = 377	Intervention group *N* = 376	p value
60 days in-hospital mortality, *n* (%)	38 (10.1)	37 (9.8)	0.91
ICU admission within 7 days of randomization, *n* (%)	6 (1.6)	7 (1.9)	0.78
New course of antibiotic therapy, *n* (%)	25 (6.6)	17 (4.5)	0.21
Antibiotic treatment for relapsing infection, *n* (%)	30 (7.9)	13 (3.4)	0.01
Length of stay, days (median, IQR)			
Overall population	15 (9–27)	15 (9–25)	0.95
Community-acquired infection	6 (3–14)[a]	5 (3–10)[b]	0.06

a260 patients.
b249 patients.

Lesprit P. et al, Clin Microbiol 2012

Post-prescription review improves the in-hospital antibiotic use: a multicenter randomized controlled trial

P. Lesprit[1], A. de Pontfarcy[1], M. Esposito-Farese[2], H. Ferrand[1], J.L. Mainardi[3], M. Lafaurie[4], P. Parize[3], C. Rioux[5], F. Tubach[2] & J.C. Lucet[5]

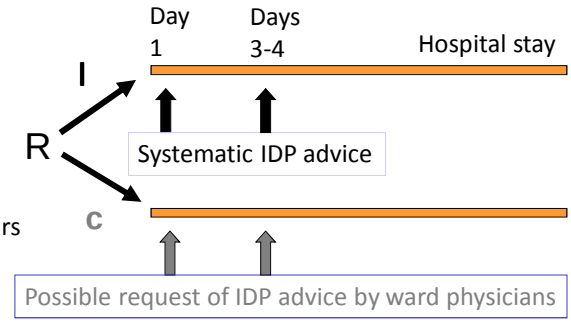
[1]Unité de Contrôle et Prévention de l'Infection, Hôpital Henri Mondor, Créteil; [2]Département d'Epidémiologie Biostatistique et Recherche Clinique, Hôpital Bichat-Claude Bernard, Paris; [3]Service de Microbiologie Clinique, Hôpital Européen Georges Pompidou: [4]Service des Maladies Infectieuses et Tropicales, Hôpital Saint-Louis, Paris;

[5]Unité de Contrôle de l'Infection, Hôpital Bichat-Claude Bernard, Paris- all in France

Eligibility criteria and study design

Setting
8 wards of 4 hospitals

Patients (n=246)*
- Aged ≥18 years
- Antibiotic prescribed by ward physician ≤ 24 hrs
- Surgery or medical
- Not prophylaxis for ≤ 24 hrs
- Not prophylaxis for OI



*All patients hospitalized in participating wards receiving antibiotic therapy at admission or during their stay were assessed for eligibility
Inclusion period consisted in 2 periods of 2 weeks separated by 6 months

Appropriateness of therapy

Variable	**Intervention group**	**Control group**	P
D1			
Antibiotic indicated	89 (72.4)	96 (78.0)	0.30
Optimal drug	61/89 (69.5)	62/96 (64.6)	0.57
Optimal administration	81/89 (91.0)	87/96 (90.6)	0.93
Optimal dosing	68/89 (76.4)	78/96 (81.2)	0.42
D3-4			
Antibiotic indicated	109 (88.6)	97 (78.9)	**0.04**
Optimal drug	82/105 (78.1)	61/99 (61.6)	**0.01**
Optimal administration	77/81 (95.1)	79/87 (90.8)	0.28
Optimal dosing	74/81 (91.6))	77/87 (88.5)	0.54
Optimal duration	72 (58.5)	55 (44.7)	**0.03**
Median duration (IQR)	7 (3-14)	10 (7-16)	**0.003**

Clinical impact

	Intervention group (n=123)	Control group (n=123)	P
Length of stay, median (IQR)	4 (2-6)	4 (2-6)	0.55
In-hospital mortality (%)	1 (0.8)	0 (0)	1
Clinical improvement at D3 (%)	99 (80.5)	95 (77.2)	0.53
Clinical improvement at discharge (%)	60/68 (88.2)	51/63 (80.9)	0.25

Rôle du médecin référent en antibiothérapie (circulaire du 2 mai 2002)

- Conseil sur le bon usage des antibiotiques sur avis sollicité par les prescripteurs
- Interventions sur alertes pharmacie, microbiologie
- Actions de formation sur le bon usage
- Diffusion des recommandations locales et du suivi des consommations d'antibiotiques
- Actions d'évaluation (audits de pratique)

Suivi des bactériémies

- Hôpital Bichat, 512 épisodes
- Suivi prospectif, 18 mois, tous services sauf réanimation
- Avant EMA : antibiothérapie

efficace/appropriée	42,8%
efficace/inappropriée	26,5%
inefficace/absente	30,7%

- Avis EMA : 94%
- Facteurs associés à une antibiothérapie inappropriée

Infection nosocomiale	RR 1.45 (1.22–1.73)
Infection associée aux soins	RR 1.59 (1.30–1.95)
Cathéter	RR 1.64 (1.33–2.03)
BMR	RR 1.38 (1.17–1.61)

Diamantis S, Eur J Clin Microbiol Infect Dis 2012

The winners ….

Le maréchal lance son interjection favorite « Allons-y » (interjection caractéristique de son langage fier et énergique qui l'a rendu fameux dans les états-majors)