5° JARI
Journée de Formation

INSTITUT MAURICE RAPIN

PCT EN PRATIQUE: UTILE POUR RÉDUIRE LES DURÉES DE TRAITEMENT ?

(HORS RÉANIMATION)

P. HAUSFATER

Hôpital Pitié-Salpêtrière et Université Pierre et Marie Curie UPMC-Paris 06, Paris

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6ème journée des biomarqueurs Pitié-Tenon

Le vendredi 20 mai 2016

jepu.anesthesie@psl.aphp.fr 01 42 17 72 42

Avons-nous une utilisation rationnelle des ATB ?

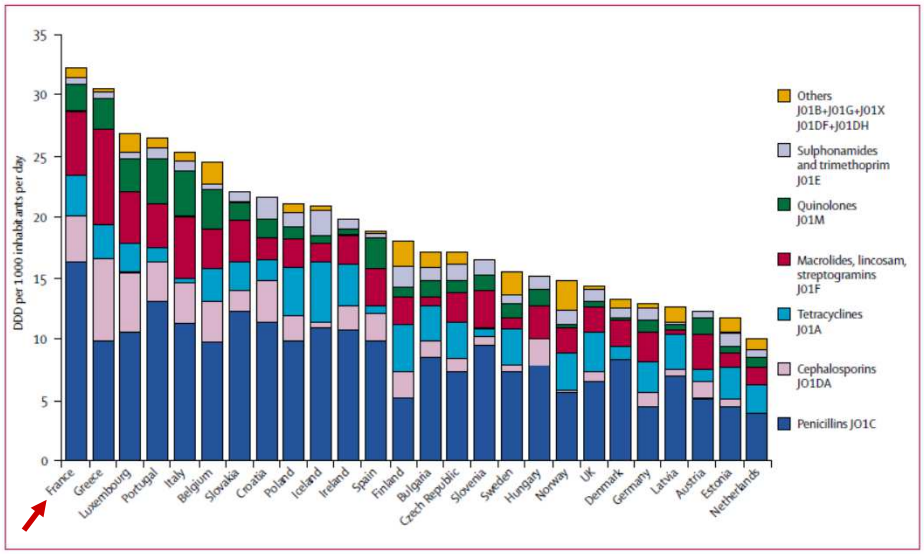


Figure 1: Total outpatient antibiotic use in 26 European countries in 2002

Lancet 2005; 365: 579–87

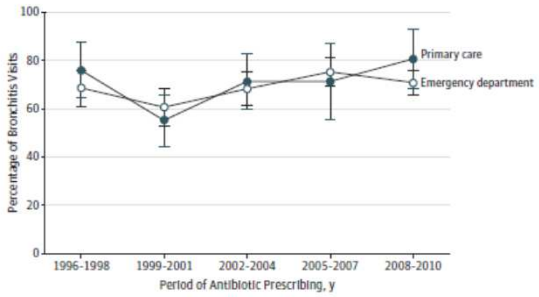
Letters

RESEARCH LETTER

Antibiotic Prescribing for Adults With Acute Bronchitis in the United States, 1996-2010

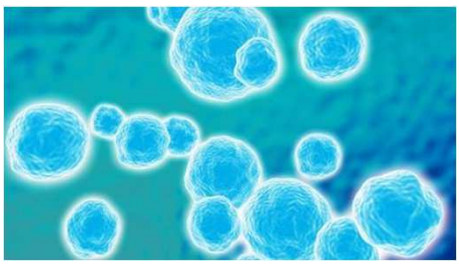
JAMA May 21, 2014 Volume 311, Number 19

Figure. Antibiotic Prescribing for Acute Bronchitis in the United States by Site of Care, 1996-2010



No. of sampled visits					
Primary care	168	167	185	217	234
Emergency department	293	401	499	462	527

« The world is headed for a post-antibiotic era, in which common infections and minor injuries which have been treatable for decades can once again kill »



World Health Organization

La PCT biomarqueur d'infection systémique

- PCT: pro-hormone de la calcitonine
- Sujets sains: < 0,1 µg/L
- [Serum] augmentent spécifiquement au cours inf bact systémiques
- Valeurs normales ou faiblement élevées au cours inf virales ou autres processus inflammatoires (≠ CRP)
- Marqueur précoce de sepsis:
  - 3 h après injection endotoxine chez l'homme
- t½: 24h
- Valeur absolue corrélée à la sévérité ++

ARTICLES

Effect of procalcitonin-guided treatment on antibiotic use and outcome in lower respiratory tract infections: cluster-randomised, single-blinded intervention trial

Mirjam Christ-Crain, Daiana Jaccard-Stolz, Roland Bingisser, Mikael M Gencay, Peter R Huber, Michael Tamm, Beat Müller

- 243 patients suspects d 'IRB aux urgences
  - 119 pts: prise en charge « standard »
  - 124 patients: traitement ATB guidé par résultat PCT:
    - PCT< 0,1: pas d 'ATB
    - PCT <0,25: pas d 'ATB recommandé
    - PCT > 0,25: ATB recommandés
    - Méthode dosage: Kryptor

Lancet 2004; 363: 600–07.

ARTICLES

Effect of procalcitonin-guided treatment on antibiotic use and outcome in lower respiratory tract infections: cluster-randomised, single-blinded intervention trial

Mirjam Christ-Crain, Daiana Jaccard-Stolz, Roland Bingisser, Mikael M Gencay, Peter R Huber, Michael Tamm, Beat Müller

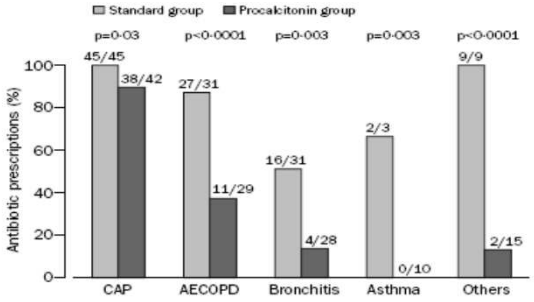


Figure 2: **Antibiotic prescriptions in different subgroups of lower respiratory tract infection comparing standard group and procalcitonin group**
CAP=community-acquired pneumonia. AECOPD=acute exacerbations of COPD.

PCT threshold: 0.25 ng/ml

Lancet 2004; 363: 600–07

PCT et durée ATB dans pneumonies

- 302 CAP, randomisation 2 groupes (groupe PCT, groupe contôle)
- Dosage PCT à J0, J4, J6, J8 *(+ 6-24h après T0 pour pts avec PCT<0.25)*
  - PCT< 0,1: pas d 'ATB
  - PCT <0,25: pas d 'ATB recommandé
  - PCT > 0,25: ATB recommandés
- Groupe PCT:
  - Réduction de 50% durée d'exposition totale aux ATB
  - Réduction initiation ATB (85% vs 99%, *p<0.001)*
  - Réduction durée tt ATB (médiane 5j *vs* 12 j, *p<0.001*)

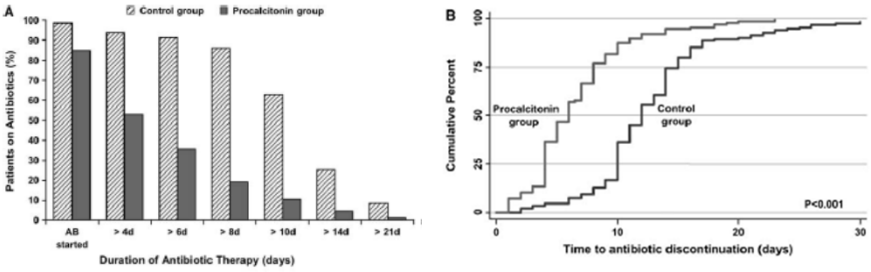
Christ-Crain et al., Am J Resp C.Care Med 2006

Procalcitonin Guidance of Antibiotic Therapy in Community-acquired Pneumonia

A Randomized Trial

Mirjam Christ-Crain, Daiana Stolz, Roland Bingisser, Christian Müller, David Miedinger, Peter R. Huber, Werner Zimmerli, Stephan Harbarth, Michael Tamm, and Beat Müller

Am J Respir Crit Care Med Vol 174. pp 84–93, 2006



Réduction de 65% de la durée de traitement ATB des PAC si guidé par la PCT

(12.9 versus 5.8 jours)

ORIGINAL INVESTIGATION

Procalcitonin-Guided Antibiotic Use vs a Standard Approach for Acute Respiratory Tract Infections in Primary Care

Matthias Briel, MD; Philipp Schuetz, MD; Beat Mueller, MD; Jim Young, PhD; Ursula Schild, RN; Charly Nusbaumer, PhD; Pierre Périat, MD; Heiner C. Bucher, MD, MPH; Mirjam Christ-Crain, MD

Arch Intern Med. 2008;168(18):2000-2007

Table 2. Summary of Primary and Secondary Outcomes

Outcome	PCT-Guided Therapy Group	Difference (95% CI) Between PCT-Guided and Standard Therapy Groups	Standard Therapy Group
Primary End Points[a]			
Per protocol analysis	n=231		n=224
Days with RAs, mean (SD)	8.7 (3.9)		8.7 (3.8)
Unadjusted difference in days (95% CI)		0.01 (–0.7 to 0.7)	
Adjusted difference in days (95% CI)[b]		0.1 (–0.5 to 0.8)	
Intention-to-treat analysis	n=232		n=226
Days with RAs, mean (SD)	8.7 (3.9)		8.6 (3.9)
Unadjusted difference in days (95% CI)		0.1 (–0.6 to 0.8)	
Adjusted difference in days (95% CI)[b]		0.2 (–0.4 to 0.9)	
Secondary End Points[c]			
Prescribed antibiotics, No. (%)	58 (25)		219 (97)
Percentage difference (95% CI)		–72 (–78 to –66)	
Adjusted odds ratio (95% CI)[b]		0.01 (0.002 to 0.02)	
Days with antibiotics, mean (SD)[d]	6.2 (2.5)		7.1 (2.2)
Adjusted difference in days (95% CI)[b]		–1.0 (–1.7 to –0.4)	
Degree of discomfort from infection score at 14 d, mean (SD)[e]	1.9 (2.7)		1.1 (1.9)
Adjusted difference in score (95% CI)[b]		0.8 (0.4 to 1.2)	
Days with adverse effects within 14 d, mean (SD)[f]	2.3 (4.6)		3.6 (6.1)
Adjusted difference in days (95% CI)[b]		–1.1 (–2.1 to –0.1)	
Days of work missed within 14 d, mean (SD)[g]	4.9 (4.6)		4.8 (4.2)
Adjusted difference in days (95% CI)[b]		0.3 (–0.6 to 1.2)	
Patients with any symptoms of ongoing or relapsing infection at 28 d, No. (%)	69 (30)		67 (30)
Adjusted odds ratio (95% CI)[b]		1.0 (0.7 to 1.5)	

Infection — Clinical and Epidemiological Study

Effect of Procalcitonin-Guided Treatment in Patients with Infections: a Systematic Review and Meta-Analysis

H. Tang, T. Huang, J. Jing, H. Shen, W. Cui

Infection 2009; 37: 497–507

Figure 2. Forrest plot of pooled odds ratios (OR) for antibiotics prescribed from four randomized trials. CI: confidence interval; PCT procalcitonin.

ATB Initiation

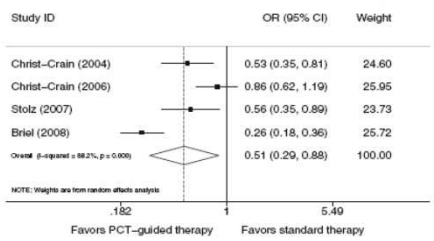
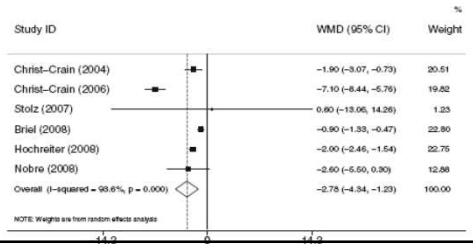


Figure 3. Forrest plot of pooled weighted mean difference for duration of antibiotic therapy from six randomized trials. WMD: Weighted mean difference. CI: confidence interval.

ATB duration



ORIGINAL INVESTIGATION

Effectiveness and Safety of Procalcitonin-Guided Antibiotic Therapy in Lower Respiratory Tract Infections in "Real Life"

An International, Multicenter Poststudy Survey (ProREAL)

Arch Intern Med. 2012;172(9):715-722

« Antibiotic therapy duration was significantly shorter if the PCT algorithm was followed compared with when it was overruled (**5.9 vs 7.4 days**; difference, −1.51 days; 95% CI, −2.04 to −0.98; *P*.001) »

Table 2. Predictors of Antibiotic Therapy Duration From Multivariable Regression

Predictor	Regression Coefficient (95% CI)[a]	*P* Value
Compliance	−1.51 (−2.04 to −0.98)	<.001
CAP (vs bronchitis)	4.4 (3.7 to 5.1)	<.001
France (vs Switzerland)	2.22 (1.41 to 3.04)	<.001
Outpatient treatment	−2.41 (−3.23 to −1.58)	<.001
PSI classes	0.21 (0.07 to 0.35)	.003
Renal failure[b]	1.21 (0.63 to 1.79)	<.001
Previous experience with algorithm	−0.71 (−1.25 to −0.17)	.01
Multilobar pneumonia	1.18 (0.16 to 2.2)	.02

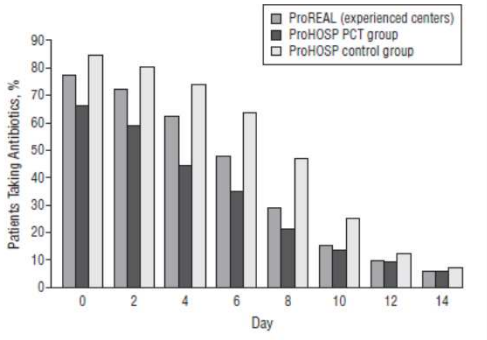


Figure 2. Antibiotic exposure compared between real-life experience (ProREAL) and a randomized controlled trial (ProHOSP procalcitonin [PCT] group and control group) (for centers participating in both).

Table 3. Safety of Initial Withholding of Antibiotic Therapy in Patients With Low PCT Values

Variable	Adjusted OR (95% CI)[a]	*P* Value
In-hospital complications[b]	0.627 (0.299 to 1.314)	.22
In-hospital mortality	1.048 (0.243 to 4.513)	.95
ICU admission	1.248 (0.368 to 4.232)	.72
Mechanical ventilation	1.701 (0.372 to 7.786)	.49
Empyema	0.812 (0.040 to 16.457)	.89
30-d Mortality	1.044 (0.330 to 3.301)	.94
Recurrences	0.655 (0.246 to 1.748)	.40
Rehospitalization	0.045 (<0.001 to >0.999)	.98
Any 30-d complication[c]	0.830 (0.444 to 1.550)	.56
Antibiotic adverse effects[d]	0.232 (0.059 to 0.908)	.04

Table 4. Safety of Early Discontinuation of Antibiotic Therapy According to PCT Value After a Decrease in the PCT Value

Variable	Adjusted OR (95% CI)[a]	*P* Value
In-hospital complications[b]	1.095 (0.609 to 1.969)	.76
In-hospital mortality	1.498 (0.360 to 6.226)	.58
ICU admission	0.002 (<0.001 to >0.999)	.81
Mechanical ventilation	0.192 (<0.001 to >0.999)	.99
Empyema	<0.001 (<0.001 to >0.999)	.91
30-d mortality	0.771 (0.328 to 1.814)	.55
Recurrence	0.939 (0.483 to 1.824)	.85
Rehospitalization	0.758 (0.097 to 5.951)	.79
Any 30-d complication[c]	0.607 (0.355 to 1.038)	.07
Antibiotic adverse effects[d]	1.113 (0.560 to 2.212)	.76

LRTI
CAP excluded++

Serum Procalcitonin Measurement and Viral Testing to Guide Antibiotic Use for Respiratory Infections in Hospitalized Adults: A Randomized Controlled Trial

Angela R. Branche,[1] Edward E. Walsh,[1,3] Roberto Vargas,[4] Barbara Hulbert,[4] Maria A. Formica,[3] Andrea Baran,[2] Derick R. Peterson,[2] and Ann R. Falsey[1,3]

JID 2015:212 (1 December)

Table 2. Comparison of Antibiotic Use Between the Intervention Group/Subgroups or Historical Controls and the Nonintervention Group

Characteristic	Intervention Group	Nonintervention Group	*P* Value
Subjects, no.	151	149	
Antibiotic use for ≤48 h	69 (46)	61 (41)	.42
Discharged receiving oral antibiotics	51 (35)[a]	64 (44)[b]	.09
Total antibiotic-days	3.0 (1.0–7.0)	4.0 (0.0–8.0)	.71

Table 3. Comparison of Antibiotic Use in the Intervention Group, by Procalcitonin (PCT) Level, and Among All Patients, by Results of Viral Testing

Characteristic	Low PCT Level	High PCT Level	*P* Value
Subjects, no.	121	30	
Antibiotic use for ≤48 h	63 (52)	6 (20)	.002
Discharged receiving oral antibiotics	32 (27)[a]	19 (63)	<.001
Total antibiotic-days	2.0 (0.0–6.0)	7.5 (5.0–10.0)	<.001
	Virus Positive	Virus Negative	
Subjects, no.	92	208	
Antibiotic use for ≤48 h	47 (51)	83 (40)	.08
Discharged receiving oral antibiotics	26 (28)	89 (45)[b]	.01
Total antibiotic-days	2.0 (1.0–6.0)	4.0 (1.0–8.0)	.07

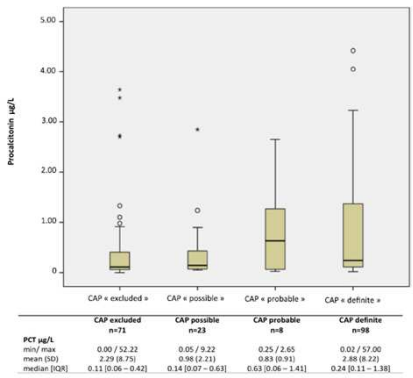
Le Bel et al. Critical Care (2015) 19:366
DOI 10.1186/s13054-015-1083-6

CRITICAL CARE

RESEARCH Open Access

Diagnostic accuracy of C-reactive protein and procalcitonin in suspected community-acquired pneumonia adults visiting emergency department and having a systematic thoracic CT scan

Josselin Le Bel[1,2*], Pierre Hausfater[3,4], Camille Chenevier-Gobeaux[5], François-Xavier Blanc[6,7], Mikhael Benjoar[8], Cécile Ficko[9], Patrick Ray[10], Christophe Choquet[11], Xavier Duval[2,12,13†], Yann-Erick Claessens[14†] and on behalf of the ESCAPED study group



PCT µg/L	CAP excluded n=71	CAP possible n=23	CAP probable n=8	CAP definite n=98
min/ max	0.00 / 52.22	0.05 / 9.22	0.25 / 2.65	0.02 / 57.00
mean (SD)	2.29 (8.75)	0.98 (2.21)	0.83 (0.91)	2.88 (8.22)
median [IQR]	0.11 [0.06 – 0.42]	0.14 [0.07 – 0.63]	0.63 [0.06 – 1.41]	0.24 [0.11 – 1.38]

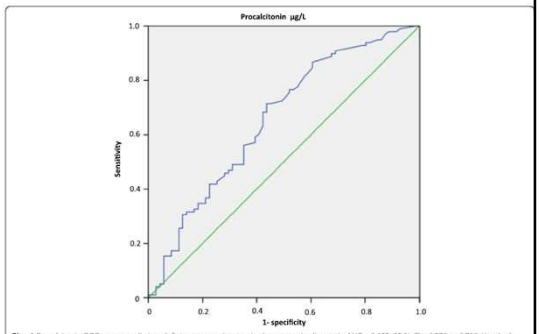


Fig. 4 Procalcitonin ROC curve predicting definite community-acquired pneumonia diagnosis. AUC = 0.655. 95 % CI = 0.570 to 0.739. Youden's index = 0.307 for an optimal PCT cut-off point at 0.13 µg/L. *ROC* receiver operative characteristic, *AUC* area under the curve, *CI* confidence interval, *PCT* procalcitonin

REVIEW ARTICLE

Procalcitonin Algorithms for Antibiotic Therapy Decisions

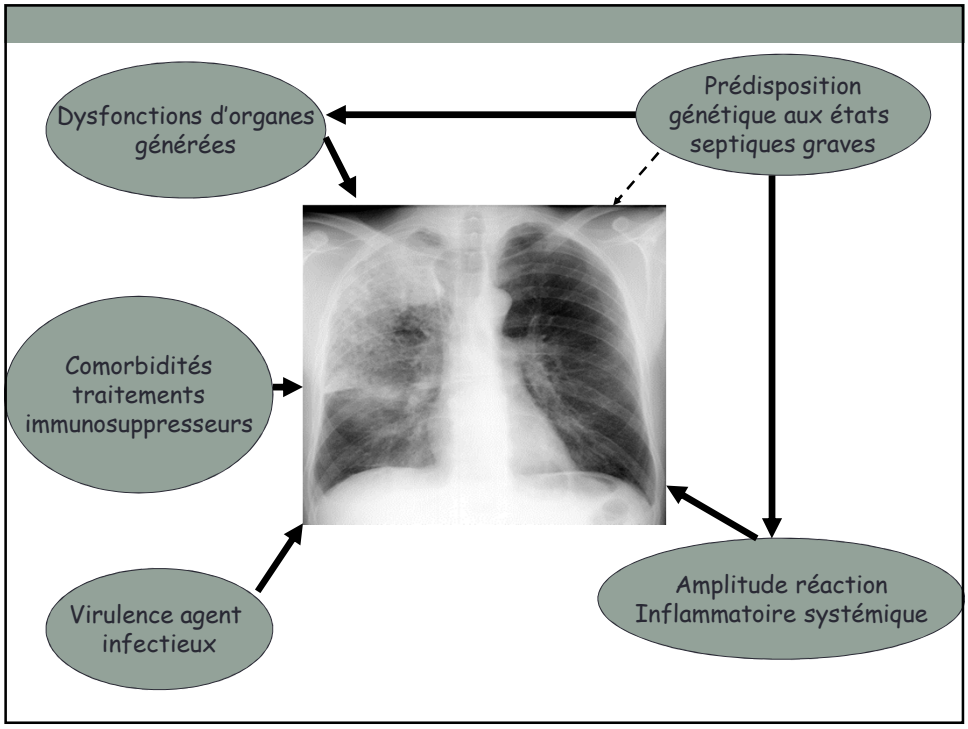
A Systematic Review of Randomized Controlled Trials and Recommendations for Clinical Algorithms

Philipp Schuetz, MD, MPH; Victor Chiappa, MD; Matthias Briel, MD, MSc; Jeffrey L. Greenwald, MD

Arch Intern Med. 2011;171(15):1322-1331

Source
Briel et al,[14] 2008
Burkhardt et al,[21] 2010
Christ-Crain et al,[22] 2004
Christ-Crain et al,[23] 2006
Stolz et al,[24] 2007
Long et al,[25] 2009
Kristoffersen et al,[26] 2009
Schuetz et al[15] 2009
Svoboda et al,[27] 2007
Nobre et al[28] 2008
Stolz et al,[29] 2009
Hochreiter et al,[30] 2009
Schroeder et al,[31] 2009
Bouadma et al,[32] 2010

- *« Measurement of procalcitonin levels for antibiotic decisions in patients with respiratory tract infections and sepsis appears to reduce antibiotic exposure without worsening the mortality rate. »*



MISE AU POINT

Antibiothérapie par voie générale dans les infections respiratoires basses de l'adulte
Pneumonie aiguë communautaire
Exacerbations de Bronchopneumopathie Chronique Obstructive

- Le principal agent pathogène impliqué dans les pneumonies aiguës communautaires (PAC) est le pneumocoque *(Streptococcus pneumoniae)*. La gravité des PAC liées à cette étiologie justifie de débuter en urgence une antibiothérapie efficace sur *S. pneumoniae* : amoxicilline 1 g x 3 par jour pendant 7 à 14 jours.

Agence Française de Sécurité Sanitaire des Produits de Santé
Juillet 2010

HAS
HAUTE AUTORITÉ DE SANTÉ

Février 2014

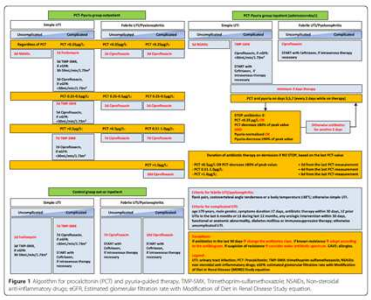
RAPPORT D'ÉLABORATION

Principes généraux et conseils de prescription des antibiotiques en premier recours

1.4 Utilisation appropriée des antibiotiques

- une durée de traitement la plus courte possible :
  - 3 jours pour une infection urinaire basse chez la femme,
  - 5 jours pour une pneumonie commune,

En dehors des infections respiratoires ?



RESEARCH ARTICLE Open Access

Procalcitonin and pyuria-based algorithm reduces antibiotic use in urinary tract infections: a randomized controlled trial

Daniel Drozdov[1,6], Stefanie Schwarz[1], Alexander Kutz[1], Eva Grolimund[1], Anna Christina Rast[1], Deborah Steiner[1], Katharina Regez[1], Ursula Schild[1], Merih Guglielmetti[1], Antoinette Conca[2], Barbara Reutlinger[2], Cornelia Ottiger[3], Florian Buchkremer[4], Sebastian Haubitz[1], Claudine Blum[1], Andreas Huber[3], Ulrich Buergi[5], Philipp Schuetz[1], Andreas Bock[4], Christoph Andreas Fux[6], Beat Mueller[1] and Werner Christian Albrich[1,6,7]*

BMC Medicine (2015) 13:104

Table 4 Antibiotic exposure by randomization group with subgroup analysis

	Control group Median (IQR), days	PCT/Pyuria group Median (IQR), days	*P* value[a]
All patients (intention-to-treat)	**(n = 64)**	**(n = 61)**	
Duration of initial antibiotic therapy	10.0 (7.0–11.0)	6.0 (4.0–8.0)	**<0.001**
Antibiotic exposure within 90 days	10.0 (7.0–16.0)	7.0 (5.0–14.0)	**0.011**
Per-protocol population	**(n = 52)**	**(n = 44)**	
Duration of initial antibiotic therapy	10.0 (7.0–11.0)	6.0 (4.0–7.0)	**<0.001**
Antibiotic exposure within 90 days	10.0 (7.5–16.0)	7.0 (5.0–14.5)	**0.025**

Table 5 Rates of adverse outcomes

	Control group	PCT/Pyuria group	Odds ratio	95% CI	*P* value[a]
All patients (intention-to-treat)	**(n = 64)**	**(n = 61)**			
Recurrence	14/63 (22%)	15/59 (25%)	1.19	0.52–2.75	0.68
Rehospitalization	17/63 (27%)	15/59 (25%)	0.92	0.41–2.07	0.85
Death	4/63 (6%)	1/59 (2%)	0.25	0.03–2.30	0.22

Conclusion: PCT pour réduire durée de traitement ATB (hors réanimation)

- Nombreuses études d'impact randomisées en faveur de l'utilisation algorithme PCT dans infections respiratoires
  - PAC
  - EABPCO
- 1er objectif: atteindre les durées de traitement recommandées !
- Pas d'étude médico-économique
- Pas d'étude pédiatrique
- Quid des autres infections communautaires (IU, dig, erysipèle…)