Risk factors for unnecessary antibiotic therapy: a major role for clinical management

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Bon Usage Antibiotique: que proposent les reco ?

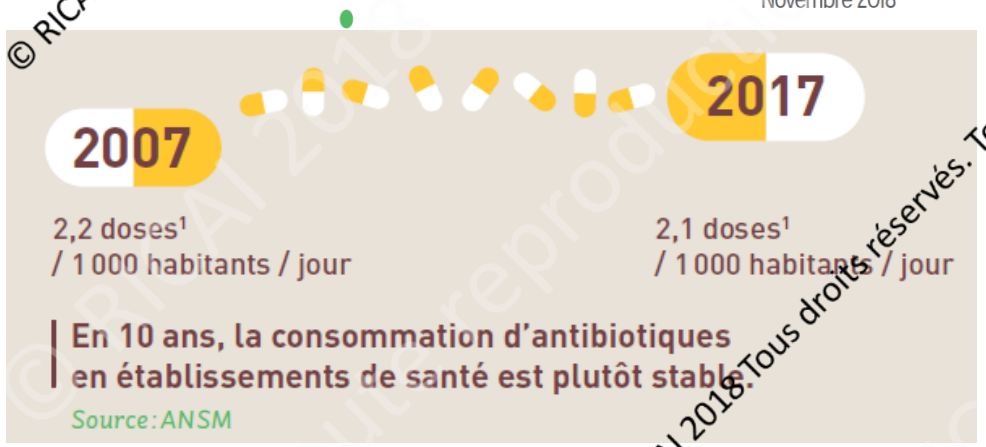
- Réduire la conso ATB pour réduire l'émergence des BMR
- Améliorer la qualité de l'antibiothérapie par un ensemble de mesures structurelles et fonctionnelles (*cf* ICATB-2)
  - Informatisation / Protocoles d'antibiothérapies probabilistes
  - Réévaluation antibiotique à J2-J3 et à J7 / Audit, RMM…
- Organisation pluridisciplinaire: alertes de la pharmacie, des laboratoires, aide EOH

Bon Usage Antibiotique: quels résultats des reco ?

CONSOMMATION D'ANTIBIOTIQUES ET RÉSISTANCE AUX ANTIBIOTIQUES EN FRANCE:

UNE INFECTION ÉVITÉE, C'EST UN ANTIBIOTIQUE PRÉSERVÉ !

Novembre 2018



	EN VILLE	EN ÉTABLISSEMENTS DE SANTÉ	EN SANTÉ ANIMALE
CÉPHALOSPORINES DE 3E ET 4E GÉNÉRATIONS	- 35,1 %	+ 35,7 %	- 84,7 %
FLUOROQUINOLONES	- 37,3 %	- 54,5 %	- 85,7 %
TÉTRACYCLINES	- 9,1 %	NE*	- 53,0%
PÉNICILLINES	+ 28,6 %	+ 3,2 %	- 11,4 %

facteurs de prescription d’une antibiothérapie inutile ?

Clinical Infectious Diseases

INVITED ARTICLE

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Measuring Appropriate Antimicrobial Use: Attempts at Opening the Black Box

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Table 2. Proposed Definitions of Terminology to Describe a Day of Therapy With a Particular Antimicrobial Agent

Term	Definition	Examples
Unnecessary	Use of antimicrobials for noninfectious syndromes, use of antibiotics for nonbacterial infections, days of therapy beyond the indicated duration of therapy absent any clinical reason for a lengthened course, use of redundant antimicrobial therapy, and/or continuation of empiric broad-spectrum therapy when cultures have revealed the infecting pathogen.	• Treatment of asymptomatic bacteriuria outside of established indications • Antibiotics for viral upper respiratory tract infections • Treating community-acquired pneumonia for 14 d instead of 5–7 in the absence of clinical data suggesting need for a longer course • Double anaerobic coverage • Continued use of vancomycin started empirically after growth of *Pseudomonas aeruginosa* in blood cultures • Continued use of empiric vancomycin and cefepime in a patient found to have sterile pancreatic necrosis
Inappropriate	Use of antimicrobials in the setting of established infection to which the pathogen is resistant or use of antimicrobials not recommended in treatment guidelines.	• Patient treated with an antibiotic not treating the bacteria recovered in cultures (bug–drug mismatch) • Use of piperacillin/tazobactam to treat uncomplicated community acquired pneumonia
Suboptimal	Use of antimicrobials in the setting of established infection that can be improved in one of the following categories: (1) drug choice, (2) drug route, and (3) drug dose.	• Use of an overly broad-spectrum agent to treat a susceptible bacterium (eg, cefepime for ampicillin susceptible *Escherichia coli* infection) • Use of intravenous fluoroquinolones when no contraindication to oral therapy • Failure to adjust doses of renally cleared drugs in the setting of acute renal failure

Méthode

Prospective, Multicentrique

Même Dossier Patient Informatisé (E-med)

Toutes antibiothérapies curatives, x 2 jours

- toutes données participant à la prescription antibiotique: motif d'hospitalisation, diagnostic énoncé…
- antibiothérapies probabilistes
- données microbiologiques
- antibiothérapies documentées
- évolution clinique des symptômes décrits initialement

Appropriateness of 453 antibiotic therapies at 17 private clinics according to the proposed definitions (1)

Unnecessary, n = 169 (37%) including insufficient drug doses, n = 20 (4%)	**Non-infectious syndromes, n = 106 (23%), comprised cases mixing any clinical or biological element for ongoing infection (n = 62, 14%), and active cancer (n = 47, 10%) and other causes of fever (n = 19, 4%). We also observed 8 cases of isolated increase of C-reactive protein and/or procalcitonin (2%)**	**Other causes of fever hematoma (n = 6), thrombo-embolisms (n = 3), necrosis (n = 3), vessel inflammation due to peripheral catheter (n = 2), inflammatory bowel diseases (n = 2), drug intolerance, haemorrhagic pleurisy, non-infectious arthritis (n = 1 each)**
	Non-bacterial infections, n = 40 (9%)	**28 urinary colonisations 7 COPD, 5 bronchitis**
	Redundant antimicrobial, n = 13 (3%)	**amox + clavulanic ac + imidazole, n = 11 imipenem + imidazole, n = 2**
	Continuation of empirical broad-spectrum antimicrobials, n = 11 (2%)	**imipenem, n = 4; ceftriaxone + gentamicin, n = 5; piperacillin + tazo, n = 2**

Inappropriate, n = 154 (34%) including insufficient drug doses, n = 36 (8%)	use of antimicrobials in the setting of a resistant pathogen, n = 29 (6%)
Suboptimal, n = 71 (16%) including insufficient drug doses, n = 39 (9%) Useless parenteral therapy: not determined	
Optimal, n = 59 (13%)	

Main characteristics of unnecessary antibiotic therapy (UAT) compared to required therapy, which was the sum of inappropriate + suboptimal + optimal antibiotic therapies (1)

	Required therapy n = 284 (63%)	UAT n = 169 (37%)	p	All, n = 453
Wards				
Medicine	137 (48)	112 (66)	< 0.001	249 (55)
Surgery	130 (46)	56 (33)	0.008	186 (41)
Intensive care	17 (6)	1 (1)	0.009	18 (4)
Antibiotic referent at the institution	249 (88)	132 (78)	0.007	381 (84)
Antibiotic referent advice	30 (11)	7 (4)	0.015	37 (8)
ID specialist at the institution	59 (21)	33 (20)	0.749	92 (20)
ID specialist advice	17 (6)	3 (2)	0.060	20 (4)
Age (years)	72±16	72±16	0.447	72±16
Sex-ratio (M/F)	1.41	1.21	0.425	1.33
Non-infectious syndromes				
active cancer	63 (22)	47 (28)	0.176	110 (24)
other putative causes of fever	20 (7)	19 (11)	0.123	39 (9)
increase in CRP and/or procalcitonin	6 (2)	8 (5)	0.200	14 (3)
at least one cause of inflammation	87 (31)	71 (42)	0.014	158 (35)
Infection as a reason for hospitalisation	161 (56)	40 (24)	< 0.001	201 (44)
Suspected or definitive diagnosis				
urinary tract infections	77 (27)	41 (24)	0.503	118 (26)
respiratory infections	48 (16)	28 (16)	0.926	76 (16)
gastrointestinal infections	57 (20)	9 (5)	< 0.001	66 (15)
cutaneous infections	26 (9)	19 (11)	0.472	45 (10)
osteoarticular infections	23 (8)	4 (2)	0.023	27 (6)
endocarditis	11 (4)	6 (4)	0.876	17 (4)
unspecified	42 (15)	62 (37)	< 0.001	104 (23)
Healthcare-associated infections	123 (43)	60 (37)	0.118	183 (40)

Main characteristics of unnecessary antibiotic therapy (UAT) compared to required therapy, which was the sum of inappropriate + suboptimal + optimal antibiotic therapies (2)

	Required therapy n = 284 (63%)	UAT n = 169 (37%)	p	All, n = 453
≥ 1 microbial test	207 (73)	89 (53)	< 0.001	296 (65)
blood cultures	99 (35)	15 (9)	< 0.001	114 (25)
urine cultures	133 (47)	79 (47)	0.985	212 (47)
any positive microbial test result	113/207 (55)	43/89 (45)	0.321	156 (53)
Antibiotic therapy				
parenteral administration	213 (75)	74 (44)	< 0.001	287 (63)
antibiotic combination	125 (44)	35 (21)	< 0.001	165 (36)
third-generation cephalosporin	99 (35)	48 (29)	0.175	147 (32)
amoxicillin + clavulanic acid	98 (34)	52 (31)	0.453	150 (33)
fluoroquinolones	92 (32)	49 (29)	0.489	140 (31)
vancomycin	29 (10)	4 (2)	0.001	33 (7)
aminoglycoside	52 (7)	12 (18)	< 0.001	64 (14)
Effective antibiotic reassessment	93 (33)	28 (17)	< 0.001	121 (27)
Insufficient drug dose	75 (26)	20 (12)	< 0.001	95 (21)
Clinical outcome				
favourable	183 (64)	66 (39)	< 0.001	249 (55)
uncertain	75 (27)	82 (49)	< 0.001	157 (35)
adverse	26 (9)	21 (12)	0.269	47 (10)
Non-bacterial infections				
urinary colonisation	14 (5)	28 (16)	< 0.001	42 (9)
others	7 (2)	12 (7)	0.017	19 (4)

Risk factors for unnecessary antibiotic therapy. Logistic regression

	AOR [95% CI]	p
Hospitalisation in a medical ward	2.11 [1.30-3.41]	0.002
Infection as an indication for hospitalisation	0.24 [0.15-0.41]	< 0.001
Gastro-intestinal infections	0.23 [0.10-0.52]	< 0.001
Unspecified diagnosis	1.83 [1.04-3.20]	0.033
Blood cultures not performed	5.26 [2.56-10.80]	< 0.001
Antibiotic administration *via* parenteral route	0.55 [0.33-0.90]	0.018
Favourable clinical outcome	0.36 [0.23-0.58]	< 0.001

Discussion

- **104 patients sans diagnostic d'infection (23%)**
  - ✓ Fièvre ou Inflammation biologique liées à un diagnostic non infectiologique, et néanmoins antibiothérapie
    - ❖ Quelques travaux menés avant 2004 montraient les mêmes données: donc pas en amélioration
  - ✓ Dans les études épidémiologiques des sepsis: incertitude diagnostique > 20%
    - ❖ Les cas cliniques / situations prototypiques pour proposer des options thérapeutiques ne rendent pas compte de cette réalité
    - ❖ Réduire ces difficultés diagnostiques : compagnonnage, formation continue, audits par les praticiens

Mise en œuvre de l'auto-évaluation accompagnée

- 296 patients bénéficiaient d'un prélèvement microbiologique (65%), 156 avaient au moins 1 prélèvement positif (53%), dont 42 colonisations bactériennes
  - ✓ Difficultés du diagnostic microbiologique, quantitative et qualitative : même approche méthodologique