



From antibiotic therapy to peri-surgical antibiotic prophylaxis: measures and interventions to influence antibiotic use and consumption

Dr Florence Lieutier-Colas, PharmD PhD, UH of Nice, France EAHP Academy Seminar 2 « ABS for beginners » 29 September 2017, Wien, Austria





No conflict of interest

Questions to the audience

- Which broad spectrum ATB provide AMR?
 - 1. Amoxicillin-clavulanate
 - 2. 3rd generation cephalosporines
 - 3. Fluoroquinolones
 - 4. Carbapenems

- Who are the leading actors in AMS?
- 1. Infectious diseases specialits?
- 2. Microbiologists?
- 3. Pharmacists?

- How many time spend peri-surgical antibiotic prophylaxis?
 - 1. 2 to 4 hours (duration of the intervention)?
 - 2. 24h?
 - 3. 3 to 5 days?

ATB, antibiotic, AMR, antimicrobial resistance, AMS, antimicrobial stewardship

Outline and plan

- Antimicrobial Resistance in France
- How are pharmacists involved in AMS in our hospital?
- And in our region ?
- Conclusion and perspectives

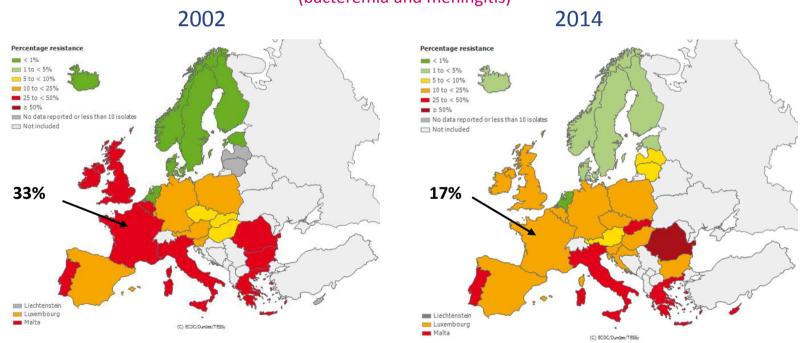








Methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from invasive infections (bacteremia and meningitis)



ECDC. Surveillance atlas of infectious diseases. Available at: http://atlas.ecdc.europa.eu/public/index.aspx. Accessed March 2017.

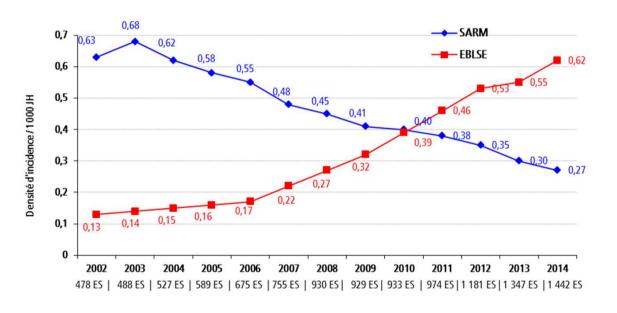








Evolution of the incidence of MRSA and ESBL Enterobacteriaceae in French hospitals (BMR-Raisin data)







ESBL, extended-spectrum betal-lactamase; MRSA, methicillin-resistant Staphylococcus aureus.
Rapport BMR-Raisin. Surveillance nationale des bactéries multirésistantes dans les établissements de santé: réseau BMR-Raisin. Available at: http://invs.santepubliquefrance.fr//bmr-raisin. Accessed March 2017.

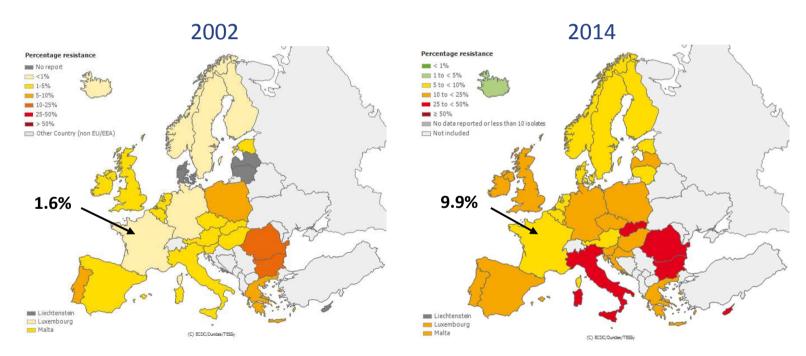








Resistance of *E. coli* to 3rd generation cephalosporins



ECDC. Surveillance atlas of infectious diseases. Available at: http://atlas.ecdc.europa.eu/public/index.aspx. Accessed March 2017.



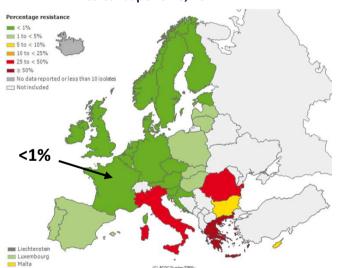




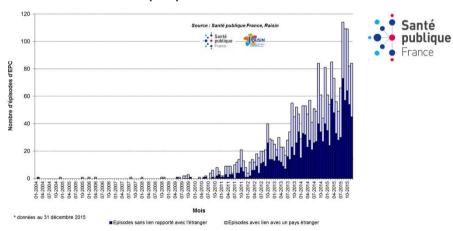


Carbapenem-resistant Enterobacteriaceae

% of isolates of *K. pneumoniae* resistant to carbapenems, 2014



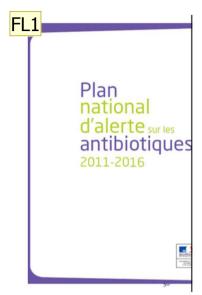
Episodes with Carbapenemase-producing Enterobacteriaceae (CPE) in France from 2004 to 2015



- 2385 episodes with CPE from 2004 (report 31.12.2015)
- Strong increase in episodes reported during the summer of 2015

CPE, Carbapenemase-producing Enterobacteriaceae.

ECDC. Surveillance atlas of infectious diseases. Available at: http://atlas.ecdc.europa.eu/public/index.aspx. Accessed March 2017; InVS, signalement des infections nosocomiales. Available at: http://invs.santepubliquefrance.fr//epc. Accessed March 2017.



National context in France

- National Medicare Campaigns since 2002
- 2016 Interdepartmental Committee for Health targeted on AMR
 - Limit prescribing of broad-spectrum antibiotics providing resistance :
 - Amoxicillin-clavulanate
 - 3rd generation cephalosporines
 - Fluoroquinolones
 - Carbapenems









Diapositive 9

FL1 Florence Lieutier; 13/09/2017

In this context how are pharmacists involved in AMS?

Responsibilities of pharmacists

- Promoting optimal uses of antimicrobial agents
 - Encouraging multidisciplinary collaboration
 - Working within the pharmacy and therapeutics committee structure
 - Operating a multidisciplinary AMS program
 - Generating and analysing quantitative data on antimicrobial drug use to perform clinical and economic outcome analyses
 - Working with the microbiology laboratory
 - Using information technology to enhance AMS through surveillance, utilization and outcome reporting, and the development of clinical decision-support tools
 - Facilitating safe medication management practices of antimicrobial agents
- Reducing the transmission of infections
- Educational activities

ASHP Statement on the Pharmacist's Role in Antimicrobial Stewardship and Infection Prevention and Control

DEVELOPED THROUGH THE ASHP COUNCIL ON PHARMACY PRACTICE AND APPROVED BY THE ASHP BOARD OF DIRECTORS ON APRIL 17, 2009, AND BY THE ASHP HOUSE OF DELEGATES ON JUNE 16, 2009

Am J Health-Syst Pharm. 2010; 67:575

How are pharmacists involved in AMS in our hospital?

Our antimicrobial stewardship since 2005

Our daily interactions



Pharmacist

- Assess the prescription according to the indication, microbiological data... •Alert the Infectious
- diseases specialist for targeted antibiotics and in other cases if necessary



- Microbiological
- documentation
- Expert advices



Physician / Patient



Pharmacologist

- **TDM (Therapeutic Drug** Monitoring)
- **Expert advices**



Infectious Disease specialist

- Answers to the clinicians' requests
- Advice for targeted antibiotics
- Ward rounds



Infection preventionist or Hospital epidemiologist

Lieutier-Colas F, personal opinion.

PP-GEP-EUR-0042 Date of preparation: March 2017



Our antimicrobial stewardship since 2005 Our daily tools in 2017

Pharmacist

•Nominative prescription for all antibiotics (ATB), in violet for ATB, in red for targeted ATB
•Assess the prescription according to the indication, microbiological data...
•Alert the Infectious diseases specialist for targeted antibiotics and in other cases if necessary



Pharmaci	Pharmacles Archet, Pasteur et St. Roch						A destination des microbiologiste infectiologues itinérants et des hygie CHU d		
		Ré	capitulatif des ale	And the second second second second second	ciblés à réé	valuer			
			Date	: 11/05/2017					
Nom	Prinom	UF	Molécule 1	Molécule 2	Molécule 1	Rédvalué	Date	Intervenant	
	DENISE	2010	CEFEPIME 2 G FL IN)						
	JACQUEUNE	7620	IMPENEM CILASTATINE 500						
	JEAN	7883	PIPERACILLINE TAZOBACTA						
	JEAN PAUL	2010	INVANZ 1G INI IV	ANTIKACINE 500 MG FLAC I					
	RITA	7241	PIPERACILLINE TAZOBACTA						
	ANNE MARIE	7241	IMPENEM CHASTATINE 500	VANCOMYCINE 1 G FL INI					
	CHRISTIAN	7814	IMIPENEM CILASTATINE 500	ZYVOXID 2MG/ML SOL POU					
	ROBERT	7200	ZYVOXID ZMG/ML SOL POU	AUGMENTIN 1G/200MG FL					
	FLORIAN	7431	IMIPENEM CILASTATINE 500	ZYVOXID 2MG/ML SOL POU					
	ALAIN	7931	CEFEPIME 2 G FL INI	METRONIDAZOLE 0,5% ECO					
	PIERRE	2210	IMIPENEM CILASTATINE 500	AMIKACINE 500 MG FLACT					

Infectious Disease specialist

- Replying to clinicians' requestsAdvice for targeted antibiotics
- •Ward rounds
- About 2000 drawn opinions from experts per year in the computerized patient file since 2008



Physician / Patient

PARACETAMOL 1G /100ML	1 g Nuit 00h, 1 g Matin, 1 g AM 16h	3 g, tous les jours (en 3 fois) Volume total :
AUGMENTIN 1G/200MG	1 g Nuit OOh, 1 g Matin, 1 g AM 16h	3 g, tous les jours (en 3 fois) Volume total :
ZYVOXID 600MG/300M	600 mg Matin, 600 mg Soir 20h	1200 mg, tous les jours (en 2 fois)

Microbiologist

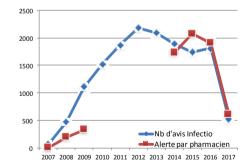


Pharmacologist



Volume total:

Infection preventionist or Hospital epidemiologist



In this context how are pharmacists involved in AMS in our hospital?

- Since February 2016, systematic clinical pharmacist intervention in the ICU at University Hospital Nice
 - 536 interventions from February 2016 to February 2017
 - 165 interventions on antimicrobial prescriptions (inadequation to protocols, drugs interactions, parenteral to oral switch, optimisation of the dose or of the administration modalities, need of therapeutic drug monitoring)
 - 95.8% of the pharmacists' interventions were accepted by the prescribers.

Our multidisciplinary experience in the South East of France: an effective AMS initiative involving pharmacists since 2005



SciVerse ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM consulte
www.em-consulte.com



Médecine et maladies i

Original article

An antibiotic stewardship program in a French teaching hospital to

Bilan d'un programme de bon usage des antibiotiques dans un CHU français

V. Mondain^a, F. Lieutier^b, S. Dumas^b, A. Gaudart^c, T. Fosse ^{c,d}, P.-M. Roger ^{a,d}, E. Bernard^a, R. Farhad^a, C. Pulcini ^{a,*,d}

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Received 9 April 2012; received in revised form 24 September 2012 accepted 31 October 2012

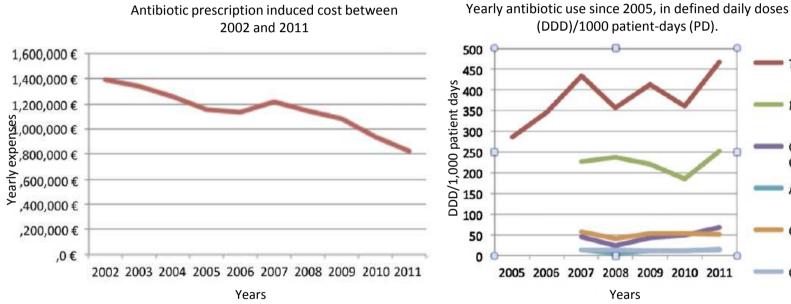
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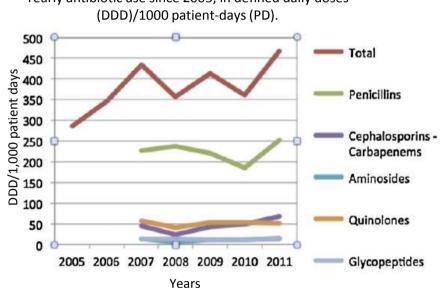
Role of the pharmacist

- •Assessing ATB prescriptions, regarding microbiological data and eventual organ dysfunctions
- •Alerting the ID specialist and other actors for targeted ATB and if necessary
- •Specific form filled out by AMT members, visible by all physicians on the patient's electronic medical record
- •Participating in the development of electronic prescriptions of drugs
- Monitoring ATB consumptions regarding to the AMR in each unit of the hospital
- •Participating to audits and feedback to prescribers, to prescribers training, to biyearly journal sent by mail on various themes of infectious diseases...

AMR, antimicrobial resistance; AMS, antimicrobial stewardship; AMT, antibiotic management team; ATB, antibiotic; ID, infectious disease. Mondain V, et al. *Med Malad Infect* 2013;43:17–21.

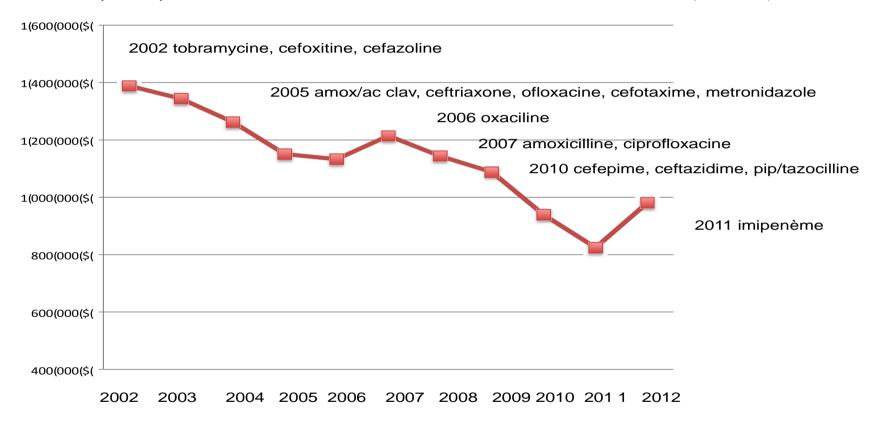
Our experience in the South East of France: an effective AMS initiative involving pharmacists since 2005. Results.





AMS, antimicrobial stewardship; DDD, daily defined dose. Mondain V, et al. Med Malad Infect 2013;43:17-21.

Antibiotic prescription induced cost between 2002 and 2012 in the UH of Nice (in euros).



The decrease in cost corresponds to the availability of generics...



Antibiotic consumptions and bacterial resistances

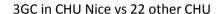
- A new tool: a National software CONSORES developed by the UH of Nancy, France
- A French National website to compare our data
- Objective? To follow simultaneously
 ATB consumptions (in DDD per day of hospitalization) and AMR in each medical unit of our hospital
- When ? Analysis by quarter or by year

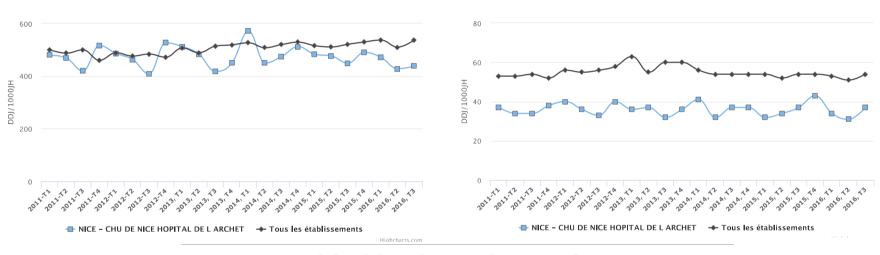




AMS initiative in Nice involving pharmacists: ATB consumptions from 2011–2016









CONSORES: UN OUTIL POUR AIDER L'INFECTIOLOGUE TRANSVERSAL



S. Boussat ¹, S. Hénard ², B. Demore ³, C. Rabaud ^{1,2}
(1) CClin-Est, CHU de Nancy ; (2) Service des Maladies Infectieuses, CHU de Nancy; (3) Pharmacie hospitalière, CHU de Nancy

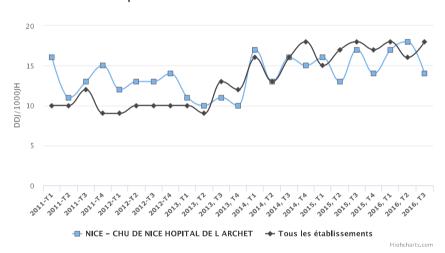
3GC, 3rd generation cephalosporins; AMS, antimicrobial stewardship; ATB, antibiotic; CHU, Centre Hospitalier Universitaire. Data from the French national website. Available at: www.consores.net. Accessed March 2017.



AMS initiative in Nice involving pharmacists: ATB consumptions from 2011–2016

Quinolones in CHU Nice vs 22 other CHU

Carbapenems in CHU Nice vs 22 other CHU

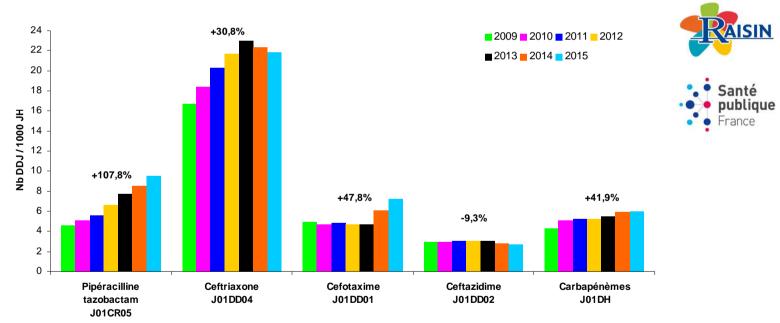


AMS, antimicrobial stewardship; ATB, antibiotic; CHU, Centre Hospitalier Universitaire.

Data from the French national website. Available at: www.consores.net. Accessed March 2017.

Antibiotic consumption in French hospitals 2009–2015

Evolution of beta-lactam consumption in DDD/1000 HD between 2009 and 2015 (N=542 hospitals)



HD, inhabitant days.
Réseau de surveillance ATB Raisin. Données préliminaires 2015. Available at: http://invs.santepubliquefrance.fr/raisin/. Accessed March 2017.

In this context how are pharmacists involved in AMS in our hospital? Perisurgical antibiotic prophylaxis



Antibioprophylaxie en chirurgie et médecine interventionnelle. (patients adultes) **Actualisation 2010**

Comité de pilotage Société française d'anesthésie et de réanimation

C. Martin (coordonnateur)

H. Dupont

A. Lepape O. Mimoz

P. Montravers I.I. Pourriat

Avec la collaboration des sociétés savantes suivantes

Société française des chirurgiens esthétiques plasticiens

Société française de chirurgie orthopédique et traumatologique

A. Lortat-Jacob

Société française de neurochirurgie

P.H. Roche

Société française et francophone de chirurgie de l'obésité

Société française de stomatologie et de chirurgie maxillo-faciale

Société française d'hygiène hospitalière

Principles and context

- PSAP important to prevent infections related to surgical site
- The good ATB for the good surgical intervention at the good time (30 minutes before incision)
- Just during the surgical intervention
- According to recommandations and protocols
- PSAP recorded in the patient medical file

PSAP perisurgical antibioprophylaxis,

Kits for perisurgical ATB prophylaxis

In practice since 2005 in the operating rooms in the hospital site Archet in Nice



Kits by indication of surgical intervention According to the up-dated recommendations

- -Kit number
- -Composition : antibiotic and dosage
- -One dose or reinjection
- To ditute in 100 ml of NaCl 0,9% or G5%
- To pass in 30 minutes

Operational organization since 2005, extended progressively to all surgical rooms of the University Hospital of Nice in 2008, 2014, and 2015 © Good collaboration between anesthesists and pharmacists!

Kits for perisurgical ATB prophylaxis

BEFORE kits

- . 26 different antibiotics
- . Stock for one month
- . Multiple storage locations

AMIKACINE **OXACILLINE** TICARCILLINE CEFTAZIDIME **CEFTRIAXONE** CEFOTAXIME VANCOMYCINE PIPERACILLINE + TAZOBACTAM OFLOXACINE RIFAMPICINE AMOXICILLINE + ACIDE CLAVULANIOUE **GENTAMYCINE AMOXICILLINE** IMIPENEM + CILASTATINE **METRONIDAZOLE CEFAZOLINE** CEFOXITINE CLINDAMYCINE **CIPROFLOXACINE PIPERACILLINE FOSFOMYCINE LEVOFLOXACINE CEFAMANDOL** CEFUROXIME **TEICOPLANINE** COTRIMOXAZOLE

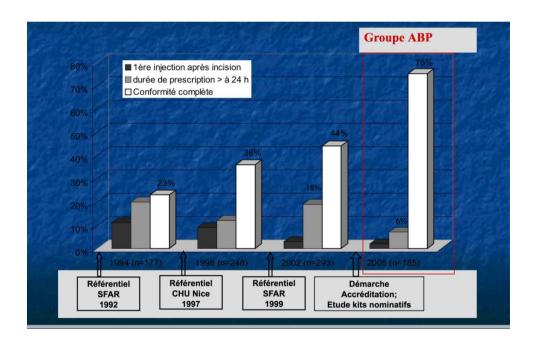
AFTER kits

- . 14 antibiotics
- . Stock for one week
- . One storage location

VANCOMYCINE
PIPERACILLINE + TAZOBACTAM
OFLOXACINE
RIFAMPICINE
AMOXICILLINE + ACIDE CLAVULANIQUE
GENTAMYCINE
AMOXICILLINE
IMIPENEM + CILASTATINE
METRONIDAZOLE
CEFAZOLINE
CEFOXITINE
CLINDAMYCINE
CIPROFLOXACINE
PIPERACILLINE

Impact of our PSAP organisation

- 4 audits performed on PSAP since
 1992 on
 - First injection after incision, less and less frequent
 - Duration of prescription > 24h
 - Global conformity
- Global conformity better and better, from 23% in 1994 to 75% with PSAP kits in 2005



Impact of our PSAP organisation

- Better compliance with recommendations evaluated by repeated audits
- Traceability of PSAP in the patient file
- Perennial organisation since 2005
- Actualized according to last recommandations
- Good collaboration between anesthesists, pharmacists and nurses

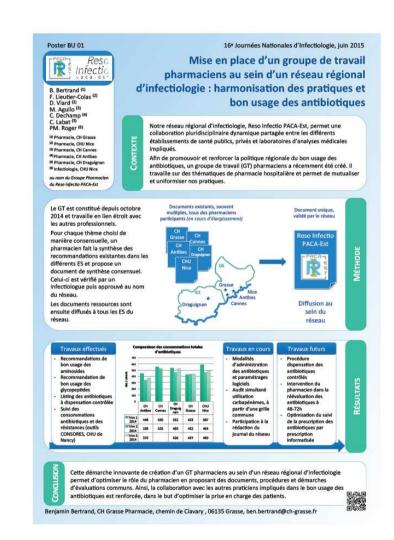
How are pharmacists involved in AMS in our region ?

2014 Creation of a regional pharmacists' network to promote good use of ATB

- •Sharing of tools (aminosides administration protocols, list of targeted ATB...)
- •Generation and analysis regional quantitative data on antimicrobial drug use
- Regional audits on carbapenems use
- •Coordination of the writing of the regional Infectious Disease newspaper

•...

AMS, antimicrobial stewardship; ATB, antibiotics.





6 numbers of our regional multidisciplinary Newsletter on Infectious Diseases named INFOH since 2014 Number 7 in preparation for November 2017







A new software to help optimize regional antimicrobial stewardship policy? Results from a two yearsurvey of antibiotic consumption and antimicrobial resistance in five hospitals in South-Eastern France

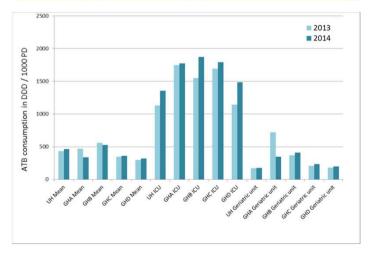
EV0707

Marion Warembourg¹, Anne-Charlotte Lombardo², Véronique Blanc³, Benjamin Bertrand⁴, Sophie Léotard⁵, Carole Labat⁶, Marine Agullo⁷, Véronique Mondain⁸, Sandrine Boussat⁹, Pierre-Marie Roger⁸, Raymond Ruimy¹⁰, **Florence Lieutier-Colas**¹ and the Regional Network Reso-Infectio-PACA-Est.

1/Pharmacy, Nice University Hospital 2/Pharmacy, Antibes Hospital, 3/ Microbiology, Antibes Hospital 4/Pharmacy, Grasse Hospital, 5/ Microbiology, Grasse Hospital, 6/Pharmacy, Draguignan Hospital, 7/Pharmacy, Cannes Hospital, 8/Infectious diseases unit, Nice University Hospital 9/Infections Control Committee, Nancy University Hospital, 10/ Microbiology, Nice University Hospital

- A new national software to survey ATB consumptions and AMR in clinical wards since 2013
- Results from a 2 year-survey (2013, 2014) in 5 hospitals in our region
- Focused on two populations of at risk-patients exposed to ATB, in intensive care units (ICU) and in geriatric wards
- ID advices were given upon request and on a weekly basis in ICU (in UH, GHB and GHD) and in geriatric units (UH and GHA).

Hospitals	Beds	ID presence (Y/N) Since when	ATB consumption in 2013 (DDD/1000PD)	ATB consumption in 2014 (DDD/1000PD)
Antibes Hospital (A)	622	Y (2013)	471	337.6
Cannes Hospital (B)	849	Y (2010)	559	527.8
Draguignan Hospital (C)	391	Y (2014)	349.0	359.8
Grasse Hospital (D)	453	Y (2015)	300.4	321.8
Nice University Hospital	1692	Y (1999)	431.4	464.6



Warembourg M, et al. ECCMID 2016. Poster EV0707.

A new software to help optimize regional antimicrobial stewardship policy? Results from a two yearsurvey of antibiotic consumption and antimicrobial resistance in five hospitals in South-Eastern France

EV0707

Marion Warembourg¹, Anne-Charlotte Lombardo², Véronique Blanc³, Benjamin Bertrand⁴, Sophie Léotard⁵, Carole Labat⁶, Marine Agullo⁷, Véronique Mondain⁸, Sandrine Boussat⁹, Pierre-Marie Roger⁸, Raymond Ruimy¹⁰, **Florence Lieutier-Colas**¹ and the Regional Network Reso-Infectio-PACA-Est.

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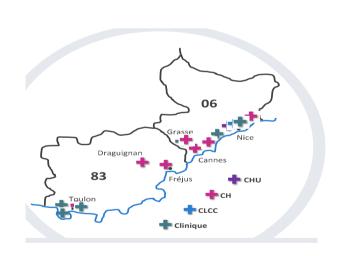
- The Reso-Infectio-PACA-Est experience enabled us to quickly survey trends and to compare practices between differents units and hospitals.
- Prospective monitoring and associated prescriptions quality audit may allow adapting guidelines to local AMR rates, identifying inappropriate ATB use, targeting improvement interventions, and evaluating the impact of those actions.
- These indicators may be useful to assess the impact of this regional multidisciplinary AMS network.

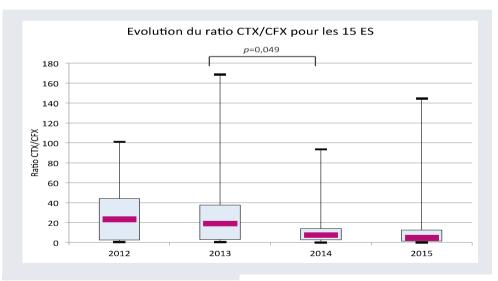
Fig 2. **Evolution** of MRSA% in the UH since 2011 to 2014. Fig 3. **Evolution** of Escherichia coli resistance (R) to ciprofloxacin and ciprofloxacin consumption at the UH from 2012 to 2014.

Warembourg M, et al. ECCMID 2016. Poster EV0707.

How are pharmacists involved in AMS in the South East of France?



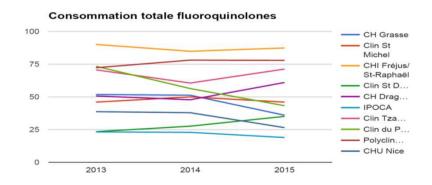




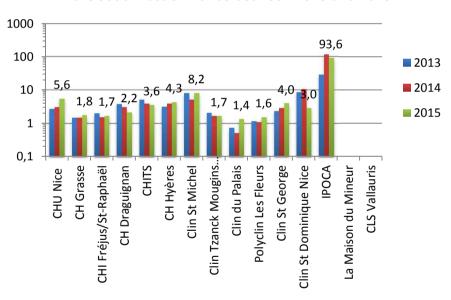
15 HCF in the South East of France: 1 UH, 7 GH, 1 Center for Cancer Control and 6 private clinics

An effective AMS initiative in France involving pharmacists: where is it today in South East of France?

- 2016: Survey of ATB consumption in 15 hospitals of the regional network at the initiative of the pharmacists' network
 - Oral antibiotic use needs to be promoted, in particular for quinolones



Evolution of the oral/parenteral quinolones use in 15 hospitals in the South East of France between 2013 and 2015*



^{*}Maison du Mineur, CL S Vallauris: no parenteral use; CH Cannes:no data. AMS, antimicrobial stewardship; ATB, antibiotic. Lieutier-Colas F, personal data.



Appropriate use of carbapenems: a regional audit in 7 hospitals

P1298

Delphine Viard¹, Florence Lieutier-Colas¹, Benjamin Bertrand², Marine Agullo³, Anne-Charlotte Lombardo⁴, Jihen Bousseta⁵, Carole Labat⁶, Isabelle Falconi⁷, Karine Risso⁸, Pierre-Marie Roger⁶, Raymond Ruimy⁶. **RésO-InfectiO-PACA-Est****Pharmacy department: 1/ Nice University Hospital 2/ Grasse Hospital 3/ Cannes Hospital 4/ Andres Hospital 5/ Toulon La Seyne s/ Mer Hospital 7/ Diaguignan Hospital 7/ Menton Hospital 8/ Infectious diseases unit, Nice University Hospital 9/ Laboratory of microbiology, Nice University Hospital

Context of the study

- •Carbapenems (CP) consumption has increased these last years in Europe and in France (+145% since 2000).
- •The frequent use of CP contributes to increase the emergence of carbapenemase producing bacteria.
- •In Europe the average rate of CP resistance for Klebsiella pneumoniae is 8% with a maximum of 59% in Grece.
- •In consequence, CP must be used as the last resort antibiotics.

Our aim was to assess the appropriateness of CP prescriptions in their indications and in the re-evaluation at 48-72 hours or at the bacteriological results.

Method proposed in 2014 by the French Society of Infectious Diseases

Results

- •7 health institutions
- •118 CP prescriptions (116 patients): 87 imipenem, 16 ertapenem, 15 meropenem
- Conformity of the indication: 63,6%
- Conformity of the reevaluation: 70,4%
- •Global appropriateness: 62,6%
- •The global conformity rate of all the HC (51,7%) is < to those of the UHC (p=0,015)

HC hospital center, UHC university hospital center. Viard D, et al. ECCMID 2016. Poster P1298.

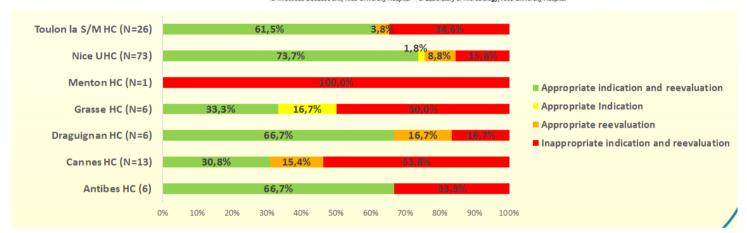


Appropriate use of carbapenems: a regional audit in 7 hospitals

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**Toulon La Seyne s/ Nieth Hospital 0/ Diaguignan Hospital 7/ Menton Hospital 8/ Infectious diseases unit. Nice University Hospital 9/ (Laboratory of microbiology. Nice University Hospital)

**Toulon La Seyne s/ Nieth Hospital 1/ Diaguignan Hos



More than 1/3 of the CP prescription were not appropriate. The differences observed in the conformity rates of each hospital and between all the HC and the UHC might be related to various internal organizations and inequal human ressources.

Suggestions for improvment:

- -to study the organizations of each hospital and and their impact on the conformity of CP prescriptions
- -to work on regional recommendation for the management of CP prescriptions
- -to implement targeted actions for each hospital and clinical units according to their respective results.

The regional network will allow us to pool our resources and share our ideas, in order to harmonize our clinical practices and organizations.

Viard D, et al. ECCMID 2016. Poster P1298.

Next steps for antimicrobial pharmacists

- Continue collaboration (local, regional, national, international)
- Continue antifungal stewardship (since 2005)
- Outpatient Parenteral
 Antimicrobial Therapy, therapeutic
 education of the patient
- Vaccination promotion (despite shortages...)

Infection (2013) 41:621-628 DOI 10.1007/s15010-013-0431-1

CLINICAL AND EPIDEMIOLOGICAL STUDY

A 6-year antifungal stewardship programme in a teaching hospital

V. Mondain · F. Lieutier · L. Hasseine · M. Gari-Toussaint · M. Poiree · C. Lions · C. Pulcini



Conclusions and perspective

- Advice to colleagues thinking of initiating such a programme
 - Multidisciplinary collaboration is essential!
 - Indicators follow-up (antimicrobial consumption, AMR, appropriate use of ATB, IV/PO ratio, acceptance of interventions,...)
 - Set goals, essential messages, evaluate the results and provide regular feedback to prescribers
 - Importance of tracing pharmaceutical interventions to evaluate their clinical and financial impact
 - Using information technology to enhance AMS and develop easy-to-use tools (guidelines and newspaper available on internet, website, poster on how to administer injectable ATB ...)
- Which lessons can be learned from the French approach to AMS?
 - Multidisciplinary collaboration between pharmacists, ID specialists, microbiologists, hygienists is essential ©

ATB, antibiotics; AMR, antimicrobial stewardship; AMS, antimicrobial stewardship; IV, intravenous; PO, oral. Lieutier-Colas F, personal opinion.





Questions to the audience

- Which broad spectrum ATB provide AMR?
 Amoxicillin-clavulanate, 3rd generation
 cephalosporines, fluoroquinolones, carbapenems
- Who are the majors actors in AMS? Infectious diseases specialits, microbiologists and pharmacists
- How many time spend peri-surgical antibiotic prophylaxis? 2 to 4 hours (duration of the intervention)





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