

Antibiotic policy and Microbiological vigilance: "why, who, how ?"

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Based on the Belgian expérience and on material kindly provided by

- Pharm. Caroline Briquet, Groupe de Gestion de l'antibiothérapie, Cliniques univ. St Luc, Bruxelles, Belgium
- Dr C. Rossi, infectiologue hygiéniste, CHU Ambroise Paré, Mons, Belgium
- Dr C. Potvliege, microbiologiste hygiéniste, CHU Tivoli, La Louvière, Belgium
- Prof. H. Goossens, microbiologist and "creator" of the Belgian Antibiotic Policy Coordination Commmittee", Antwerp, Belgium
- Prof. A. Simon, microbiologiste hygiéniste, Clin. univ. St-Luc, Bruxelles, Belgium
- Dr A. Apisarnthanarak, Division of Infectious Diseases, Thammasat University Hospital, Thailand.

¹ member of the Association for the Prudent Use of Antibiotics (APUA: http://www.apua.org)

But before that, where are you from ?



WBI - HUP cooperation - Bach Mai Hospital, Hanoi, Vietnam

And what do you do in Belgium ?



antibiotics: from molecules to man

Our laboratory has a long-lasting experience in the training foreign graduate fellows

doctoral fellows



post-docs



students















group leaders



And also experience in academic partnerships













Vrije Universiteit Brussel





PENNSTATE HERSHEY			
	Milton S. Hershey Medical Center		











UNIVERSITY^{OF} BIRMINGHAM

11/10/2011

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In this context, we had for 2 years and half a very active Vietnamese post-doctoral fellow

- supported first by the programme "Research in Brussels" of the "Région Bruxelloise" (in 2007)
- and then by the "Fonds de la Recherche Scientifique" (in 2008-2009)



11/10/2011

And he was successful...



Prix "AORIC" remis à Paris, France, pour le meilleur travail d'antibiothérapie expérimentale

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2009, p. 1434–1442 0066-4804/09/\$08.00+0 doi:10.1128/AAC.01145-08 Copyright © 2009, American Society for Microbiology. All Rights Reserved. Vol. 53, No. 4

Intracellular Activity of Antibiotics in a Model of Human THP-1 Macrophages Infected by a *Staphylococcus aureus* Small-Colony Variant Strain Isolated from a Cystic Fibrosis Patient: Pharmacodynamic Evaluation and Comparison with Isogenic Normal-Phenotype and Revertant Strains[⊽]†

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Université Catholique de Louvain, Louvain Drug Research Institute, Unité de Pharmacologie Cellulaire et Moléculaire,¹ and Hôpital Erasme, Department of Microbiology, Laboratoire de Référence MRSA-Staphylocoques,² Hôpital des Enfants Reine Fabiola, Département de Maladies Infectieuses Pédiatriques,³ and CHU Saint Pierre-Huderf-CHU Brugmann, Département Interhospitalier de Dermatologie,⁴ Université Libre de Bruxelles, Brussels, Belgium

11/10/2011

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ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2009, p. 1443–1449 0066-4804/09/\$08.00+0 doi:10.1128/AAC.01146-08 Copyright © 2009, American Society for Microbiology. All Rights Reserved. Vol. 53, No. 4

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Based on what he learned in Belgium, the following seemed possible at UPH and Hanoi ...

- Launching clinical pharmacy in Vietnam...
 - Creating a strong basis for
 Pharmacokinetics/Pharmacodynamics of antibiotics in
 Vietnamese hospitals and at the University of Pharmacy
 - Creating a "Drug Information Center" for the country
 - Creating the basis for a strong Pharmacoeconomy group
 - helping to address the "antibiotic crisis" in Vietnam (but also present in other Asian Countries)

"Core program" of the Wallonie-Bruxelles project

Now, Belgium is by no means perfect...

P. aeruginosa from HAP / VAP patients in 6 hospitals in Belgium



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Belgium is certainly not perfect...

Consumption of Antibiotics in the Community



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Inorderly use of antibiotics causes major problems !



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Antimicrobial resistance is a major problem in hospitals ...

Factors that may increase antimicrobial resistance in hospitals.

Greater severity of illness of hospitalized patients More severely immunocompromised patients Newer devices and procedures in use Increased introduction of resistant organisms from the community Ineffective infection control and isolation practices and compliance Increased use of antimicrobial prophylaxis Increased empiric polymicrobial antimicrobial therapy High antimicrobial usage per geographic area per unit time

NOTE. Modified from McGowan JE Jr.

You can act upon these parameters by a rational policy of use !

Shlaes et al. Infect Control Hosp Epidemiol. 1997 Apr;18(4):275-91

But what can we do?

- Local
 - organism isolation (efficiency)
 - susceptibility pattern and reporting
 - Antibiotic Management Team
 - Isolation and Hygiene
- Regional/National
 - resistance and antibiotic consumption data
 - setting up guidelines
 - coordination

- "No organism isolated" means the doctor is blind ...
- Setting of pro-active programme to improve isolation success
 - local team (nursing) training for correct sampling
 - fast delivery to the laboratory
 - enough personnel and means to handle the daily load and pply the mots approriate technique
 - record success / failures by ward and main suspected infection and compare
 - with literature data
 - other hospitals
 - over time

to detect low level of performance and indentify the causes

Examples of techniques for success *

- Abcesses
 - Aspirate of pus or fluid in anaerobic transport vial is preferred; swabs usually have insufficient material for Gram stain and culture.
 - Clean surface of closed abscess with 70% alcohol; collect specimens at margins of abscess.
 - Aspirates in anaerobic transport tubes are acceptable for aerobic and anaerobic bacterial, fungal, and mycobacterial cultures.
 - Specify location of abscess for optimal processing; provide all other pertinent information (e.g., surgical infection, trauma, bite wound).
- Catheter
 - Intravascular: Remove aseptically, cut at least a 2-inch segment from tip, and place segment in sterile container. Transport rapidly to prevent drying out.
- Skin Lesion
 - Scrape skin at active edge of lesion; avoid blood. Place in sterile petri dish; biopsy may be more definitive than swabs of lesion. Transport swabs in transport media to prevent drying out; specify specific organism if one is suspected (e.g., dermatophyte, Sporothrix, Mycobacterium, etc.).

^{*} from Mandel's Principles and Practice of Infectious Diseases, 7th Edition, Elsevier

Examples of techniques for success

• Sputum, expectorated

- Have patient rinse or gargle with water to remove excess oral flora; instruct patient to cough deeply and expectorate secretions from lower airways; collect and transport in a sterile container.
- Collect 1 mL for bacterial culture; 5 mL or more for mycobacterial culture and molds.
- Presence of abundant epithelial cells is indicative of contamination with oral flora; a contaminated specimen is unacceptable for routine bacterial culture, but can be processed for mycobacteria or molds.

• Urine (midstream)

- Instruct women to hold labia apart, discard the first portion of voided urine, and collect a midstream portion in a sterile container.
- Instruct men to retract the foreskin, discard the first portion of voided urine, and collect a midstream portion in a sterile container.
- Collect first voided urine for Chlamydia trachomatis and N. gonorrhoeae tests.
- Keep refrigerated and transport to laboratory promptly, or submit in urine tube with boric acid to prevent overgrowth of contaminating organisms
- Cleansing before voiding does not consistently improve the quality of the specimen; however, if the patient is unable to provide a proper specimen, cleansing and supervised collection may be necessary.

Susceptibility pattern and reporting

Susceptibility pattern and reporting

- Follow the techniques proposed by annually reviewed standards (CLSI, EUCAST, CA-SFM, BSAC, ...) but with a critical eye and if appropriate to where you are
- Use reporter antibiotics to increase your diagnostic abilities (e.g. norfloxacin to detect efflux)
- Use automated systems but check for the quality of their answer (heteroresistance will be poorly detected)
- Keep track of the real MIC as much as possible for difficult cases, and compare values with those of the wild type distribution and with breakpoints
- Use E-test and microdilution when needed (e.g., detection of heteroresistance)
- Report MICs for (i) epidemiological surveys; (ii) any difficult case (with appropriate comment to the prescriber)

Looking at local hospital MIC distributions...

P. aeruginosa from HAP / VAP patients in 6 hospitals in Belgium



Going from the lab to the ward

- Does <u>your microbiologist</u> discuss infection cases in ICU with you ?
 - 1. Each case
 - 2. Few cases
 - 3. Upon asking
 - 4. Never



Addressing the questions you always wanted to ask ...

- Does your microbiologist gives MIC of antibiotics apart from sensitivity in ICU infections ?
 - 1. Each case
 - 2. Few cases
 - 3. upon asking
 - 4. Never



Looking at local <u>regional</u> MIC distributions...



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And making decisions....



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European Society of Clinical Microbiology and Infectious Diseases

EUCAST

Amoxicillin EUCAST rationale document

5. Pharmacodynamics

	Enterobacteriaceae	Streptococcus pneumoniae	Haemophilus influenzae		
%/T>MIC for st asis : exp	30 – 35	25 35	25 35		
%fT>MIC for 2 log drop : exp		35 – 45	35 - 45		
%/T>MIC from climical data		40	40		
References	 Gerber AU et al. J Infect Disease 1986; 153: 90-97 Craig WA et al. 33rd ICAAC 1993; Abstract 86 Craig WA. In Antimicrobial Pharmacodynamics Theory and Clinical Practice Ambrose. Marcel Dekker Inc, Basel: 1-22 MacGowan AP. Clin Microbiol Infect 2004: 52: 6-11 				

 $http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Rationale_documents/Amoxicillin_rationale_Nov2010_v_1.0.pdf$



Amoxicillin EUCAST rationale document: Target attainment rate*



Depending on the dose and schedule, you may cover bacteria with MIC from 0.5 to 8 mg/L

Graph prepared from data in http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Rationale_documents/Amoxicillin_rationale_Nov2010_v_1.0.pdf

30 years and Antibacteriak Therapy, Istan MBlurkey UP cooperation of Bach Mai Hospital, Hanoi, Vietnam

X EUCAS

European Society of Clinical Microbiology and Infectious Diseases

Performing longitudinal surveys



Vanhoof RLM, et al. 19th European Congress of Clinical Microbiology and Infectious Diseases. May, 16-19 2009, Helsinki.

Antibiotic Management team



Milestones in Belgium

- 1997: « package deal » for antibioprophylaxis in surgery
- 1998: Copenhagen conference « the microbial threat »
- 1999: launching of a Belgian Antibiotic Policy Coordination Committee
- 2001: European conference on AB use in Europe, Brussels, Belgium
- 2002: Pilot projects of antibiotic policy control groups in a few hospitals

3 major papers describing the role of an antibiotic policy committee...

JAMA. 1996 Jan 17;275(3):234-40.

Strategies to Prevent and Control the Emergence and Spread of Antimicrobial-Resistant Microorganisms in Hospitals. A challenge to hospital leadership.

Goldmann DA, Weinstein RA, Wenzel RP, Tablan OC, Duma RJ, Gaynes RP, Schlosser J, Martone WJ.

Department of Medicine, Children's Hospital, Boston, Mass 02115, USA.

Infect Control Hosp Epidemiol. 1997 Apr;18(4):275-91.

Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: guidelines for the prevention of antimicrobial resistance in hospitals.

Shlaes DM, Gerding DN, John JF Jr, Craig WA, Bornstein DL, Duncan RA, Eckman MR, Farrer WE, Greene WH, Lorian V, Lew S, McGowan JE Jr, Paul SM, Ruskin J, Tenover FC, Watanakunakorn C.

Wyeth-Ayerst Research, Pearl River, NY 10965, USA.

<u>Clin Infect Dis.</u> 2007 Jan 15;44(2):159-77. Epub 2006 Dec 13.

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship.

Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP, Huskins WC, Paterson DL, Fishman NO, Carpenter CF, Brennan PJ, Billeter M, Hooton TM; Infectious Diseases Society of America; Society for Healthcare Epidemiology of America.

Harborview Medical Center and the University of Washington, Seattle, USA.

Antibiotic Management team

Multidisciplinary team ...



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History project

- October 2002 ASTs in <u>37</u> acute care hospitals (*Financing: Royal Decree 25 April 2002*)
- July 2006 ASTs in <u>61</u> acute care hospitals (*Financing: Royal Decree 10 November* 2006)
- July 2007 acute care hospitals and chronic care hospitals with >150 beds
 (*Financing: Royal Decree 19 June 2007*) (*Tasks: Royal decree 12 February 2008*)

Position within the hospital organigram

Direction médicale



Priority tasks

Mandatory interventions

- Hospital formularium

Required interventions

- Guidelines
- Local epidemiology

• Priority interventions

- Evaluation of consumption
- Link between consumption and epidemiology
- Providing advice about antibiotic use
- Limitation and control of antibiotic usage
- Staff education
- Annual report for the commission coordinating antibiotic policy

A. How to set up an antibiotic policy control group ?

1. Clearly establish the main goals of the working group.
 → improve antibiotic usage (efficacy AND security)
 → reduce the cost without altering quality of care

 Convince the medical direction of the need
 → self-supported by cost savings and improving of quality of care

3. Examine the local situation

- \rightarrow number and type of beds
- \rightarrow number and type of hospital stays
- \rightarrow type of activities (surgery, ICU, oncology, ...)

Financial support

- Annual budget of 3 609 208 euro (federal funding for antibiotic managers)
- According to number of beds
- Range: 10 000- 81 700 euro per hospital

A. How to set up an antibiotic policy control group ?

4. Determine human resources that are needed ... and available

5. Describe the current situation



6. Establish a working plan for YOUR hospital

Proactive core strategies

- Prospective audit of AB use with direct intervention and feedback to prescriber (A-I)
- Formulary restriction and preauthorization requirements for specific agents (A-II)

Supplemental strategies

- Education (A-III)
- Guidelines and clinical pathways (A-I)
- Streamlining/de-escalation of empirical therapy (A-II)
- Parenteral to oral conversion (A-I)
- Dose optimization (A-II)
- Antimicrobial order forms (B-II)
- Combination therapy (C-II)
- Antimicrobial cycling (C-II)

1. « Face to Face » interventions



- Prospective and direct interaction between the prescriptor and the infectiologist/clinical pharmacist and feed-back
- Des-escalation (if empirical treatement) based on lab data
- Dose adaptation
- IV-Oral switch

⇒ Very efficient to reduce inappropriate usage !

2. Formularium

- list of antibiotics that are available in the hospital
- list of « reserved » antibiotics (broad spectrum) with specific modalities of use

⇒ Very efficient to reduce consumption !

- 3. At the level of the laboratory
- modalities of sample collection why, when, how ?
- data interpretation
 - criteria used colonisation vs infection sample quality

testings

antibiograms vs MIC which antibiotics to test ?

• epidemiology

how often ? which type of sample ?



- 4. At the level of the pharmacy
- consumption data (per ward)
- detailed evaluation of specific antibiotics carbapenems fluoroquinolones glycopeptides
- tables to improve antibiotic use

dose compatibilities and storage interactions, ...



5. Education



- guidelines
- analysis and feed back of data (resistance and consumption)

Should be accompanied by active interventions to be efficient

6. Evaluation



- compliance to guidelines
- reasons for non-observance

Propose new measures to improve at the next round !

Evaluation of impact

- Process measure: antimicrobial use (B-III)
- Outcome measure: resistance patterns (B-III)

3. Antibiotic formulary and guidelines

• Antibiotic formulary:

96.3% of the acute care hospitals

• Guidelines for empirical and etiological antibiotic therapy:

91.7% of the acute care hospitals

 Guidelines for antibiotic prophylaxis: 98.2% of the acute care hospitals

Successes and Difficulties of the antibiotic management teams

- accepted as a reference in the hospital for
- evaluation of consumption
- prescription habits
- detection of inappropriate use
- reminding of guidelines

- Diffusion of information
- Communication
- Data availability
- unlinked softwares (laboratory vs pharmacy)
- Heaviness of evaluation

Isolation and Hygiene

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Isolation and Hygiene

- Overpopulation must be avoided and/or corrected for
- Patients with multi-resistant organisms must be promptly diagnosed and isolated (with specific personnel)
- Cohorting is an useful approach to avoid dissemination while minimizing the costs and personnel burden
- Sound and consistent disinfection procedures must be enforced (hand washing, medical materials, plants and fruits from external and internal sources, ...)

Isolation and Hygiene: the problem



Isolation and Hygiene: knowing what you have

Results from recent European prevalence surveys



Belgium was 6 % in 2007

Hygiene: the most simple but most effective measure

Hand Hygiene (HH) is the most simple and effective measure to prevent healthcare associated infections.



Does everyone in you hospital agree???

Hand hygiene must be comprehensive

Journal of Hospital Infection (2007) 67, 9-21



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www.elsevierhealth.com/journals/jhin

REVIEW

'My five moments for hand hygiene': a user-centred design approach to understand, train, monitor and report hand hygiene

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^c School of Nursing, Mailman School of Public Health, Columbia University, New Y

^d Hospital of Saint Raphael, New Haven, CT, USA





Hand hygiene must be comprehensive

Your 5 moments for HAND HYGIENE ß PE CLEAN AD

BEFORE TOUCHING A PATIENT		2 BEFPROT	CEDURE CEPTIC	
				ING A
3 AFTER E EXPOSUR	SODY FUR			PATIENT
·			SURROUN	DINGS

BEFORE TOUCHING	WHEN? Clean your hands before touching a patient when approaching him or her
A PATIENT	WHY? To protect the patient against harmful germs carried on your hands
2 BEFORE CLEAN/ ASEPTIC PROCEDURE	WHEN? Clean your hands immediately before performing a clean/aseptic procedure WHY? To protect the patient against harmful germs, including the patient's own germs, entering his or her bod
3 AFTER BODY FLUID	WHEN? Clean your hands immediately after an exposure risk to body fluids (and after glove removal)
EXPOSURE RISK	WHY? To protect yourself and the health-care environment from harmful patient germs
4 AFTER TOUCHING	WHEN? Clean your hands after touching a patient and his or her immediate surroundings when leaving
A PATIENT	WHY? To protect yourself and the health-care environment from harmful patient germs
5 AFTER TOUCHING PATIENT SURROUNDINGS	WHEN? Clean your hands after touching any object or furniture in the patient's immediate surroundings, when leaving - even without touching the patient WHY? To protect yourself and the health-care environment from harmful patient germs
SURROUNDINGS	Corms Wash your hands of

Germs. wash your hands of them.

The hand hygiene campaigns in Belgium



Measurement of HH compliance: Gold standard

- Direct (overt or covert) observation
- By trained observers (IC practitioner or reference nurses for hospital hygiene)
- Standardised observation grid
- Observation period of 30 minutes, 24/24h, 7/7d
- Minimum 150 opportunities for HH per unit
- At least intensive care units
- Same methodology before and after campaign

Results are obtained sequentially ...

Campaig n	Messages	Participation	Hand hygien	e compliance %
		>80%	Before campaign	After campaign
2005	Just Do It		48	68
2006- 2007	Do It correctly		53	69
2008- 2009	Without jewels and with appropriate use of gloves		58	69
2010- 2011	Doctor, don't forget, it works and you have a role model		63	74.9



Incidence of healthcare associated MRSA in Belgian hospitals 1994-2009



National surveillance MRSA, Bea Jans

Surveillance of ESBL-producing Enterobacter aerogenes in Belgian hospitals



BAPCOC effect ? (Implementation of GGA)

Hand hygiene National campagnes ?

BICS guidelines for infection control of MRSA in hospitals ?

Decrease in proportion / incidence of ESBL+ E. aerogenes since 2006/2 No difference in incidence by hospital nbr of bed size 2,5 fold higher incidence in hospitals with DMS >9 days ISP/WIV report 2008/2

Can isolation / hygiene be applied in a country of limited resources ?

Resource-full

- Molecular epidemiology
- Environmental culture
- Active Surveillance
- Enhanced environmental cleaning
- Enhanced isolation precaution
- Antibiotic management

Resource-Limited

- Stratified unit specific infection rate
- Line listing and/or case-control study (identify common source outbreak)
- Implement emergency measure for highly alert pathogen
- Initial environmental culture (per finding from line listing)
- Modified Active Surveillance
- Enhanced isolation precaution
- Environmental cleaning
- Antibiotic management program

PDR-Acinetobacter baumannii: Can it be controlled?

Anucha Apisarnthanarak, MD, Division of Infectious Diseases, Thammasat University Hospital, Thailand Presented at the 8th Internatonal Sympoisum on Antibiotic Resistance (ISAR), Seoul, Korea, April 2011

Hand Hygiene Compliance Rate in Thailand



Urinary Tract Infection Intervention



Apisarnthanarak A, et al. Effectiveness of multifaceted hospital wide quality improvement program featuring intervention to remove IUC in a tertiary care center in Thailand. ICHE, 2007

Creating cohort area to limit transmission of PDR-A. baumannii in a medical unit

- October 2007, first case of *PDR-A. baumannii* was detected in a medical unit. The nurse to patient ratio was 1: 8 in this medical unit.
- IC measured were implemented within 24 hours including 1) enhanced contact isolation, 2) ASCs, 3) environmental cleaning, 3) enhanced hand hygiene program
- During period 1 (4-28 October), 6 cases of PDR-A. baumanii were detected by ASCs; infection and colonization rate 2.4/1000 patientdays & acquisition rate 6/1000 patient-days.

Apisarnthanarak A, et al. Creating cohort area to limit transmission of *PDR-A. baumannii* in a medical unit. CID, 2009

Regional / National activities

Regional / National activities

- Antibiotic consumption data
 - global
 - per hospital with feed back and comparisons
- Guidelines
 - for general practice \rightarrow guide sent to all GP's
 - for hospital: through Scientific Societies with the help of the Ministry of Health and the Social Security
- Centers for <pathogen> (Pneumococci, Pseudomonas, Staphylococci, …)
 - reference centers for clinical microbiology laboratories (indentification, novel resistance mechanisms, alerts...)
 - stable collections for evaluation of novel (or "come back") antibiotics