

#### La Gestione Multidisciplinare delle Infezioni Complicate delle Vie Urinarie nel Terzo Millennio

Ferrara, 5 Maggio 2017 Azienda Ospedaliera-Universitaria Ferrara Nuovo "Arcispedale S. Anna", Cona Aula Congressi

## Aspetti clinici e nuove opportunità terapeutiche

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The generally accepted definition of complicated UTI includes infection in the presence of factors that predispose to persistent or relapsing infection, such as

- foreign bodies (e.g., calculi, indwelling catheters or other drainage devices);
- obstruction;
- immunosuppression;
- renal failure;
- renal transplantation;
- urinary retention from neurologic disease
- infection in men,
- pregnant women,
- children,
- patients who are hospitalized or in health care-associated settings may be considered complicated



International Study of the Prevalence and Outcomes of Infection in Intensive Care Units

JL Vincent et al; JAMA 2009, 302:2323-2329

## · Point prevalence study

- International ICUs (n=1,265)
  - Population: 13,796 patients; 51% infected

## · Cohort

- Mean SOFA score: 6.3
- 28% medical, 72% surgery/trauma
- 56% on mechanical ventilation

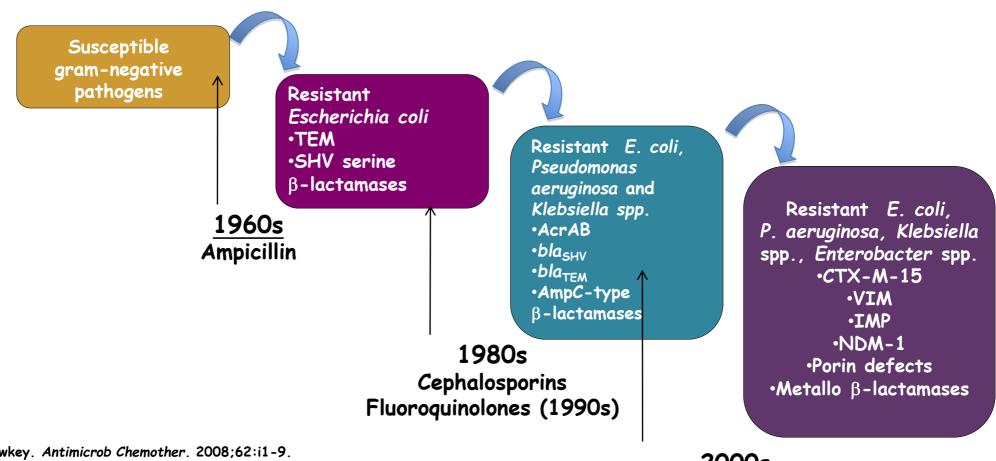
## International Study of the Prevalence and Outcomes of Infection in Intensive Care Units

JL Vincent et al; JAMA 2009, 302:2323-2329

			N	lo. (%) <sup>a</sup>					
Site of Infection	All	North America	Western Europe	Eastern Europe	Central/ South America	Oceania	Africa	Asia	
No. (%)	7087 (51.4)	607 (48.4)	3683 (49)	426 (56.4)	1290 (60.3)	285 (48.2)	89 (46.1)	707 (52.6)	
Respiratory tract	4503 (63.5)	345 (56.8)	2332 (63.3)	305 (71.6)b	851 (66)	165 (57.9)	41 (46.1) <sup>b</sup>	464 (6 5.6)	
Abdominal	1392 (19.6)	101 (16.6)	778 (21.1)	93 (21.8)	228 (17.7)b	50 (17.5)	16 (18)	126 (17.8)	
Blood stream	1071 (15.1)	157 (25.9)	546 (14.8)	53 (12.4)	139 (10.8) <sup>b</sup>	49 (17.2)	16 (18)	111 (15.7)	
Renal/urinary tract	1011 (14.3)	135 (22.2)	411 (11.2)	84 (19.7) <sup>b</sup>	222 (17.2) <sup>b</sup>	33 (11.6)	15 (16.9)	111 (15.7) <sup>b</sup>	
Skin	467 (6.6)	26 ( 4.3)	242 (6.6)	37 (8.7)	73 (5.7)	30 (10.5)	8 (9.0)	51 (7.2)	
Catheter- related	332 (4.7)	16 (2.6)	171 (4.6)	21 (4.9)	73 (5.7)	15 (5.3)	4 (4.5)	32 (4.5)	
CNS	208 (2.9)	14 ( 2.3)	100 (2.7)	20 (4.7)	40 (3.1)	11 (3.9)	4 (4.5)	19 (2.7)	
Others	540 (7.6)	62 (10.2)	289 (7.8)	31 (7.3)	87 (6.7)	22 (7.7)	14 (15.7) <sup>b</sup>	35 (5.0)b	

Infection	Pathogens				
Complicated UTI					
Most Common	Enterobacteriaceae, Pseudomonas aeruginosa, Acinetobacter spp.				
Less Common	MRSA, Enterococcus spp. (including VRE), Candida spp., Fastidious organisms possible				
Complicated IAI					
Gram-negative Bacteria	Enterobacteriaceae (E. coli, Enterobacter spp., Klebsiella spp., Proteus spp) Non-fermenting (P. aeruginosa, A. baumannii)				
Gram-positive Bacteria	Enterococci, Staphylococcus aureus, Coagulase-negative Staphylococci				
Anaerobic Bacteria	Bacteroides fragilis, Clostridium spp.				
Yeasts	Candida spp.				
Pneumonia (Nosocomial and Healthcare-associated)					
Most Common	P. Aeruginosa, Klebsiella spp., E. coli, Acinetobacter spp., S. aureus, S. pneumoniae, H. influenzae				
Less Common	Serratia spp., Legionella, spp., Influenza A virus, RSV, Parainfluenza virus, adenovirus				

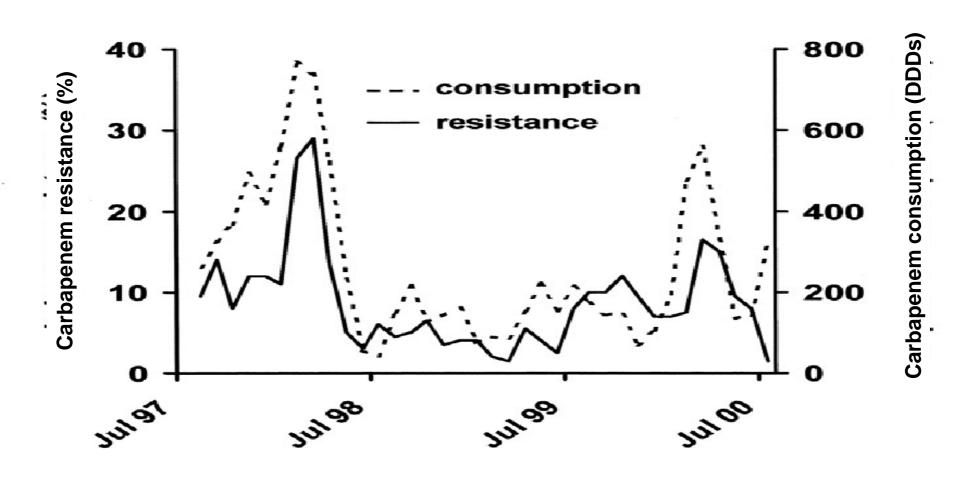
## Evolution of Gram-neg pathogens has caused widespread drug resistance



- 1. Hawkey. Antimicrob Chemother. 2008;62:i1-9.
- 2. Hawkey and Jones. J Antimicrob Chemother. 2009;64:i3-10.
- 3. Bush. Antimicrob. Agents Chemother. 2010;54:969-76.
- 4. Livermore. Clin Infect Dis. 2002;34:634-40.
- 5. Olivares et al. Front Microbiol. 2013:4:103.

2000s Carbapenems

# Correlation between carbapenem consuption and *P.aeruginosa* resistance



Lepper PM, et al. Antimicrob Agents Chemother. 2002;46:2920-2925.



#### 25 Feb 2017

# GLOBAL PRIORITY LIST OF ANTIBIOTIC-RESISTANT BACTERIA TO GUIDE RESEARCH, DISCOVERY, AND DEVELOPMENT OF NEW ANTIBIOTICS

**Chair:** E. Tacconelli (Infectious Diseases, DZIF Center, Tübingen University, Germany) and N. Magrini (WHO, EMP Department)

Coordinating group: Y. Carmeli, Tel Aviv University, Israel; S. Harbarth, University of Geneva, Switzerland; G. Kahlmeter, University of Uppsala, Sweden; J. Kluytmans, University Medical Center Utrecht, Netherlands; M. Mendelson, University of Cape Town, Groote Schuur Hospital, Cape Town, South Africa; C. Pulcini, University of Lorraine and Nancy University Hospital, France; N. Singh, George Washington University, USA; U. Theuretzbacher, Center for Anti-infective Agents, Austria

\*Advisory board: M. Cavaleri, Anti-infectives and Vaccines, European Medicine Agency (EMA); E. Cox U.S. Food and Drug Administration, Silver Spring; Lindsay Grayson, University of Melbourne, Australia; C. Houchens, Antibacterials Program at Biomedical Advanced Research and Development Authority (BARDA); D.L. Monnet, European Centre for Disease Prevention and Control, Stockholm, Sweden; M. Ouellette, Université Laval and Canadian Institutes for Health Research, Canada; K. Outterson, Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator CARB-X, Boston University, USA; J. B. Patel, Office of Antimicrobial Resistance, Centers for Diseases Control and prevention (CDC), Atlanta, USA

#### **Priority 1: CRITICAL**

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

*Enterobacteriaceae*, carbapenem-resistant, 3<sup>rd</sup> generation cephalosporin-resistant

### **Priority 2: HIGH**

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella spp., fluoroquinolone-resistant

*Neisseria gonorrhoeae*, 3<sup>rd</sup> generation cephalosporin-resistant, fluoroquinolone-resistant

## **Priority 3: MEDIUM**

Streptococcus pneumoniae, penicillin-non-susceptible

Haemophilus influenzae, ampicillin-resistant

Shigella spp., fluoroquinolone-resistant

## Resistance in Gram- pathogens: Challenges and opportunities

- Resistance = ↑ morbidity & mortality
- · Resistant Gram- in community & hospital settings
- · Enhanced infection control practices required
- Different mechanisms of resistance cause different relative change in MIC from wild type
  - Porin / Efflux / Target site → modest ↑ in MICs
  - Enzyme mediated → ↑ in MICs
- · PD optimize dosing can overcome modest MIC increases
- Enzyme mediated ↑ MICs require different Tx strategies

## Optimize antimicrobial exposures

- Anticipate impact of host on exposure
  - Increased clearance
  - Increased volume of distribution
- Determine MICs of target pathogen(s)
- Optimize PD using:
  - Highest tolerated doses
  - Altered infusion techniques (i.e., Prolonged or Continuous infusion)
  - Combination therapy
- · Consider availability of new potent agents
- Most expensive antibiotic is the one that doesn't work  $\rightarrow$   $\uparrow$  FAILURE  $\rightarrow$   $\uparrow$  LOS & Cost of Care

# Gram- negative resistance: Four major areas of need

Resistant Gram- negative Phenotype	CDC Threat Level	Estimated Cases & Attributable Deaths in US per Year				
ESBL-producing	Serious	26,000 cases				
Enterobacteriaceae	Jerious	1,700 deaths				
MDD P convoinage	Serious	6,000 cases				
MDR P. aeruginosa	Serious	400 deaths				
Carbapenem-resistant		9,300 cases				
Enterobacteriaceae (e.g. KPC)	Urgent	610 deaths				
Metallo-β-lactamase- producers	N/A	Very rare				

CDC, Antibiotic Resistance Threats in the US, 2013.

## Ceftolozane/ Tazobactam

Superior antipseudomonal activity compared to ceftazidime

- Active against most ESBL and Amp C-producing organisms
- · Covers most ESBL-producing E. coli, Klebsiella pneumoniae, and other Enterobacteriaceae

- Covers most AmpC producers
- · Does not have activity against KPC or MBLs

In 2013, the Centers for Disease Control and Prevention identified CRE as "nightmare bacteria" and an immediate public health threat that requires "urgent and aggressive action"

## The virtues of Avibactam

• Avibactam inactivates most important  $\beta$ -lactamases except metallo types and Acinetobacter OXA carbapenemases

 Even metalloenzymes can be overcome by combining avibactam with aztreonam, which is stable to metallo- β-lactamases, but vulnerable to the ESBLs and AmpC enzymes that often accompany them

## Activity of CAZ / AVI

 Activity against ESBLs and some carbapenem resistant Enterobacteriaceae

Most KPC producers are susceptibile

 Strains which are carbapenem resistant due to porin loss plus production of an ESBL or AmpC are susceptible **CEFTOLOZANE/TAZOBACTAM** is indicated for the treatment of the following infections in adults:

- Complicated intra-abdominal infections;
- Acute pyelonephritis;
- ·Complicated urinary tract infections

**CEFTAZIDIME/AVIBACTAM** is indicated for the treatment of the following infections in adults:

- ·Complicated intra-abdominal infection (cIAI)
- ·Complicated urinary tract infection (cUTI), including pyelonephritis
- ·Hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP).

Ceftazidime/avibactam is also indicated for the treatment of infections due to aerobic Gram-negative organisms in adult patients with limited treatment options.

MA a ME SERVONO ANTIBIOTICI per INFEZIONI delle VIE URINARIE, INFEZIONI di CUTE e TESSUTI MOLLI, INFEZIONI ADDOMINALI

#### oppure

#### **ANTIBIOTICI per MDR ????**

..... problema regolatorio/registrativo .....



TI PIACE VINCERE FACILE?



#### TERAPIA ANTI-INFETTIVA - CRITICITA'

Scarsa cultura specifica nel mondo medico tutti prescrivono tutto molti usano male

Nessun coinvolgimento degli infermieri nella responsabilità prescrittiva

Poca aderenza al concetto di gradualità della prescrizione il massimo ai pazienti gravi il minimo ai pazienti stabili

Utilizzo sub-ottimale delle risorse della microbiologia

Scarsa cultura rispetto alla necessità di approccio multidisciplinare in specifici contesti

## Current evidence and expert opinion support the following elements as effective to support the prudent use of antimicrobials in healthcare:

- 1. International organisations and agencies
- 2. National, regional and local governments
- 3. Healthcare facilities (resources, systems and processes)
- 4. Clinical microbiologists
- 5. Infectious disease specialists
- 6. Prescribers
- 7. Pharmacists
- 8. Nurses
- 9. Infection control practitioners
- 10. Public/patients
- 11. Professional associations and scientific societies
- 12. Research funders
- 13. Pharmaceutical industry
- 14. Diagnostics industry

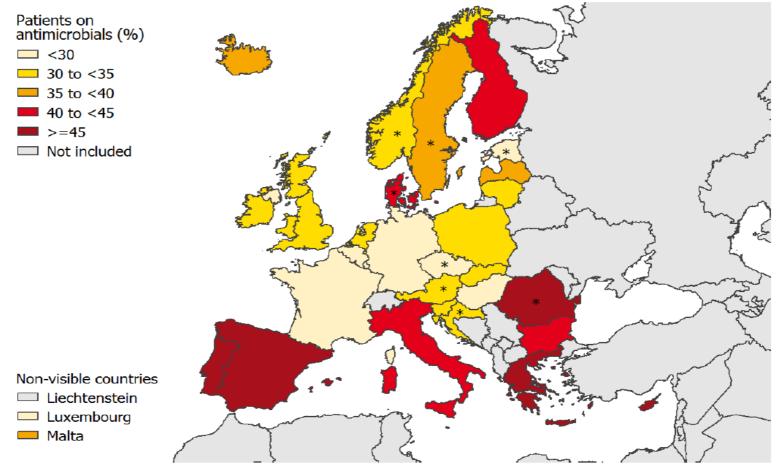


**TECHNICAL REPORT** 

Proposals for EU guidelines on the prudent use of antimicrobials in humans

European Centre for Disease Prevention and Control, 2017

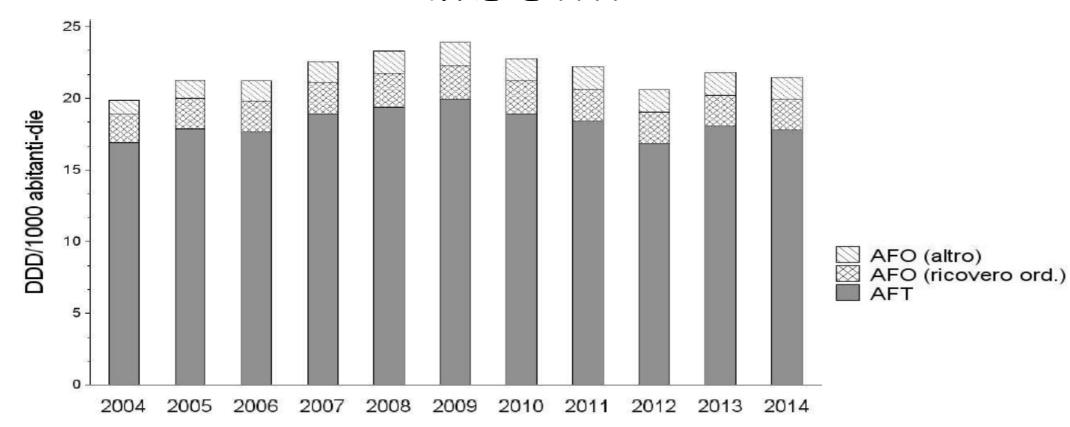
## Prevalence of antimicrobial use (percentage of patients receiving at least one antimicrobial agent) in European hospitals, by country, ECDC PPS 2011-2012



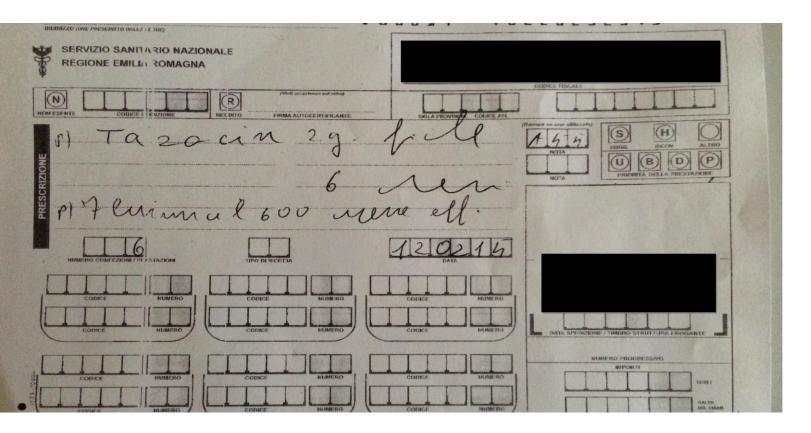
An asterisk indicates that reported PPS data did not provide a proper representation of the situation in a given country.

Representativeness of PPS data was poor in Austria, Croatia, the Czech Republic, Estonia, Norway and Romania, and very poor in Denmark and Sweden.

AMS
WHERE ????



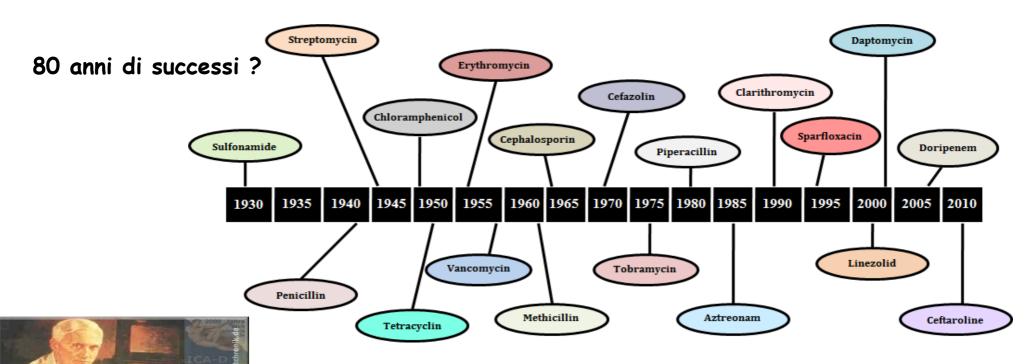
Tasso di consumo di antibiotici in Emilia-Romagna, espresso in DDD/1.000 abitanti-die (AFT e AFO 2004-2014)











80 anni di sconfitte?

#### Antimicrobial Resistance

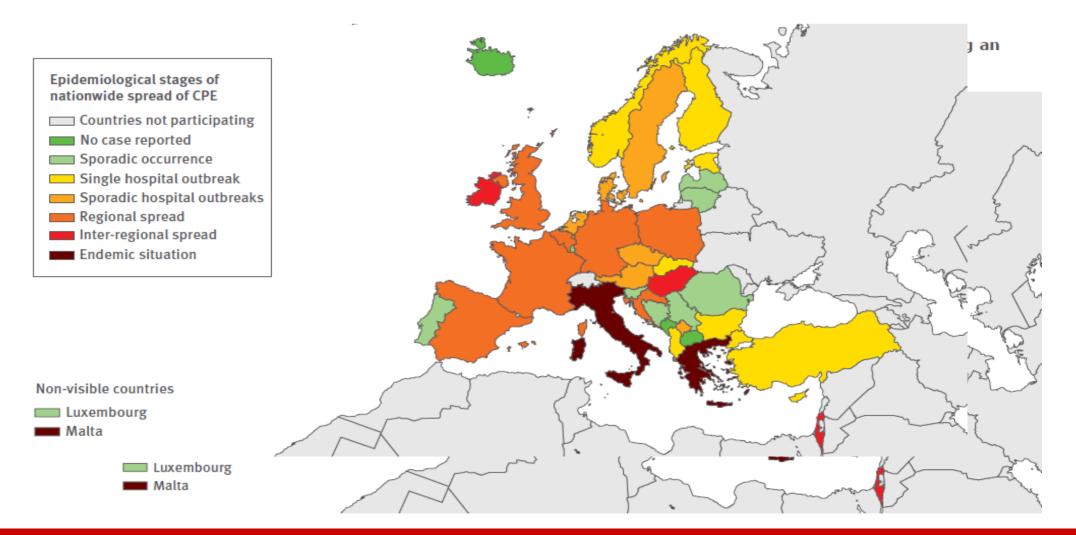
#### HD Marston et al; JAMA 2016, 316:1193-1204

Class	Antibiotic	Year of Approval or Introduction to Market								
β-Lactams	Penicillin	1942				Time	From	Antibioti	ic Appr	oval or
	Methicillin	1960						iction to		
	Cephalothin	1964				R	esistan	ice in Cl	inical S	iamples
	Amoxicillin-clavulanic acid	1984								
Carbapenems	Imipenem-cilastatin	1985								
Amphenicols	Chloramphenicol	1950								
Tetracyclines	Tetracycline	1953								
Aminoglycosides	Streptomycin	1946								
Macrolides	Erythromycin	1952								
Glycopeptides	Vancomycin	1958								
Quinolones	Nalidixic acid	1964								
Streptogramins	Quinupristin-dalfopristin	1999								
Oxazolidinones	Linezolid	2000								
Lipopeptides	Daptomycin	2003								
			0	5	10	15	20	25	30	35
			Years From Approval or Introduction to							

Market to First Clinical Report of Resistance

<u>European Centre for Disease Prevention and Control.</u> Last-line antibiotics are failing: options to address this urgent threat to patients and healthcare systems. *Stockholm: ECDC; 2016* 

Figure 1. Occurrence of carbapenemase-producing Enterobacteriaceae<sup>2</sup> in 38 European countries, using an epidemiological scale indicating the level of national spread, 2013



## LA CRISI DEGLI ANTIBIOTICI: QUALI RISPOSTE

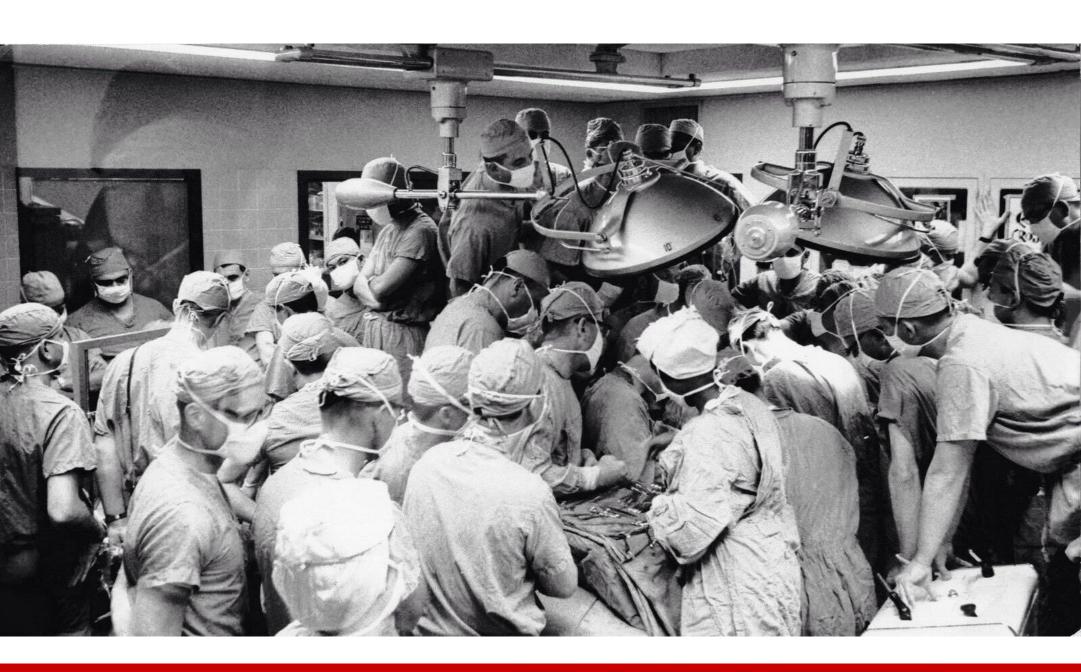
Nuovi farmaci

Terapie alternative

## Strategie di prevenzione

## Anti-Microbial Stewardship

AMS: visione "di sistema" della terapia antimicrobica. Uscire dall'individualismo terapeutico per passare ad una filosofia di utilizzo ecologico degli antimicrobici









## Preventing surgical site infections



## Patient who needs a surgical procedure

#### **Preoperative**

#### **Ensure that:**

- a clinical risk assessment for meticillin resistant Staphylococcus aureus (MRSA) screening is undertaken
- hair is not removed if at all possible; if hair removal is necessary, do not use razors
- the patient has showered (or bathed/washed if unable to shower) on day of or day before surgery using soap
- prophylactic antibiotic is prescribed as per local antibiotic policy/SIGN guideline, for the specific operation category
- the antibiotic is administered within 60 minutes prior to the operation (blade to skin)

#### **Perioperative**

#### Ensure that:

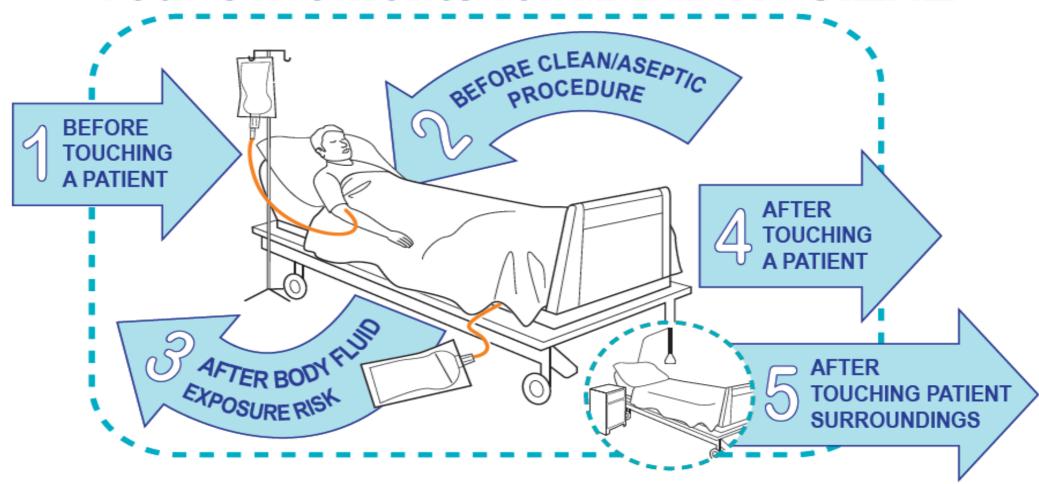
- 2% chlorhexidine gluconate in 70% isopropyl alcohol solution is used for skin preparation (if patient sensitive, use povidone-iodine)
- the patient's body temperature is maintained above 36°C in the perioperative period (excludes cardiac patients)
- the diabetic patients glucose level is kept at < I Immol/I throughout the operation</li>
- the patient's haemoglobin saturation is maintained above 95% (or as high as possible if there is underlying respiratory insufficiency)
- the wound is covered with a sterile wound dressing at the end of surgery

#### Postoperative **P**

#### Ensure that:

- the wound dressing is kept in place for 48 hours after surgery unless clinically told otherwise
- aseptic technique is used, if there is excess wound leakage and need for a dressing change
- hand hygiene is performed immediately before every aseptic dressing change (WHO Moment 2)

## **Your 5 moments for HAND HYGIENE**





## A Program to Prevent Catheter-Associated Urinary Tract Infection in Acute Care 5 Saint et al, NEJM 2016; 374:2111-9

Recommendation	Example of Intervention					
Primary						
Conducting daily assessment of the presence of and need for an indwelling urinary catheter	Conducting daily nursing rounds to review urine-collection strategies, including indications for continued urinary- catheter use					
Avoiding use of an indwelling urinary catheter by considering alternative urine-collection methods	Promoting the use of condom catheters, bladder scanners, intermittent straight catheterization, and accurate measurement of daily weight (all in lieu of indwelling urinary catheters)					
Emphasizing the importance of aseptic technique during catheter insertion and proper maintenance after insertion	Developing or updating the catheter-insertion policy to in- clude all the proper steps, developing competencies for health care workers who insert catheters, and considering periodic audits of catheter placement					
Additional						
Providing feedback to the units regarding urinary- catheter use and catheter-associated UTI rates	Providing nurses and physicians with data on urinary-catheter use, with monthly feedback on use and catheter-associated UTIs					
Addressing any identified gaps in knowledge of urinary management processes†	Conducting an evaluation for gaps in knowledge of infectious and noninfectious consequences of urinary-catheter use; developing tailored educational materials to fill identified gaps; using multiple venues for education, including bedside and electronic; incorporating education into annual competency testing for nurses; and using multiple venues for physicians (formal presentations and meetings, with one-to-one discussions for physicians with high use)					

# NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

MARCH 2015



XVII LEGISLATURA — ALLEGATO A AI RESOCONTI — SEDUTA DEL 21 GENNAIO 2016

552. Allegato A

# DOCUMENTI ESAMINATI NEL CORSO DELLA SEDUTA COMUNICAZIONI ALL'ASSEMBLEA

MOZIONI CAPUA, LENZI, NIZZI, CALABRÒ, GIGLI, LOCATELLI ED ALTRI N. 1-01055, RONDINI ED ALTRI N. 1-01092, PALESE ED ALTRI N. 1-01094 E GREGORI ED ALTRI 1-01096 CON-CERNENTI INIZIATIVE PER IL CONTRASTO DELLE INFE-ZIONI IN AMBIENTE OSPEDALIERO E SANITARIO We all have a moral obligation to work together to improve care for patients.

(Pronovost & Vohr, 2010, p. 137)



## The Health and Social Care Act 2008

Code of Practice on the prevention and control of infections and related guidance

Title: The Health and Social Care Act 2008 Code of Practice of the prevention and control of infections and related guidance

Author: Public and International Health Directorate, Health Protection and Emergency Response Division, Infectious Diseases Branch 10200

**Document Purpose:** 

Guidance

Publication date:

July 2015

Target audience:

CCG's CEs, NHS Trust CEs, Foundation Trust CEs, Medical Directors, Directors of PH, Directors of Nursing, Local Authority CEs, Directors of Adult SS, NHS Trust Board Chairs, Allied Health Professionals, GPs, Primary care organisations, dentists, independent healthcare and adult social care organisations, directors of infection prevention and control, infection prevention and control leads, Care Quality Commission

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July 2015



ALMA MATER STUDIORUM UNIVERSITÀ DI BOLOGNA

Policlinico S. Orsola-Malpighi





## CODICE DI COMPORTAMENTO

AZIENDALE (REVISIONE
APPROVATA CON DELIBERAZIONE
N. 154 DEL 30.3.2015)

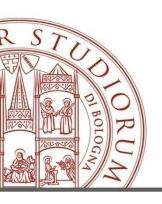
#### RELAZIONI INTERNE - CORRETTEZZA NEI COMPORTAMENTI NEI LUOGHI DI LAVORO

I destinatari:

- a) nell'ambito delle proprie competenze, si tengono informati ed aggiornati per offrire risposte soddisfacenti e indicazioni quanto più possibile chiare, complete e comprensibili a tutti gli interlocutori, interni ed esterni
- b) nell'ambito della propria posizione e nel rispetto del ruolo rivestito all'interno dell'Azienda, assumono un comportamento improntato a criteri di lealtà, probità e non prevaricazione, evitando ogni condotta che possa creare disagi e garantendo un proficuo rapporto collaborativo con i colleghi
- c) esprimono pensieri e opinioni personali in modo tale da non arrecare offesa a colleghi o danno all'Azienda
- d) ai fini del costante miglioramento della performance complessiva dell'Azienda e della comunità, collaborano allo svolgimento delle attività di controllo svolte dagli organi competenti, affinché sia resa agli stessi organi un'informazione veritiera, onesta, completa e trasparente
- e) operano nel rispetto delle norme di sicurezza previste dalla legge e dalle procedure interne, allo scopo di prevenire possibili conseguenze pregiudizievoli a danno di persone siano esse lavoratori, utenti o terzi o cose di proprietà dell'Azienda o di soggetti terzi
- f) utilizzano e valorizzano pienamente tutte le professionalità presenti nella struttura, mediante l'adozione delle iniziative disponibili al fine di favorire la crescita e lo sviluppo dei propri collaboratori
- g) assicurano l'assegnazione delle risorse in funzione delle specifiche competenze ed esperienze
- si astengono dal turpiloquio o, comunque, da un linguaggio non consono e offensivo verso colleghi e superiori

#### J. PROTEZIONE DELLA SALUTE

I destinatari, nell'ambito delle funzioni e delle responsabilità affidate, adottano e contribuiscono ad adottare le misure necessarie per proteggere l'integrità fisica e psicologica delle persone e ad utilizzare, ove previsto, i presidi antinfortunistici.



#### La Gestione Multidisciplinare delle Infezioni Complicate delle Vie Urinarie nel Terzo Millennio

Ferrara, 5 Maggio 2017 Azienda Ospedaliera-Universitaria Ferrara Nuovo "Arcispedale S. Anna", Cona Aula Congressi

## Aspetti clinici e nuove opportunità terapeutiche

Fabio Tumietto

Programma Epidemiologia e Controllo del Rischio Infettivo Correlato alle Organizzazioni Sanitarie Clinica Malattie Infettive – Bologna