Convegno Nazionale

La Gestio e Appropriat
delle Infezioni

Ferrara, 20 giugno 2019

INFEZIONI DELLE VIE URINARIE COMPLICATE NEL MIELO E CEREBROLESO

REGIONE AUTONOMA FRIULI VENEZIA GIULIA
azienda per l'assistenza sanitaria
5 Friuli Occidentale

Massimo Crapis

Responsabile S.S. Malattie Infettive

Responsabile *Antimicrobial Stewardship*

AAS 5 "Friuli Occidentale"

L'INSOSTENIBILE LEGGEREZZA … DELLE DEFINIZIONI

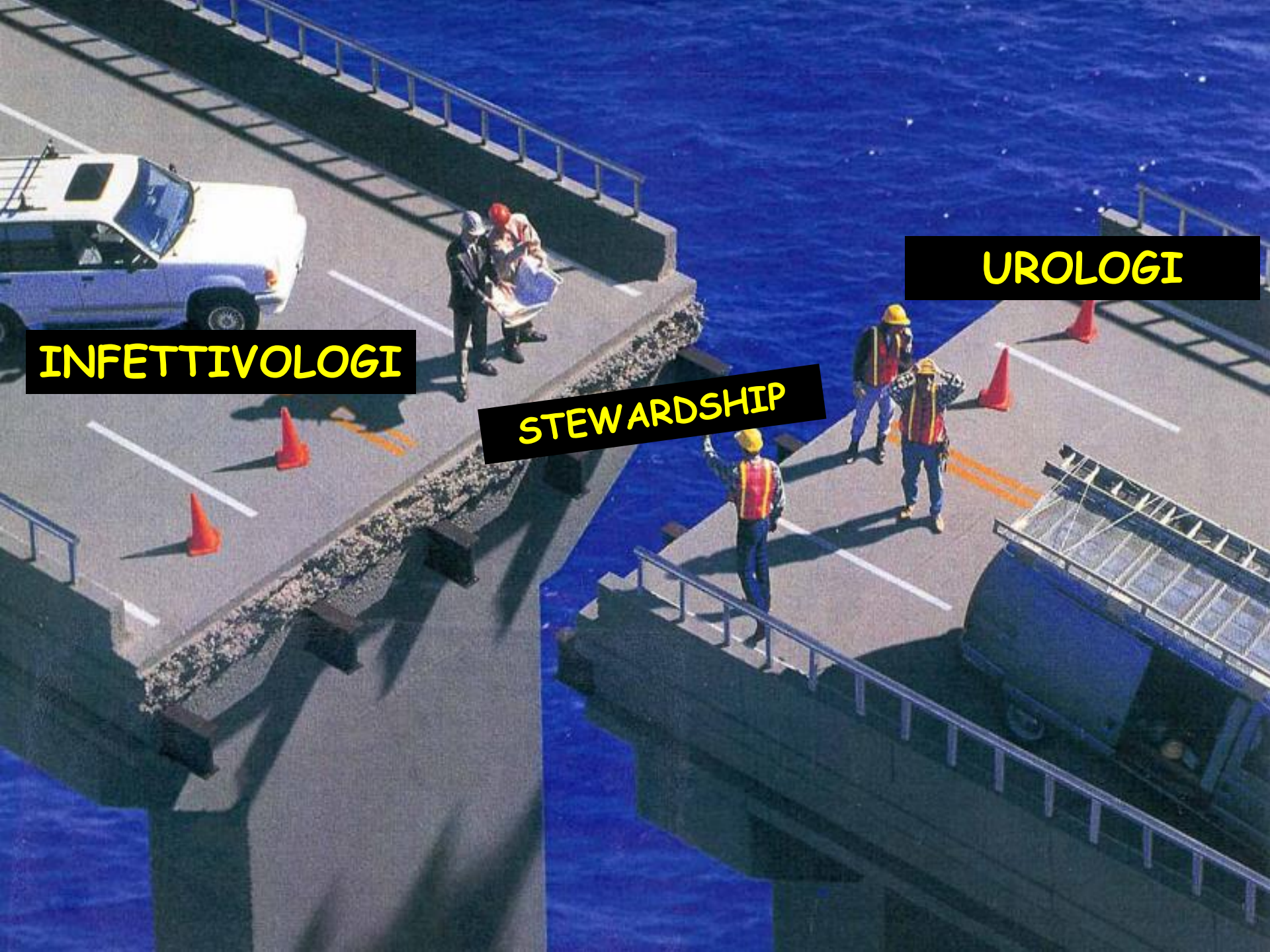
Complicated Urinary Tract Infections
Sabih A, LeslieSW *StatPearls Pub* 2019

Examples of a complicated UTI include:

- Infections occurring despite the presence of anatomical protective measures (UTI in males are by definition considered complicated UTI)
- Infections occurring due to anatomical abnormalities, for example, an obstruction, hydronephrosis, renal tract calculi, or colovesical fistula
- Infections occurring due to an immune compromised state, for example, steroid use, post chemotherapy, diabetes, elderly population, HIV)
- Atypical organisms causing UTI
- Recurrent infections despite adequate treatment (multi-drug resistant organisms)
- Infections are occurring in pregnancy (including asymptomatic bacteriuria)
- Infections are occurring after instrumentation, nephrostomy tubes, ureteric stents or bladder catheters
- Infections in renal transplant patients
- Infections are occurring in patients with impaired renal function
- Infections following prostatectomies or radiotherapy

Definition of Complicated Urinary Tract Infection
JR Johnson *CID* 2017

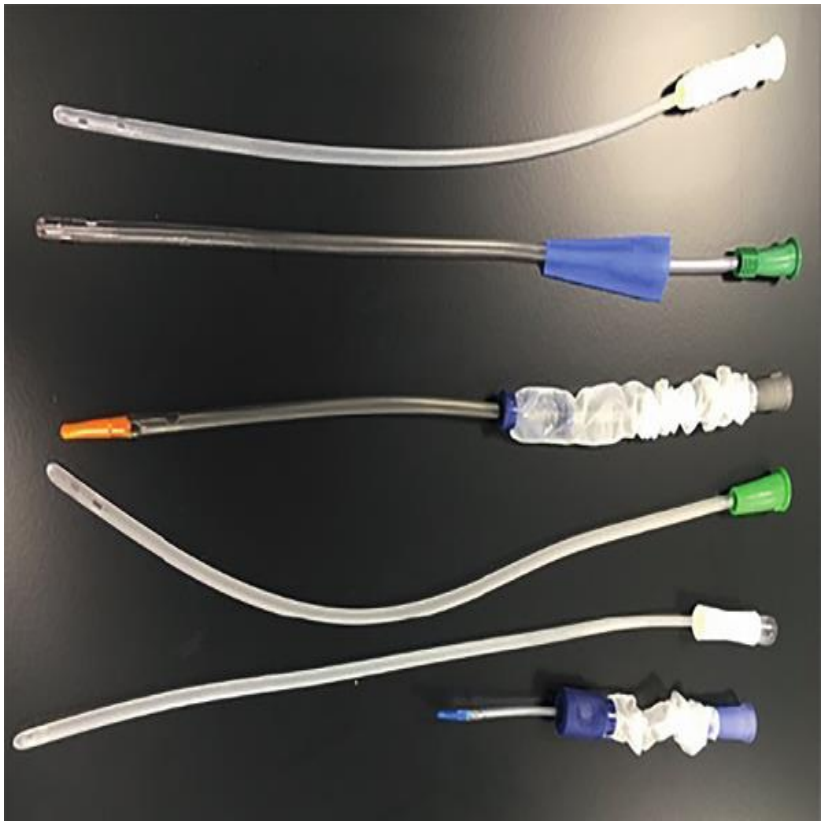
To the extent that different physicians interpret complicated UTI inconsistently, guidelines and treatment recommendations for complicated vs uncomplicated UTI risk being misapplied, even by conscientious providers. It may be time to find a different term than complicated UTI for UTIs that occur in patients with underlying predisposing factors, since this term seems hopelessly mired in ambiguity.


INFETTIVOLOGI
STEWARDSHIP
UROLOGI


“Il vero viaggio non
è cercare nuove terre
ma avere occhi nuovi.”
Marcel Proust

Review of Catheter-Associated Urinary Tract Infections and In Vitro Urinary Tract Models

Cortese YJ et al *J Healthcare Engineering* 2018



(a)

(b)

FIGURE 1: Various intermittent catheters (a): the upper five are male catheters, the lowest one is a female catheter. Two indwelling catheters with retention balloons inflated (b).

Review of Catheter-Associated Urinary Tract Infections and In Vitro Urinary Tract Models

Cortese YJ et al *J Healthcare Engineering* 2018

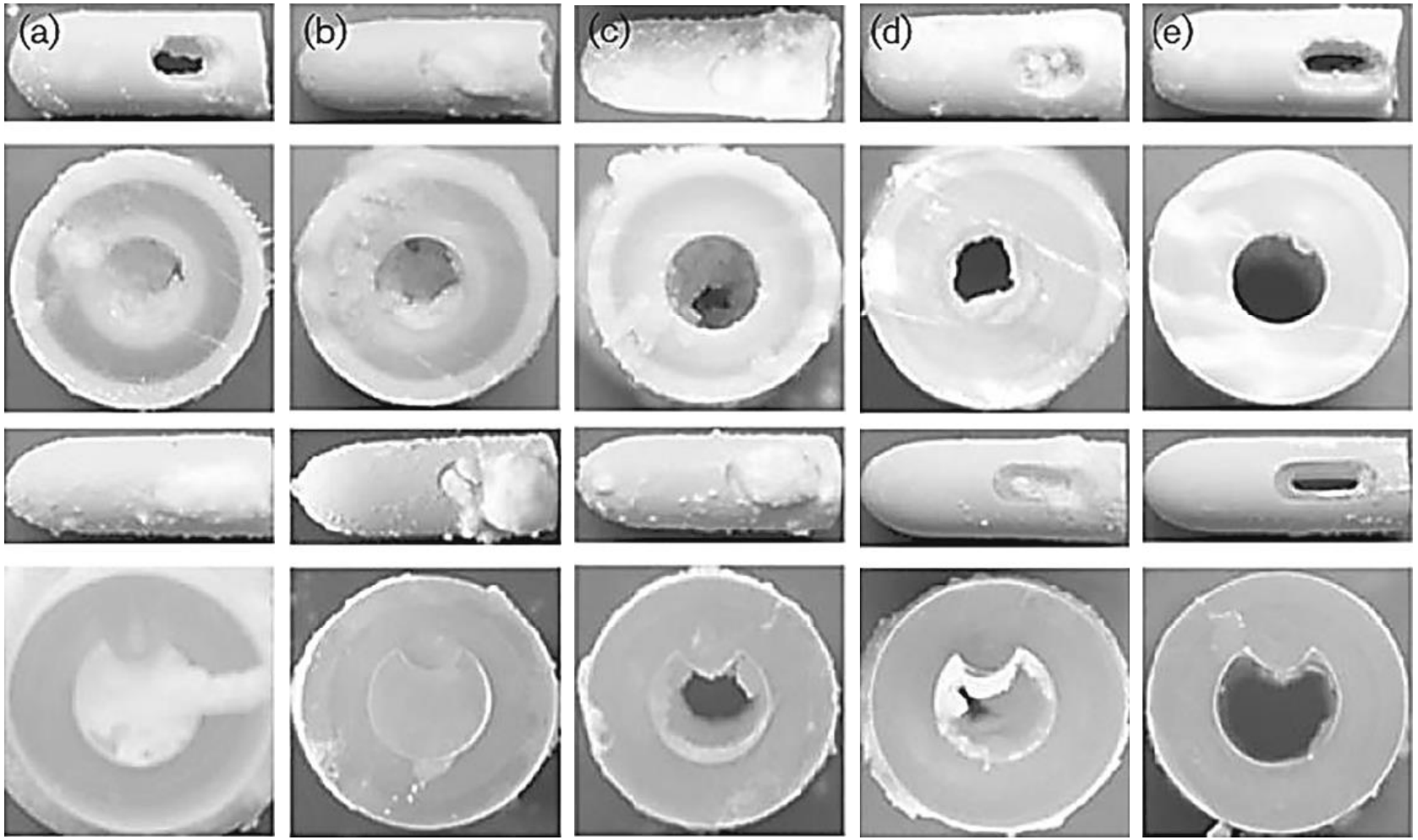


Figure 2: Examples of catheters encrusted by crystalline biofilms created by various bacteria: (a) *Proteus mirabilis,* (b) *Proteus vulgaris,* (c) *Providentia rettgeri,* (d) *Morganella morganii,* and (e) *Staphylococcus aureus*. The top two rows are silver/latex catheters, and the bottom two rows are nitrofurazone/silicone catheters [26].

Current controversies in urinary tract infections: ICI-RS 2017
Averbeck MA et al *Neurour Urodyn* 2018

	Definition of CAUTI
2016 Guidelines on Neuro Urology of the European Association of Urology (EAU)[9]	Signs and/or symptoms accompanied by laboratory findings of a UTI (bacteriuria, leucocyturia,[a] and positive urine culture). Significant bacteriuria in persons performing IC is present with $>10^2$ cfu/mL, $>10^4$ cfu/mL in clean-void specimens, and any detectable concentration in suprapubic aspirates.
Centers for Disease Control and Prevention (CDC) definition[12]	Patient must meet 1, 2, and 3 below: 1. Patient had an indwelling urinary catheter that had been in place for >2 days on the date of event (day of device placement = Day 1) AND was either: • Present for any portion of the calendar day on the date of event, OR • Removed the day before the date of event. 2. Patient has at least one of the following signs or symptoms: • fever (>38.0°C) • suprapubic tenderness • costovertebral angle pain or tenderness[b] • urinary urgency[b] • dysuria[b] 3. Patient has a urine culture with no more than two species of organisms identified, at least one of which is a bacterium of $\geq 10^5$ colony-forming units (cfu)/mL.
2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America (IDSA)[13]	Symptoms or signs compatible with UTI with no other identified source of infection along with $\geq 10^3$ cfu/mL of ≥1 bacterial species in a single catheter urine specimen or in a midstream voided urine specimen from a patient whose urethral, suprapubic, or condom catheter has been removed within the previous 48h[c].

[a]Leucocyturia is defined as 10 or more leucocytes in centrifuged urine samples per microscopic field (400×).
[b]These symptoms cannot be used when catheter is in place. An indwelling urinary catheter in place could cause patient complaints of "frequency" "urgency" or "dysuria".
[c]In the catheterised patient, pyuria is not diagnostic of CA-bacteriuria or CA-UTI, and the presence, absence, or degree of pyuria alone does not, by itself, differentiate catheter-associated asymptomatic bacteriuria from CAUTI. However, the absence of pyuria in a symptomatic catheterised patient suggests a diagnosis other than CAUTI.

Stigma and self-management: an Interpretative Phenomenological Analysis of the impact of chronic recurrent urinary tract infections after spinal cord injury

Hearn JH et al *Spinal Cord Ser Cas* 2018

CONCLUSIONS

The results of the present study suggest that UTIs after SCI are a source of **physical, emotional and social distress and disruption**. However, the depth of understanding obtained from the present study supports previous literature indicating that UTIs have a broader impact than that related to physical issues alone. This information can be used to improve the services provided by those involved in care of people with SCI as well as the treatment of UTIs. The findings provide **subjective support for continually improving the availability, reliability and effectiveness of psychological and social support for those with recurrent UTIs**, which will likely have an important role in reducing the stigma and improving the wellbeing of those living with SCI and recurrent UTIs.

Management of patient's expectations

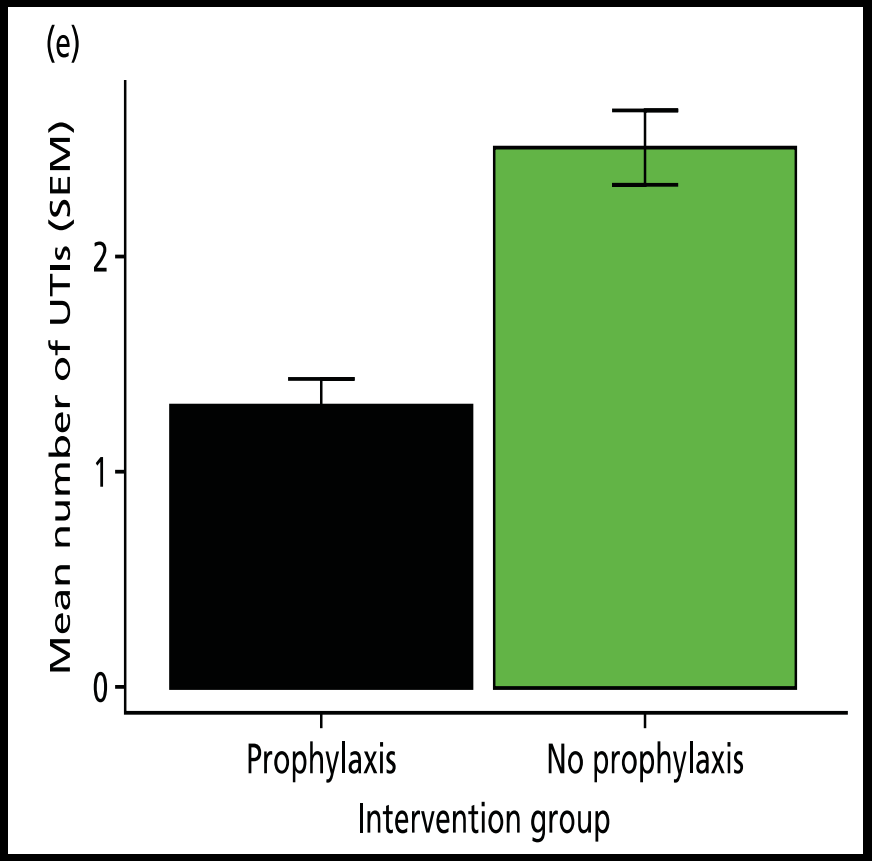
Patient and clinician perceptions of UTI symptoms and their severity can differ significantly, which may impair patient care, quality of life and potentially increase antibiotic resistance. Problems in communication between the patient and clinician have been reported as a major factor in this context; however, it is further complicated by conflicting guidelines on the management of UTI and variations between countries. A review by Christaens et al considered evidence and cultural factors when comparing four European guidelines on uncomplicated "cystitis." They reported that differences between guidelines seemed to be influenced by cultural aspects such as habits, the patient's expectations and healthcare service organization.

Patients have positive attitudes towards antibiotics, but poor knowledge about them and the diseases for which they are taken. This confusion has led to reduced patient satisfaction in practices with frugal antibiotic prescribing

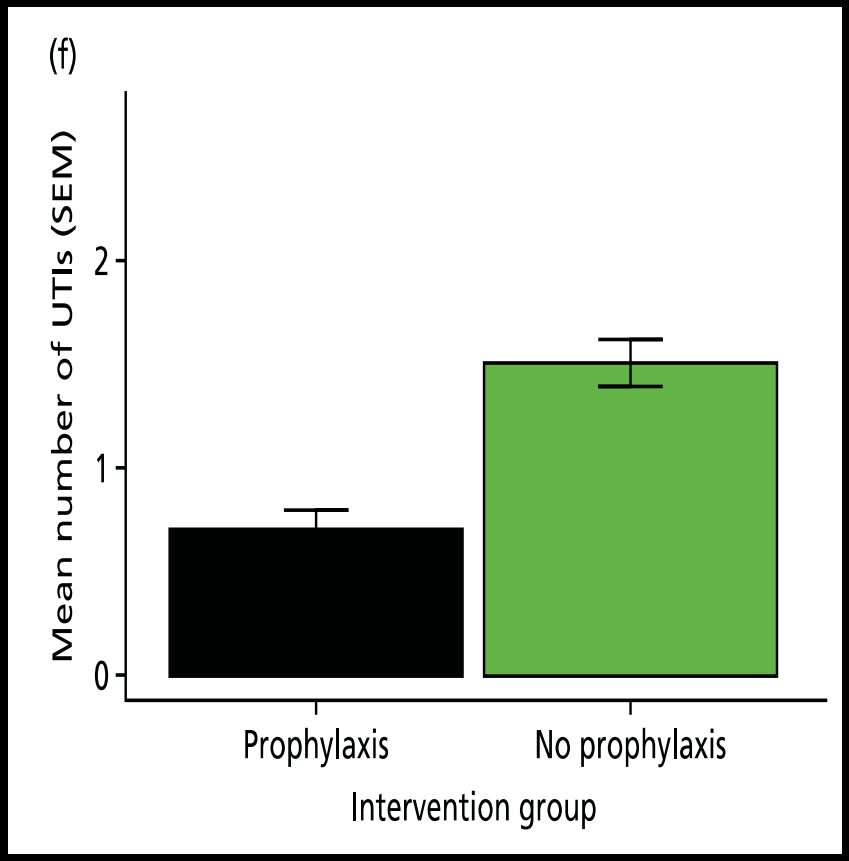
ATTENZIONE ALLE SIRENE AMMALIATRICI DELLA PROFILASSI …

Continuous low-dose antibiotic prophylaxis to prevent urinary tract infection in adults who perform clean intermittent self-catheterisation: the AnTIC RCT

Pickard R et al *Health Tech Assesm* 2018



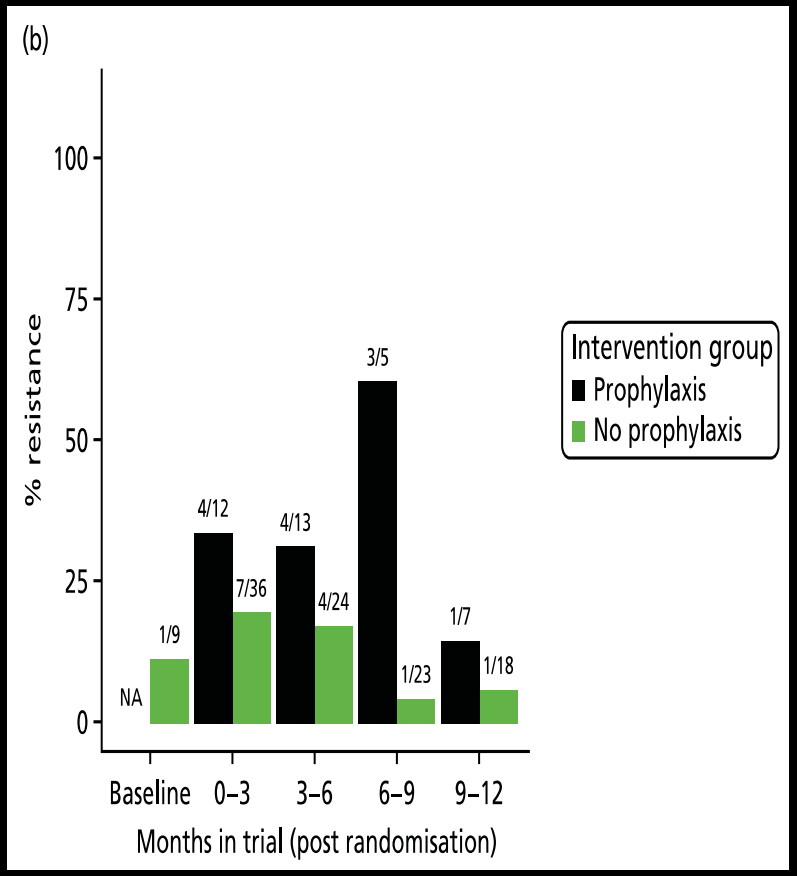
UTI sintomatiche

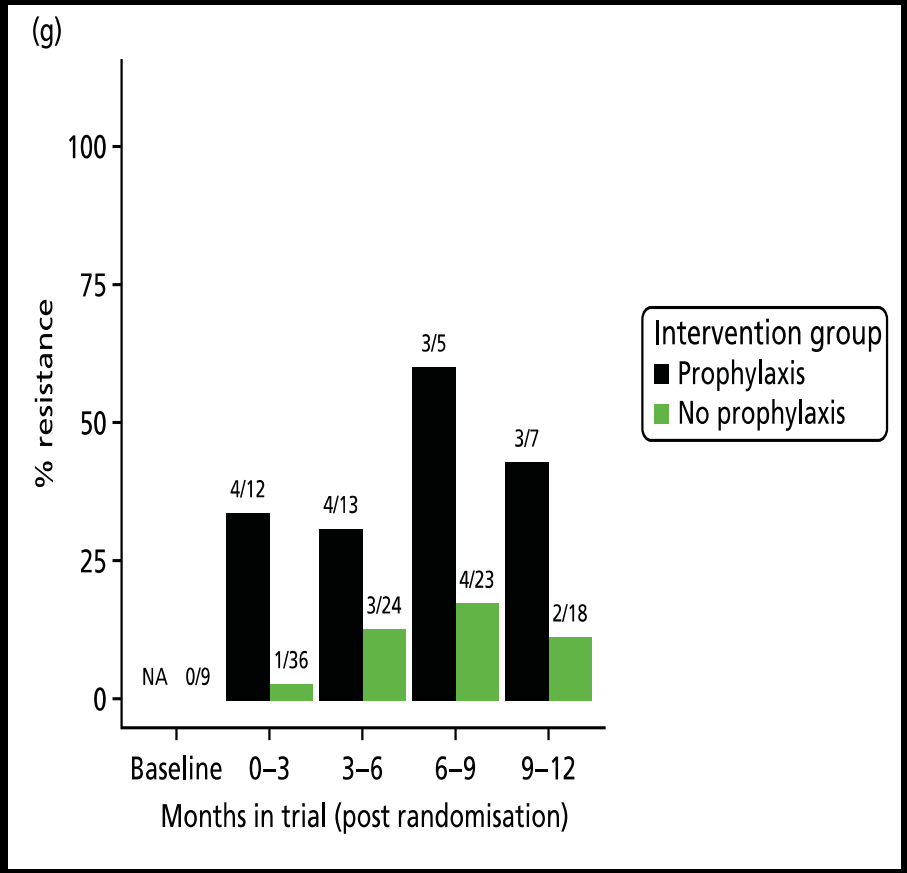


UTI sintomatiche e microbiologicamente confermate

Continuous low-dose antibiotic prophylaxis to prevent urinary tract infection in adults who perform clean intermittent self-catheterisation: the AnTIC RCT

Pickard R et al *Health Tech Assesm* 2018





Continuous low-dose antibiotic prophylaxis to prevent urinary tract infection in adults who perform clean intermittent self-catheterisation: the AnTIC RCT

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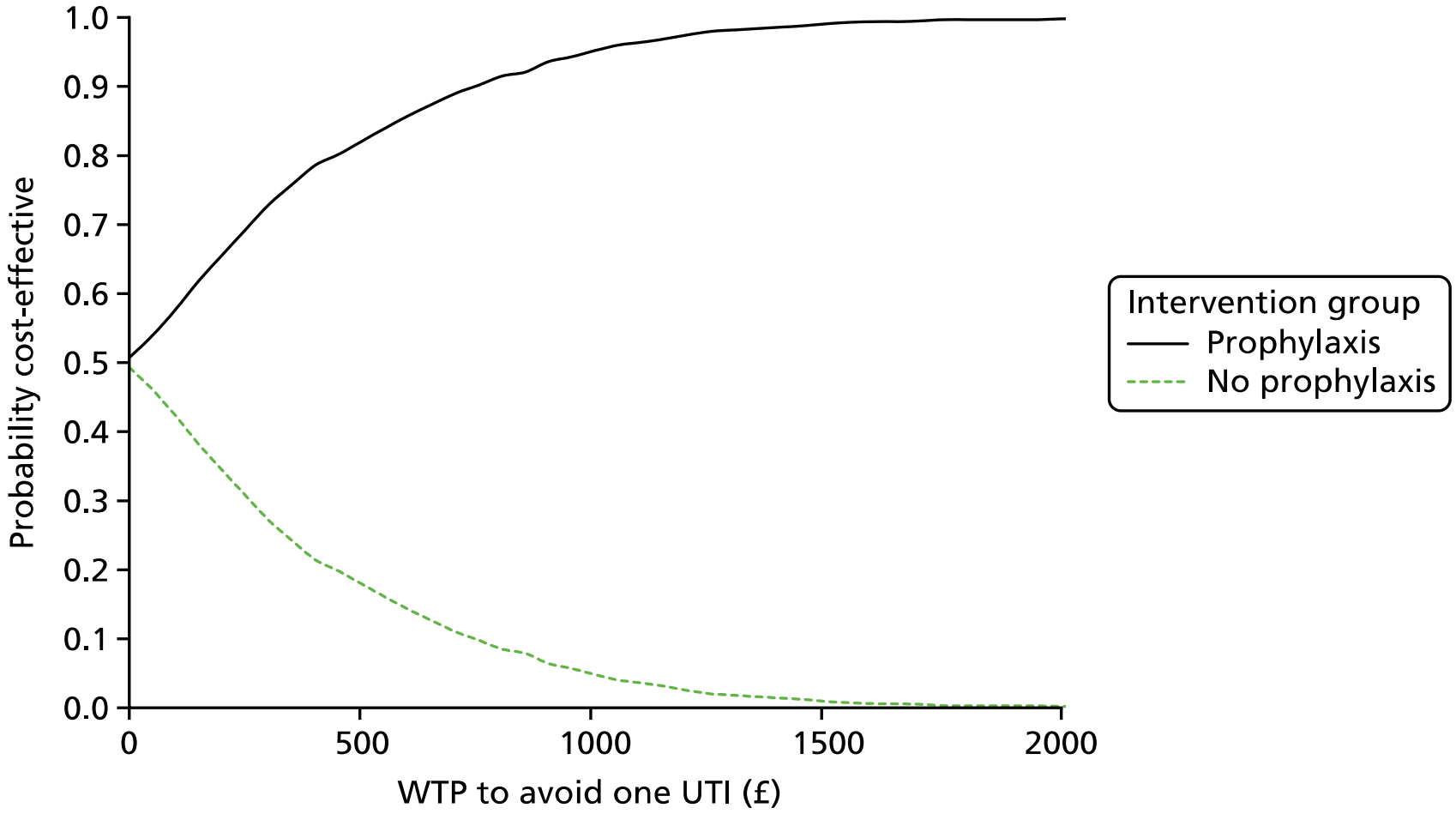


Complicated Urinary Tract Infections
Sabih A, LeslieSW *StatPearls Pub* 2019

Patients with permanent catheters such as suprapubic tubes should avoid prophylactic antibiotics. They should be treated only when symptomatic.

Infectious Diseases Society of America Guidelines for the Diagnosis and Treatment of Asymptomatic Bacteriuria in Adults

Nicolle LE et al CID 2005

Screening for or treatment of asymptomatic bacteriuria is NOT recommended for the following persons.

Premenopausal, nonpregnant women (A-I).

Diabetic women (A-I).

Older persons living in the community (A-II).

Elderly, institutionalized subjects (A-I).

Persons with spinal cord injury (A-II).

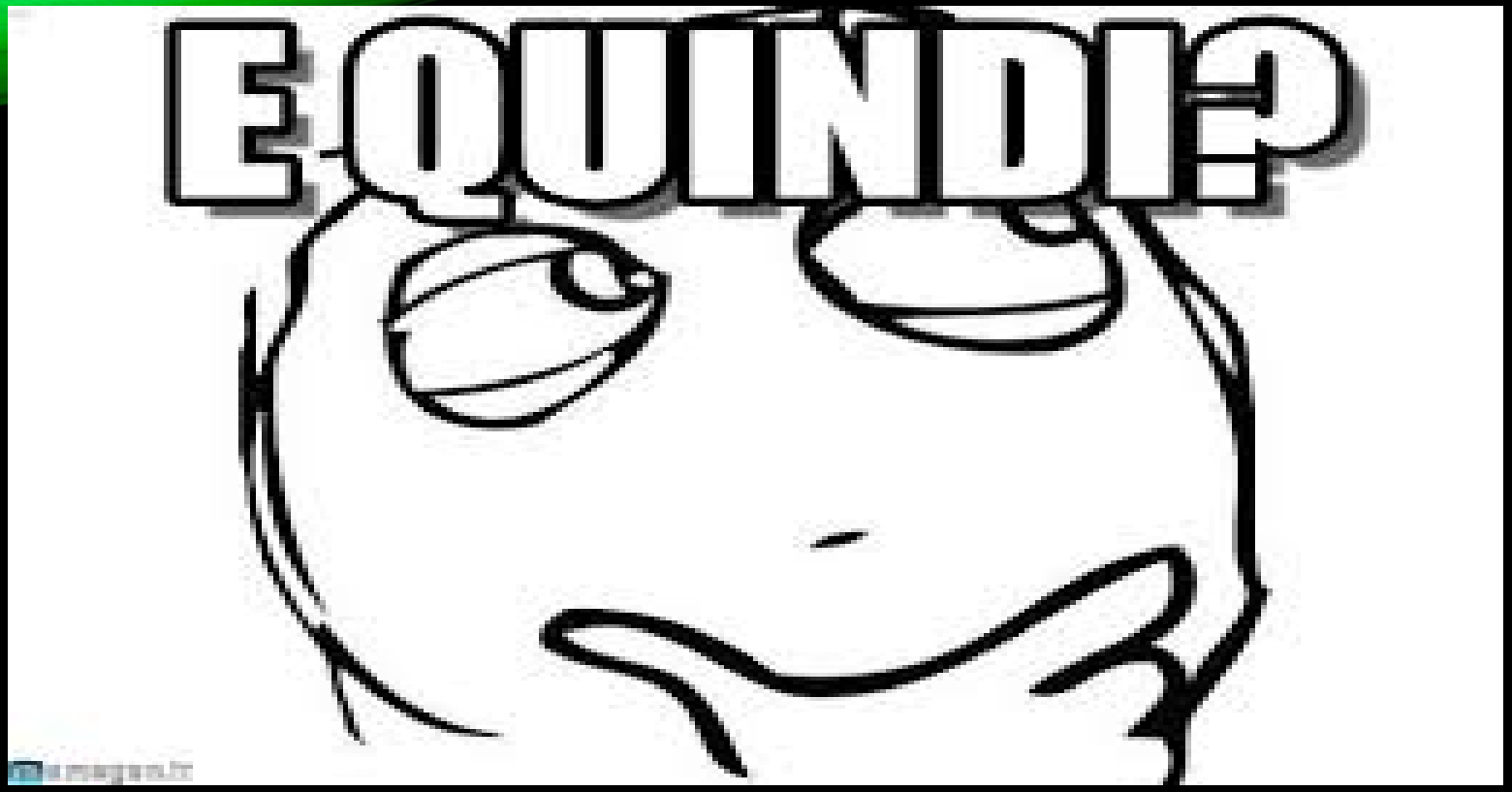
Catheterized patients while the catheter remains in situ (A-I).

La prima strategia per la salvaguardia degli antibiotici è valutare la reale indicazione ad eseguire terapia …

NON SI TRATTA LA BATTERIURIA ASINTOMATICA TANTO Più SE RECIDIVANTE o PERSISTENTE!!!

PER LO STESSO MOTIVO NON SI RICHIEDE UROCOLTURA SE NON VI E' INDICAZIONE O SOSPETTO CLINICO.

IN PARTICOLARE SARA' SEMPRE FUORVIANTE ESEGUIRE UROCOLTURE IN PAZIENTE PORTATORE DI CATETERE VESCICALE



CHI, COME E QUANDO TRATTARE?

Diagnosis, Prevention, and Treatment of CatheterAssociated Urinary Tract Infection in Adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America

Hooton TM et al CID 2010

In the catheterized patient, pyuria is not diagnostic of CA-bacteriuria or CA-UTI (AII).
The presence, absence, or degree of pyuria should not be used to differentiate CA-ASB from CA-UTI (A-II).
Pyuria accompanying CA-ASB should not be interpreted as an indication for antimicrobial treatment (A-II).
The absence of pyuria in a symptomatic patient suggests a diagnosis other than CA-UTI (A-III).

Signs and symptoms compatible with CA-UTI include new onset or worsening of fever, rigors, altered mental status, malaise, or lethargy with no other identified cause; flank pain; costovertebral angle tenderness; acute hematuria; pelvic discomfort; and in those whose catheters have been removed, dysuria, urgent or frequent urination, or suprapubic pain or tenderness (A-III).

In patients with spinal cord injury, increased spasticity, autonomic dysreflexia, or sense of unease are also compatible with CA-UTI (A-III).

INFEZIONE

CORRETTA COLLOCAZIONE DEL PAZIENTE E DELLA TIPOLOGIA DI INFEZIONE PER UNA APIA ANTIBIOTICA

SIMPLE & SAVING

ano e lontano»
roverbio

MELY & AGGRESSIVE

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFCM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

Editorial page 757

Author Video Interview, Author Audio Interview, and JAMA Report Video at jama.com

Related articles pages 762 and 775

CME Quiz at jamanetworkcme.com and CME Questions page 816

IMPORTANCE Definitions of sepsis and septic shock were last revised in 2001. Considerable advances have since been made into the pathobiology (changes in organ function, morphology, cell biology, biochemistry, immunology, and circulation), management, and epidemiology of sepsis, suggesting the need for reexamination.

OBJECTIVE To evaluate and, as needed, update definitions for sepsis and septic shock.

PROCESS A task force (n = 19) with expertise in sepsis pathobiology, clinical trials, and epidemiology was convened by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine. Definitions and clinical criteria were generated through meetings, Delphi processes, analysis of electronic health record databases, and voting, followed by circulation to international professional societies, requesting peer review and endorsement (by 31 societies listed in the Acknowledgment).

KEY FINDINGS FROM EVIDENCE SYNTHESIS Limitations of previous definitions included an excessive focus on inflammation, the misleading model that sepsis follows a continuum through severe sepsis to shock, and inadequate specificity and sensitivity of the systemic inflammatory response syndrome (SIRS) criteria. Multiple definitions and terminologies are currently in use for sepsis, septic shock, and organ dysfunction, leading to discrepancies in reported incidence and observed mortality. The task force concluded the term severe sepsis was redundant.

RECOMMENDATIONS Sepsis should be defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. For clinical operationalization, organ dysfunction can be represented by an increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more, which is associated with an in-hospital mortality greater than 10%. Septic shock should be defined as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. Patients with septic shock can be clinically identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia. This combination is associated with hospital mortality rates greater than 40%. In out-of-hospital, emergency department, or general hospital ward settings, adult patients with suspected infection can be rapidly identified as being more likely to have poor outcomes typical of sepsis if they have at least 2 of the following clinical criteria that together constitute a new bedside clinical score termed quickSOFA (qSOFA): respiratory rate of 22/min or greater, altered mentation, or systolic blood pressure of 100 mm Hg or less.

CONCLUSIONS AND RELEVANCE These updated definitions and clinical criteria should replace previous definitions, offer greater consistency for epidemiologic studies and clinical trials, and facilitate earlier recognition and more timely management of patients with sepsis or at risk of developing sepsis.

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The Sepsis Definitions Task Force members are the authors listed above.

Corresponding Author: Clifford S. Deutschman, MD, MS, Departments of Pediatrics and Molecular Medicine, Hofstra-Northwell School of Medicine, Feinstein Institute for Medical Research, 350 Community Dr, Manhasset, New Hyde Park, NY 11040 (cdeutschman@nshs.edu).

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

qSOFA

CORRETTA COLLOCAZIONE DEL PAZIENTE E DELLA TIPOLOGIA DI INFEZIONE PER UNA SCELTA APPROPRIATA DI TERAPIA ANTIBIOTICA

«Hit h lich

SIMPLE & SAVING

TIMELY & AGGRESSIVE

FONDAMENTALE CORRELAZIONE CON LOCALIZZAZIONE DI INFEZIONE (VIE URINARIE INFERIORI vs SUPERIORI)

ANTIBIOTICI IDROFILI

- Beta-lattamici
  - ✓Penicilline
  - ✓Cefalosporine
  - ✓Carbapenemi
  - ✓Monobactami
- Glicopeptidi
- Ami

Da Preferire in cistiti-IVU inferiori

- ✓ Basso volume di distribuzione
- ✓ Incapacità ad attraversare m. plasmatica
- ✓ Inattivi su patogeni intracellulari
- ✓ Eliminazione prevalentemente renale
- ✓ Assorbimento orale variabile non sempre ottimale

ANTIBIOTICI LIPOFILI

- Macrolidi
- Fluorochinoloni
- Tetracicline
- Tigeciclina
- Rifampi

Da Preferire in pielonefriti-IVU superiori e prostatiti

- ✓ me di distribuzione
- ✓ ttraversamento m. plasmatica
- ✓ Attivi su patogeni intracellulari
- ✓ Eliminazione dopo metabolismo epatico
- ✓ Miglior assorbimento orale

Courtesy of F. Pea modified

CISTITI – INFEZIONE VIE URINARIE INFERIORI

NITROFURANTOINA

Preferibile dosaggio 100 mg x4/die per 5 gg
(50 mg x4/die se ClCr <50 ml/min)

PRO
- Tasso di resistenza bassissimo
- Ben tollerata

CONTRO
- 4 volte al giorno
- Controindicata in IR (<ClCr 30 ml/min)

TMP/SMX

Possibile salire a 1cp x 3/die
(1/2 cp x 3/die se ClCr <50 ml/min)

PRO
- Buona efficacia
- Ben tollerato per brevi periodi

CONTRO
- Elevati tassi di resistenza
- Troppo spesso sottodosato

FOSFOMICINA SALE DI TROMETAMOLO

Possibile incremento dose a 3g ogni 24 ore per 3-4 somministrazioni

PRO
- Ottima efficacia
- Tasso di resistenza bassissimo
- Facile somm.ne con pochi eff collaterali

CONTRO
- Sensib. Da preservare per utilizzo ev
- Monosomm.ne ad elevato rischio di insuccesso
- Facile somm.ne con pochi eff collaterali

The revival of fosfomycin

Michalopoulos AS *Int J Inf Dis* 2011

Fosfomycin is rapidly absorbed following oral administration and is converted to the free acid, fosfomycin. Bioavailability is around 40% for fosfomycin tromethamine .
30–60% of fosfomycin tromethamine is excreted unchanged in the urine

Fosfomycin has a relatively long elimination half-life, which varies between 4 and 8 h

Fosfomycin has good distribution into tissues, achieving clinically relevant concentrations in serum, kidneys, bladder wall, prostate, lungs, inflamed tissues, bone, cerebrospinal fluid, abscess fluid, and heart valves.

For uncomplicated cystitis, a single dose of fosfomycin (3 g) is adequate. For complicated cystitis, a single dose of fosfomycin (3 g) administered every 2–3 days is necessary. In total, three doses of fosfomycin are needed. In the case of oral administration, no dosage adjustment is necessary in patients with hepatic or renal failure.

INOLTRE CONSIDERARE ANCHE …

AMOXICILLINA/CLAVULANATO
1 cp ogni 8 ore (8-16-24) per 3-5 giorni

CEFALOSPORINE ORALI (accattivanti ma … adeguate solo sulla carta…)
Opzioni NON ottimali in quanto biodisponibilità orale molto bassa (<50%). Se utilizzate prediligere
CEFTIBUTEN 400 mg/die (digiuno) o CEFPODOXIME 200 mg ogni 12 ore (peraltro *off label*)

HA CITATO 6 FARMACI E NON HA CITATO I FLUOROCHINOLONI?

MAI FLUOROCHINOLONI!!!
E POI …

NOTA INFORMATIVA IMPORTANTE CONCORDATA CON LE AUTORITA' REGOLATORIE EUROPEE E L'AGENZIA ITALIANA DEL FARMACO (AIFA)

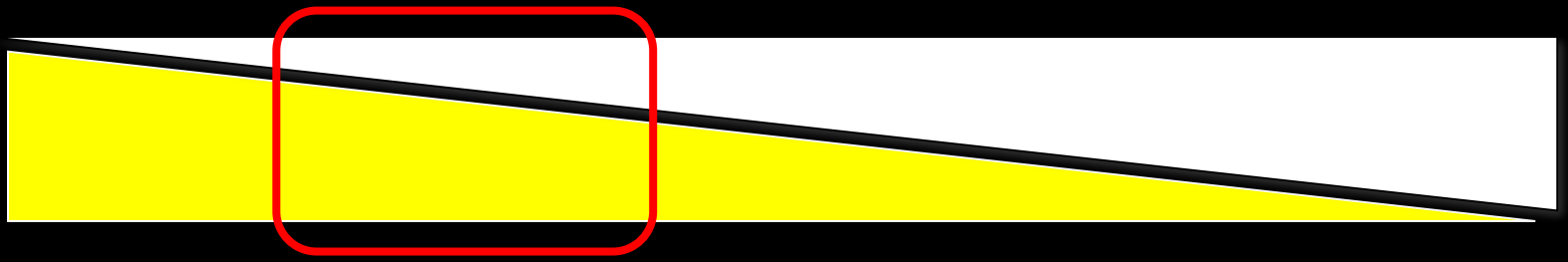
Aprile 2019

Antibiotici chinolonici e fluorochinolonici per uso sistemico e inalatorio

Rischio di effetti indesiderati invalidanti, di lunga durata e potenzialmente permanenti e restrizioni d'uso

- per il trattamento di infezioni non gravi o autolimitanti (quali faringite, tonsillite e bronchite acuta);
- per la prevenzione della diarrea del viaggiatore o delle infezioni ricorrenti delle vie urinarie inferiori;
- per infezioni non batteriche, per esempio la prostatite non batterica (cronica);
- per le infezioni da lievi a moderate (incluse la cistite non complicata, l'esacerbazione acuta della bronchite cronica e della broncopneumopatia cronica ostruttiva – BPCO, la rinosinusite batterica acuta e l'otite media acuta), a meno che altri antibiotici comunemente raccomandati per queste infezioni siano ritenuti inappropriati ;
- ai pazienti che in passato abbiano manifestato reazioni avverse gravi ad un antibiotico chinolonico o fluorochinolonico.

INFEZIONE VIE URINARIE SUPERIORI



FR PRINCIPALI nella *REAL LIFE*

ESBL

- Pregressa colonizzazione e/o infezione da ESBL
- Prolungata ospedalizzazione (mediana di 10 giorni) (in particolare in UTI, RSA, *hospice*)
- Catetere vescicali a permanenza
- PEG
- Multipli cicli di terapia antibiotica (FQ, betalatt, cefalo)

Pseudomonas

- Pregressa colonizzazione e/o infezione da *P.aeruginosa*
- Bronchiectasie)
- Fibrosi cistica
- Prolungato utilizzo della terapia steroidea
- DM non controllato
- Multipli cicli di terapia antibiotica (FQ)

Colonizzazione e/o infezione negli ultimi 12 mesi
Multipli cicli di tp atb: almeno 5-10 giorni negli ultimi 30

Maseda E et al. Exp Rev of Anti-infec Ther 2015; DOI:10.1586/14787210.2016.1120669
Augustin Pet al. Crit Care 2010;14:R20
Lee DS et al. Int J Colorectal Dis. 2015;30:497-504
Trouillet JL et al, Am J Respir Crit Care Med 1998; 157:531-539
American Thoracic Society, Am J Respir Crit Care Med 2005; 171:388-416

Prediction of infection caused by extended-spectrum beta-lactamase-producing Enterobacteriaceae: development of a clinical decision making nomogram

Table 1. Demographic data, clinical characteristics and risk factor exposition in the study population.

Variable	ESBL positive ($n = 416$)	ESBL negative ($n = 1108$)	p
Age (years)	72.6 ± 20.5	54.7 ± 29.8	<0.0001
Male gender	169 (40.6)	386 (34.8)	0.036
Nursing home residency	157 (38.2)	100 (9.04)	<0.0001
Hospital stay in preceding 3 months	151 (36.3)	182 (16.4)	<0.0001
Hemodialysis	2 (0.5)	2 (0.2)	0.3
Comorbidity: disease			
Diabetes mellitus	150 (36.1)	238 (21.5)	<0.0001
Chronic renal failure	74 (17.8)	114 (10.3)	<0.0001
Immunodeficiency	45 (10.8)	106 (9.6)	0.46
Neoplasia	82 (19.7)	140 (12.6)	0.0005
Severe underlying disease	194 (46.6)	332 (30)	<0.0001
Recurrent UTI	159 (38.2)	188 (17)	<0.0001
Lithiasis	26 (6.2)	55 (5)	0.31
Hospital admission during past year	239 (57.5)	326 (29.4)	<0.0001
Medical department	167 (40.1)	196 (17.7)	<0.0001
Surgical department	50 (12)	120 (10.8)	0.51
ICU	21 (5.05)	10 (0.9)	<0.0001
Number of stays	2.2 ± 1.5	1.8 ± 1.4	<0.0001
Invasive procedure in preceding 3 months			
Abdominal surgery	46 (11.1)	77 (7)	<0.0001
Non-urological invasive procedure	75 (18)	122 (11)	0.0003
Urological surgery	49 (11.8)	54 (4.9)	<0.0001
Urological invasive procedure	200 (48.1)	271 (24.5)	<0.0001
Permanent urinary catheter	60 (14.4)	60 (5.4)	<0.0001
Antibiotic use in preceding 3 months	211 (50.7)	274 (24.7)	<0.0001
Fluorquinolones	100 (47.4)	78 (28.5)	<0.0001
Fosfomycin	37 (17.5)	42 (15.3)	0.50
Amoxicillin–clavulanic acid	93 (44.1)	137 (50)	0.19
Aminoglycosides	9 (4.3)	10 (3.6)	0.73
TMP-SMX	21 (10)	31 (11.3)	0.63
Nitrofurantoin	1 (0.5)	9 (3.3)	0.05

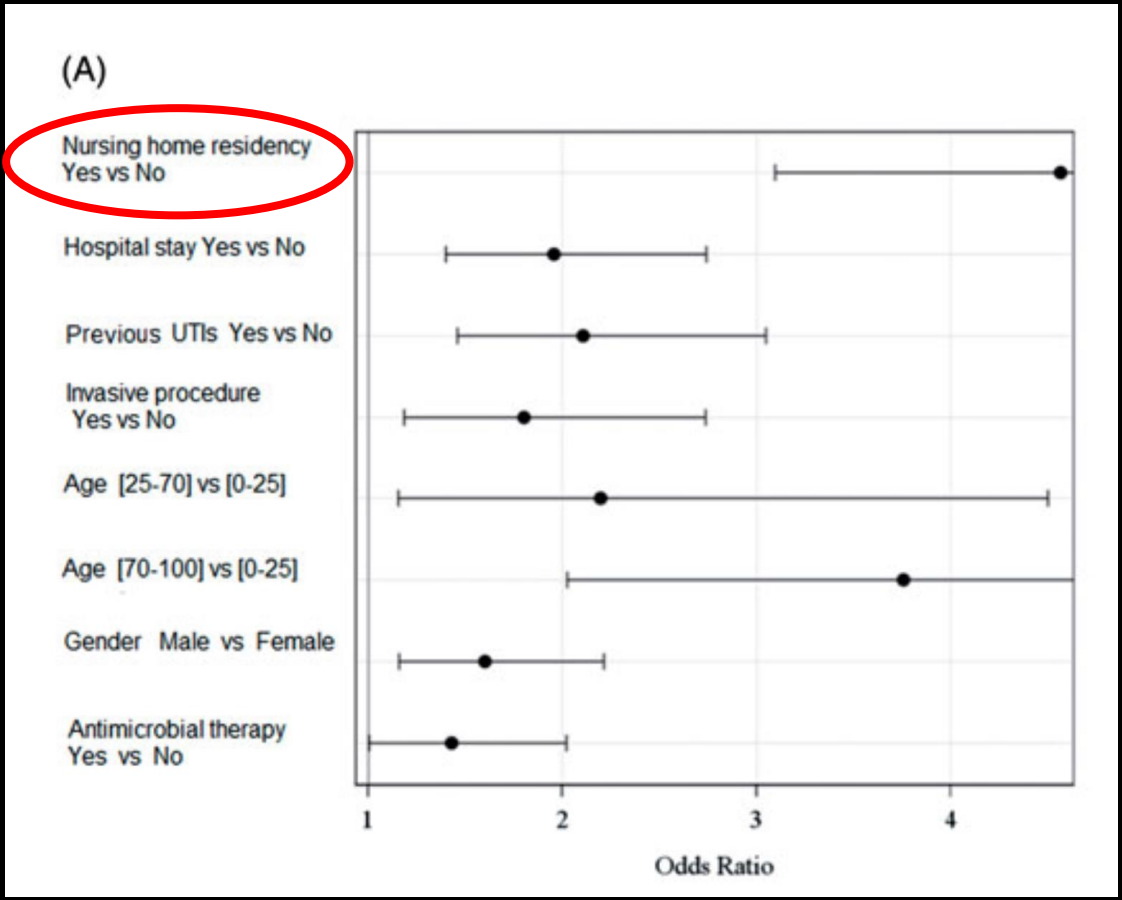
Table 2. Clinical features, microbiological data and outcome in the study population.

Variable	ESBL positive ($n = 416$)	ESBL negative ($n = 1108$)	p
Nosocomially acquired infection	115 (27.64)	160 (14.4)	<0.0001
Medical department	75 (18)	90 (8.1)	<0.0001
Surgical department	23 (5.5)	46 (4.15)	0.25
ICU	16 (3.85)	17 (1.5)	0.006
Length of hospital stay (days)	18.2 ± 29.7	11.3 ± 16.7	<0.0001
Community healthcare system-related infection	188 (45.2)	200 (18)	<0.0001
Diagnosis			
UTI	297 (71.4)	680 (61.4)	0.0003
Pyelonephritis	42 (10.1)	289 (26.1)	<0.0001
Prostatitis	18 (4.3)	81 (7.3)	0.035
Orchiepididymitis	7 (1.7)	16 (1.4)	0.73
Sepsis	52 (12.5)	41 (3.7)	<0.0001
Microorganism			
Escherichia coli	345 (82.9)	844 (76.2)	0.0045
Klebsiella sp.	64 (15.4)	151 (13.6)	0.38
Drug resistance			
Ciprofloxacin	352 (84.6)	235 (21.2)	<0.0001
Gentamicin	159 (38.2)	78 (7.1)	<0.0001
Amoxicillin–clavulanic acid	190 (45.7)	138 (12.5)	<0.0001
Carbapenem	0	0	–
Fosfomycin	101 (24.3)	115 (10.4)	<0.0001
Nitrofurantoin	39 (9.4)	125 (11.3)	0.27
TMP-SMX	262 (63)	300 (27.1)	<0.0001
Appropriate empirical treatment	192 (46.1)	924 (83.4)	<0.0001
Global mortality	32 (7.7)	24 (2.2)	<0.0001
Secondary to infection	9 (2.2)	11(1)	0.07
Other cause	23 (5.5)	13 (1.2)	<0.0001

Garcia-Tello A et al. *Scand J Urology* 2017

Prediction of infection caused by extended-spectrum beta-lactamase-producing Enterobacteriaceae: development of a clinical decision making nomogram

Fattori predittivi di infezioni da ESBL



Garcia-Tello A et al. *Scand J Urology* 2017

Comunitarie (minor rischio di *P. aeruginosa* e/o batteri ESBL-prod)

NO Sepsi

AMOXICILLINA/CLAVULANATO ev 2.2 g ogni 6 ore o
AMPICILLINA/SULBACTAM ev 2/1 g ogni 6 ore

Se FR per *P. aeruginosa* (portatori CV o stent ureterali a permanenza pluritrattati)

CEFTAZIDIME 2g in 2 ore poi 6 g in IC

Correlate a pratiche assistenziali (maggior rischio di *P. aeruginosa* e/o batteri ESBL-prod)

NO Sepsi

PIPERACILLINA/TAZOBACTAM 4.5 g in 2 ore poi 18g in IC

O

CEFTAZIDIME 2g poi 6g in infusione continua +
GENTAMICINA 3-5 mg/Kg/die

NON DIMENTICARE:

Se disponibilità di isolato microbiologico de-escalare la terapia il prima possibile cercando di sospendere piperacillina/tazobactam

DURATA: 7-10 giorni (se *P. aeruginosa* 14 giorni)

UROSEPSI

Proposta di terapia empirica per il trattamento di urosepsi

FATTORI DI RISCHIO	PAZIENTE CRITICO
Nessun FR	Amoxicillina/clavulanato + gentamicina O Cefotaxime + gentamicina
FR per ESBL	Meropenem + gentamicina o Fosfomicina O Piperacillina/tazobactam + gentamicina o Fosfomicina
FR per P. aeruginosa	Ceftazidime + amikacina
FR per P. aeruginosa MDR	Ceftolozane/tazobactam + amikacina
FR per CRE	Meropenem HD + fosfomicina + gentamicina

AMINOGLICOSIDI

Spiccata attività battericida

Fortemente concentrazione-dipendente

Prolungato effetto post-antibiotico (PAE)

Effetto sinergico sia vs Gram-negativi che vs Gram-positivi

Spettro antimicrobico davvero ampio (anche vs ESBL, KPC)

Ma … nefrotossici e ototossici (spt per tempi di terapia medio-lunghi)

Quindi … single shot o max 48-72 ore

The effect of short-course gentamicin therapy on kidney function in patients with bacteraemia a retrospective cohort study

Carlsen S et al *Eur J Clin Microbiol Infect Dis* Sep 2018

		OR*	95% CI	*p* value
All patients	AKI overall (KDIGO ≥ stage 1)	0.90	0.68–1.20	0.475
Patients with no ICU treatment	AKI overall (KDIGO ≥ stage 1)	0.94	0.70–1.28	0.701
	KDIGO stage 1	0.99	0.71–1.37	0.945
	KDIGO stage 2	0.70	0.43–1.30	0.143
	KDIGO stage 3	1.02	0.63–1.65	0.932
Patients with ICU treatment	AKI overall (KDIGO ≥ stage 1)	0.66	0.11–3.85	0.643
	KDIGO stage 1	0.56	0.08–3.80	0.554
	KDIGO stage 2	2.24	0.24–21.0	0.480
	KDIGO stage 3	0.56	0.08–3.94	0.561

*Adjusted for age, sex, CT with contrast, severe liver disease, diabetes, cancer, hypertension, coronary vascular disease, peripheral vascular disease, origin of infection, polymicrobial infection, appropriateness of treatment, focus of infection and baseline and admission level SCr threshold

		HR*	95% CI	*p* value
All patients	30-day mortality	1.20	0.94–1.55	0.144
	90-day mortality	1.02	0.84–1.25	0.814
Patients with no ICU treatment	30-day mortality	1.25	0.95–1.64	0.107
	90-day mortality	1.01	0.82–1.25	0.900
Patients with ICU treatment	30-day mortality	1.13	0.49–2.59	0.777
	90-day mortality	1.37	0.65–2.89	0.402

*Adjusted for age, sex, CT with contrast, severe liver disease, diabetes, cancer, hypertension, coronary vascular disease, peripheral vascular disease, origin of infection, polymicrobial infection, appropriateness of treatment, focus of infection and baseline and admission level SCr threshold

Conclusion: We did not find gentamicin to be a triggering factor for AKI in this study. In conclusion, short-course treatment (≤ 3 days) with gentamicin seems to be a safe regimen with respect to nephrotoxicity and mortality.

IN EPOCA DI *ANTIMICROBIAL STEWARDSHIP*

De-escalation

- Semplificare la terapia antibiotica appena disponibile antibiogramma e/o se paziente non più febbrile.
- Valutare attentamente (epidemiologia locale!!) se proseguire PIPERACILLINA/TAZOBACTAM se antibiogramma evidenzia sensibilità ad altro antibiotico di più bassa capacità si selezione di resistenza (es. aminopenicilline, cefalosporine, aminoglicosidi)
- Proseguire con soli AMINOGLICOSIDI in monosomministrazione se sensibilità documentata e pazienti non nefropatici

Durata

Durata della terapia 7-10 giorni; fino a 10-14 se urosepsi da P.aeruginosa


CHIUSO
PER SONNO
riapriremo a breve...