

Antibiotici, approfondimenti e buone pratiche

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Anestesia e Rianimazione

Ospedale di Lanusei



Prescrizione dei farmaci: avvicinamento della pratica allo standard

Hotel Mediterraneo, Lotzorai, 17.6.2016

Antibiotico-Resistenza

The 2009 Garrod Lecture: The evolution of antimicrobial resistance: a Darwinian perspective

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Microbes have evolved over 3.5 billion years and are arguably the most adaptable organisms on earth. Restricted genetically by their inability to reproduce sexually, bacteria have acquired several additional mechanisms by which to exchange genetic material horizontally. Such mechanisms have allowed bacteria to inhabit some of the most inhospitable environments on earth. It is thus hardly surprising that when faced with a barrage of inimical chemicals (antibiotics) they have responded with an equal and opposite force. This article compares and contrasts the evolution of antimicrobial resistance to β -lactam antibiotics over the last 70 years in two bacterial species, namely *Staphylococcus aureus*, a highly evolved human pathogen, and *Pseudomonas aeruginosa*, an opportunistic nosocomial pathogen.

Batteri multiresistenti

Multi Drug Resistant (MDR)

Extensively Drug Resistant (XDR)

Pan Drug Resistant (PDR)



Nuovi antibiotici

Fidaxomicina (2011)

Bedaquilina (2012)

Telavancina (2013)

Dalbavancina (2014)

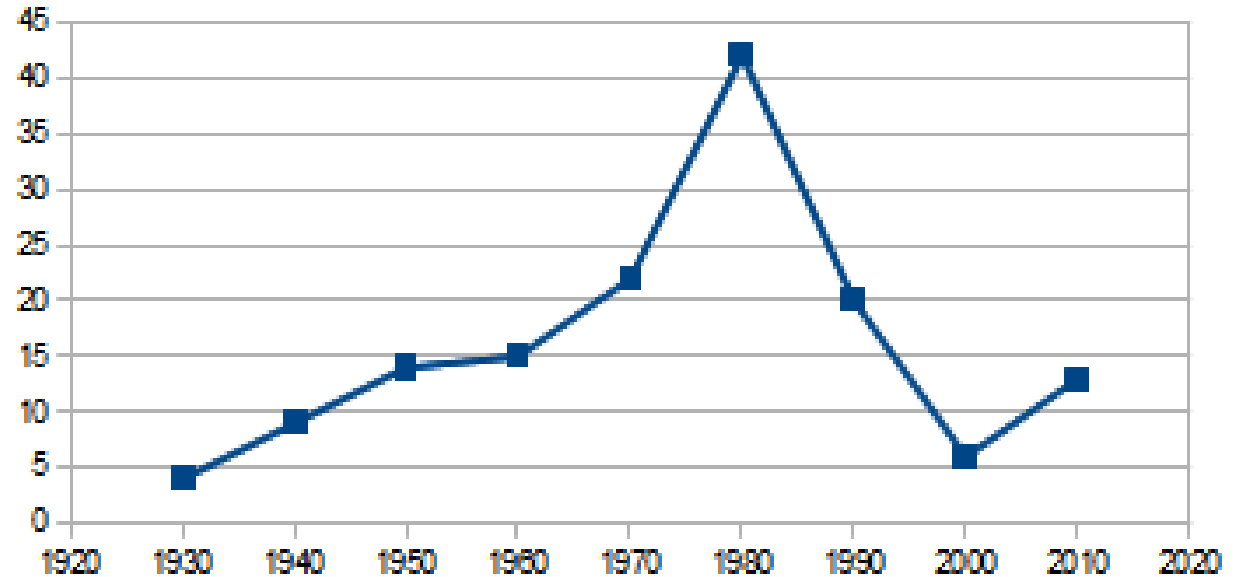
Oritavancina (2014)

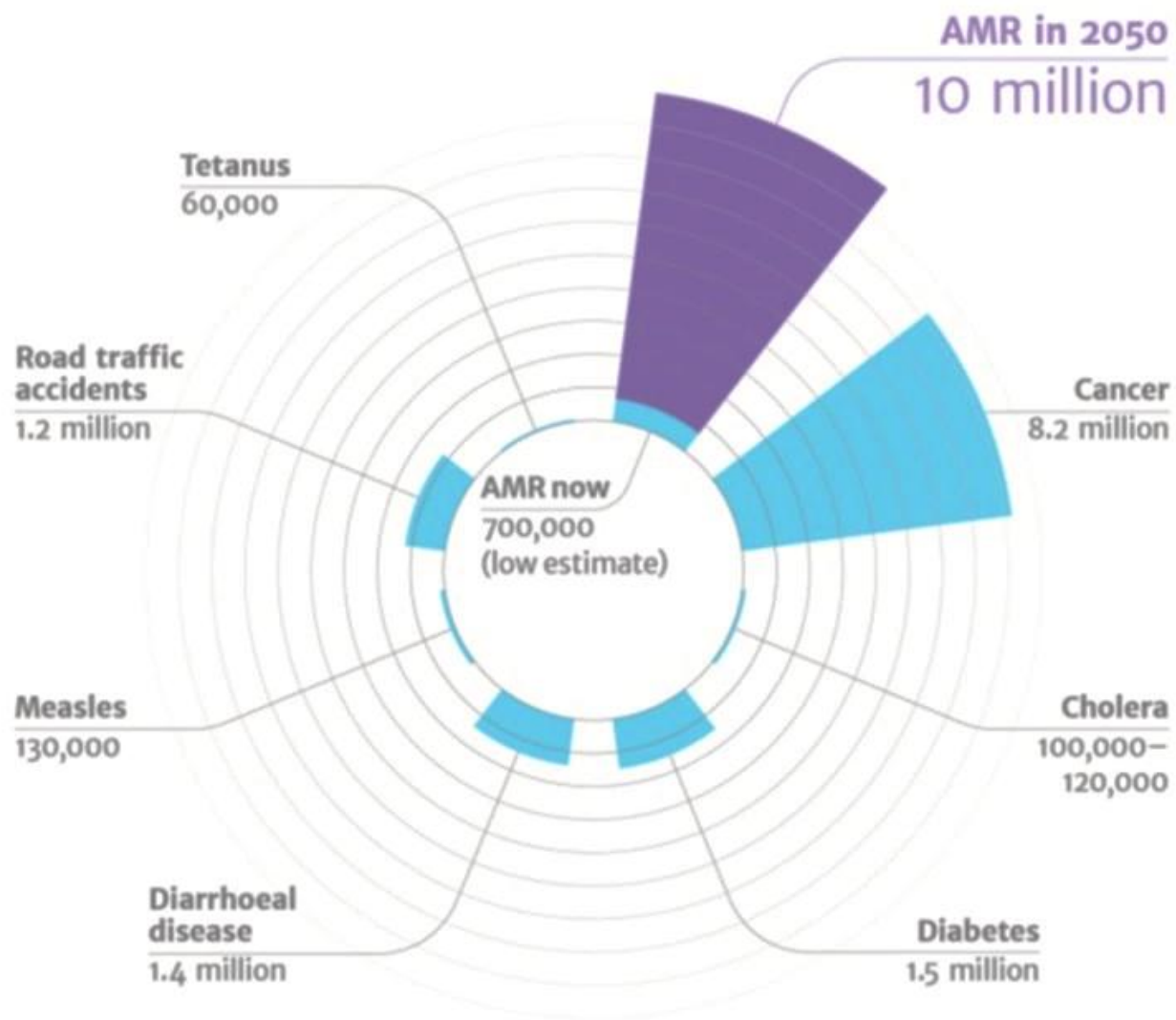
Tedizolid (2014)

Ceftolozane-Tazobactam (2014)

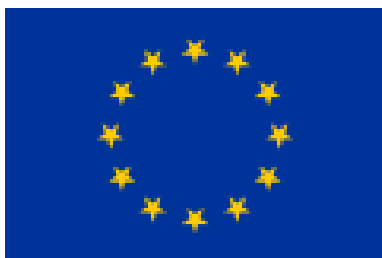
Ceftazidime-Avibactam (2015)

Individual Antibiotics Approved Per Decade

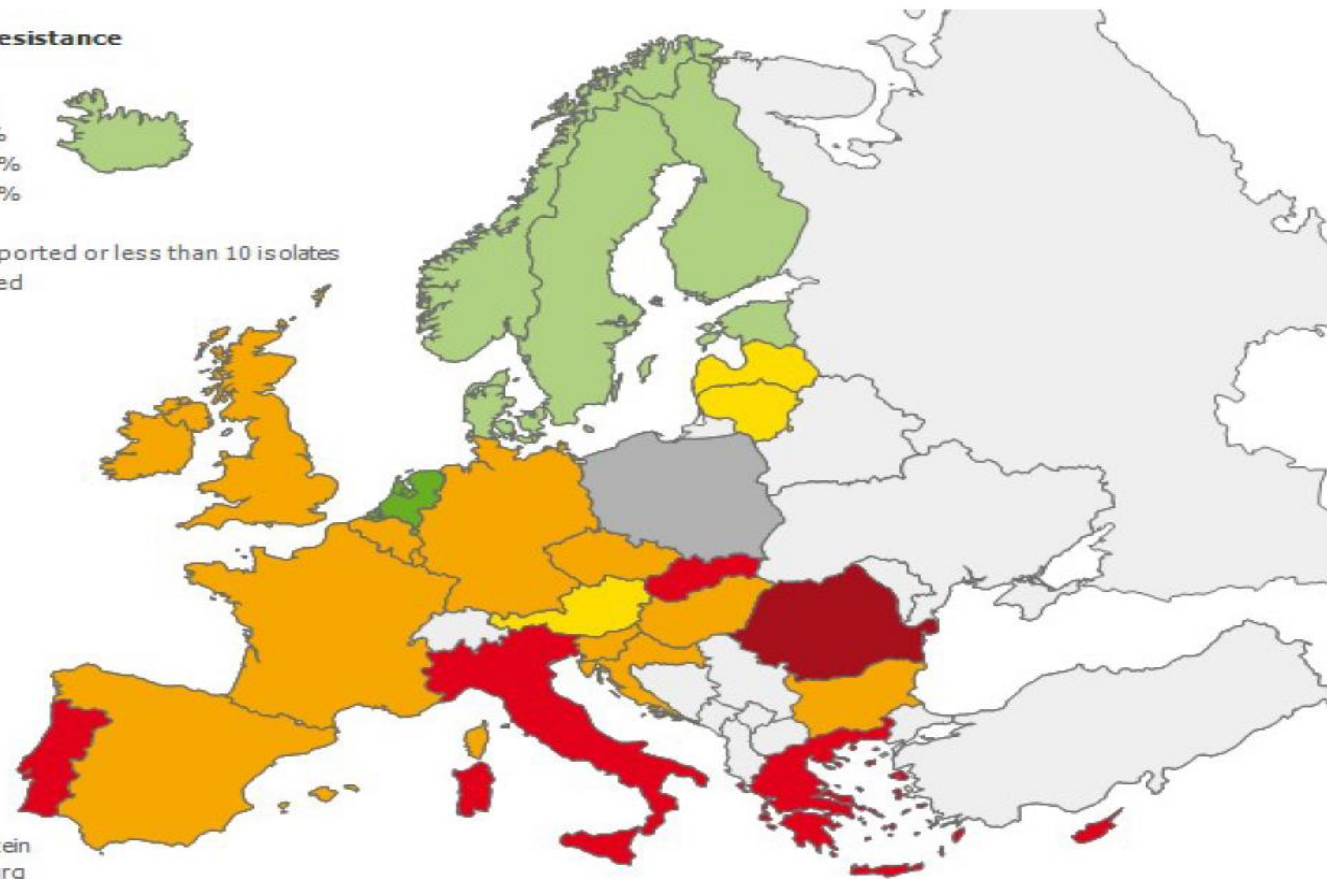
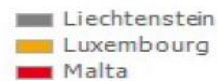
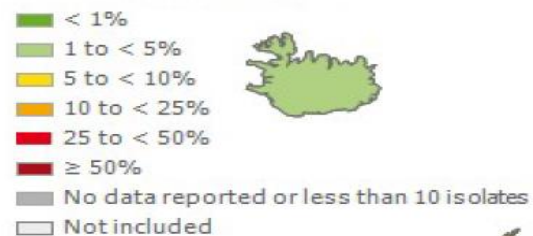




Proportion of Methicillin Resistant *Staphylococcus aureus* (MRSA) Isolates in Participating Countries in 2014



Percentage resistance



(C) ECDC/Dundas/TESSy

ASL 4 Lanusei

Faringotonsilliti da *S. pyogenes*



-R penicilline 8%

-R cefalosporine 0%

-R macrolidi 7%

Infezioni delle vie urinarie da *E. coli*



-R penicilline 49%

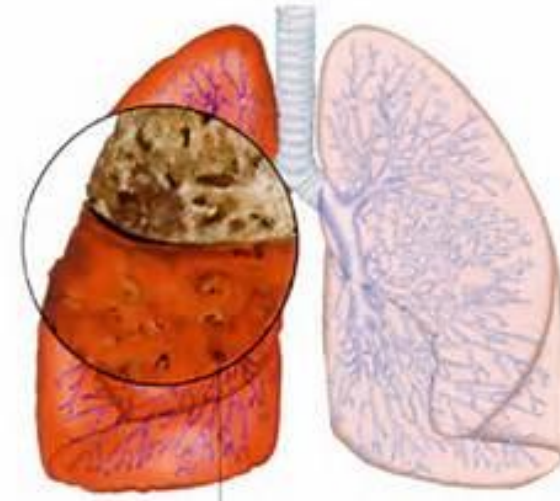
-R cefalosporine 26%

-R chinoloni 37%

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Polmoniti acquisite in comunità

-R Aminopenicilline	70%
-R Cefalosporine	50%
-R Chinoloni	30%
-R Aminoglicosidi	4%
-R Glicopeptidi	0%



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Infezioni invasive sostenute da E. coli (Gram -)

% SENSIBILITA'

Amino Penicilline		Amino Glicosidi		Cefalosporine 3° gen		Fluoro Chinoloni		Carba Penemici	
ITA	LAN	ITA	LAN	ITA	LAN	ITA	LAN	ITA	LAN
35%	15%	75%	65%	70%	55%	50%	35%	100%	100%

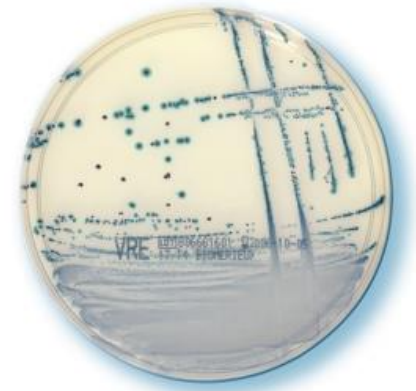


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Infezioni invasive sostenute da *E. faecalis* (Gram +)

% SENSIBILITA'

Aminopenicilline		Aminoglicosidi		Glicopeptidi	
ITA	LAN	ITA	LAN	ITA	LAN
90%	75%	45%	35%	99%	100%



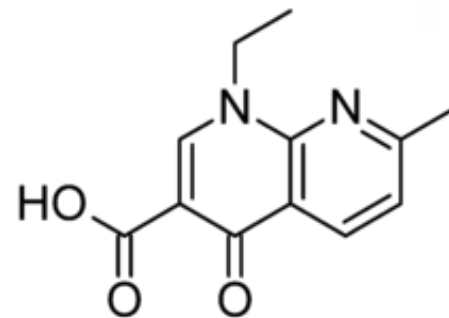
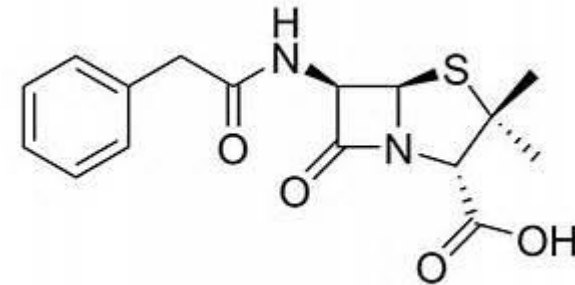
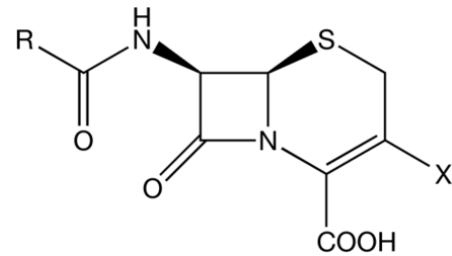
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Antibiotici più prescritti:

-Penicilline \pm inibitori delle β -lattamasi

-Cefalosporine

-Fluoroquinoloni



ASL 4 Lanusei

Inf. comunitarie «banali»

(IVU - E. coli/FT - S. pyogenes)

Inf. comunitarie «serie»

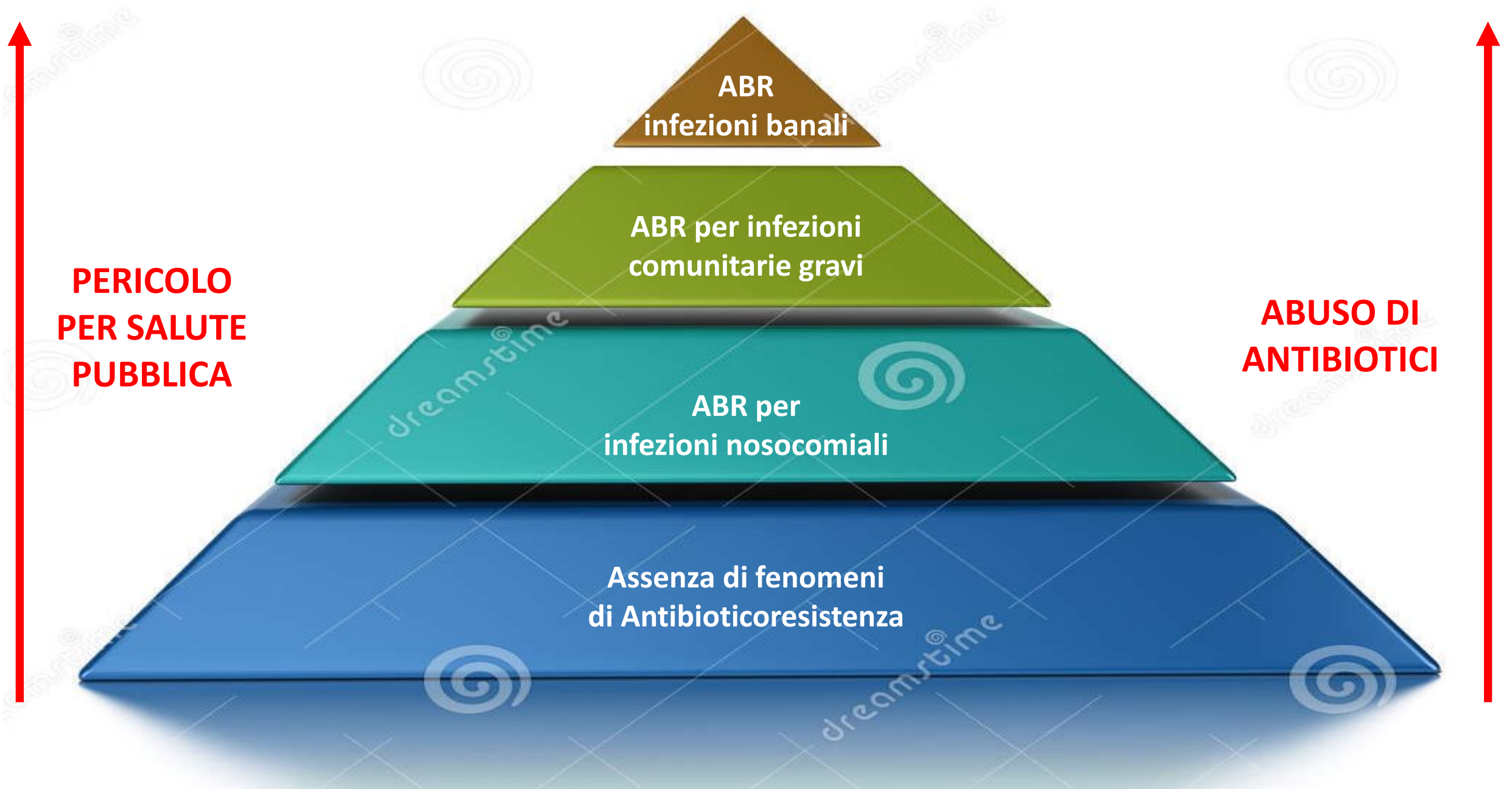
(Polmoniti acquisite in comunità)

Infezioni invasive

**Profili ABR
«accettabili»**

**Profili ABR
«pericolosi»**

**ABR correla
con AB
+ prescritti**



ABR
infezioni banali

ABR per infezioni
comunitarie gravi

ABR per
infezioni nosocomiali

Assenza di fenomeni
di Antibioticoresistenza

**PERICOLO
PER SALUTE
PUBBLICA**

**ABUSO DI
ANTIBIOTICI**

Materiale: BRONCOASPIRATO

ESAME COLTURALE

Microorganismo 1 **Enterobacter aerogenes**

ANTIBIOTICI	Microorganismo 1	
	MIC	
Amikacina	≤ 2	S
Amoxicillina/A.CLAV.	≥ 32	R
Cefepime	≤ 1	S
Cefotaxime	4	R
Cefoxitina	≥ 64	R
Ceftazidime	4	I
Ciprofloxacina	2	R
Colistina	$\leq 0,5$	S
Ertapenem	$\leq 0,5$	S
Fosfomicina	≥ 256	R
Gentamicina	≤ 1	S
Imipenem	$\leq 0,25$	S
Meropenem	$\leq 0,25$	S
Piperacillina/tazobactam	16	I
Trimetoprim/Sulfam.	≤ 20	S



Infezione nosocomiale da batterio MR comunitario

Batterio colonizza tratto digerente/urinario/respiratorio



Abuso di Antibiotici

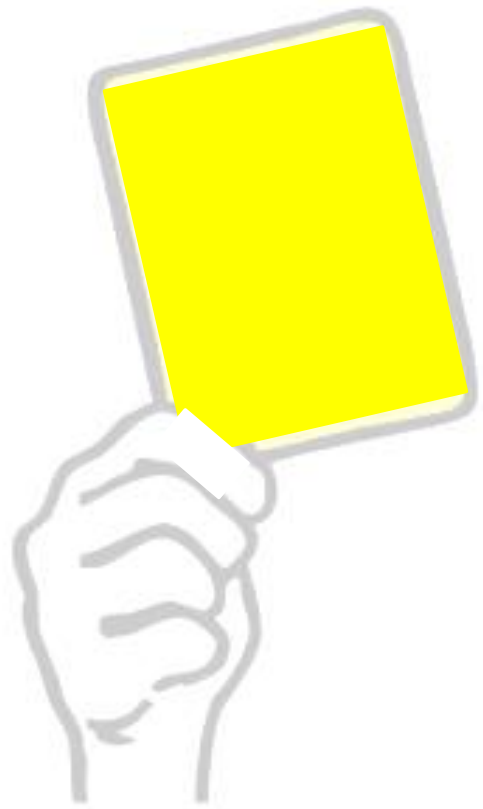
Selezione di ceppi batterici resistenti agli antibiotici



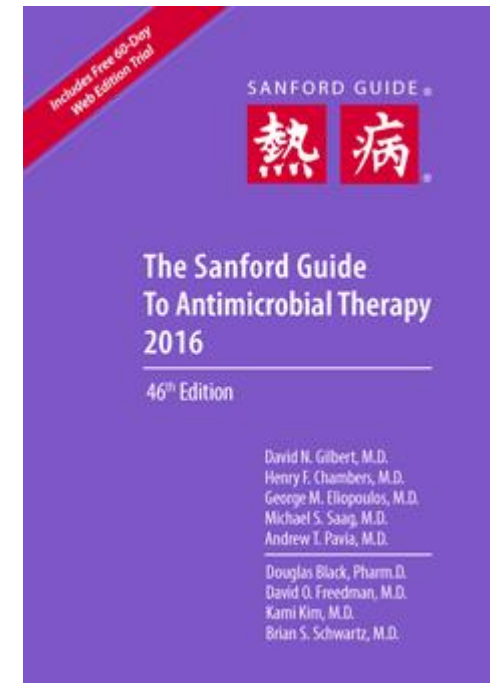
Trauma/Intervento chirurgico/
Stress/F immunosoppressori

Abbassamento difese immunitarie

Infezione da batterio
multiresistente



Somministrazione Antibioticoterapia Secondo Linee Guida



Infezioni del tratto respiratorio

FARINGITE

Diagnosis of GAS:

- In approximately 10% of adults with sore throat, the etiology is GAS
- Need symptom score over 1: one point each for history of fever, absence of cough, presence of tender cervical lymph nodes, presence of tonsillar exudates
- If associated rhinitis, hoarseness, or cough, likely etiology is viral; testing for GAS is not necessary

SINUSITE

Acute rhinosinusitis is usually obstruction of sinus ostia from inflammation caused by viral infection or allergens. Treatment is oral fluids and perhaps nasal saline irrigations.

Antibiotic therapy indicated in one of 3 situations:

- At initial evaluation: fever ($39 \text{ }^\circ\text{C}$ in children), intense facial pain, and purulent nasal discharge justifies treatment as bacterial sinusitis.
- If, despite withholding antibiotics, patient is still symptomatic after 10 days, treat as bacterial sinusitis.

OTITE MEDIA

Diagnosis of AOM in children is based on presence of moderate to severe bulging of the TM or new onset otorrhea. May diagnose with mild bulging *and* recent (<48 hours) onset of ear pain (holding, tugging, rubbing of the ear in a nonverbal child) or intense erythema of the TM.

Infezioni del tratto respiratorio

BPCO RIACUTIZZATA

Acute bacterial exacerbation of chronic bronchitis (ABECB) in adults. Almost always in smokers with chronic obstructive pulmonary disease (COPD).

Severe ABECB means increased dyspnea, increased sputum viscosity/purulence, increased sputum volume. NOTE: none of the three parameters can be quantified which confounds interpretation of clinical trials.

POLMONITE

Community-acquired pneumonia (CAP) occurs in individuals of all ages not recently hospitalized and lacking healthcare associated risk factors (e.g., indwelling vascular catheter, renal replacement therapy, resident in a long-term care facility).

Presentation

- Acute onset of fever, chills, cough, shortness of breath, and chest pain but can be mimicked by many disease processes.

Infezioni del tratto urinario

BATTERIURIA ASINTOMATICA

Preschool children

- Base regimen on culture and sensitivity, not empiric

Pregnancy ,

Invasive urologic procedure

No therapy for asymptomatic bacteriuria in the following patient populations:

- Premenopausal, nonpregnant women
- Diabetic women
- Older persons living in the community
- Elderly, institutionalized subjects
- Persons with spinal cord injury

CISTITE

Acute uncomplicated urinary tract infection (UTI) (cystitis, urethritis) in women without signs and symptoms of upper urinary tract infection.

Empiric therapy: routine urine culture is not necessary.

Infezioni del tratto urinario

INFEZIONI VIE URINARIE COMPLICATE

Complicated urinary tract infections (UTI): obstruction, reflux, azotemia, transplant.

Foley catheter-related infection.

Important to rule out obstruction.

PIELONEFRITE

Usually presents in women age 18–40 years, temperature $>102^{\circ}\text{F}$, definite costovertebral tenderness.

Culture of urine and blood prior to therapy.

If male, look for obstructive uropathy or other complicating pathology.

Complicated pyelonephritis connoted by presence of obstruction, underlying renal disease, male sex, immunosuppression, stone disease, anatomic or functional urinary tract abnormality.

Infezioni del tratto digerente

DIVERTICOLITE

3 presentations:

- Outpatient: mild diverticulitis or drained perirectal abscess.
- Inpatient: mild to moderate disease, focal peri-appendiceal peritonitis, peri-diverticular abscess and endomyometritis.
- Severe, life-threatening disease.

COLECISTITE

Various manifestations of gallbladder infection: cholecystitis, cholangitis, biliary sepsis and common duct obstruction

GASTROENTERITE

Severe

- ≥ 6 unformed stools per day
- \pm temperature $\geq 101^\circ\text{F}$, tenesmus, blood or fecal leukocytes
- Severe afebrile bloody diarrhea should increase suspicion of E. coli 0157:H7 infection—causes

Profilassi antibiotica

PROCEDURE ODONTOIATRICHE

Predisposing cardiac conditions and/or type of dental procedure guide prophylaxis recommendation.

Antibiotic prophylaxis is recommended for patients with the following predisposing cardiac conditions:

- Prosthetic cardiac valve or prosthetic material used for cardiac valve repair.
- Previous infective endocarditis (IE).
- Congenital heart disease (CHD)
- Cardiac transplantation recipients who develop cardiac valvulopathy.

INTERVENTI CHIRURGICI

Breast, Herniorrhaphy

Cardiovascular

Colorectal

Gastroduodenal, Biliary

Head and Neck

Neurosurgery

Ob- Gyn

Orthopedic

Peritoneal Dialysis Catheter

Urologic

Indicatori di uso inappropriato di Antibiotici



	Influenza	Raffreddore comune	Laringotracheite	Faringite Tonsillite	Bronchite in assenza di BPCO	Batteriarria asintomatica
ANALISI GEOGRAFICA						
Nord	26,5	17,4	42,4	21,7	19,2	35,4
Centro	33,3	25,8	52,1	21,1	31,0	38,3
Sud e Isole	31,3	21,9	56,2	21,6	45,4	36,2
ANALISI PER GENERE						
Maschi	28,5	19,5	48,9	20,6	28,9	43,1
Femmine	29,0	21,0	49,5	22,3	29,3	34,8
ANALISI PER ETA'						
≤45	25,9	17,4	47,0	21,7	20,4	33,5
46-65	27,0	19,8	50,2	21,2	28,5	39,4
66-75	51,1	39,3	51,1	22,6	34,8	-
>75	51,5	37,0	51,8	20,4	35,8	-

BPCO: broncopneumopatia ostruttiva cronica

Gli antibiotici sono dei farmaci innocui?



Effetti collaterali/eventi avversi AB-correlati

ANTIBIOTIC CLASS	ANTIBIOTIC CLASS MEMBERS	MOST COMMON SIDE EFFECTS	ADDITIONAL CLINICAL COMMENTS
Penicillins	penicillin, amoxicillin, amoxicillin-clavulanate, ampicillin, piperacillin-tazobactam, nafcillin, oxacillin	rash, diarrhea, abdominal pain, nausea/vomiting, drug fever, hypersensitivity (allergic) reactions	if bloody stools, anaphylaxis, severe skin reaction, fever occur contact health care provider immediately; ampicillin may cause pseudomembranous colitis
Cephalosporins	cephalexin, cefaclor, cefuroxime, ceftibuten, cefdinir, cefixime, ceftriaxone	rash, diarrhea, nausea/vomiting (rare), hypersensitivity (allergic) reactions, serum sickness, vaginal candidiasis	cross-hypersensitivity may occur in patients with documented penicillin allergy
Quinolones	ciprofloxacin (Cipro), levofloxacin (Levaquin), moxifloxacin (Avelox), ofloxacin (Floxin)	nausea/vomiting, diarrhea, abdominal pain, headache, lethargy, insomnia, photosensitivity (can be severe)	Avoid prolonged sunlight exposure; use sunscreen, wear protective clothing; moxifloxacin associated with higher rates of side effects [shehab]; tendon rupture (rare) more common in age > 60, with corticosteroid use, in kidney, heart, lung transplant recipients

Problematiche legali?

bollettino di farmacovigilanza dell'AIFA

AIFA N. 13 - LUGLIO 2009

Il medico di famiglia è stato chiamato per una visita domiciliare; in base alla storia e all'esame obiettivo (ronchi diffusi all'ascoltazione del torace) diagnostica una bronchite. Nei giorni precedenti il medico aveva consigliato a Paolo di usare ketoprofene per bocca e mucolitici, ma dopo la visita decide di iniziare una terapia antibiotica.

Nella prescrizione di un farmaco va sempre tenuto conto del rapporto tra i benefici attesi e il rischio, inevitabile, della somministrazione. Utilizzare una cefalosporina di terza generazione per via iniettiva quando potrebbero essere sufficienti altri antibiotici a largo spettro per via orale vuol dire esporre il paziente a un rischio non giustificato di reazione allergica grave (che è solitamente più grave con la somministrazione parenterale) e, soprattutto, favorire la creazione di resistenze batteriche senza ragione.

Dopo circa 15 minuti dalla prima iniezione Paolo però comincia a notare un eritema diffuso su tutto il corpo e a lamentare una forte dispnea, con sensazione di mancamento e sudorazione profusa. La moglie di Paolo chiama immedia-

Uno shock anafilattico evitabile



Utilizzo degli Antibiotici in Terapia Intensiva

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Utilizzo degli Antibiotici in Terapia Intensiva

- Monitoraggio flora batterica locale**
- Scelta ABT empirica più appropriata**
- Scelta ABT mirata più appropriata**



Utilizzo degli Antibiotici in Terapia Intensiva

- A parità di sensibilità → antibiotico più economico**
- Adattamento delle LG → profili di AB-Resistenza locale**
- Incidenza infezioni noscomiali < media nazionale**

QUELLA PILLOLA CHE
PUBBLICIZZANO SEMPRE IN TV.
NON SONO SICURA COS'E',
MA LA VOGLIO !

