



Germi multiresistenti in medicina umana e veterinaria

Valeria Gaia
Servizio di microbiologia EOLAB
Bellinzona

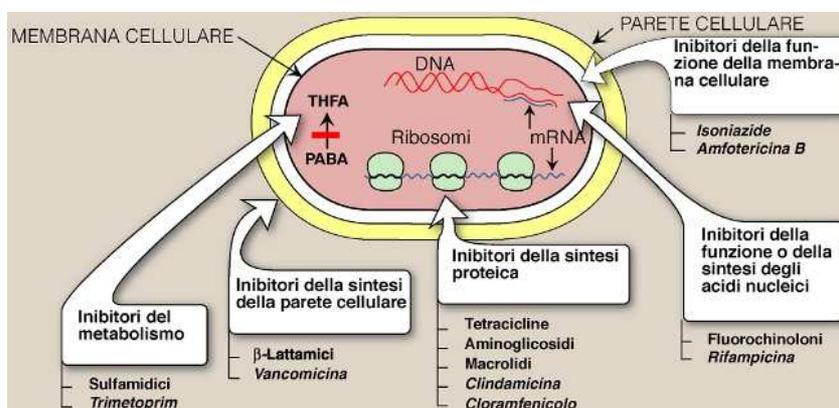
eoc



Le resistenze agli antibiotici

come si sviluppano
come si trasmettono

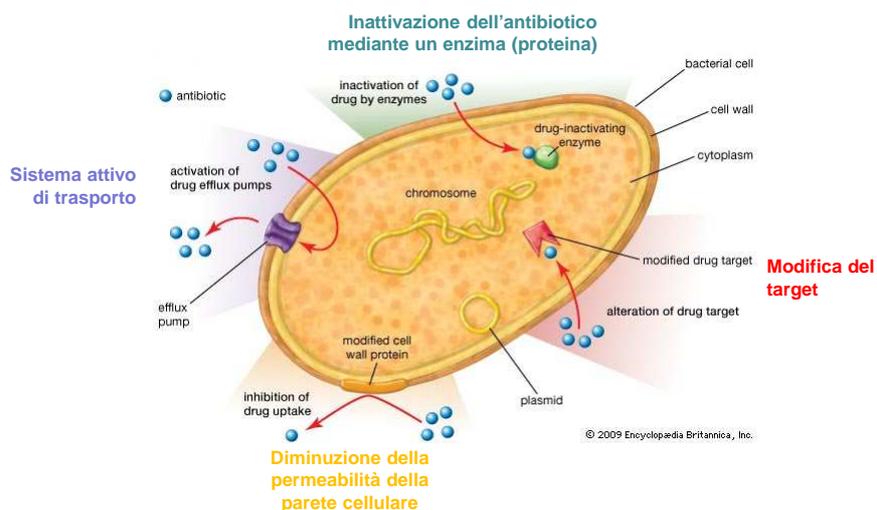
Antibiotici: target specifici



Germi multiresistenti in medicina umana e veterinaria

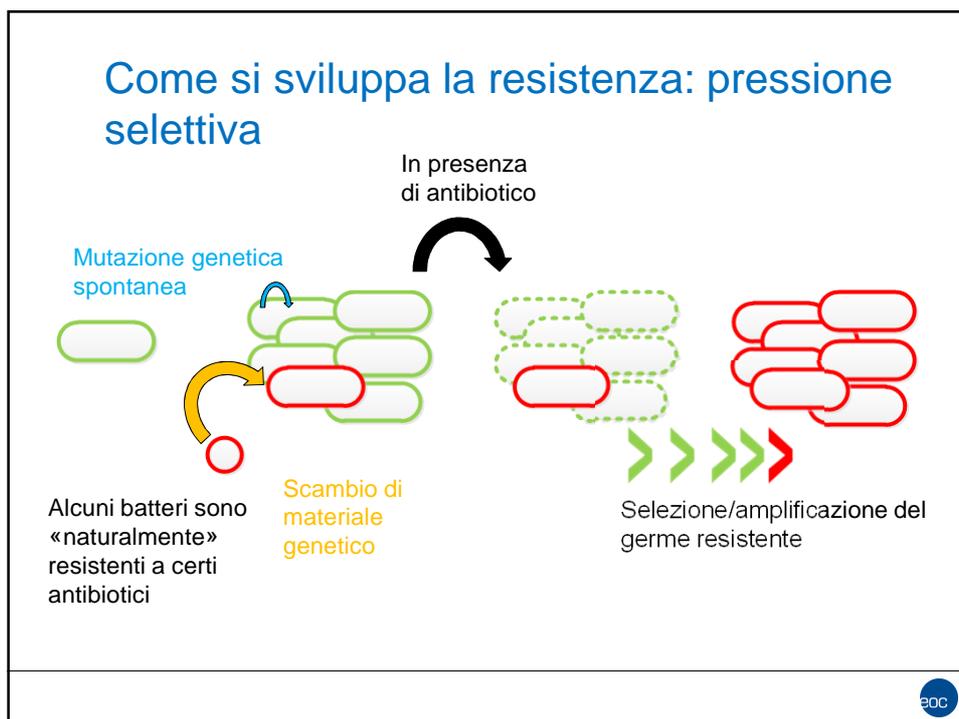


Microrganismi: meccanismi di resistenza



Germi multiresistenti in medicina umana e veterinaria





Escherichia coli

— Projekt Tierpathogenenmonitoring 2015/2016

u^b
UNIVERSITÄT BERN

Isolate aus Tiere mit vorgängiger Antibiotika-Behandlung zeigen signifikant höhere Resistenzraten !

Monitoring of antimicrobial resistance in animal pathogens - significance of choosing the appropriate isolates

Master thesis
Tobias Manuel Hübner

Antimicrobial agent	untreated	pretreated	P-value	H0 rejected, HA accepted at $\alpha = 0.05$?
Sulfamethoxazole (SMX)	5.7	36.6	0.0038	Yes
Trimethoprim (TMP)	2.9	33.3	0.0017	Yes
Ciprofloxacin (CIP)	11.4	36.6	0.0203	Yes
Tetracyclin (TET)	5.7	30	0.0174	Yes
Meropenem (MERO)	0	0		
Azithromycin (AZI)	2.9	10	0.3277	No

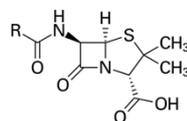
FIG 3 Fisher's Exact Test for difference in percentage of antimicrobial resistance rate of *E.coli* isolated from untreated, unkr treatment status and pretreated dogs.

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Penicillina



- Scoperta nel 1928 da Alexander Fleming
- Inibisce la sintesi della parete cellulare
- Nel 1940 prima resistenza alla penicillina
- Utilizzata durante la 2a guerra mondiale per la cura delle ferite dei soldati
- Osservata in parallelo anche una diminuzione delle infezioni veneree (gonorrea e sifilide)



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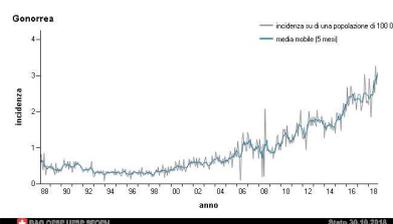
Neisseria gonorrhoeae

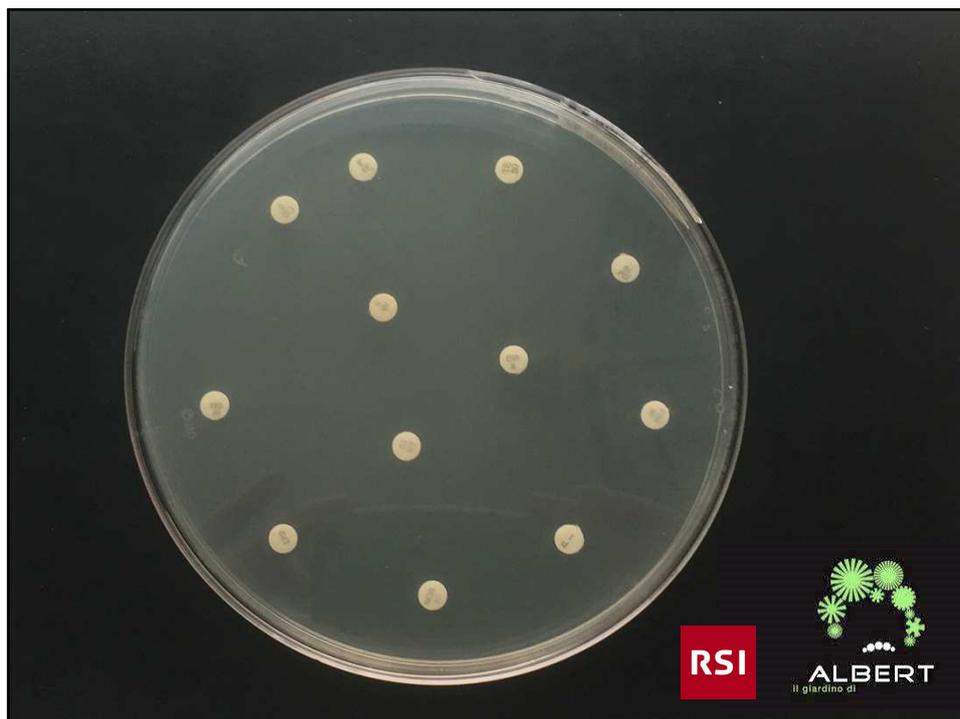


- In CH: Ca. 2500 casi/anno
- Diagnosi via PCR
 - Poche Colture
 - Pochi dati sulla resistenza

Antibiotico	Classe	Numero di casi
Amoxicillina	Penicillina	13
Penicillina G	Penicillina	13
Flucloxacillina	Penicillina	13
Amoxicillina/Cloxacillina	Beta-lattamici	13
Piperacillina/Tazobactam	Beta-lattamici	13
Cefotaxime	3G Cephalosporini	13
Ceftazidime	Cephalosporini	13
Ceftriaxone	Cephalosporini	13
Ciprofloxacina	Fluoroquinoloni	55
Levofloxacina	Fluoroquinoloni	55
Moxifloxacina	Fluoroquinoloni	55
Norfloxacina	Fluoroquinoloni	55
Ofloxacina	Fluoroquinoloni	55
Azithromicina	Macrolidi	64
Clarithromicina	Macrolidi	64
Erytromicina	Macrolidi	64

Terapia consigliata:
Ceftriaxone / Azitromicina





Umana

EUCAST
CLSI

Veterinaria

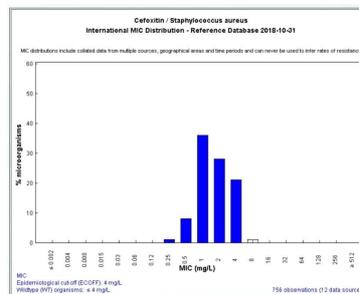
→ VetCAST
CLSI/SFM/EUCAST/

 **EUCAST** EUROPEAN COMMITTEE
ON ANTIMICROBIAL
SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

20 October 2017

Organization: _____
EUCAST News: _____ The European Committee on Antimicrobial
Clinical breakpoints: _____ Susceptibility Testing - EUCAST

EUCAST Clinical breakpoints: Nel processo vengono considerati dosaggio, farmacocinetica, meccanismi di resistenza, distribuzione CMI, distribuzione diametri, farmacodinamica e valori di cutoff epidemiologici (ECOFFs) → indicazioni per un probabile successo terapeutico



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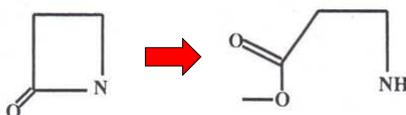
Resistenze ai beta lattamici nei bacilli Gram negativi

Resistenze da sorvegliare a livello nosocomiale

- ESBL
- CRE
- *Pseudomonas aeruginosa*
- *Acinetobacter baumannii/calcoaceticus complex*
- *Stenotrophomonas maltophilia*

1. Extended Spectrum Beta Lactamases

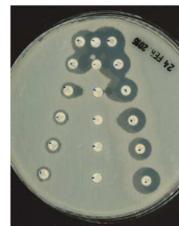
- β -lattamasi ad ampio spettro: inattivazione (idrolisi) dell'antibiotico mediante rottura dell'anello β -lattamico



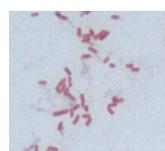
	Trasmissibile ?	Penicilline	Cefalosporine 3a gen	Cefalosporine 4a gen	Carbapenemi
Penicillinasi	NO	☹️	😊	😊	😊
ampC crom.	NO	☹️	☹️	😊	😊
ampC plas.	SI	☹️	☹️	😊	😊
➔ ESBL	SI	☹️	☹️	☹️	😊

ESBL

- Germania 1983: isolato il primo ESBL in *Klebsiella pneumoniae*
- Distribuzione globale: Asia > EU > USA
- Fino alla fine degli anni '90: problema ospedaliero: *Klebsiella pneumoniae*
- Dal 2000 aumento esponenziale dei casi in comunità: *E. coli*
- Rilevati nelle *Enterobacteriacee*, Bacilli Gram negativi che colonizzano soprattutto il tratto intestinale



Escherichia coli
Klebsiella spp.
Proteus spp.
Enterobacter spp.
Citrobacter spp.
Serratia spp.



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Ceppo sensibile Ceppo ESBL

coli	
Ampicillina	S (<2)
Augmentine	S (<2)
Tazobactam (Pi)	S (<4)
Ceftriaxone	S (<0.5)
Ceftazidima	S (<0.5)
Cefuroxima	S (<2)
Cefoxitina (scre)	S (<4)
Cefpodoxime	S
Tienam	S (<0.25)
Meropenem	S (<0.25)
Ertapenem	S (<0.25)
Aztreonam	S (<1)
Gentamicina	S (<1)
Ciprofloxacina	S (<0.125)
Norfloxacina	S (<0.5)
Bactrim	S (<1)

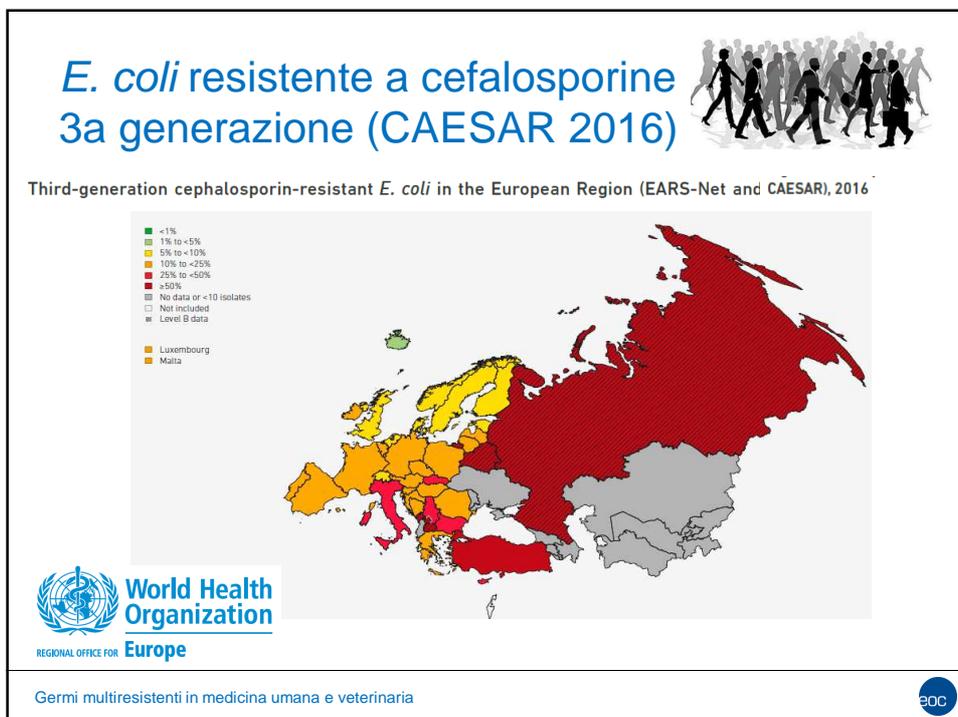
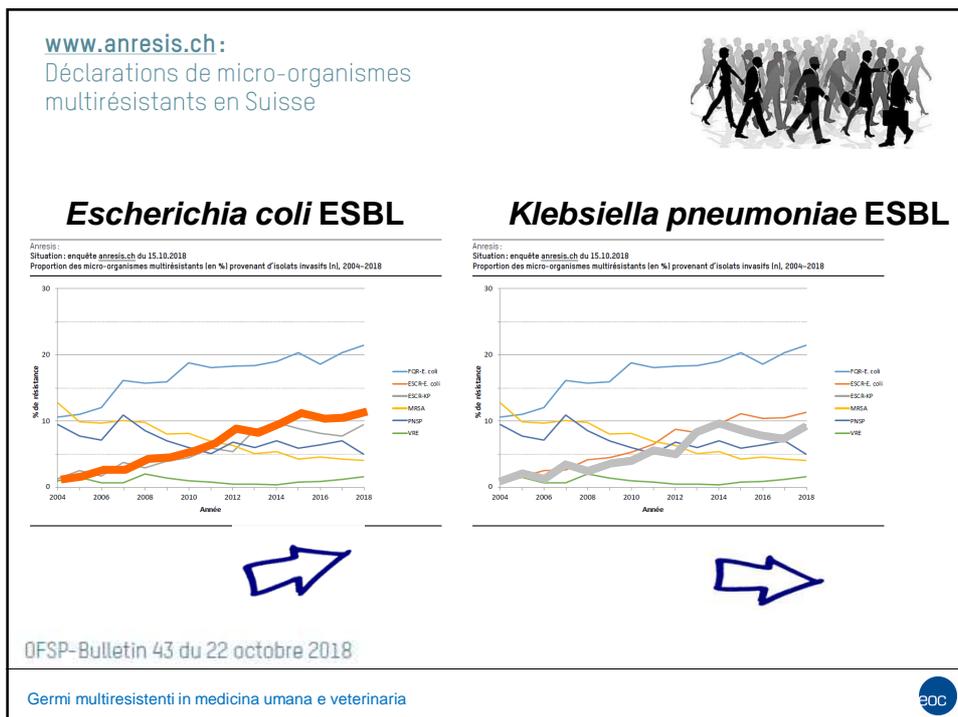


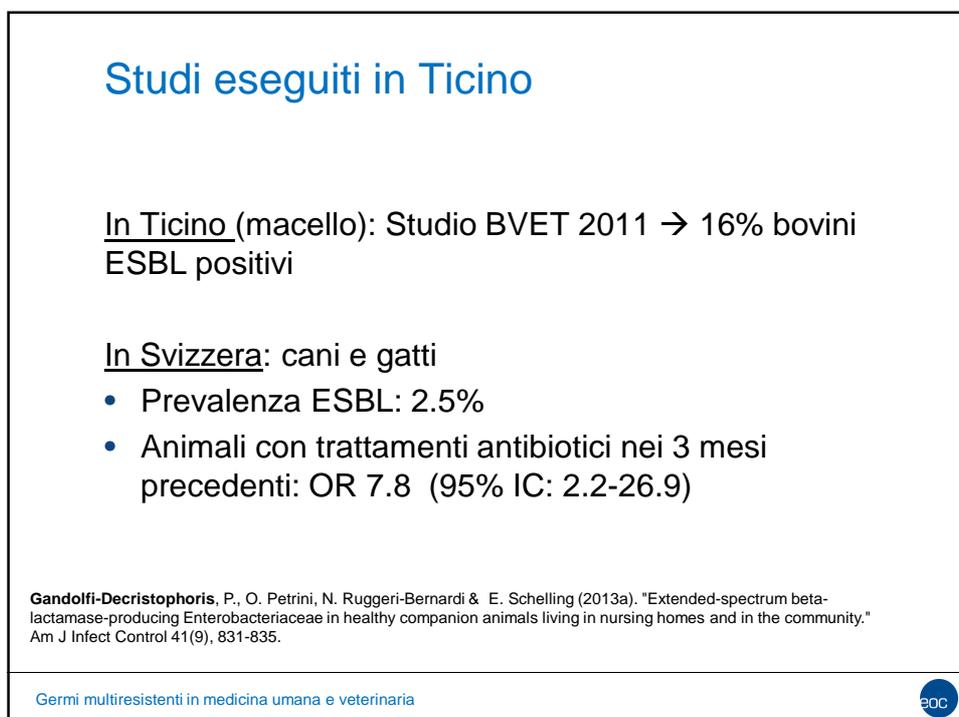
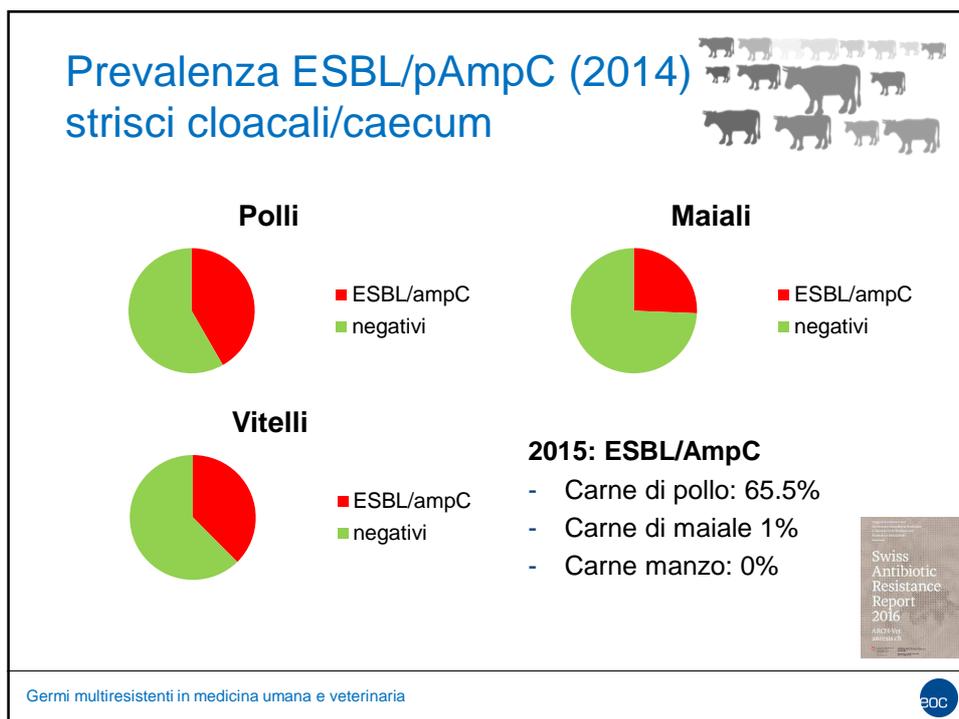
kpn	
Ampicillina	R
Augmentine	R
Tazobactam (Pi)	R
Ceftriaxone	R
Ceftazidima	R
Cefuroxima	R
Cefoxitina (scre)	R
Cefpodoxime	R
Tienam	S
Meropenem	S
Ertapenem	S
Aztreonam	R
Gentamicina	S
Ciprofloxacina	R
Norfloxacina	R
Bactrim	R



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2. Enterobatteriacee produttrici di Carbapenemasi (CPE o CRE)

- Inattivazione di tutti i betalattamici, inclusi i carbapenemi
- Possono essere presenti anche in *Pseudomonas* e *Acinetobacter*
- **Alternative terapeutiche:**
 - Colistina
 - Ceftazidima/Avibactam (Zavicefta, Pfizer; non ancora venduto in Svizzera)

	Trasmisibile ?	Penicilline	Cefalosporine 3a gen	Cefalosporine 4a gen	Carbapenemi
CPE A/B	SI	☹️	☹️	☹️	☹️
CPE D	SI	☹️	😬	😬	☹️

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Antibiogrammi

Ceppo sensibile

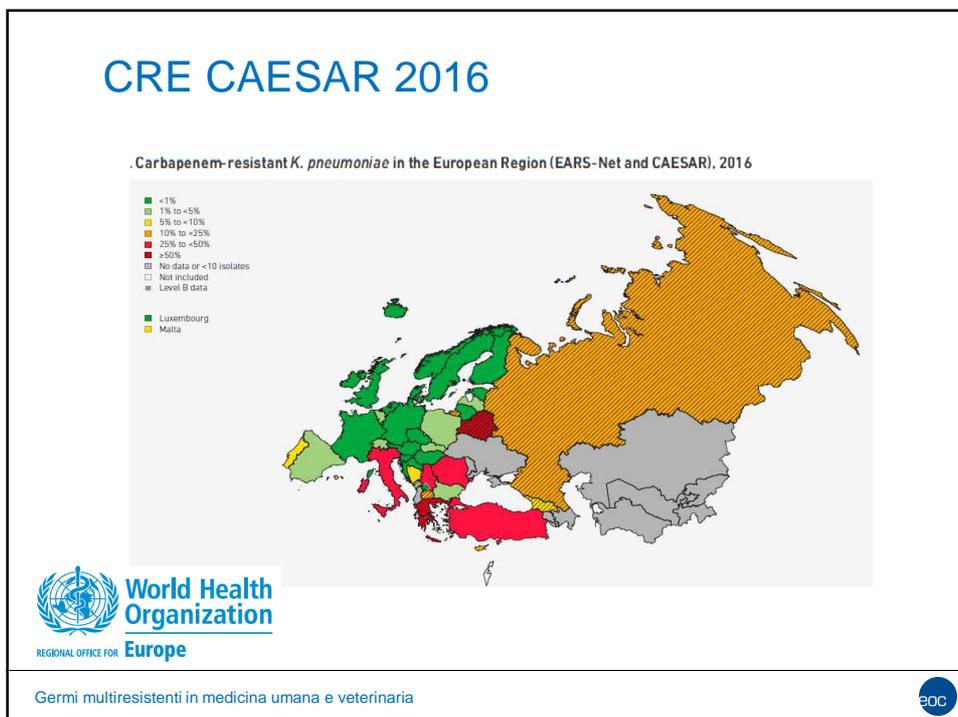
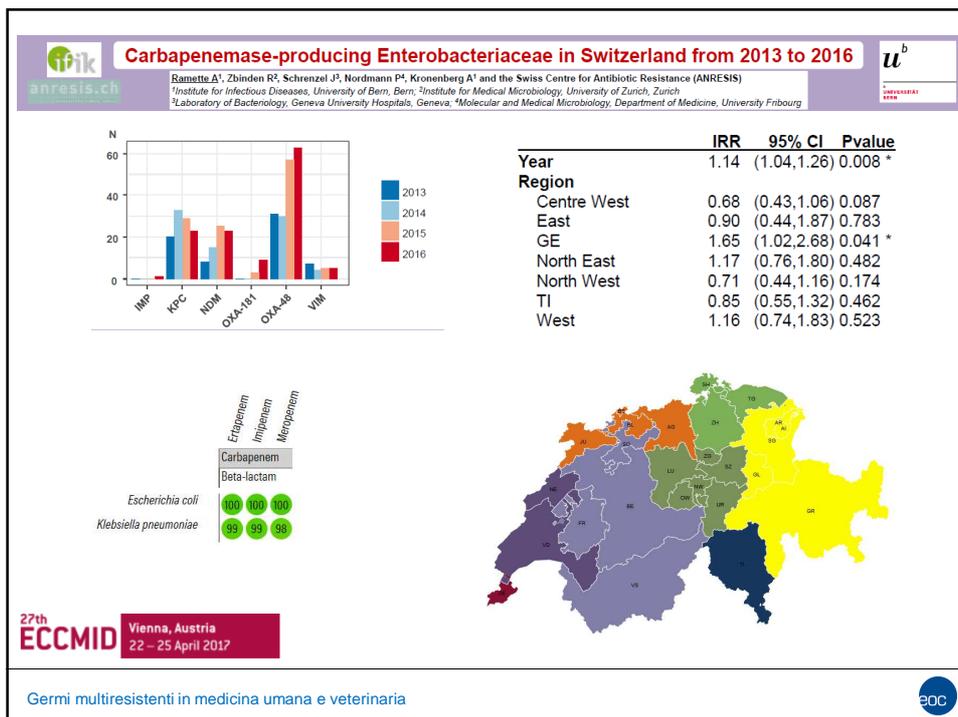


ESBL



CPE classe B







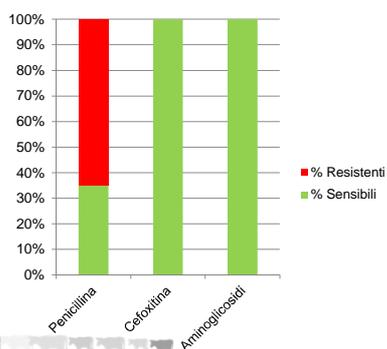
Ente Ospedaliero Cantonale

Resistenze negli stafilococchi dorati

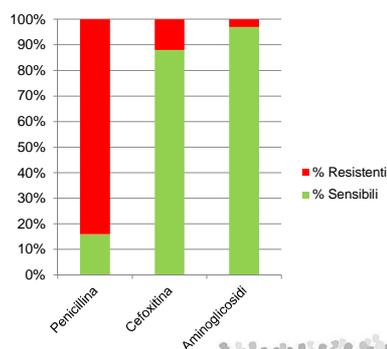
Resistenze da sorvegliare a livello nosocomiale

- MRSA
- VISA
- hVISA

S. aureus Genotipo B nei bovini (SAGB) *S. aureus* in medicina umana



Dati dal pre-progetto UVC 2016



Dati SMIC 2018

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Ceppo Ceppo sensibile MRSA

	stau
Penicillina	S (0,06)
Ampicillina	S
Floxapen	S
Augmentine	S
Tazobactam (P)	S
Cefazolina	S
Cefuroxima	S
Cefoxitina (scre	S
Gentamicina	S (<0,5)
Tetraciclina	S (<1)
Eritromicina	S (1)
Ciprofloxacina	S (<0,5)
Vancomicina	S (<0,5)
Teico (screen)	N
Bactrim	S (<10)
Clindamicina	S (0,25)
Rifampicina	S (<0,03)
Fucidina	S (<0,5)

	stau
Penicillina	R
Ampicillina	R
Floxapen	R
Augmentine	R
Tazobactam (P)	R
Cefazolina	R
Cefuroxima	R
Cefoxitina (scre	R
Gentamicina	S
Tetraciclina	S
Eritromicina	S
Ciprofloxacina	R
Vancomicina	S (2)
Teico (screen)	S
Bactrim	S
Clindamicina	S
Rifampicina	S (0,000)
Fucidina	S
Linezolid	S (3)

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Staphylococcus aureus MRSA

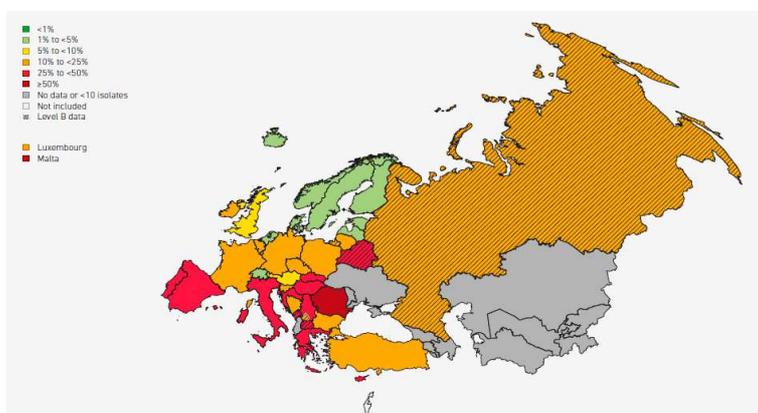
Anysisis
Situation : enquête anysisis.ch du 15.10.2018
Proportion des micro-organismes multirésistants (en %) provenant d'isolats invasifs (n), 2004-2018

Année	FQR-E. coli	ESCR-E. coli	ESCR-KP	MRSA	PNSP	VRE
2004	10	10	10	10	10	10
2006	15	10	10	10	10	10
2008	18	10	10	10	10	10
2010	18	10	10	10	10	10
2012	18	10	10	10	10	10
2014	19	10	10	10	10	10
2016	20	10	10	10	10	10
2018	22	10	10	10	10	10

OFSP-Bulletin 43 du 22 octobre 2018

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MRSA 2016 (CAESAR Report 2017)



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Prevalenza MRSA (2014-2015) (caecum)



Vitelli



Maiali



- In Ticino: cani e gatti
0% MRSA positivi

Carne pollo: 6.9%
Carne manzo: 0%
Carne maiale: 0.7%



Gandolfi-Decristophoris, P., G. Regula, O. Petrini, J. Zinsstag & E. Schelling (2013b). "Prevalence and risk factors for carriage of multi-drug resistant Staphylococci in healthy cats and dogs." J Vet Sci 14(4), 449-456.



MRSA nelle persone a contatto con animali da reddito ?

V. Post 2017 (UK/Davos/Basilea)

- 2% (tra 1166 chirurghi medicina umana)
- 5% (tra 60 chirurghi veterinari)

K. Wettstein Rosenkranz, 2014 (Uni Berna)

- 3.8% (di 340) veterinari portatori MRSA
 - Grandi animali: LA-MRSA
 - Piccoli animali: HA-MRSA

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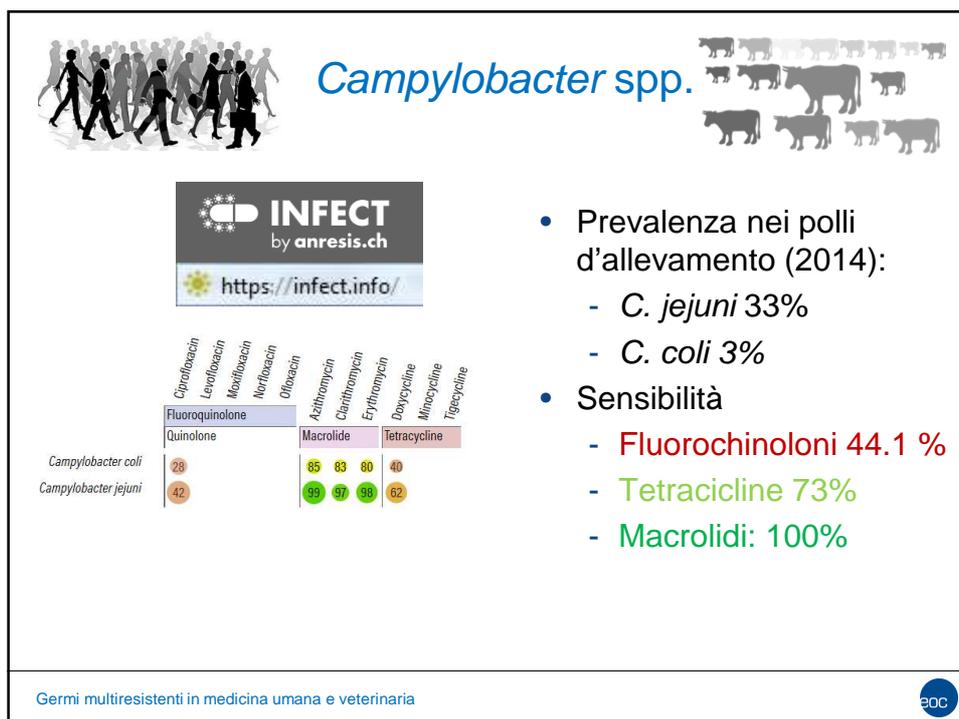


Ente Ospedaliero Cantonale

Zoonosi

Campylobacter spp.

Salmonella spp.



eoc
Ente Ospedaliero Cantonale

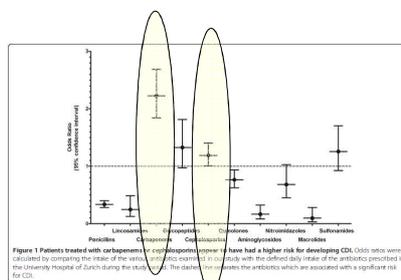
Un caso particolare

Clostridioides difficile

Clostridioides difficile



- *Clostridium difficile* infection (CDI)
- Colite pseudomembranosa associata agli antibiotici (tossine CD)
- Incidenza nei casi comunitari e nosocomiali molto simile (11.16 vs. 12.1/100'000/anno)
- *C. difficile* sensibile a metronidazolo e vancomicina
- Pazienti trattati con carbapenemi e cefalosporine sono associati in modo significativo a un rischio maggiore di CDI



BMC Infect Dis. 2014; 14: 807.
Published online 2014 Nov 26. doi: [10.1186/s12879-014-0907-z]

PMCID: PMC4247760
PMID: 25425433

Antibiotic susceptibility of *Clostridium difficile* is similar worldwide over two decades despite widespread use of broad-spectrum antibiotics: an analysis done at the University Hospital of Zurich

Andrea C Büchler, Silvana K Rampini, Simon Stelling, Bruno Ledergerber, Silke Peter, Alexander Schweiger, Christian Ruef, Reinhard Zbinden, and Roberto F Speck¹

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Clostridioides difficile



- Non è un germe a dichiarazione obbligatoria
- Incidenza?
- Integrazione in anresis.ch ?

In Ticino

Prevalenza nei ruminanti (2011): 6.6 %

- 12.7% vitelli
- 1.5% bovini
- 7.5% capre
- 26.6% aziende
- 21% campioni di feci

Romano, V., F. Albanese, S. Dumontet, K. Krovacek, O. Petri & V. Pasquale (2012). "Prevalence and genotypic characterization of *Clostridium difficile* from ruminants in Switzerland." Zoonoses Public Health 59(8), 545-548.

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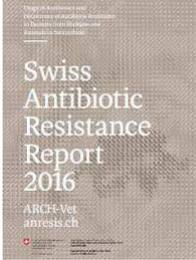
Dati Svizzeri



Swiss Centre for Antibiotic resistance



<https://infect.info/>



Swiss Antibiotic Resistance Report 2016
ARCH-Vet
anresis.ch



Usage of Antibiotics and Occurrence of Antibiotic Resistance in Bacteria from Humans and Animals in Switzerland

Swiss Antibiotic Resistance Report 2018

anresis.ch
ARCH-Vet

Presentato in conferenza stampa il 12.11.2018

Germi multiresistenti in medicina umana e veterinaria





<https://infect.info/>

Name	Penicillin		Cephalosporin				Carbapenem	Mon	Rizatriquinolone		Aminogly	Macrolide	Linc	Glycopept	Dapt	Tetracycline	Sul	Acid	Fluo	Lipo	Nitro	Fol	Rif
	Beta-lactam	PenV	Beta-lacta	1G C	2G C	3G Cephalosporin			4G C	Quinolone													
<i>Acinetobacter</i> sp.																							
<i>Acinetobacter</i> sp.	1		4	7	1	1	5	2	2	2	2	2	2										
<i>Actinomyces</i> sp.																							
<i>Bacteroides fragilis</i>																							
<i>Burkholderia</i> sp.																							
<i>Campylobacter</i> sp.																							
<i>Campylobacter jejuni</i>																							
<i>Citrobacter koseri</i>																							
<i>Citrobacter</i> sp. non-jejuni																							
<i>Enterobacter</i> sp.																							
<i>Enterococcus faecalis</i>																							
<i>Enterococcus faecium</i>																							
<i>Escherichia coli</i>																							
<i>Haemophilus influenzae</i>																							
<i>Haemophilus pylori</i>																							
<i>Klebsiella oxytoca</i>																							
<i>Klebsiella pneumoniae</i>																							
<i>Moraxella catarrhalis</i>																							
<i>Morganella morganii</i>																							
<i>Neisseria gonorrhoeae</i>																							
<i>Neisseria meningitidis</i>																							
<i>Propionibacterium acnes</i>																							
<i>Proteus mirabilis</i>																							
<i>Proteus</i> sp. 'non-mirabilis'																							
<i>Providencia</i> sp.																							
<i>Pseudomonas aeruginosa</i>																							
<i>Serratia</i> sp.																							
<i>Serratia</i> sp.																							
<i>Shigella</i> sp.																							
<i>Staphylococcus aureus</i>																							
<i>Staphylococcus epidermidis</i>																							
<i>Staphylococcus</i> sp. coagulase-negative																							

