# Pojava bakterije *Acinetobacter baumannii* u prirodnom okolišu

## Seminar I

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Poslijediplomski doktorski studij biologije

Prirodoslovno-matematički fakultet

hrzz
Hrvatska zaklada za znanost

# *Acinetobacter*

- 53 vrste

| | | | |
|---|---|---|---|
| Commonly found human pathogens | | | |
| *A. baumannii* (genospecies 2) | | | |
| *A. nosocomialis* (genospecies 13TU) | | | |
| *A. pittii* (genospecies 3) | | | |
| *A. calcoaceticus* (genospecies 1) | | | |
| Uncommon organisms in clinical infections | | | |
| *A. baylyi* | *A. guillouiae* | *A. lwoffii* | *A. soli* |
| *A. beijerinckii* | *A. gyllenbergii* | *A. nectaris* | *A. tandoii* |
| *A. bereziniae* | *A. haemolyticus* | *A. parvus* | *A. tjernbergiae* |
| *A. boissieri* | *A. harbinensis* | *A. puyangensis* | *A. towneri* |
| *A. bouvetii* | *A. indicus* | *A. qingfengensis* | *A. ursingii* |
| *A. brisouii* | *A. johnsonii* | *A. radioresistens* | *A. venetianus* |
| *A. gerneri* | *A. junii* | *A. rudis* | |
| *A. grimontii*[a] | *A. kookii* | *A. schindleri* | |

http://apps.szu.cz/anemec/Classification.pdf

Review

# Clinical relevance of the ESKAPE pathogens

Jack N Pendleton, Sean P Gorman & Brendan F Gilmore

Pages 297-308 | Published online: 10 Jan 2014

 http://dx.doi.org/10.1586/eri.13.12



## Abstract

In recent years, the Infectious Diseases Society of America has highlighted a faction of antibiotic-resistant bacteria (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter* spp.) – acronymically dubbed 'the ESKAPE pathogens' – capable of 'escaping' the biocidal action of antibiotics and mutually representing new paradigms in pathogenesis, transmission and resistance. This review aims to consolidate clinically relevant background information on the ESKAPE pathogens and provide a contemporary summary of bacterial resistance, alongside pertinent microbiological considerations necessary to face the mounting threat of antimicrobial resistance.

Keywords:: *Acinetobacter*, antibiotics, antimicrobial resistance, *Enterobacter*, ESKAPE pathogens, hospital-acquired infection, *Klebsiella*, MRSA, multidrug resistance, *Pseudomonas*, VRE

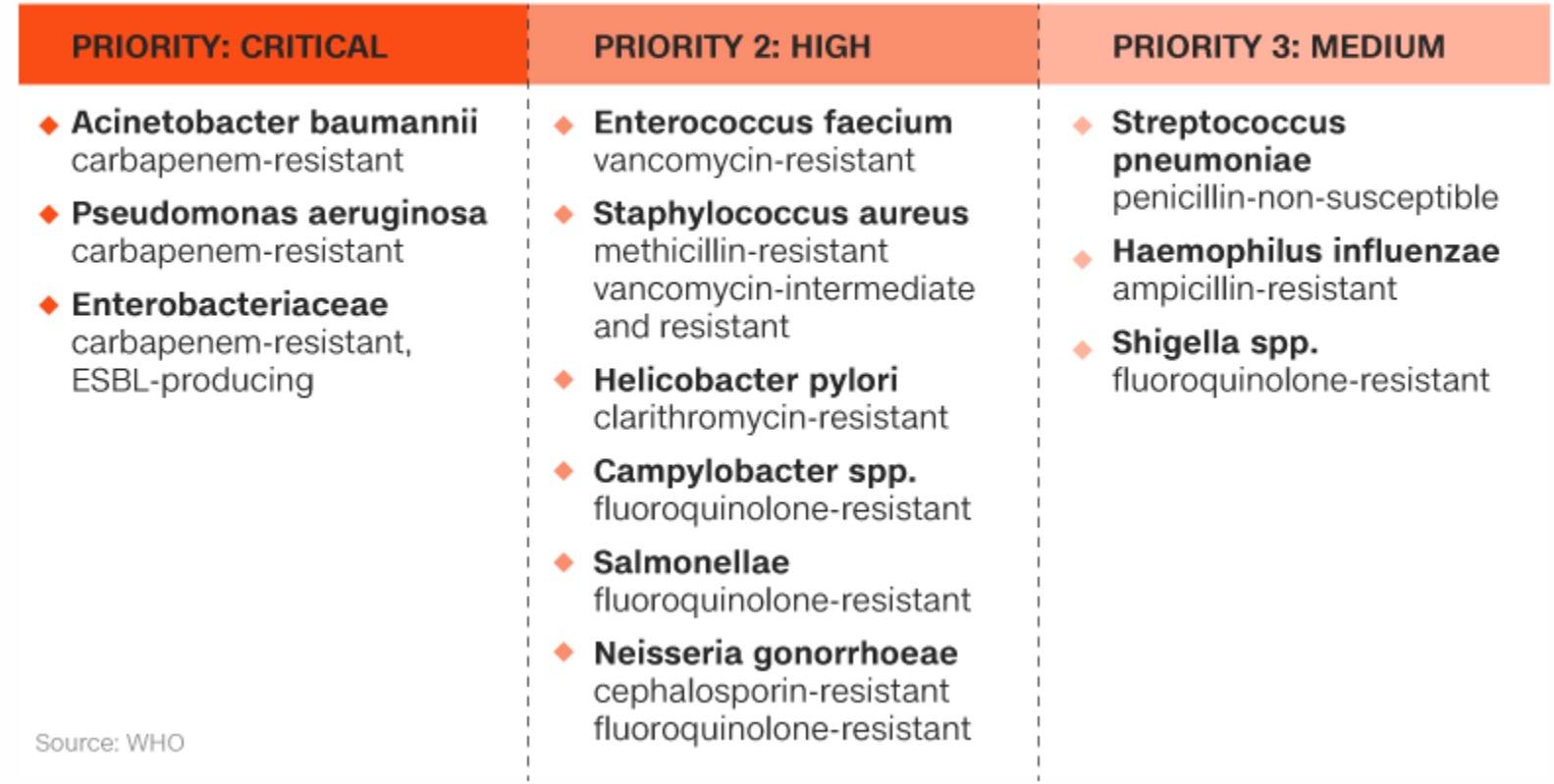
## Bad Bugs, No Drugs: No ESKAPE! An Update from the Infectious Diseases Society of America FREE

Helen W. Boucher ✉, George H. Talbot, John S. Bradley, John E. Edwards, David Gilbert, Louis B. Rice, Michael Scheld, Brad Spellberg, John Bartlett

Clin Infect Dis (2009) 48 (1): 1-12. **DOI:** https://doi.org/10.1086/595011

**Published:** 01 January 2009 **Article history** ▾

## The WHO priority list



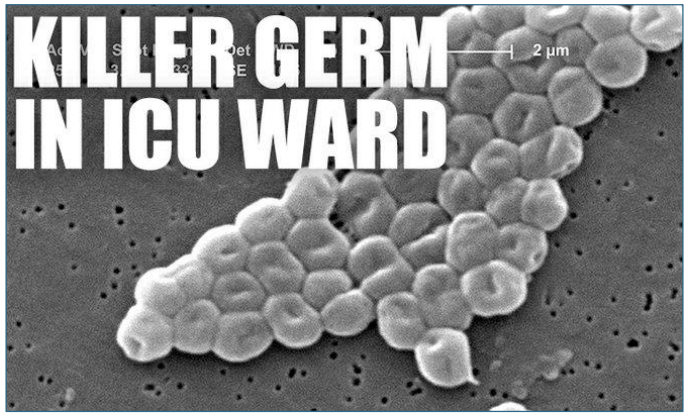
| PRIORITY: CRITICAL | PRIORITY 2: HIGH | PRIORITY 3: MEDIUM |
|---|---|---|
| **Acinetobacter baumannii** carbapenem-resistant | **Enterococcus faecium** vancomycin-resistant | **Streptococcus pneumoniae** penicillin-non-susceptible |
| **Pseudomonas aeruginosa** carbapenem-resistant | **Staphylococcus aureus** methicillin-resistant vancomycin-intermediate and resistant | **Haemophilus influenzae** ampicillin-resistant |
| **Enterobacteriaceae** carbapenem-resistant, ESBL-producing | **Helicobacter pylori** clarithromycin-resistant | **Shigella spp.** fluoroquinolone-resistant |
| | **Campylobacter spp.** fluoroquinolone-resistant | |
| | **Salmonellae** fluoroquinolone-resistant | |
| | **Neisseria gonorrhoeae** cephalosporin-resistant fluoroquinolone-resistant | |

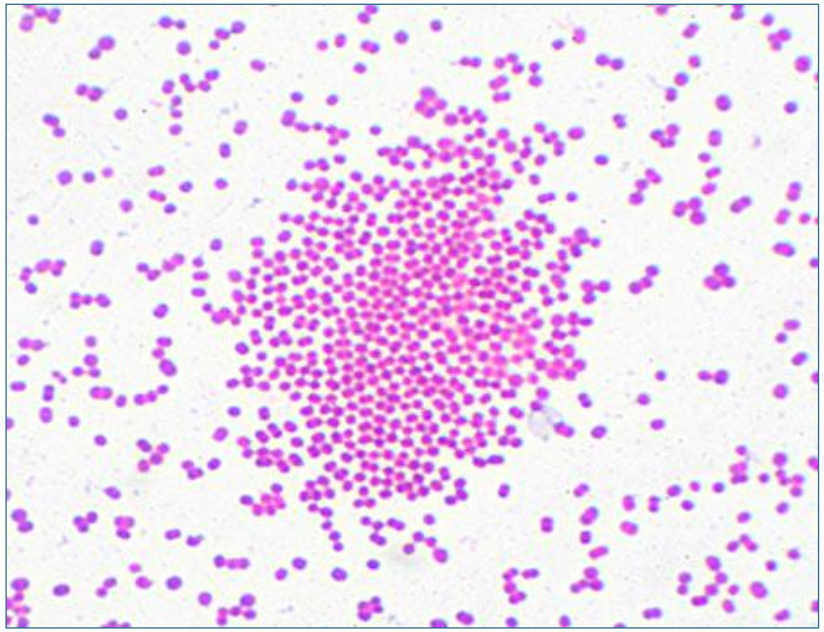
Source: WHO

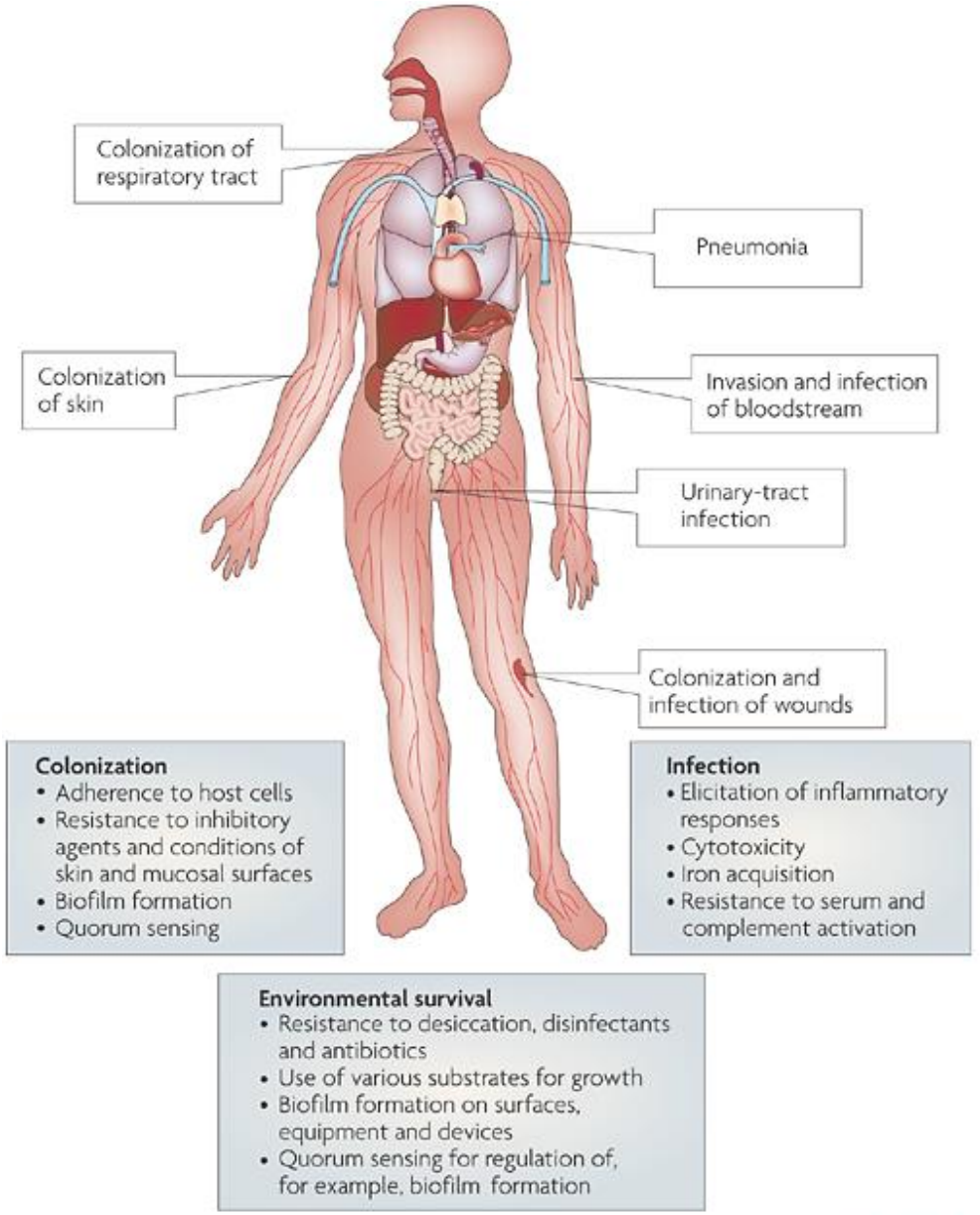
- Rezistencija na karbapenemske antibiotike u Hrvatskoj povećala se sa 10% u 2008. do 87% u 2015. godini (Croatian Academy of Medical Sciences. Antibiotic resistance in Croatia, 2015. Zagreb: CAMS; 2016.)

# *Acinetobacter baumannii*

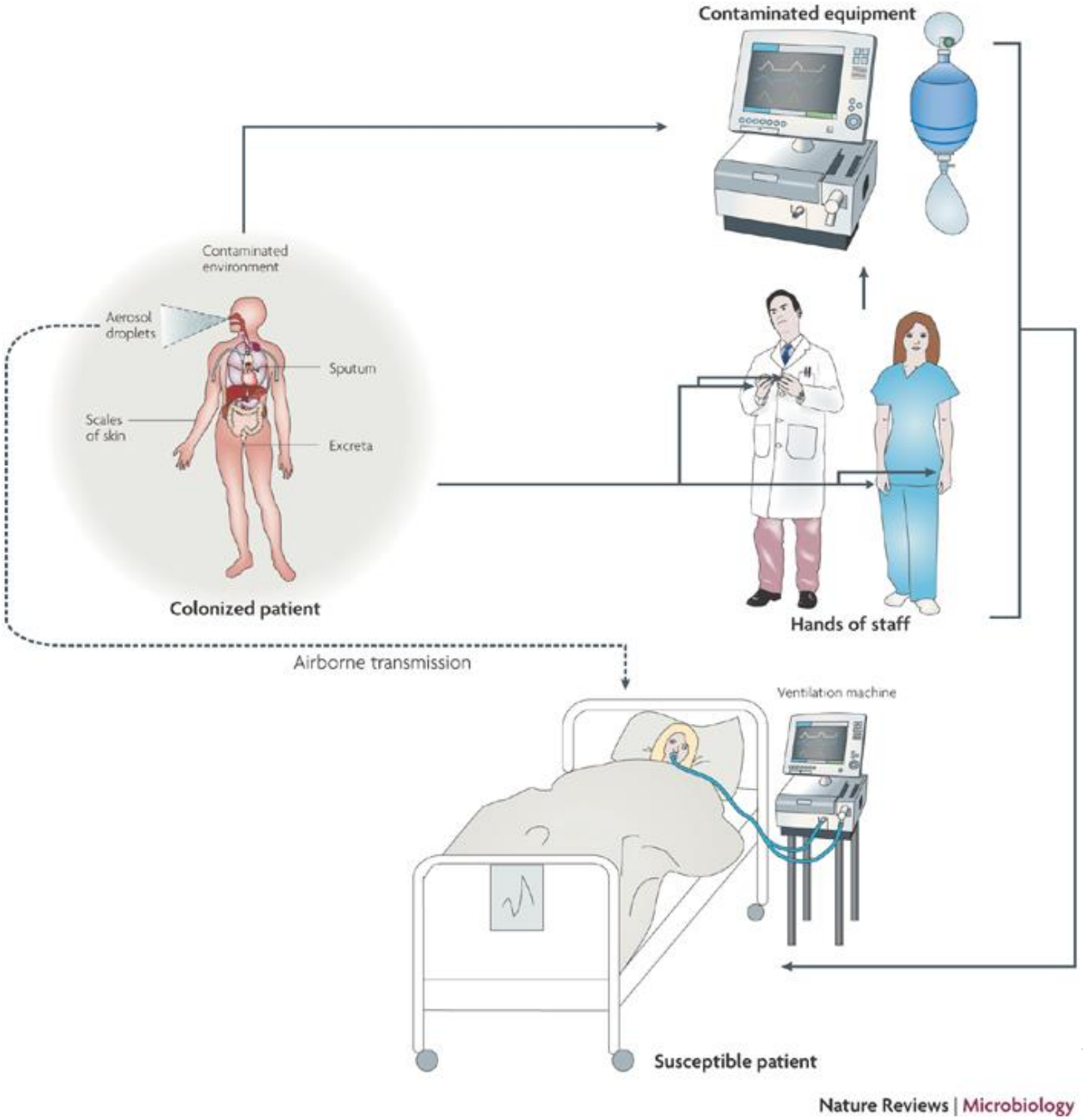
- Gram negativni kokobacilus
- Emergentni humani oportunistički patogen
- Infekcije većinom vezane uz bolnički okoliš





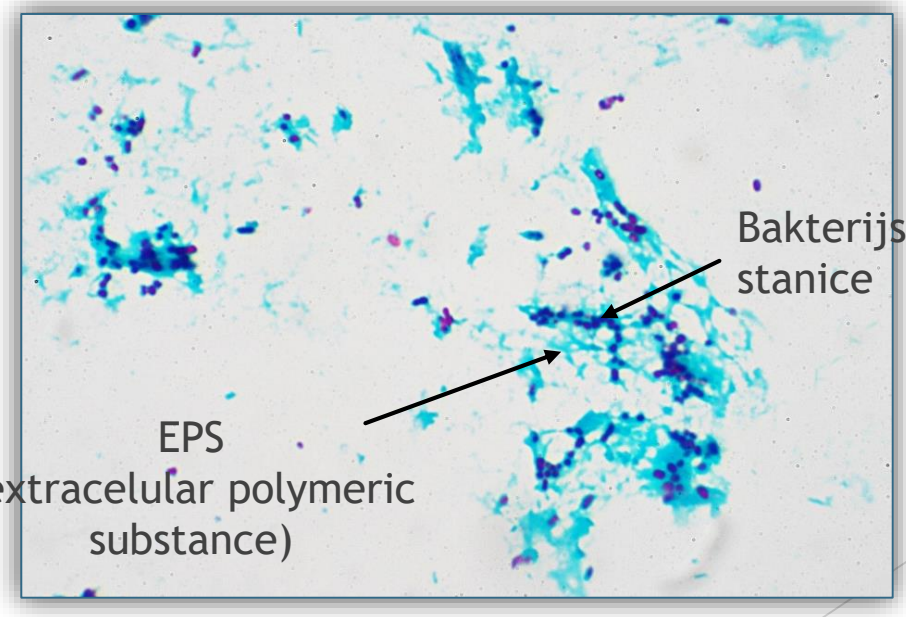

Nature Reviews | Microbiology


Contaminated equipment
Contaminated environment
Aerosol droplets
Sputum
Scales of skin
Excreta
Colonized patient
Hands of staff
Airborne transmission
Ventilation machine
Susceptible patient
Nature Reviews | Microbiology

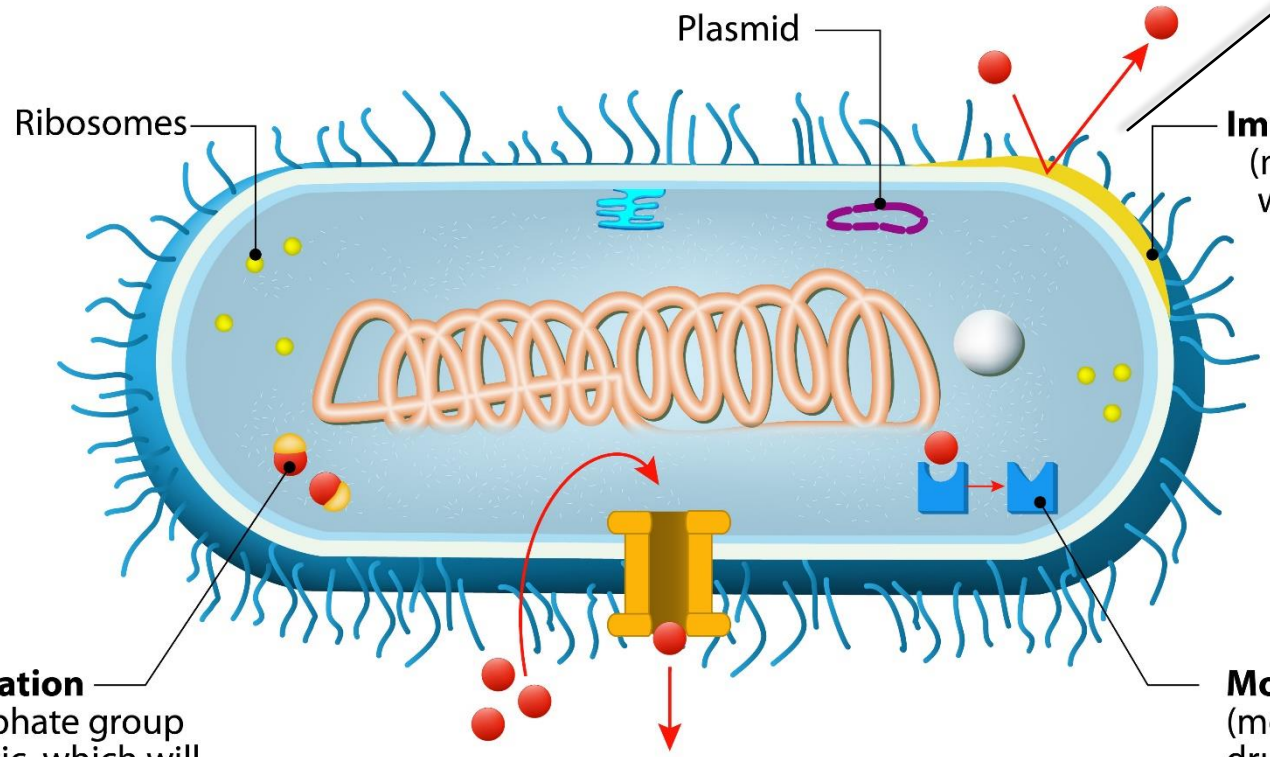
# Iraqibacter

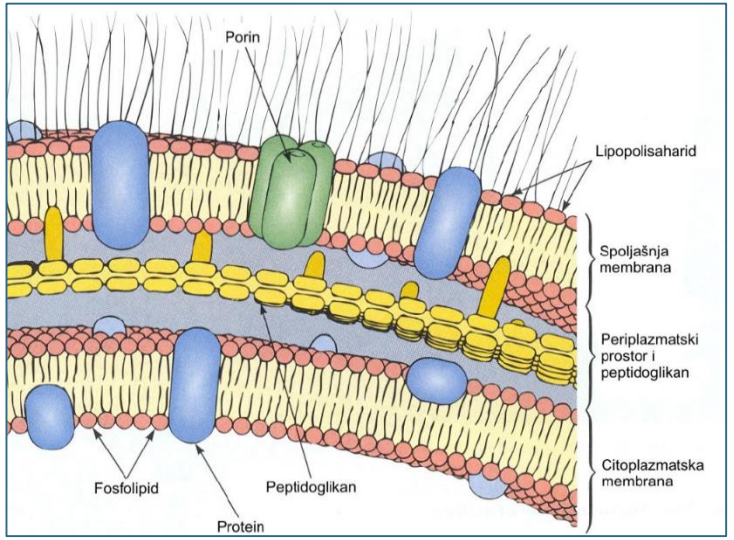
# Razlozi uspješnosti

- Rezistencija na antibiotike- MDR, XDR, PDR
- Stvaranje biofilma na biotskim i abiotskim površinama
- Površinska pokretljivost trzanjem i rojenjem
- Otpornost na komercijalne dezinficijense koji se uobičajeno koriste

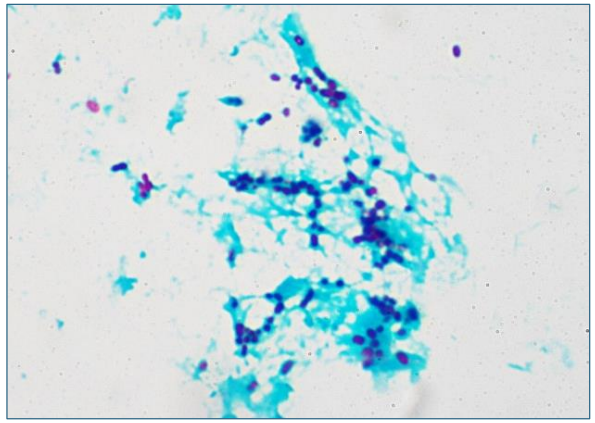




# MECHANISMS OF ANTIMICROBIAL RESISTANCE


**Impermeability** (modified cell wall protein)



Biofilm

**Inactivation** (add an phosphate group on the antibiotic, which will reduce its ability to bind to the bacterial ribosomes)

**Pumping out** (increasing active efflux of the drugs)

**Modification** (modified drug target)

https://www.thermofisher.com/blog/behindthebench/wp-content/uploads/sites/9/2016/04/Mechanism-of-antibiotic-resistance-1.jpg

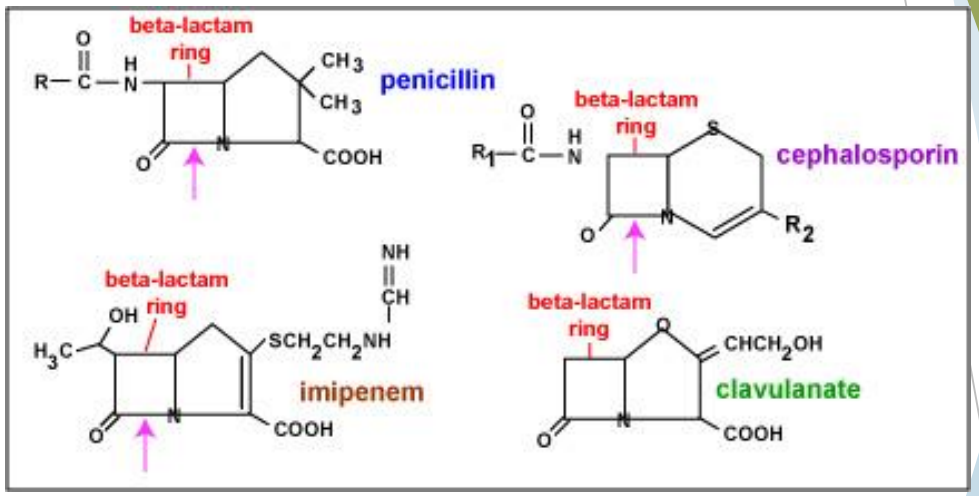
**Table 2.** The mechanism of antimicrobial resistance of Acinetobacter baumannii:[3]

| Resistance mechanisms | Antimicrobial agents |
|---|---|
| Produce antibiotics inactivated enzyme | |
| β-lactamas | β-lactams |
| Class A: extended-spectrum-β-lactamases (ESBLs): TEM, PER type | |
| Class B: the metallo-lactamases (MBLs): IMP, VIM, SIM type | |
| Class C: AmpC cephalosporinases | |
| Class D: serine carbapenemases (OXA type) | |
| Aminoglycoside-modifying enzymes (AMEs): APHs, AACs | Aminoglycosides |
| Alter the action sites of antibiotics | |
| Topoisomerase mutations in the genes gyrA and parC | Quinolones |
| Ribosomal (16S rRNA) methylation: armA | Aminoglycosides |
| Alteration in penicillin-binding proteins (PBPs) | β-lactams |
| Reduce the concentration of antibiotics in cells | |
| Decreased permeability of the outer membrane | Multidrug |
| Efflux pumps | |
| Plasmid-mediated transport protein: TetA, TetB, TetK | Tetracyclines |
| RND efflux systems: AdeABC, AdeDE, AdeXYZ, AdeIJK | Multidrug |
| Biofilm formation | Multidrug |

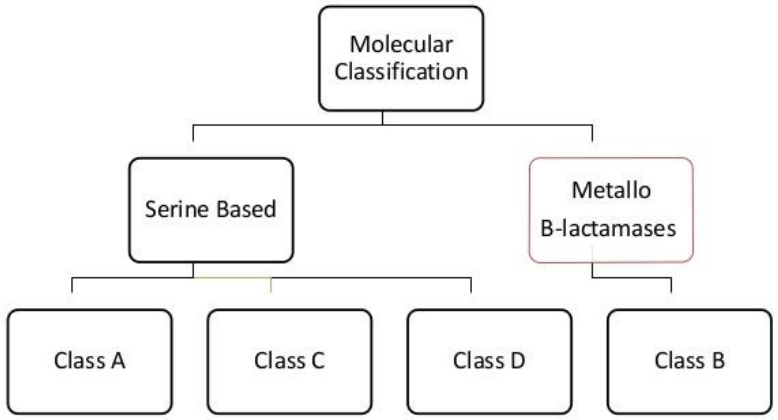
http://www.wjem.org/default/articlef/index/id/240

# ß- laktamaze

- ß-laktamaze - enzimi koji hidroliziraju ß-laktamske antibiotike
  - Penicilini
  - Cefalosporini
  - Monobaktami
  - Karbapenemi
- Klasifikacija:
  - Richmond & Sykes klasifikacija (1973)
  - Sykes and Matthew (1976)
  - Od 1990 Bush-Jacoby-Medeiros klasifikacija (podjela u grupe, ovisno o supstratu, osjetljivosti na inhibitore te molekularnoj strukturi)
  - Po Ambleru grupe A, B, C i D



## Beta-Lactamase Enzyme




# Carbapenemases

| Classification | Enzyme | Most Common Bacteria |
|---|---|---|
| Class A | KPC, SME, IMI, NMC, GES | Enterobacteriaceae (rare reports in *P. aeruginosa*) |
| Class B (metallo-β-lactamse) | IMP, VIM, GIM, SPM | *P. aeruginosa* Enterobacteriacea *Acinetobacter* spp. |
| Class D | OXA | *Acinetobacter* spp. |

TABLE 6. Carbapenemase subgroups of the OXA family of β-lactamases

| Cluster | Enzyme subfamily | Additional OXA member(s) | Reference |
|---|---|---|---|
| 1 | OXA-23 (ARI-1) | OXA-27, OXA-49 | 225 |
| 2 | OXA-24 | OXA-25, OXA-26, OXA-40, OXA-72 | 225 |
| 3 | OXA-51 | OXA-64 to OXA-71, OXA-75 to OXA-78, OXA-83, OXA-84, OXA-86 to OXA-89, OXA-91, OXA-92, OXA-94, OXA-95 | 213, 225 |
| 4 | OXA-58 | None | 225 |
| 5 | OXA-55 | OXA-SHE | 225 |
| 6 | OXA-48 | OXA-54, OXA-SAR2 | 225 |
| 7 | OXA-50 | OXA-50a to OXA-50d, PoxB | 225 |
| 8 | OXA-60 | OXA-60a to OXA-60d | 225 |
| 9 | OXA-62 | None | 192 |


- Queenan, A.M., Bush, K. Carbapenemases: the versatile beta-lactames. Clin. Microbiol. Rev. 2007, 20(3):440-58
- https://www.slideshare.net/saurav9119/beta-lactam-antibiotics-43630735
- https://www.slideshare.net/doctorrao/carbapenem-resistance-in-clinical-care-34157044

# *A. baumannii* OXA grupe

- Urođena rezistencija
  - OXA-51, OXA-51 like (IS*Aba1*)
- Stečena rezistencija
  - OXA-23 (IS*Aba1*)
  - OXA-40
  - OXA-58 (IS*Aba3*)
  - OXA-143
  - OXA-235 (IS*Aba1*)

TABLE 6. Carbapenemase subgroups of the OXA family of β-lactamases

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| 8 | OXA-60 | OXA-60a to OXA-60d | 225 |
| 9 | OXA-62 | None | 192 |

# Bolnička otpadna voda

- Brazil
  - Otpadna voda iz 3 bolnice
  - 3 izolata
- Kina
  - Otpadna voda iz 4 bolnice
  - 10 izolata
- Hrvatska
  - Specijalna bolnica za plućne bolesti, Zagreb
  - 10 izolata

**Presence of OXA-23-Producing Isolates of *Acinetobacter baumannii* in Wastewater from Hospitals in Southern Brazil**

**To cite this article:**
Alessandra E. Ferreira, Desirée P. Marchetti, Lyvia M. De Oliveira, Carolina S. Gusatti, Daiane B. Fuentefria, and Gertrudes Corção. Microbial Drug Resistance. May 2011, 17(2): 221-227. https://doi.org/10.1089/mdr.2010.0013

**Higher Isolation of NDM-1 Producing *Acinetobacter baumannii* from the Sewage of the Hospitals in Beijing**

**Chuanfu Zhang[1☯], Shaofu Qiu[1*☯], Yong Wang[1☯], Lihua Qi[1☯], Rongzhang Hao[1☯], Xuelin Liu[1☯], Yun Shi[1☯], Xiaofeng Hu[1☯], Daizhi An[1☯], Zhenjun Li[2☯], Peng Li[1☯], Ligui Wang[1☯], Jiajun Cui[1], Pan Wang[1], Liuyu Huang[1], John D. Klena[3], Hongbin Song[1*]**

**1** Institute of Disease Control and Prevention, Academy of Military Medical Science, Beijing, People's Republic of China, **2** State Key Laboratory for Infectious Disease Prevention and Control, China Center of Disease Control and Prevention, Beijing, People's Republic of China, **3** United States Centers for Disease Control and Prevention, China –US Collaborative Program on Emerging and Re-emerging Infectious Diseases, Beijing, People's Republic of China

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Journal of Hospital Infection

Available online 11 April 2017

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**Emission of extensively-drug-resistant *Acinetobacter baumannii* from hospital settings to the natural environment**

M. Seruga Music[a], J. Hrenovic[a], I. Goic-Barisic[b], B. Hunjak[c], D. Skoric[a], T. Ivankovic[a]

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https://doi.org/10.1016/j.jhin.2017.04.005

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# Uređaj za pročišćavanje otpadnih voda

## Carbapenem-resistant isolates of *Acinetobacter baumannii* in a municipal wastewater treatment plant, Croatia, 2014

J Hrenovic [1], I Goic-Barisic [2], S Kazazic [3], A Kovacic [4], M Ganjto [5], M Tonkic [2]
1. University of Zagreb, Faculty of Science, Department of Biology, Zagreb, Croatia
2. University Hospital Centre Split, Department of Clinical Microbiology and University of Split School of Medicine, Split, Croatia
3. Ruđer Boskovic Institute, Division of Physical Chemistry, Zagreb, Croatia
4. Institute of Public Health of Split and Dalmatia County, Split, Croatia
5. Zagreb Wastewater - Management and Operation Ltd., Zagreb, Croatia

Correspondence: Jasna Hrenovic (jasna.hrenovic@biol.pmf.hr)

21 izolat

## Emergence of Oxacillinases in Environmental Carbapenem-Resistant *Acinetobacter*

## Pan Drug-Resistant Environmental Isolate of *Acinetobacter baumannii* from Croatia

To cite thi
Goic-Barisi
June 2017

ıg Resistance.

Published
Online Ah

*Int.J.Curr.Microbiol.App.Sci* (2017) *6*(3): 1697-1709

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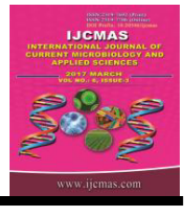
*International Journal of Current Microbiology and Applied Sciences*
*ISSN: 2319-7706* Volume 6 Number 3 (2017) pp. 1697-1709
Journal homepage: http://www.ijcmas.com




**Original Research Article**

https://doi.org/10.20546/ijcmas.2017.603.195

## Virulence Factors of *Acinetobacter baumannii* Environmental Isolates and Their Inhibition by Natural Zeolite

Svjetlana Dekic[1], Jasna Hrenovic[1]*, Blazenka Hunjak[2], Snjezana Kazazic[3], Darko Tibljas[1] and Tomislav Ivankovic[1]

24 izolata

# Prirodne vode

- Francuska, rijeka Sena
  - 1 izolat
- Hrvatska, rijeka Sava
  - Nizvodno od ispusta efluenta iz Centralnog uređaja za pročišćavanje otpadnih voda
  - 4 izolata u 10 mL vode

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Jan. 2010, p. 578–579 Vol. 54, No. 1
0066-4804/10/$12.00 doi:10.1128/AAC.00861-09


## Letters to the Editor

### First Isolation of the *bla*$_{OXA-23}$ Carbapenemase Gene from an Environmental *Acinetobacter baumannii* Isolate$^{\nabla}$

*Acinetobacter baumannii* is frequently associated with nosocomial infections, and its increasing resistance to carbapenems may significantly reduce the choice of effective antibiotics (2). Since the first description of a carbapenem-hydrolyzing class D β-lactamase (CHDL), ARI-1 (renamed OXA-23), from a clinical isolate of *A. baumannii* in Scotland in 1995 (11), the corresponding *bla*$_{OXA-23}$ gene has been detected in many *A. baumannii* clinical isolates worldwide (Brazil, Spain, Belgium, Singapore, Portugal, and France) and once in *Proteus mirabilis* in France (1). The *bla*$_{OXA-23}$ gene can be plasmid or chromosome borne (12). Three main groups of oxacillinases (OXA-23, poorly expressed (10). That species is rarely involved in human infections but is known to be present in the environment. Therefore, it is hypothesized that genetic exchanges between the two *Acinetobacter* species may lead to acquisition and expression of the *bla*$_{OXA-23}$ gene in *A. baumannii*. This might occur in aquatic environments, where *A. baumannii* and *A. radioresistens* could be in close contact. The *A. baumannii* B9 isolate was not recovered in the immediate vicinity of a hospital wastewater discharge site. Pulsed-field gel electrophoresis (PFGE) analysis of ApaI-restricted DNA from *A. baumannii* B9 and from clinical *A. baumannii* isolates from different geo- l origins showed that *A. baumannii* B9 was clonally o a human *A. baumannii* isolate previously identified

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## Emission of extensively-drug-resistant *Acinetobacter baumannii* from hospital settings to the natural environment

M. Seruga Music[a], J. Hrenovic[a], I. Goic-Barisic[b], B. Hunjak[c], D. Skoric[a], T. Ivankovic[a]

Show more

https://doi.org/10.1016/j.jhin.2017.04.005

# Tlo

- Pula – kiselo paleotlo (95% minerali glina)
  - Ilegalno odlagalište otpada
  - 1 izolat u 0,1g
- Rijeka- tehnotlo
  - Sovjak odlagalište industrijskog otpada
  - 3 izolata u 0,01-0,1g

AEM Journals.ASM.org

## Occurrence of an Environmental *Acinetobacter baumannii* Strain Similar to a Clinical Isolate in Paleosol from Croatia

**Jasna Hrenovic,[a] Goran Durn,[b] Ivana Goic-Barisic,[c] Ana Kovacic[d]**

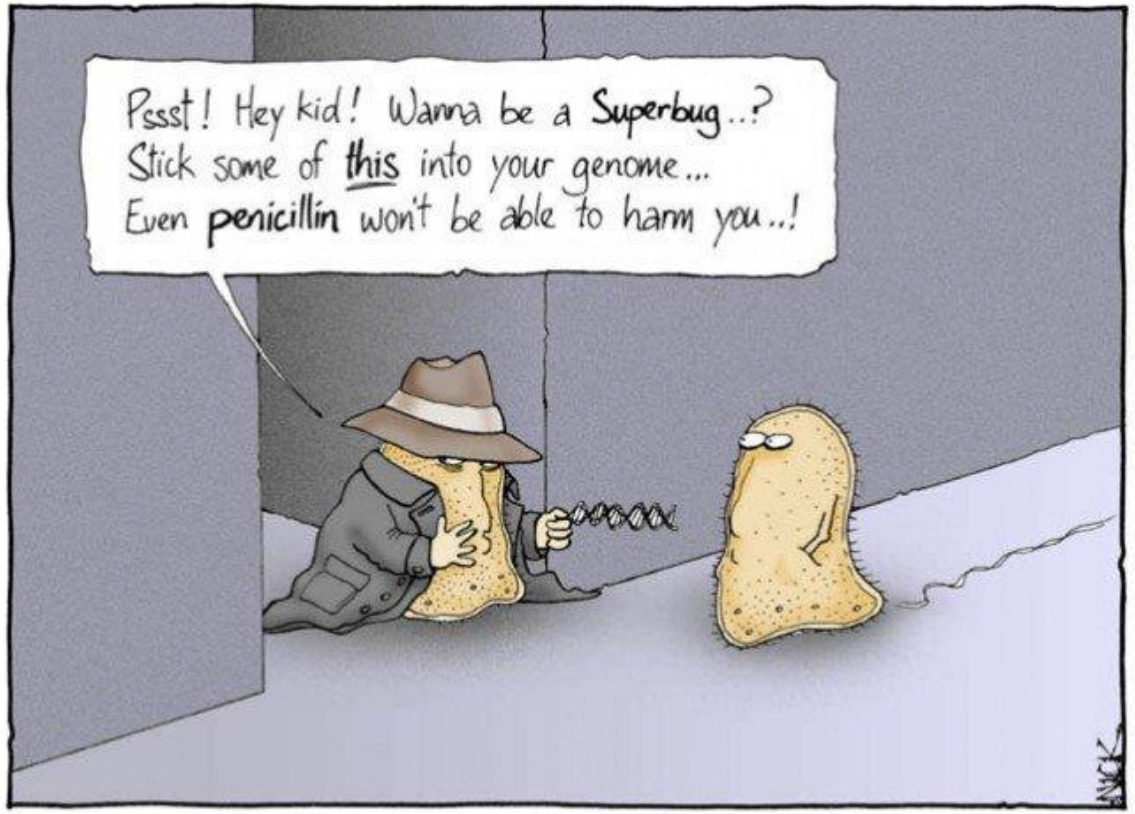
University of Zagreb, Faculty of Science, Division of Biology, Zagreb, Croatia[a]; University of Zagreb, Faculty of Mining, Geology and Petroleum Engineering, Zagreb, Croatia[b]; Department of Clinical Microbiology, University Hospital Centre Split and University of Split School of Medicine, Split, Croatia[c]; Institute of Public Health of Split and Dalmatia County, Split, Croatia[d]

**Over the past decade, bacteria of the genus *Acinetobacter* have emerged as a leading cause of hospital-acquired infections. Out-breaks of *Acinetobacter* infections are considered to be caused exclusively by contamination and transmission in hospital envi-ronments. The natural habitats of clinically important multiresistant *Aci* report an incidental finding of a viable multidrug-resistant strain of *Acin* paleosol from Croatia. The environmental isolate of *A. baumannii* showe trimeth siccatio origin**

# Zaključak

- Bakterija *A. baumannii* u okolišu se može naći u vodi i tlu pod utjecajem ljudskog krutog i tekućeg otpada
- Potrebno je uvesti predtretman bolničke vode prije ispusta u skupni kanalizacijski sustav i pravilno gospodariti krutim infektivnim otpadom kako bi se spriječilo širenje multiplo-rezistentnih bakterija u okoliš

# Hvala na pažnji!




It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.