Healthcare-associated infections

2nd Faculty of Medicine, Charles University

December 11, 2023

Alexandr Nemec

Laboratory of Bacterial Genetics
Centre for Epidemiology and Microbiology
Institute of Public Health, Prague
https://szu.cz/anemec

Focus on

- **Epidemiological typing of hospital-associated bacterial pathogens**
- **Genetics and epidemiology of antibiotic resistance in *Acinetobacter baumannii***

Lecture outline

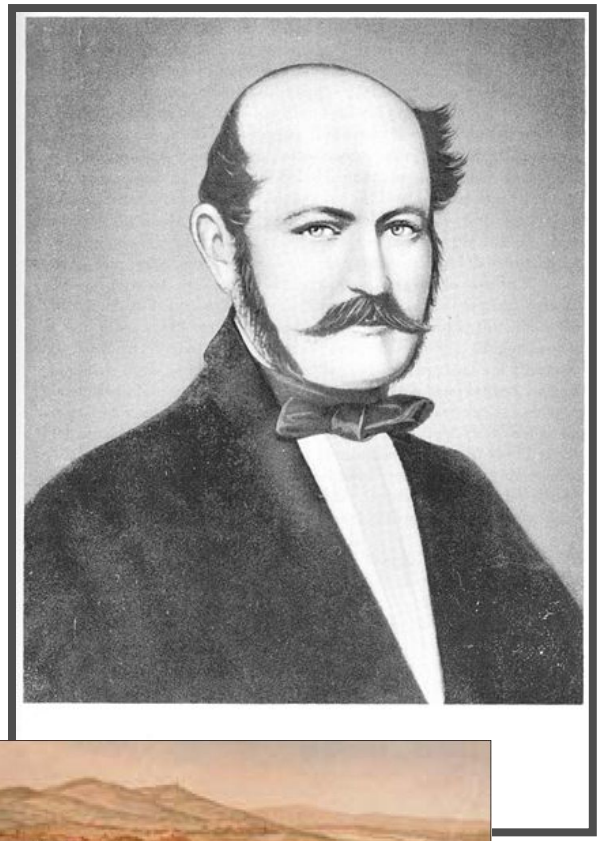
1. **Legacy of Ignaz Semmelweis**

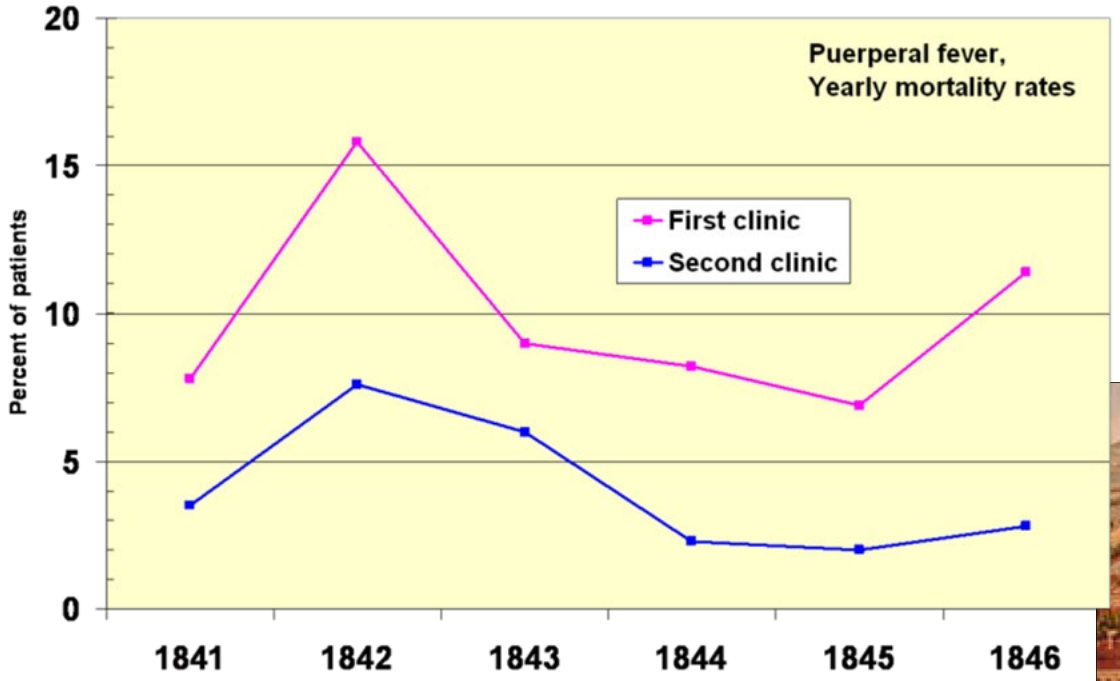
2. **Health care-associated infections (HAIs)**

3. **Multidrug-resistant HAI bacterial pathogens** with *Acinetobacter baumannii* as a model organism

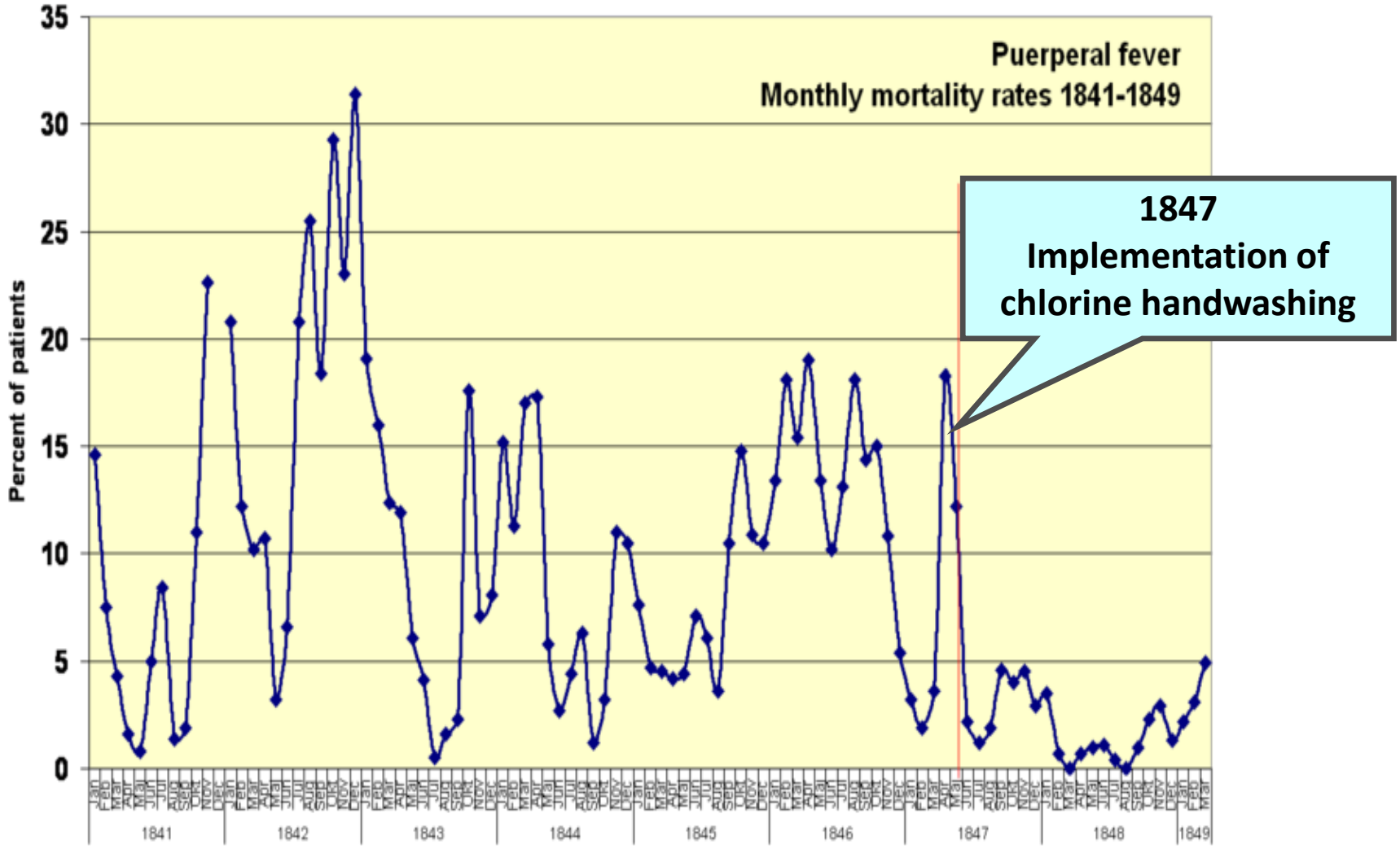
Ignaz Semmelweis (1818–1865)

- *https://en.wikipedia.org/wiki/Ignaz_Semmelweis*
- **1846 The first maternity clinic at the Vienna general hospital**
- **„Puerperal fever“ (*Febris puerperalis*)**





Ignaz Semmelweis

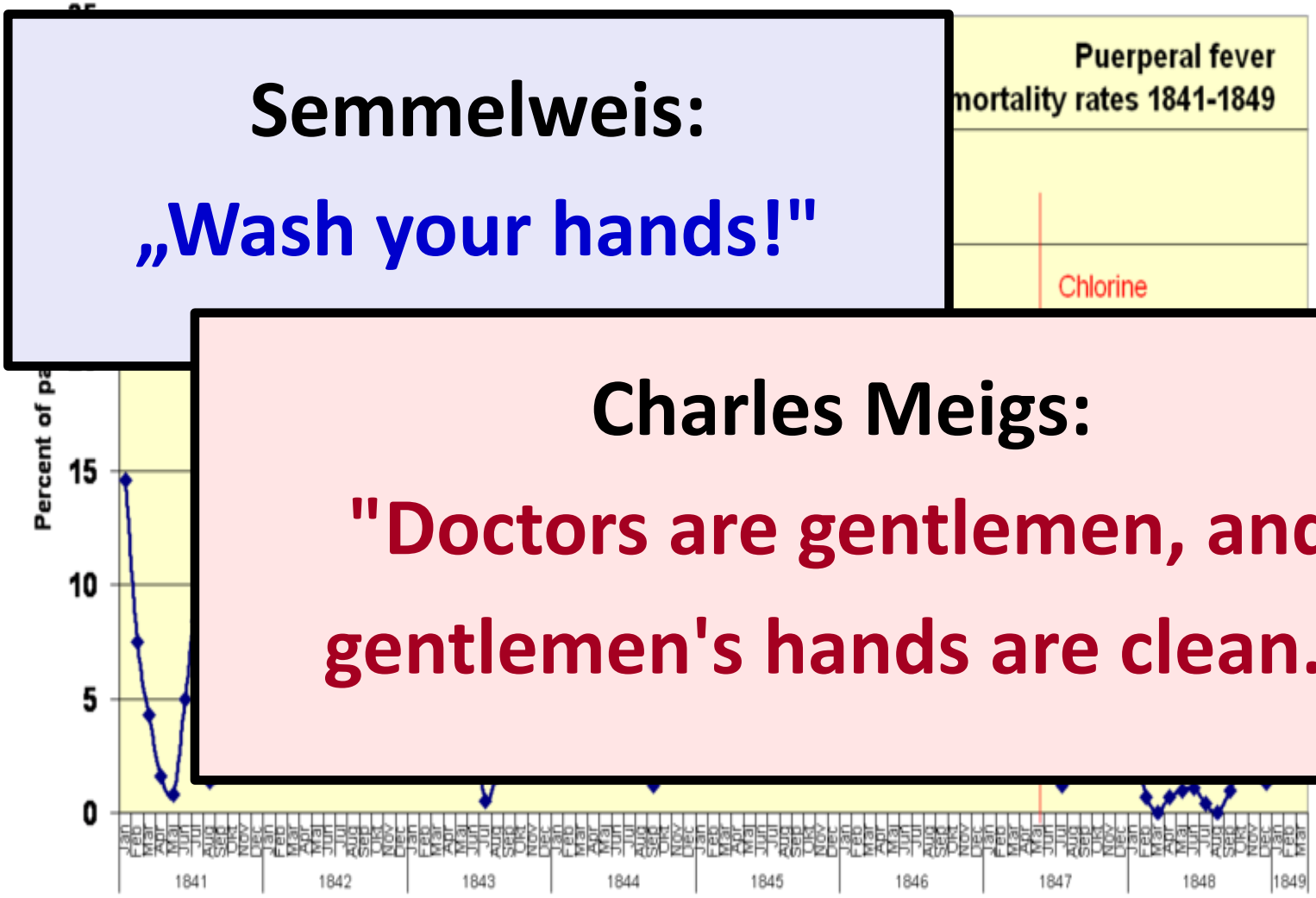


Ignaz Semmelweis

Semmelweis:

„Wash your hands!"

Ignaz Semmelweis



Semmelweis:

„Wash your hands!"

Charles Meigs:

"Doctors are gentlemen, and gentlemen's hands are clean."

Lecture outline - part 2

- **Health care-associated infection (HAI)**
  - **Definitions**
  - **Impact**
  - **Preventability**
  - **Main clinical types**
    - **Bloodstream infections**
    - **Pneumonia**
    - **Surgical site infections**

HAI definitions & classifications

- **Healthcare Associated Infections (HAIs)**

  hospital acquired infections / nosocomial infections

- **Diseases/pathologies related to the presence of an infectious agent or its products in association with exposure to healthcare (HC) facilities or HC procedures or treatments**
- **Infections that are acquired in a hospital or a HC facility**

  - the infection not present or incubating at the time of contact with the HC environment

  - typically, symptom onset >48 h after contact with a HC facility provides evidence for HAI

- **Exogenous / endogenous**
- **Preventable / non-preventable**
- **Hospital, primary, ambulatory, long-term care-associated**

European point prevalence survey (EPPS) 2011–2012

- *www.ecdc.europa.eu/en/publications-data/point-prevalence-survey-healthcare-associated-infections-and-antimicrobial-use-0*
- **The first Europe-wide point prevalence survey on HAIs and antimicrobial use**
- **Data from a total of 273,753 patients in 1,149 hospitals in 30 European countries** submitted to ECDC in order to estimate the prevalence of HAIs in Europe
- It estimates that on any given day, about 80,000 patients [one in 18 (5.6%) patients] have at least one HAI
- ECDC has made recommendations to be further developed and implemented across Europe, incl. increasing the skills for surveillance of HAIs and antimicrobial use

Impact of HAIs in Europe (2009)
mortality, extra costs and hospital stay

• No. of inhabitants (EU 27)	498,000,000
• No. of hospital admissions	81,000,000
• Admissions per 100,000	16,247
• No. of HAI cases	4,131,000
• **Incidence of HAI**	**5.1%**
• **No. of deaths (directly related)**	**37,179**
• No. of deaths (indirect)	111,537
• Extra hospital stay (pt. days)	16,000,000
• **Extra costs**	**4,480,000,000 €**

Council recommendation on patient safety incl. prevention and control of healthcare associated infections 2009, Impact assessment report

HAIs: type distribution (EPPS 2011–2)

Table 11. Prevalence of HAI by HAI type and relative frequency of HAI types, ECDC PPS 2011–2012

	N of patients with HAI	HAI%	N of HAIs	Rel%
All HAI types	**13829**	**6.0**	**15000**	**100**
Pneumonia	2902	1.3	2907	19.4
Other lower respiratory tract infections	607	0.3	609	4.1
Surgical site infections	2933	1.3	2941	19.6
Urinary tract infections	2848	1.2	2848	19.0
Bloodstream infections	1576	0.7	1585	10.6
Catheter-related infections without bloodstream infection	233	0.1	233	1.6
Cardiovascular system infections	203	0.1	204	1.4
Gastro-intestinal system infections[(a)]	1130	0.5	1134	7.6
Skin and soft tissue infections	598	0.3	599	4.0
Bone and joint infections	243	0.1	245	1.6
Central nervous system infections	97	0.0	97	0.6
Eye, ear, nose or mouth infection	454	0.2	454	3.0
Reproductive tract infections	87	0.0	87	0.6
Systemic infections[(b)]	933	0.4	934	6.2
Other/unknown	123	0.1	123	0.8

(a) including Clostridium difficile *infections 3.6%.*
(b) including clinical sepsis 5.4%.

72,7%

Device-associated HAIs (CDC)

- **Central Line-Associated BloodStream Infection (CLABSI)**
- **Ventilator-Associated Pneumonia (VAP)**
- **Surgical Site Infection (SSI)**
- **Catheter-associated Urinary Tract Infections (CAUTI)**

are considered as principal contributors to HC hazard and threat to patient safety as they can cause prolonged hospital stay, sepsis, and mortality in the ICU

HAIs: impact and trends in USA

- **≈ 2,000,000 HAI cases per year**
- **≈ 500,000 intensive care-associated cases** (VAP, BSI)
- **≈ 90,000 HAI-associated deaths per year (the 5th most frequent cause of death)**

Year	Hospitalisation	Lenght	HAI/1,000 pt. days
1975	38,000,000 ↓	7.9 days ↓	7.2 ↑
1995	36,000,000	5.3 days	9.8

Stone et al. A systematic audit of economic evidence linking nosocomial infections and infection control interventions: 1990-2000. Am J Infect Control 2002; 30(3): 145-52.

Preventability of HAI

Targeted infection control based on surveillance

SENIC study (USA 1975, ≈ 400 hospitals):

• **Surveillance + infection control**	**32 % decrease**
• Infection control without surveillance	6 % decrease
• No precautions	18 % increase

Space for improvement

Umscheid et al. Infect Control Hosp Epidemiol 2011

• Catheter-related bloodstream infection	**65–70% (100%)**
• Surgical site infections	55%
• Ventilator associated pneumonia	55%
• Urinary tract infections (catheter assoc.)	**65–70%**

HAIs are solvable to a great extent by rigorous adherence to guidelines on antiepidemic and hygienic measures

HAI etiological agents – overview

Bacteria

Gram-positive cocci

- Coagulase-negative staphylococci
- *Staphylococcus aureus*
- *Streptococcus* spp.
- *Enterococcus* spp.

Clostridioides difficile

Nontuberculous mycobacteria

Enterobacterales

- *Klebsiella* spp.
- *Escherichia coli*
- *Proteus mirabilis*
- *Enterobacter* spp.

Non-fermenters

- *Pseudomonas aeruginosa*
- *Acinetobacter* spp.
- *Burkholderia cepacia*

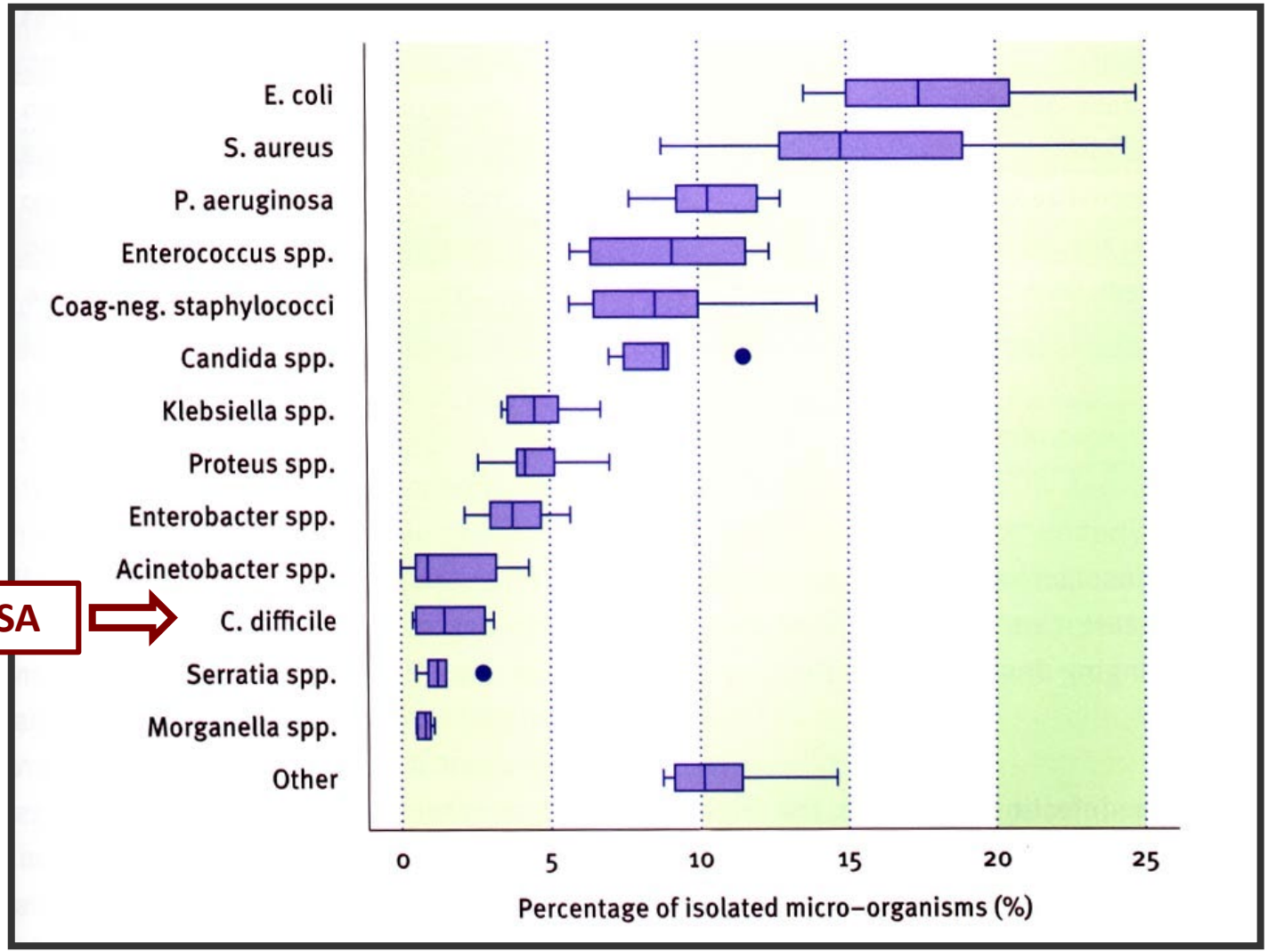
Fungi

- *Candida* spp.
- *Aspergillus fumigatus*

Viruses

- Hepatitis B and C viruses
- HIV virus
- Influenza virus
- Norovirus
- Rhinovirus
- Cytomegalovirus
- Herpes simplex virus

HAI etiological agents – prevalence



15% in USA

ECDC: Annual epidemiological report on communicable diseases in Europe 2008

Bloodstream infections (BSI)
(EPPS 2011–2)

	Number of HAIs	Percentage
Origin of bloodstream infections (BSI)[a]		
Total BSI	1585	100.0
Catheter-related (C) BSI[e]	626	39.5
C-CVC	527	33.2
Of which CRI3-CVC	345	65.5
C-PVC	99	6.2
Of which CRI3-PVC	52	52.5
Secondary (S) BSI[f]	456	28.8
S-Pulmonary infection	65	4.1
S-Urinary tract infection	127	8.0
S-Surgical site infection	79	5.0
S-Digestive tract infection	78	4.9
S-Skin/soft tissue infection	35	2.2
S-Other infection sites	72	4.5
BSI of unknown origin & missing	503	31.7
BSI of unknown origin[g]	310	19.6
Missing BSI origin	193	12.2

Nosocomial BSI (USA)

Clinical Infectious Diseases **2004; 39:309–17**

Nosocomial Bloodstream Infections in US Hospitals: Analysis of 24,179 Cases from a Prospective Nationwide Surveillance Study

Hilmar Wisplinghoff,[1,2] Tammy Bischoff,[1] Sandra M. Tallent,[1] Harald Seifert,[2] Richard P. Wenzel,[1] and Michael B. Edmond[1]

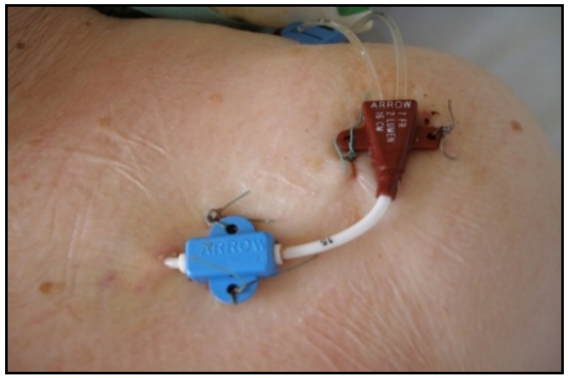
Surveillance of nosocomial BSI (49 hospitals, 1995–2002)

- **Average occurrence:** **60 cases per 10,000 admissions**
- Median/range: 48/6–252 cases per 10,000 admissions

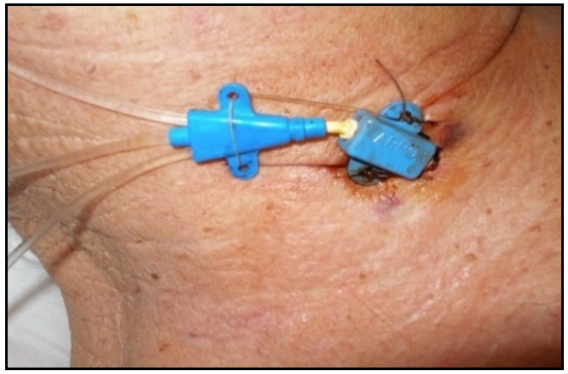
- **Crude mortality rate:** **48%**
- **Intensive care-related:** **51% cases**

Catheter-related infections
central venous catheters – different risks of BSI

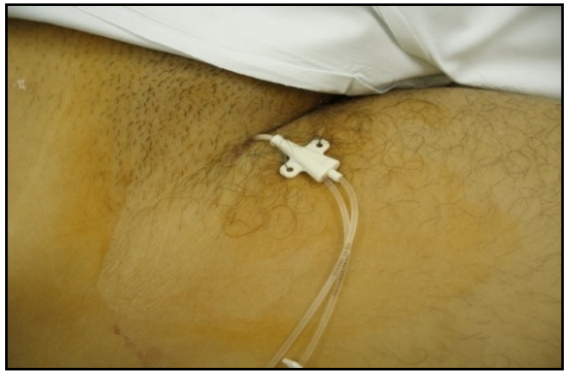
Subclavian vein



Jugular vein

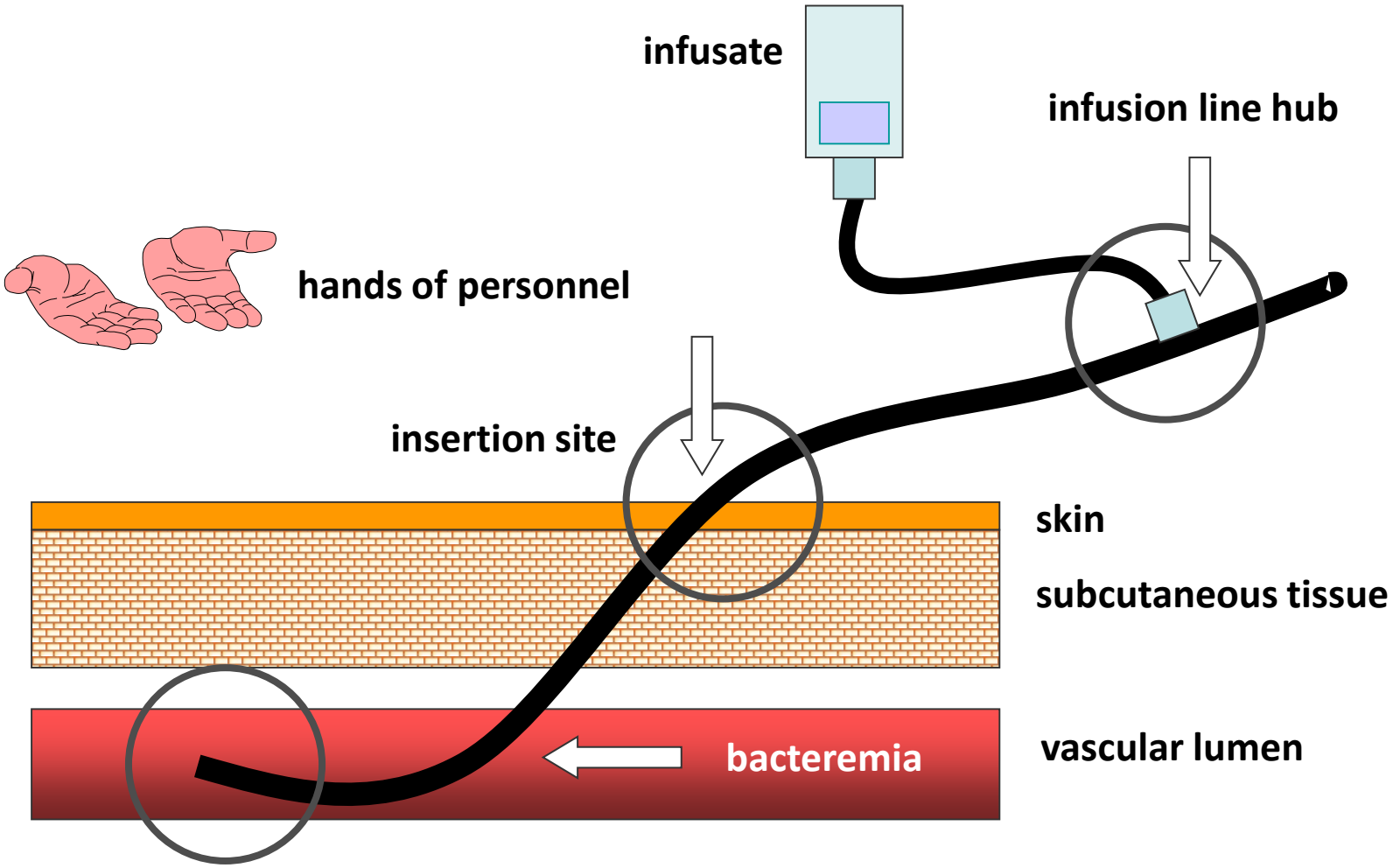


Femoral vein

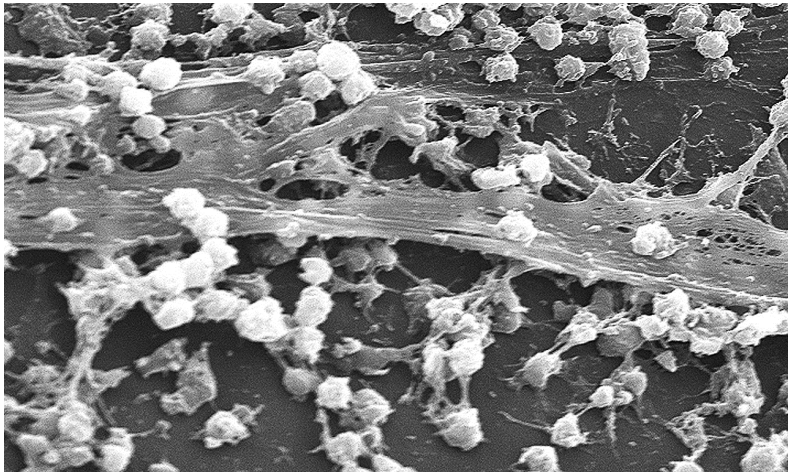


Risk of HAI

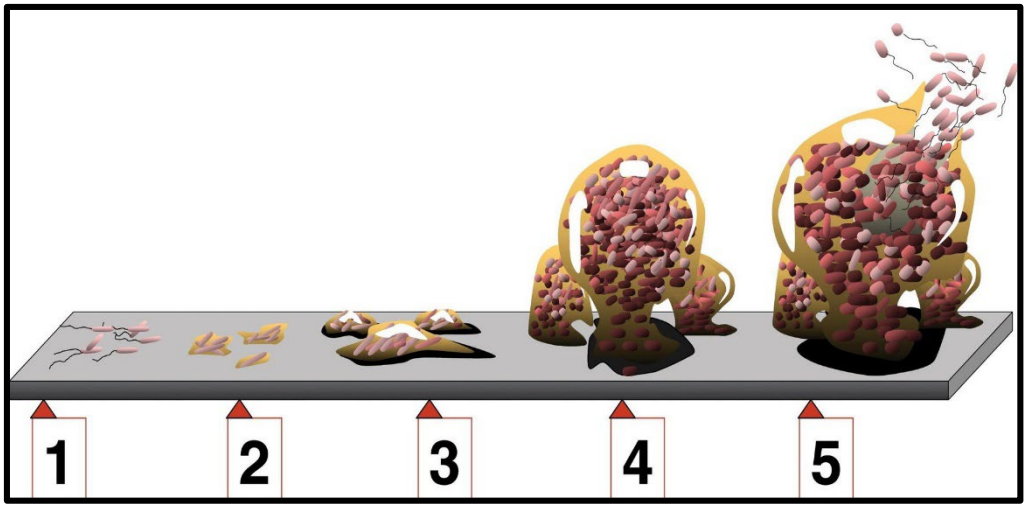
Catheter-related infections
colonisation and infection

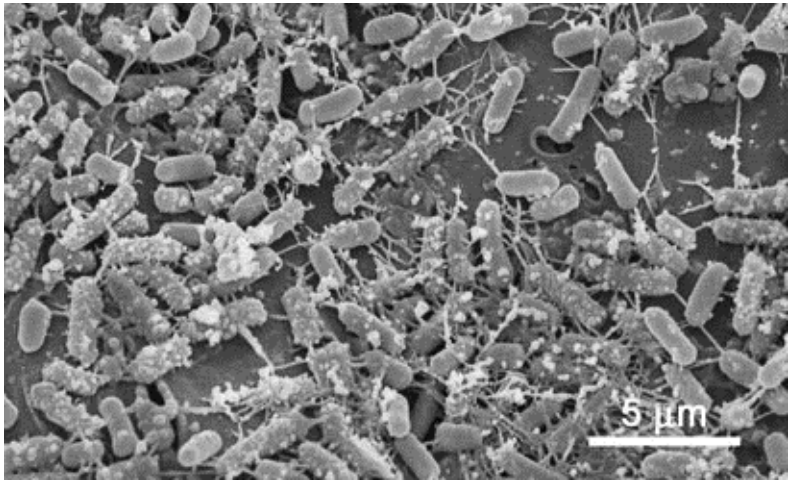


Catheter-related infections
bacterial biofilm



S. aureus **biofilm on a catheter**





E. coli **biofilm**

Biofilm development

1. Initial attachment
2. Irreversible attachment
3. Maturation I
4. Maturation II
5. **Dispersion**

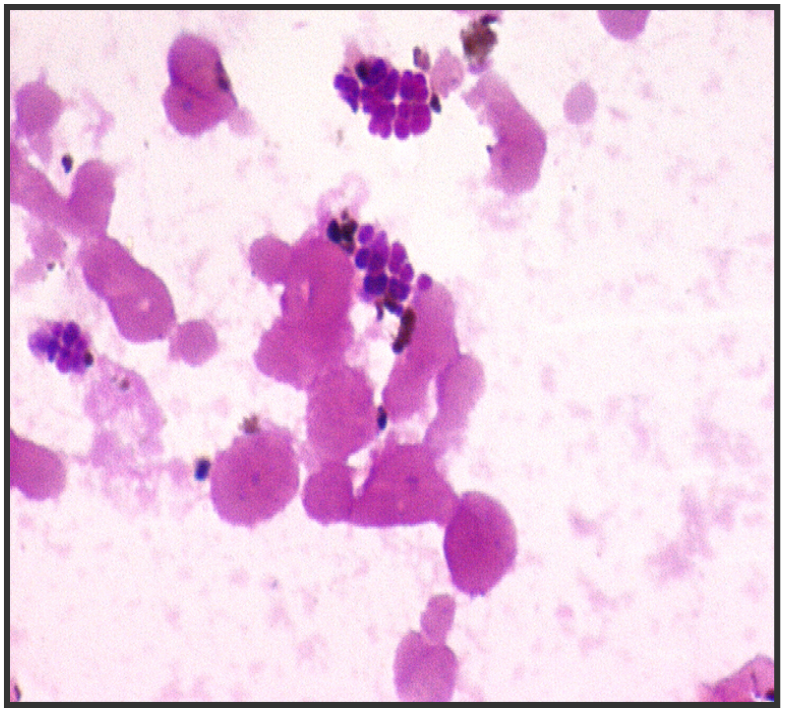
https://en.wikipedia.org/wiki/Biofilm

Nosocomial BSI (CDC, USA)
Etiology: trends 1975–1989

1975	%	1983	%	1986–1989	%
▶ *S. aureus*	14.3	▶ CN staph.	14.2	▶ CN staph.	27.7
E. coli	14.1	▶ *S. aureus*	12.9	▶ *S. aureus*	16.3
Klebsiella spp.	9.1	*Klebsiella* spp.	9.1	▶ **Enterococci**	**8.5**
▶ CN staph.	6.5	▶ **Enterococci**	**7.3**	▶ *Candida* spp.	7.8
Bacteroides spp.	6.3	*Enterobacter* spp	6.9	*E. coli*	6.0
▶ **Enterococci**	**6.0**	*P. aeruginosa*	6.1	*Enterobacter* spp.	5.0
Enterobacter spp.	5.7	▶ *Candida* spp.	5.6	*Proteus mirabilis*	5.0
P. aeruginosa	4.5	*Bacteroides* spp.	3.4	*Klebsiella* spp.	4.5
Proteus spp.	3.9	*Serratia* spp.	2.8	*P. aeruginosa*	4.4
Serratia spp.	3.8	Streptococci	2.8	Streptococci	3.8

Catheter-related infections
high risk pathogens

Staphylococcus aureus

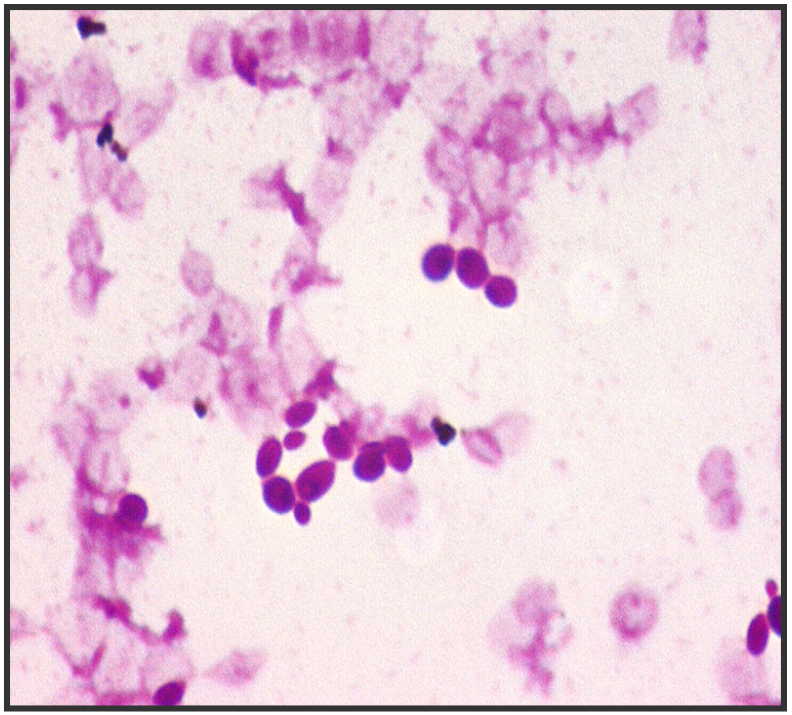


- **High virulence**
- **Frequently (severe) sepsis**
- **Risk of metastatic and recurrent infections**
- **Risk of complications** (septic vasculitis, endocarditis**)**
- **Risk of endovascular implant infections** (hematogenous spread)
- **Catheter extraction necessary**
- **Antibiotic therapy essential** (10–14 days)

Catheter-related infections
high risk pathogens

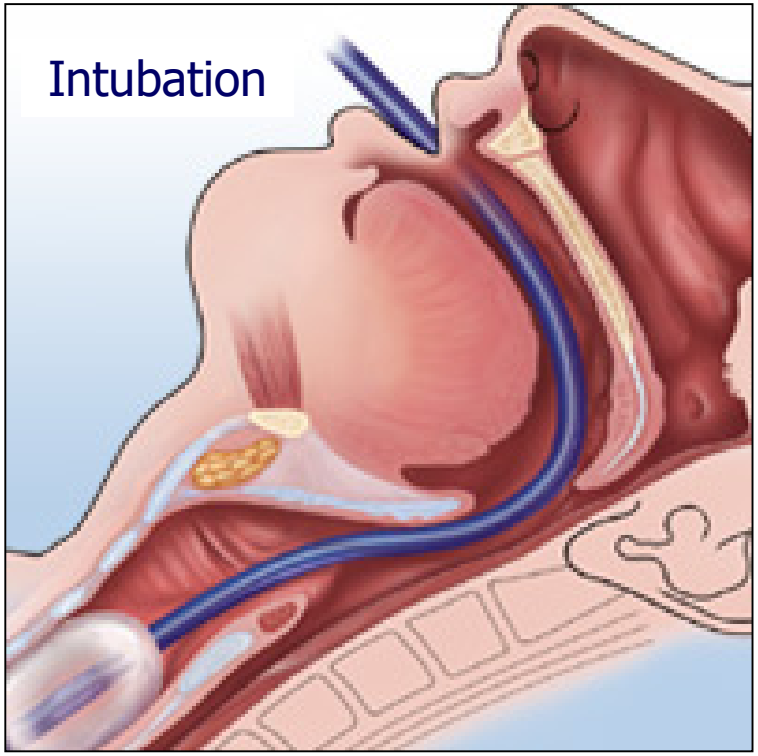
Candida spp.

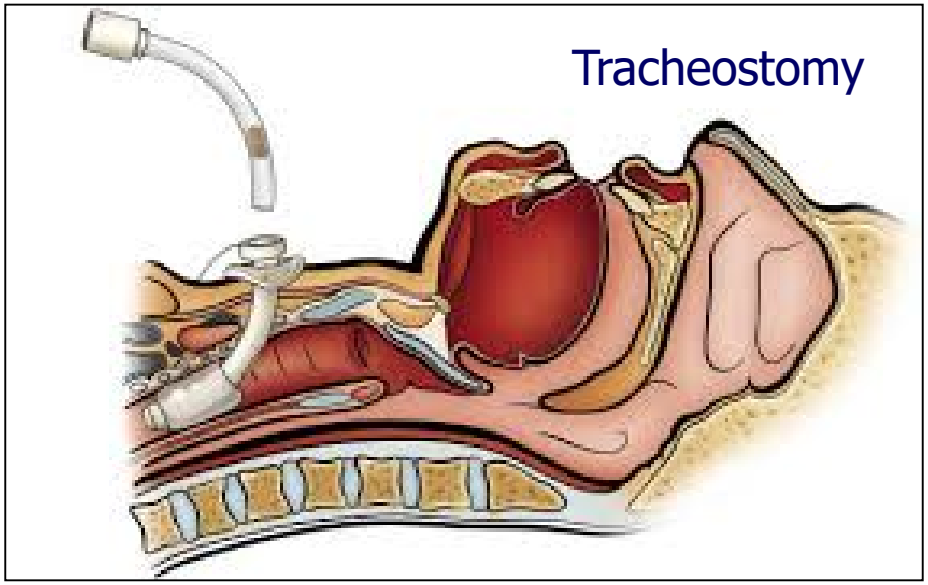
- **High ability to cause severe infection with poor prognosis**
- **Risk of metastatic and recurrent infections**
- **Risk of complications** (endophthalmitis)
- **Risk of endovascular implant infections** (hematogenous spread)
- **Catheter extraction necessary**
- **Antimycotic therapy essential** (14 days)



Nosocomial pneumonia

- **Intubation-associated pneumonia**
- **Ventilator-associated pneumonia (VAP)**





Ventilator-associated pneumonia
classification and etiology

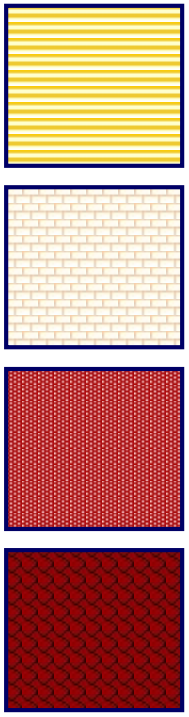
VAP early onset × VAP late onset

- **VAP early onset** (day 3–5 of hospitalization; good ATB susceptibility)
  - *Staphylococcus aureus*
  - *Streptococcus pneumoniae*
  - *Haemophilus influenzae*
  - Enterobacteria (*Escherichia coli*, *Klebsiella pneumoniae*)

- **VAP late onset** (≥ day 6, MDR, worse prognosis; contamination via e.g. suction of aspirate, intestinal source via a nasogastric tube).
  - *Pseudomonas aeruginosa* (incl. MDR)
  - *Staphylococcus aureus* (risk of MRSA)
  - Enterobacteria (incl. MDR)
  - *Acinetobacter* (incl. MDR)

- **Rare/unusual agents**
  - *Candida* spp. (except immunocompromised individuals)
  - Enterococci

Surgical site infections
classification



Skin

Subcutaneous

Fascia, muscles

Organs, body spaces

Superficial incisional infection

Deep incisional infection

Organ-space infections

Surgical site infections
etiology

Surgical discipline	*S. aureus*	CN staph.	Streptococci	G- rods	Anaerobes
Cardiothoracic surgery	XX	XX			
Vascular surgery	XX	XX			
Neurosurgery	XX	XX	X		X
Orthopaedics	XX	XX		X	
Thoracic surgery	XX	XX	X	X	X
Head and neck surgery	XX		XX		XX
Abdominal surgery			X	XX	XX
Gynaecology			XX	XX	XX
Urology			XX	XX	

Lecture outline - part 3

- **Multidrug-resistant HAI bacterial pathogens**
  - **Hospital ecosystem *versus* bacteria**
  - **High-priority (ESKAPE) pathogens**
  - ***Acinetobacter baumannii* - a HAI pathogen prototype**
    - **Resistance to antibiotics**
    - **Epidemiology**
    - **Surveillance in Europe**
    - **Evolution of MDR/XDR *A. baumannii* populations in Czechia**
    - **Hospital outbreak caused by MDR/XDR strains**

Hospital ecosystem × HAI pathogens

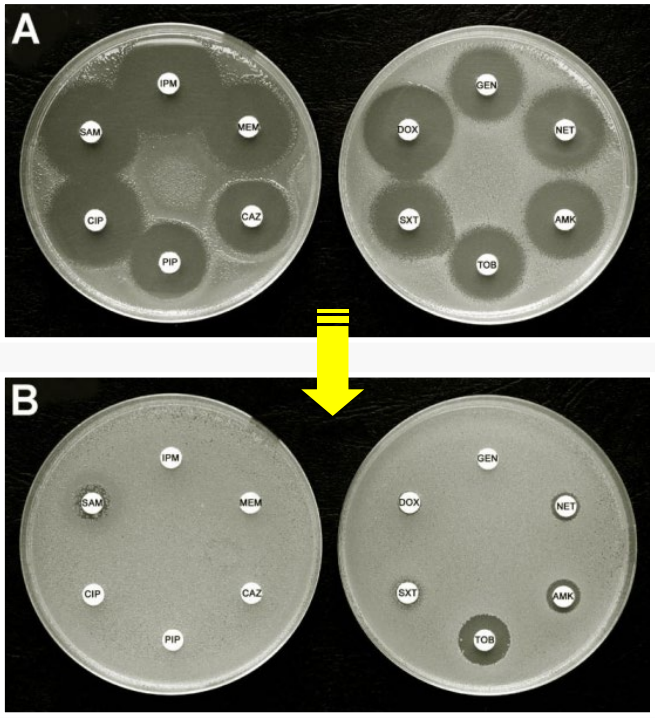
- Extensive use of disinfection, biocides and antibiotics
- Patients with severe underlying diseases and impaired defensiveness/ immunity
- Invasive therapeutic and diagnostic procedures
- High-risk departments
  - intensive care
  - neonatal
  - burn
- Ubiquitous organisms capable of surviving in hostile external environments
- Primarily resistant to many biocides and antibiotics
- Further development of resistance
- Low pathogenicity

Multidrug-resistant HAI agents - ESKAPE

Clinical Infectious Diseases 2009; 48:1–12

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

Helen W. Boucher,[1] George H. Talbot,[2] John S. Bradley,[3,4] John [illegible]wards, Jr,[5,6,7] David Gilbert,[8] Louis B. Rice,[9,10] Michael Scheld,[11] Brad Spellberg,[5,6,7] and John Bartlett[12]



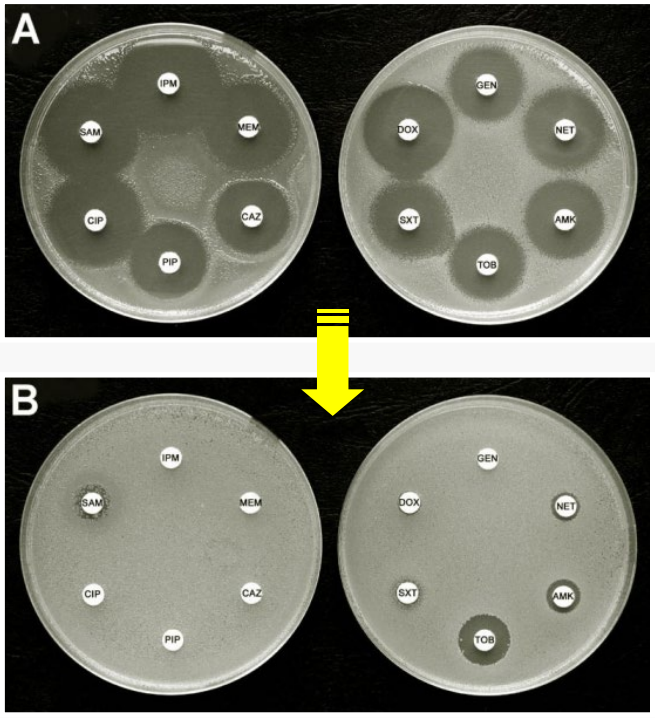
Pathogens that cause the majority of US hospital infections and effectively "escape" the effects of antibacterial drugs

Multidrug-resistant HAI agents - ESKAPE

Clinical Infectious Diseases 2009; 48:1–12

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

Helen W. Boucher,[1] George H. Talbot,[2] John S. Bradley,[3,4] John [illegible]wards, Jr,[5,6,7] David Gilbert,[8] Louis B. Rice,[9,10] Michael Scheld,[11] Brad Spellberg,[5,6,7] and John Bartlett[12]



Enterococcus faecium
Staphylococcus aureus
Klebsiella pneumoniae
Acinetobacter baumannii
Pseudomonas aeruginosa
***Enterobacter* spp.**

WHO 2017 Priority Pathogens List

World Health Organization

WHO PRIORITY PATHOGENS LIST FOR R&D OF NEW ANTIBIOTICS

Priority 1: CRITICAL#

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

Enterobacteriaceae*, carbapenem-resistant, 3rd 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, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

Streptococcus pneumoniae, penicillin-non-susceptible

Haemophilus influenzae, ampicillin-resistant

Shigella *spp.*, fluoroquinolone-resistant

WHO 2017 Priority Pathogens List

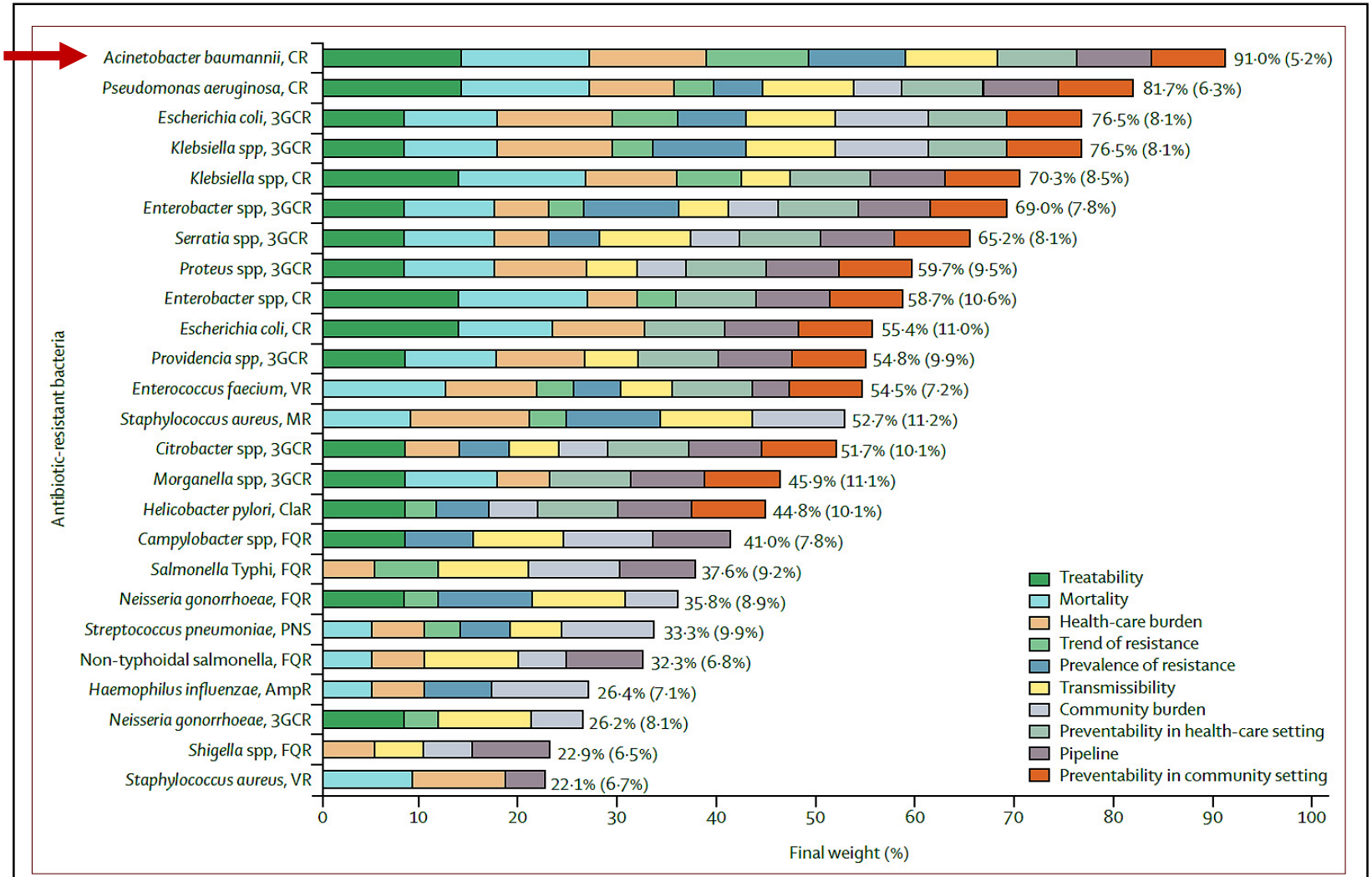


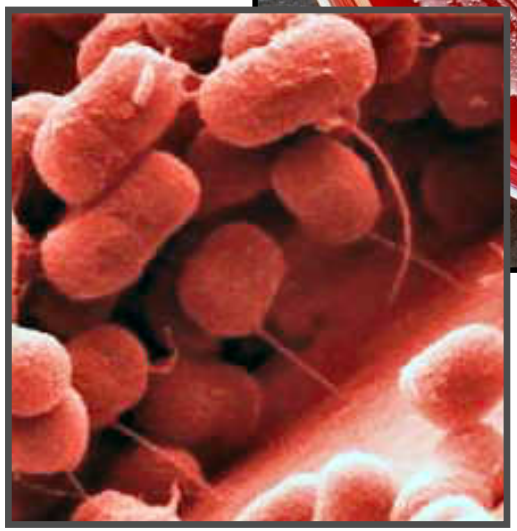
***Figure 2*: Final ranking of antibiotic-resistant bacteria**

Mean (SD) pathogen weights were derived by the software from the survey participants' preferences. The segments represent the contribution of each criterion to each pathogen's final weight. CR=carbapenem resistant. 3GCR=third-generation cephalosporin resistant. VR=vancomycin resistant. MR=meticillin resistant. ClaR=clarithromycin resistant. FQR=fluoroquinolone resistant. PNS=penicillin non-susceptible. AmpR=ampicillin resistant.

Tacconelli et al. Lancet Infect Dis 2018

Acinetobacter baumannii

- **Nonmotile** (no flagella)
- **Strictly aerobic** (capable of neither fermentative nor anaerobic respiration)
- **Low pathogenicity** (rare infections in community)
- **Colonization** more common than infection
- **Primary resistance** to desiccation and other physical/chemical factors
- **Acquired resistance** to antibiotics
- **HAIs** in critically ill patients
- **Epidemic spread** in/between hospitals
- **Prototype of an HAI pathogen**



Resistance to antibiotics

Multidrug-, extensively drug- & pandrug-resistant bacteria (MDR, XDR & PDR

- **Magiorakos *et al*. 2012.** Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. ***Clin Microbiol Infect* 18(3): 268-81.**
- **Standardized international terminology to categorize acquired resistance profiles in *S. aureus*, *Enterococcus* spp., Enterobacteriaceae, *P. aeruginosa* and *Acinetobacter* spp., all often responsible for HAIs and prone to developing multidrug resistance.**

Multidrug-, extensively drug- & pandrug-resistant bacteria (MDR, XDR & PDR)

***Acinetobacter*:**

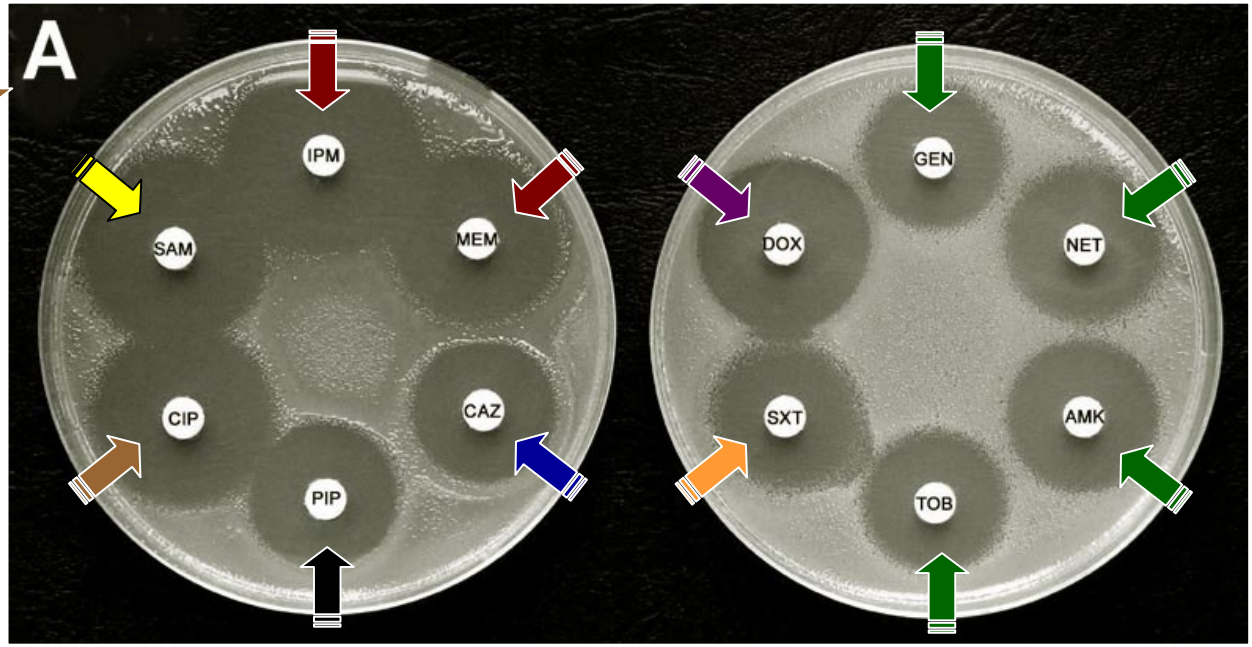
- **Magiorakos *et al*. 2012.** Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. ***Clin Microbiol Infect* 18(3): 268-81.**
- **Standardized international terminology to categorize acquired resistance profiles in *S. aureus*, *Enterococcus* spp., Enterobacteriaceae, *P. aeruginosa* and *Acinetobacter* spp., all often responsible for HAIs and prone to developing multidrug resistance.**

Antimicrobial category	Antimicrobial agent
Aminoglycosides	Gentamicin
	Tobramycin
	Amikacin
	Netilmicin
Antipseudomonal carbapenems	Imipenem
	Meropenem
	Doripenem
Antipseudomonal fluoroquinolones	Ciprofloxacin
	Levofloxacin
Antipseudomonal penicillins + β-lactamase inhibitors	Piperacillin-tazobactam
	Ticarcillin-clavulanic acid
Extended-spectrum cephalosporins	Cefotaxime
	Ceftriaxone
	Ceftazidime
	Cefepime
Folate pathway inhibitors	Trimethoprim-sulphamethoxazole
Penicillins + β-lactamase inhibitors	Ampicillin-sulbactam
Polymyxins	Colistin
	Polymyxin B
Tetracyclines	Tetracycline
	Doxycycline
	Minocycline

Criteria for defining MDR, XDR and PDR in *Acinetobacter* spp.
MDR: non-susceptible to ≥1 agent in ≥3 antimicrobial categories.
XDR: non-susceptible to ≥1 agent in all but ≤2 categories.
PDR: non-susceptible to all antimicrobial agents listed.

Antibiotics against *A. baumannii*

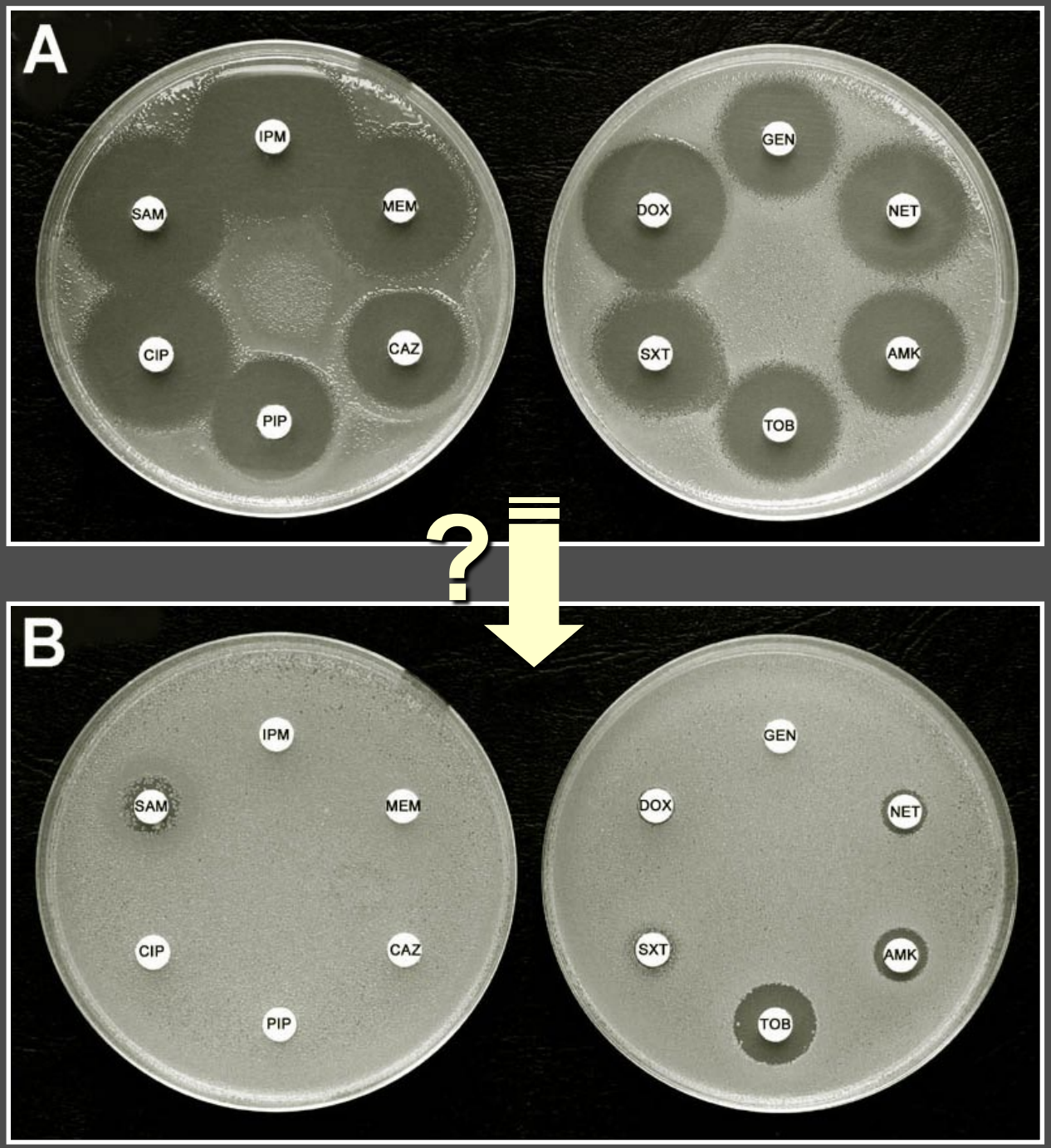
- **Antipseudomonal penicillins** (piperacillin)
- **Antipseudomonal cephalosporins** (ceftazidime)
- **Carbapenems**
- **Sulbactam**
- **Aminoglycosides**
- **Fluoroquinolones**
- **Co-trimoxazole**
- **Doxycycline**
- **Colistin**



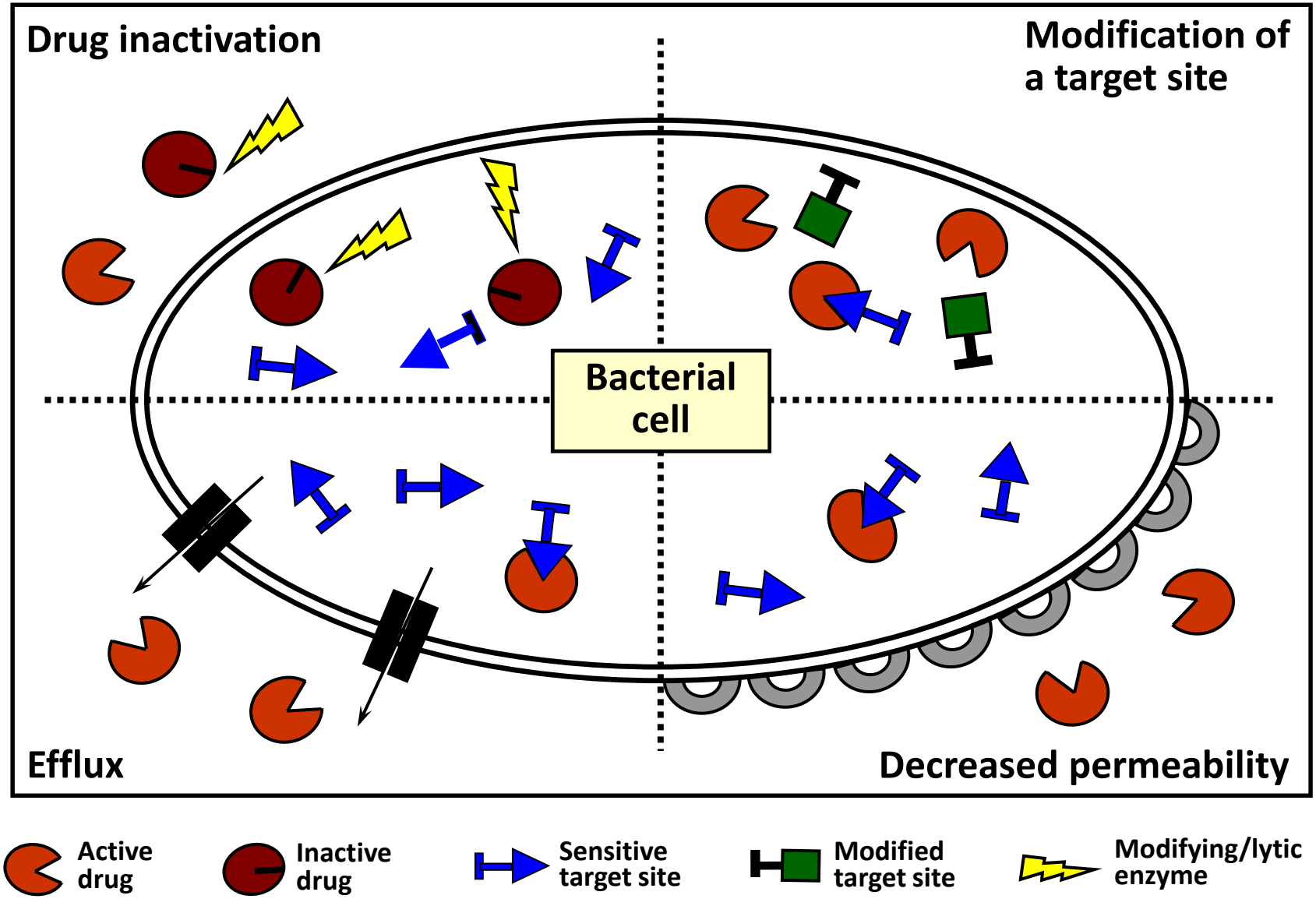
Disk diffusion test

Fully susceptible *A. baumannii*

Multidrug-resistant *A. baumannii*



Bacterial resistance mechanisms



Acquired antibiotic resistance

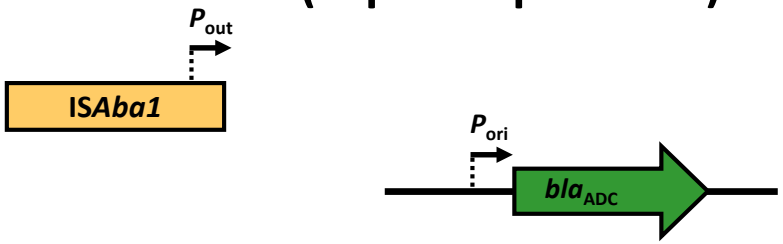
- **Intrinsic origin - genetic changes of already present systems**
  - **Regulatory genes > upregulation (activity)**
  - **Structural genes > decreased affinity to a target**

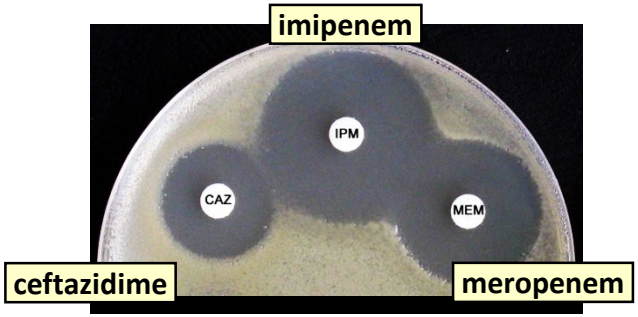
- **Acquisition of resistance genes via horizontal gene transfer (HGT)**
  - **Conjugation**
  - **Transformation**
  - **Transduction**

Overexpression of intrinsic β-lactamases

ADC

(cephalosporinase)

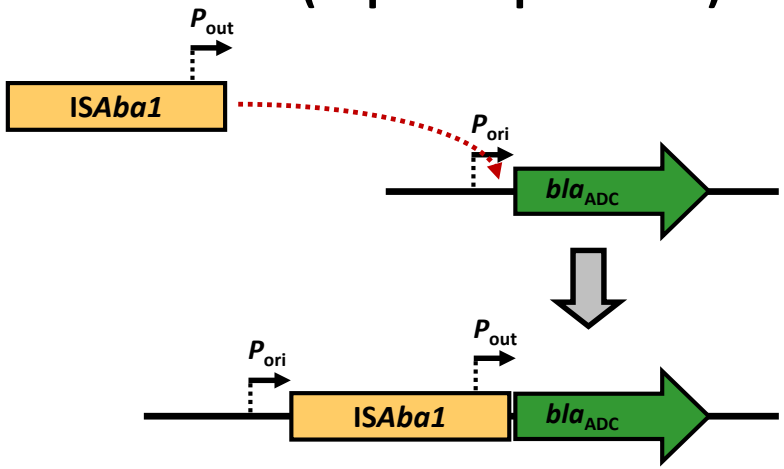


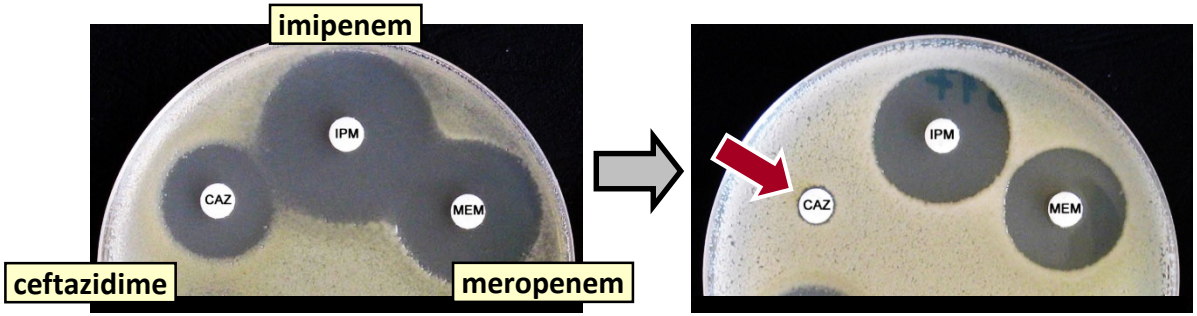


Overexpression of intrinsic β-lactamases

ADC

(cephalosporinase)

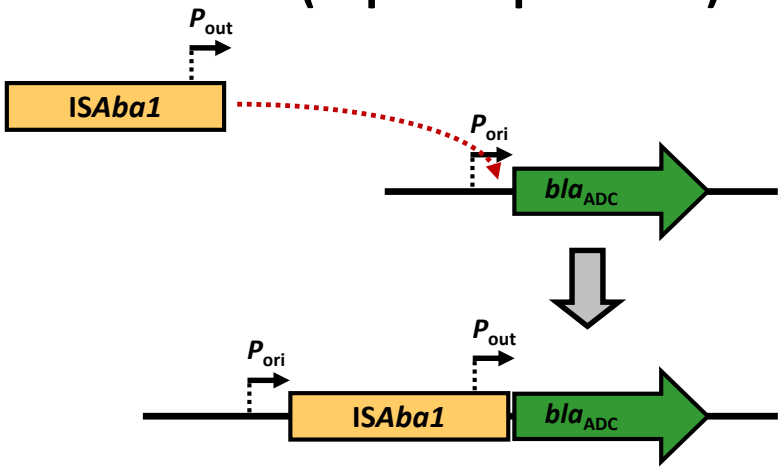




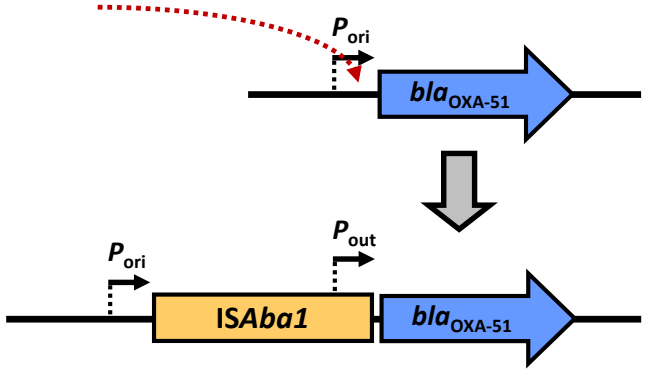
Resistance to third-generation cephalosporins

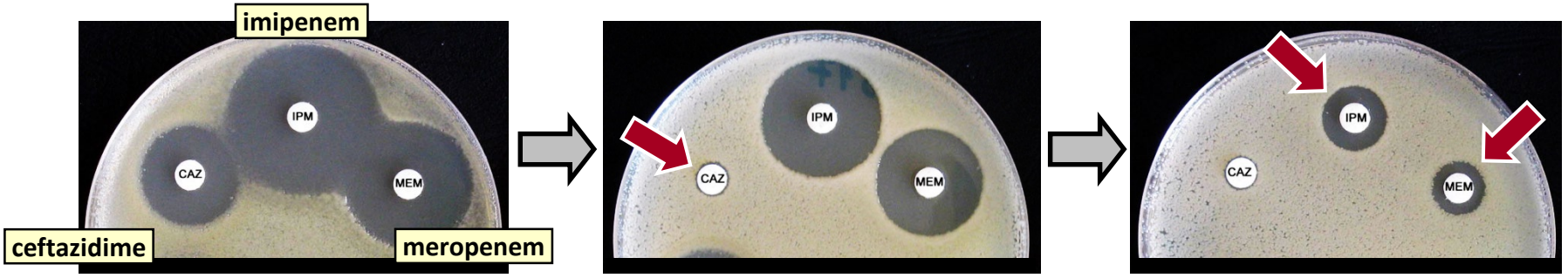
Overexpression of intrinsic β-lactamases

ADC
(cephalosporinase)



OXA-51
(carbapenemase)



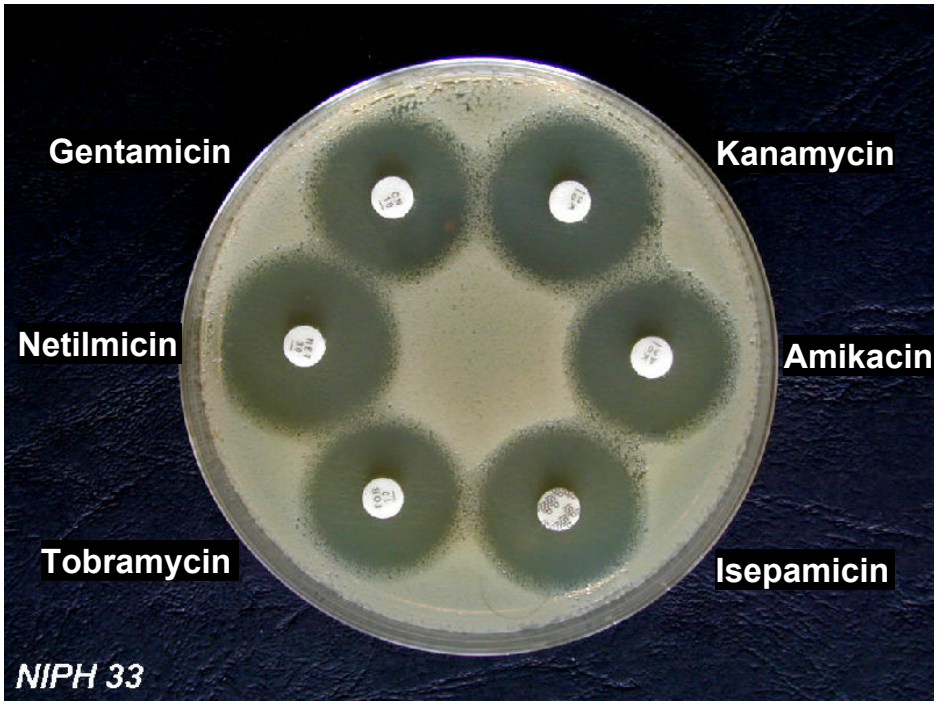


Resistance to
third-generation cephalosporins

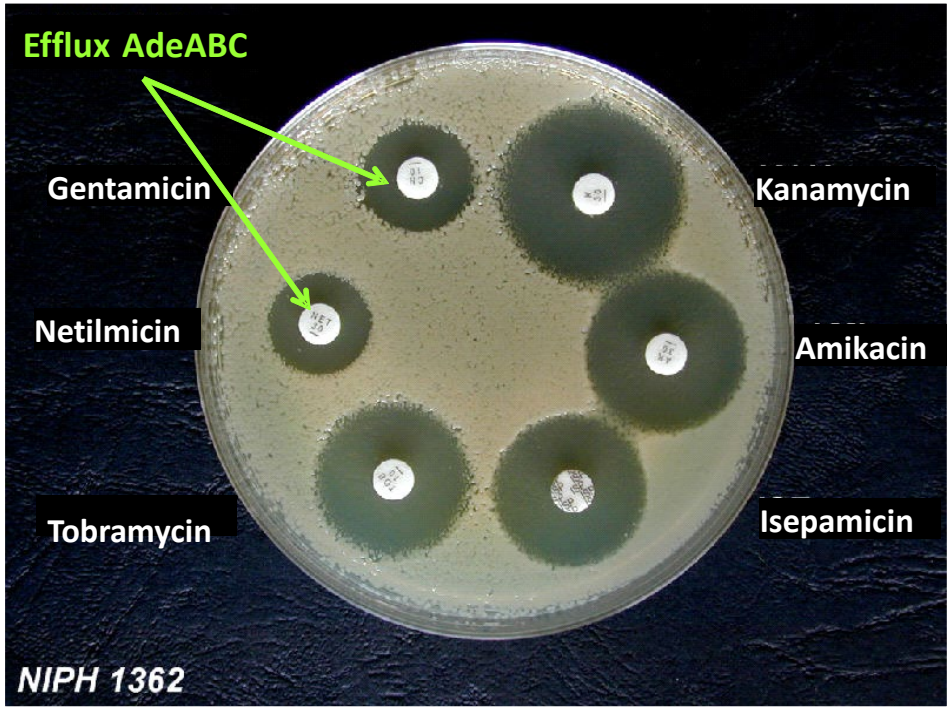
Resistance to
carbapenems

Successive acquisition of genes via HGT: resistance to aminoglycosides

1. Wild-type susceptible

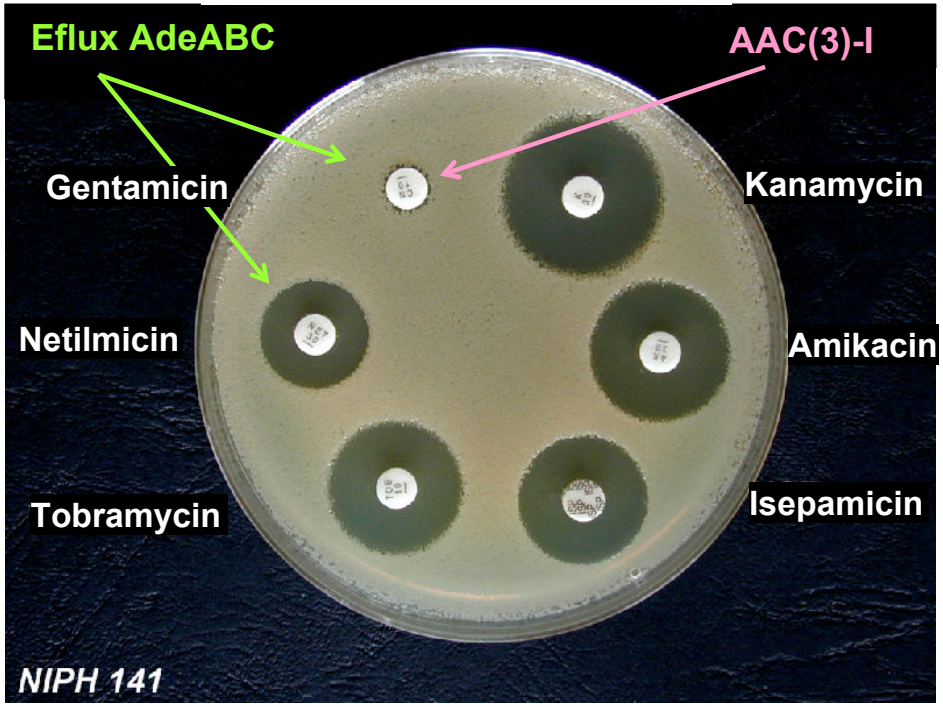


2. Overexpression of the AdeABC efflux

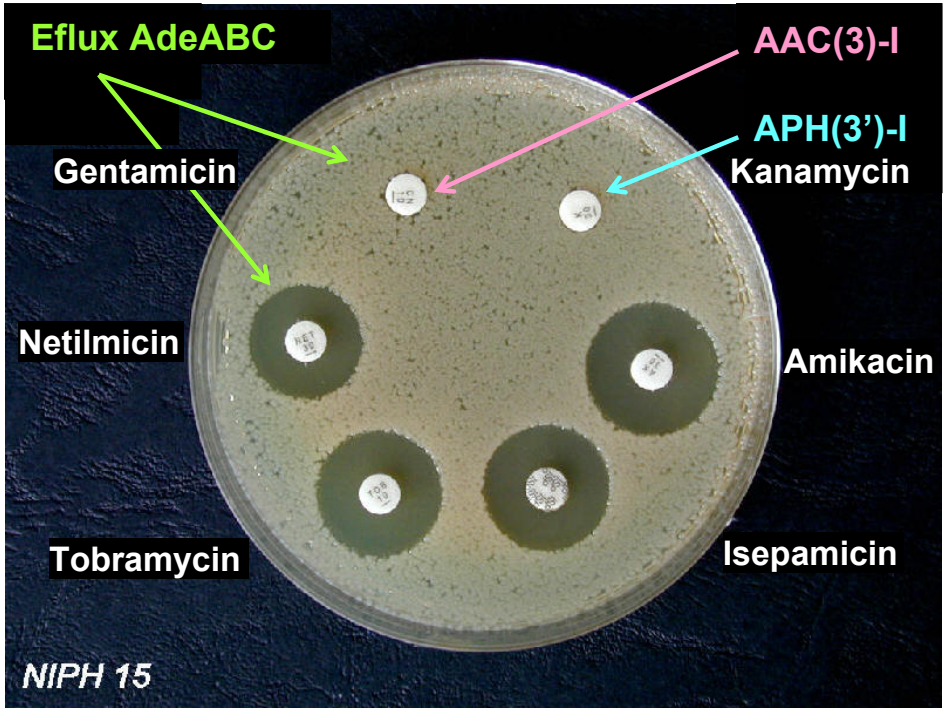


Successive acquisition of genes via HGT: resistance to aminoglycosides

3. Gentamicin resistance:
gene for acetyltransferase AAC(3)-I

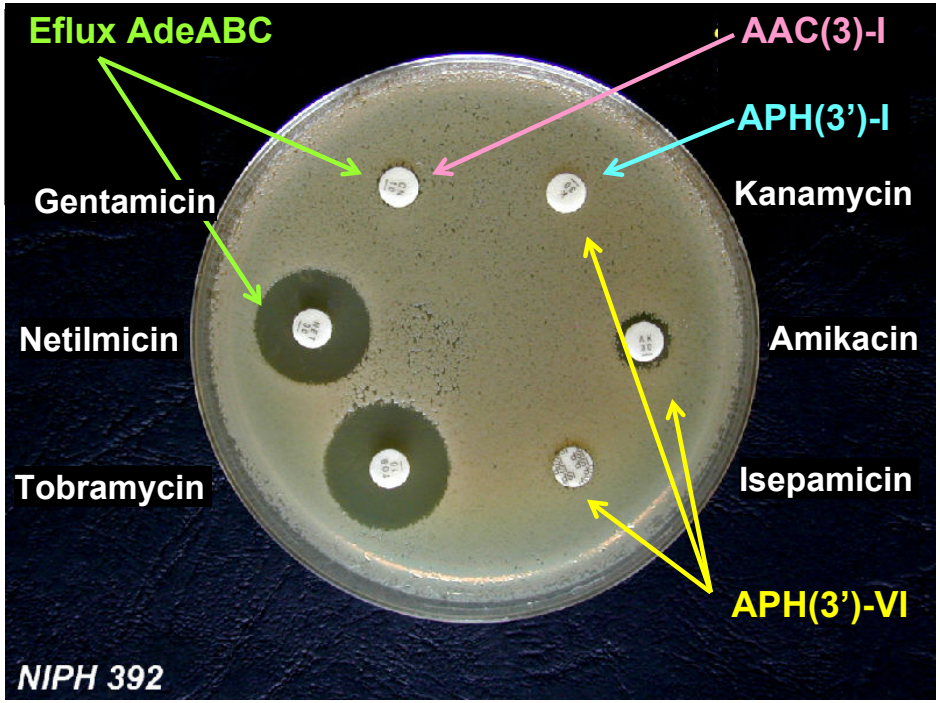


4. Kanamycin resistance:
gene for phosphotransferase APH(3')-I

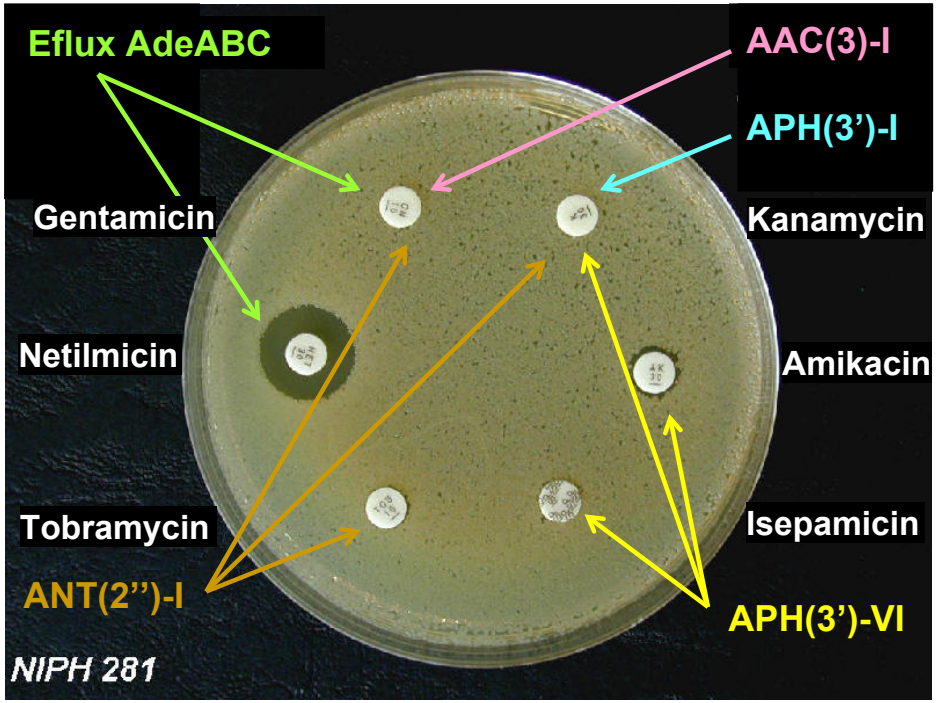


Successive acquisition of genes via HGT: resistance to aminoglycosides

5. Amikacin/isepamicin resistance:
gene for phosphotransferase APH(3')-VI

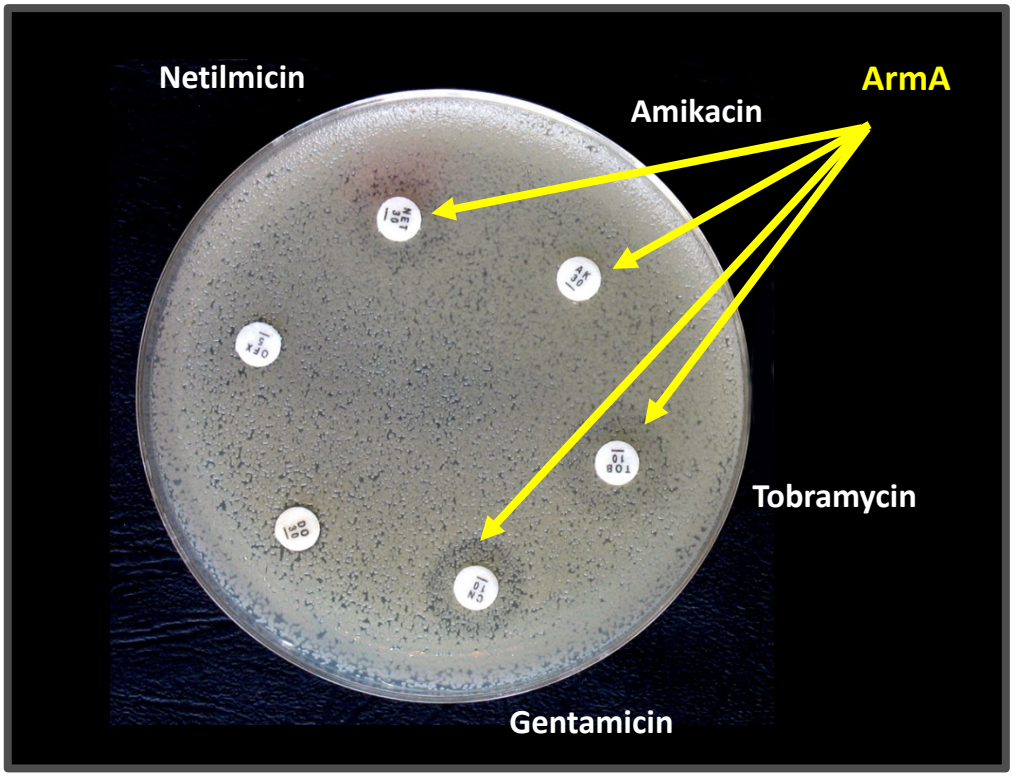


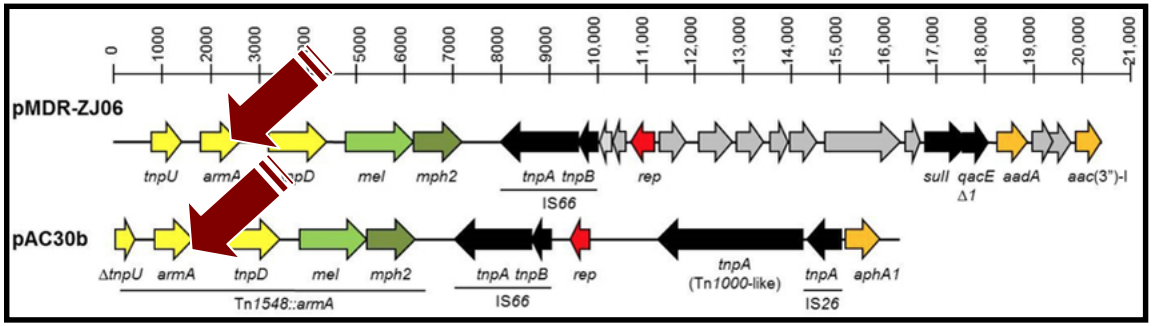
6. Tobramycin resistance:
gene for nucleotidyltransferase ANT(2'')-I



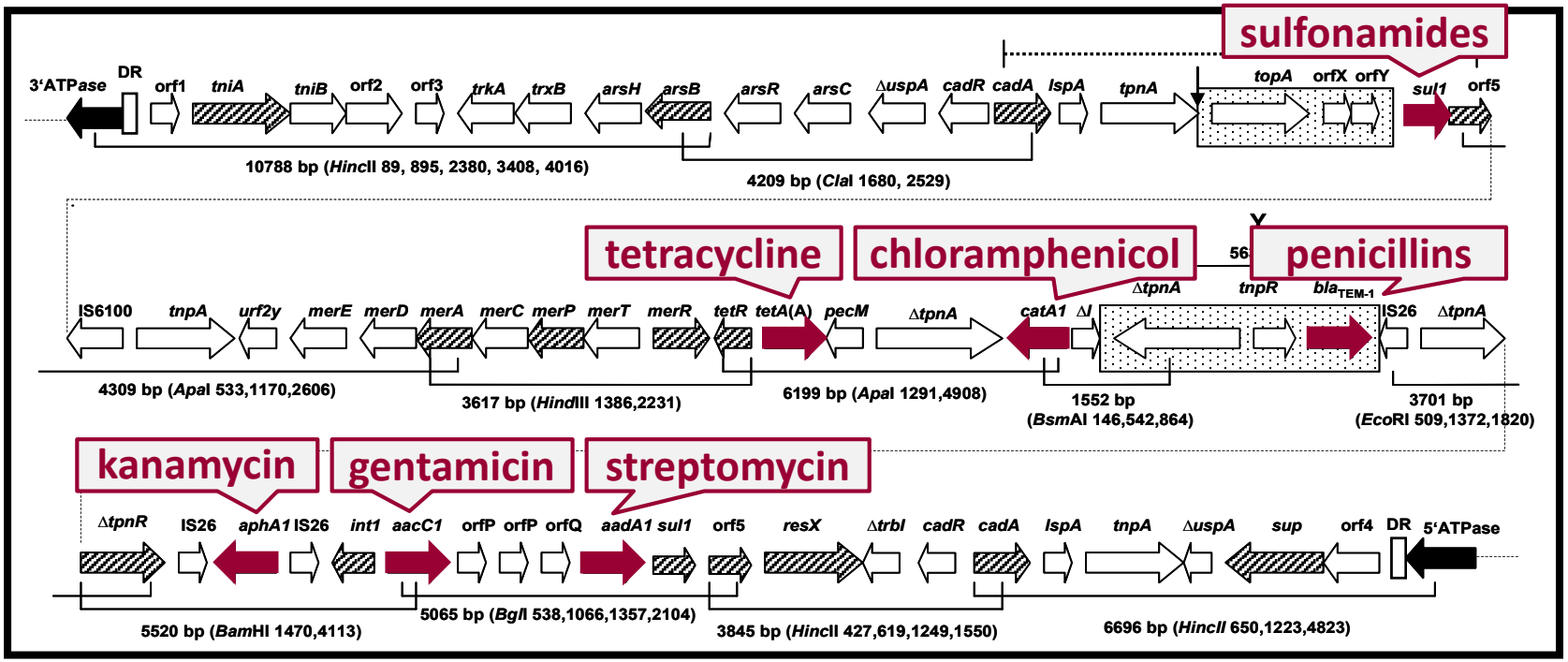
One-step acquisition of pandrug resistance to aminoglycosides via HGT

- **ArmA** (16S rRNA m^7G-methyltransferase) - **posttranscriptional methylation of rRNA** (modification of a target site)
- **Resistance to kanamycin, amikacin, gentamicin, netilmicin and tobramycin**
- **Carried by transposon Tn*1548***





Resistance genomic island



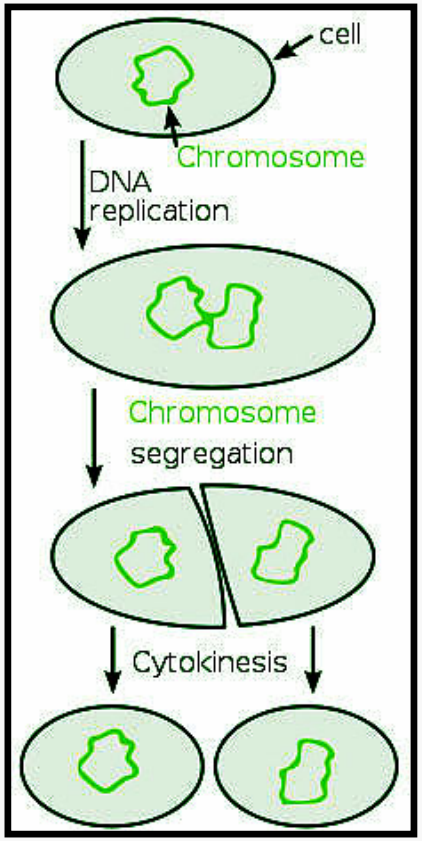
Krizova & Nemec JAC 2010; 65: 1915

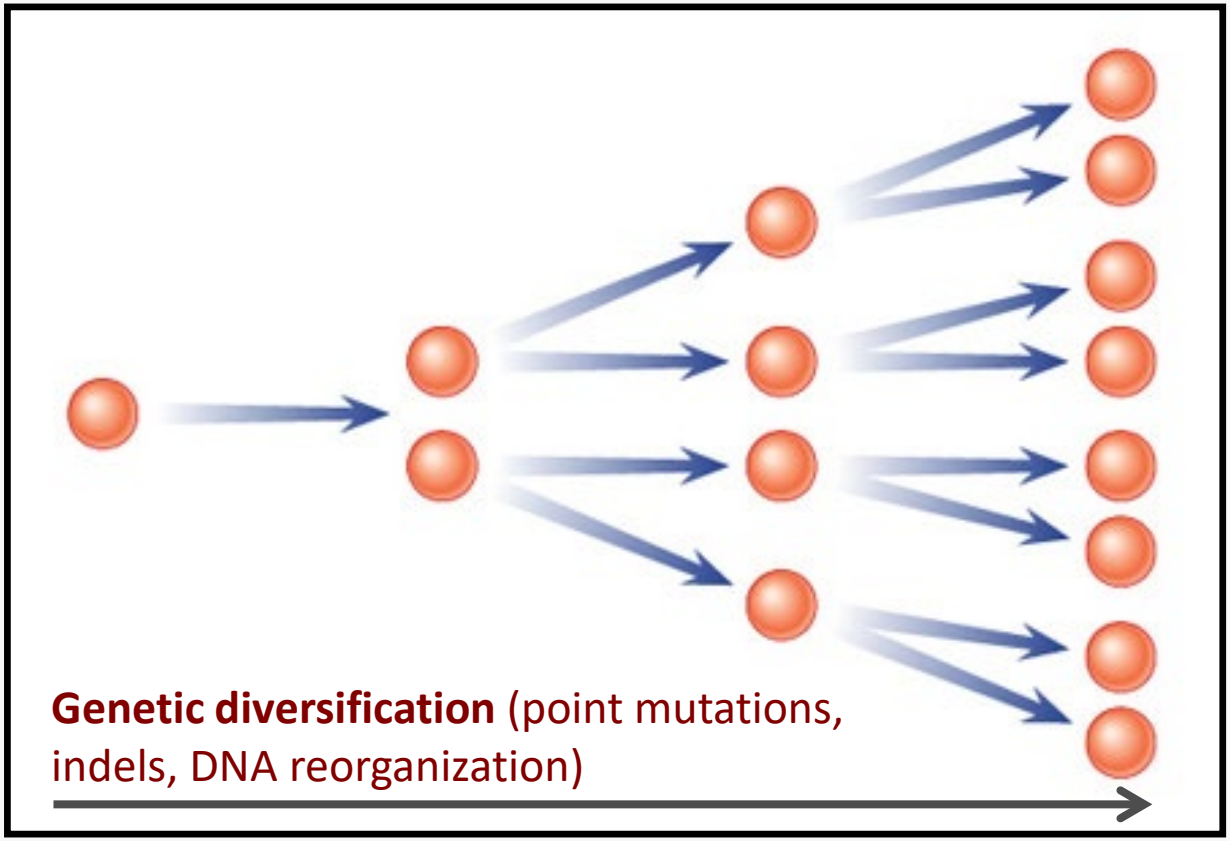
- **Resistance genomic island AbaR3** (63 kb) present in isolates of epidemic clone IC1 predominating in Europe in 1980s–1990s
- An AbaR3 variant, **AbaR1** (86 kb), is the largest resistance island found in bacteria
- Resistance to antibiotics widely used in 1970s–1980s

Epidemiology

Bacteria are haploid & clonal

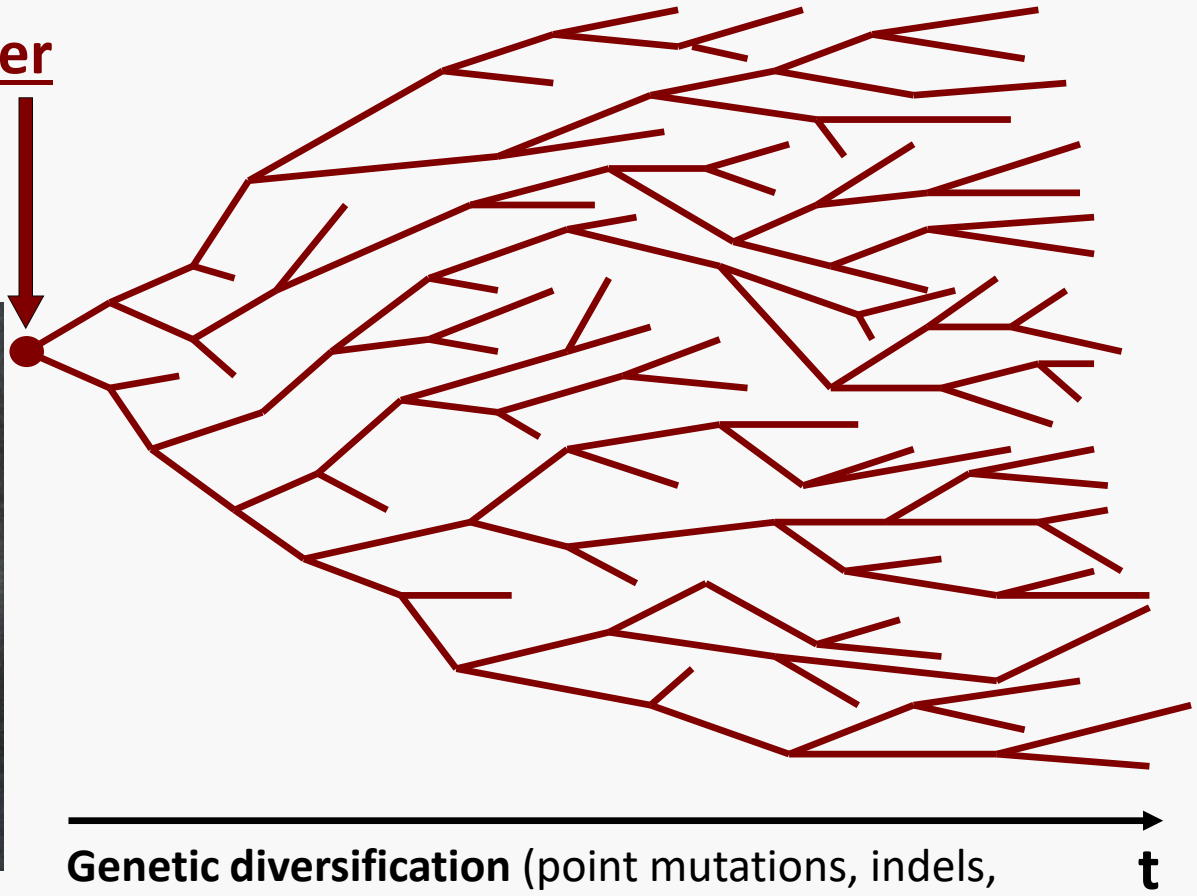
- Bacteria are haploid and reproduce asexually by binary fission
- "Clonal propagation": multiplication of genetically "identical" organisms by asexual reproduction





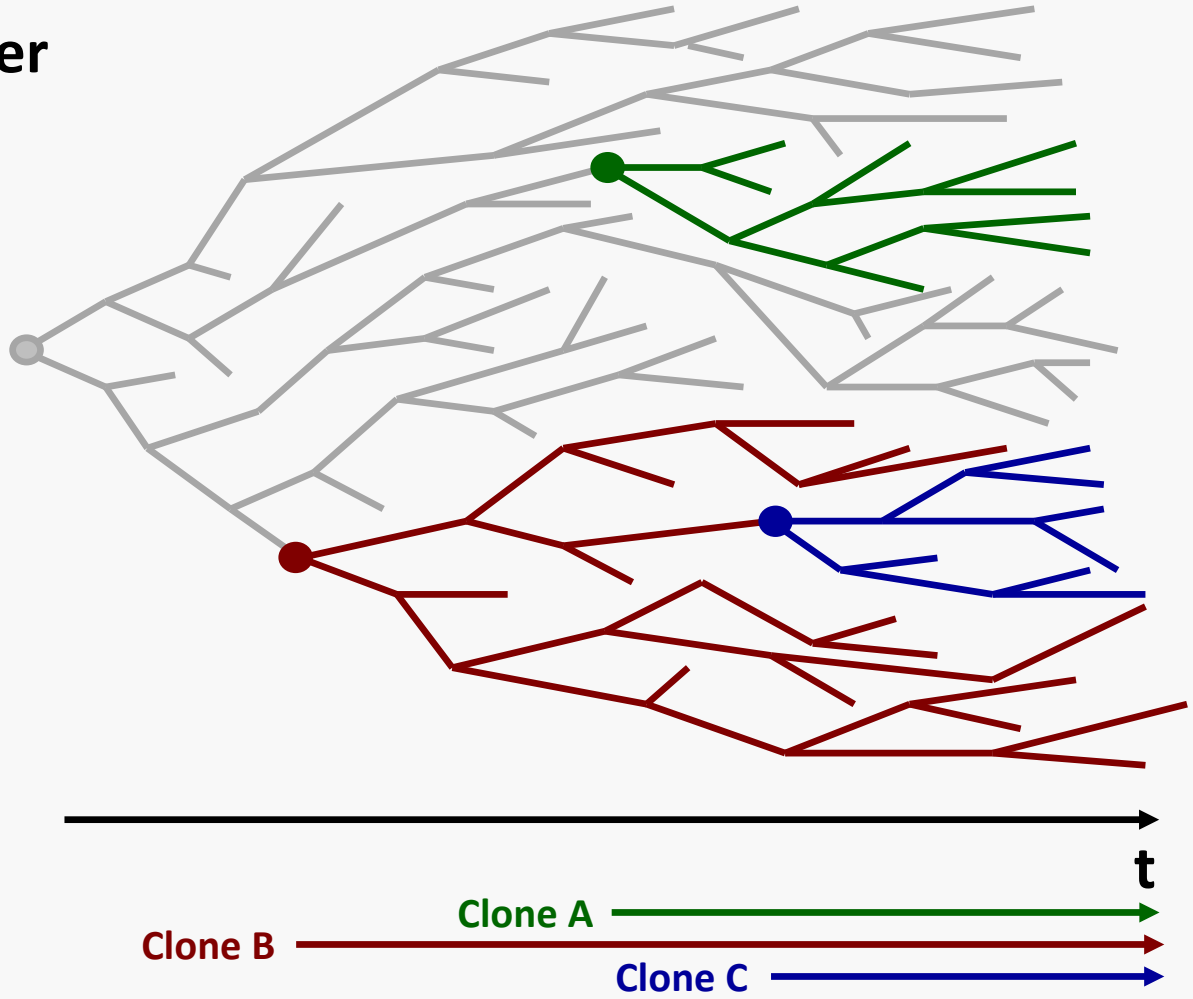
Clone in bacteria

- **A relative category depending on time scale/number of bacterial generations**
- **Defined by a founder**



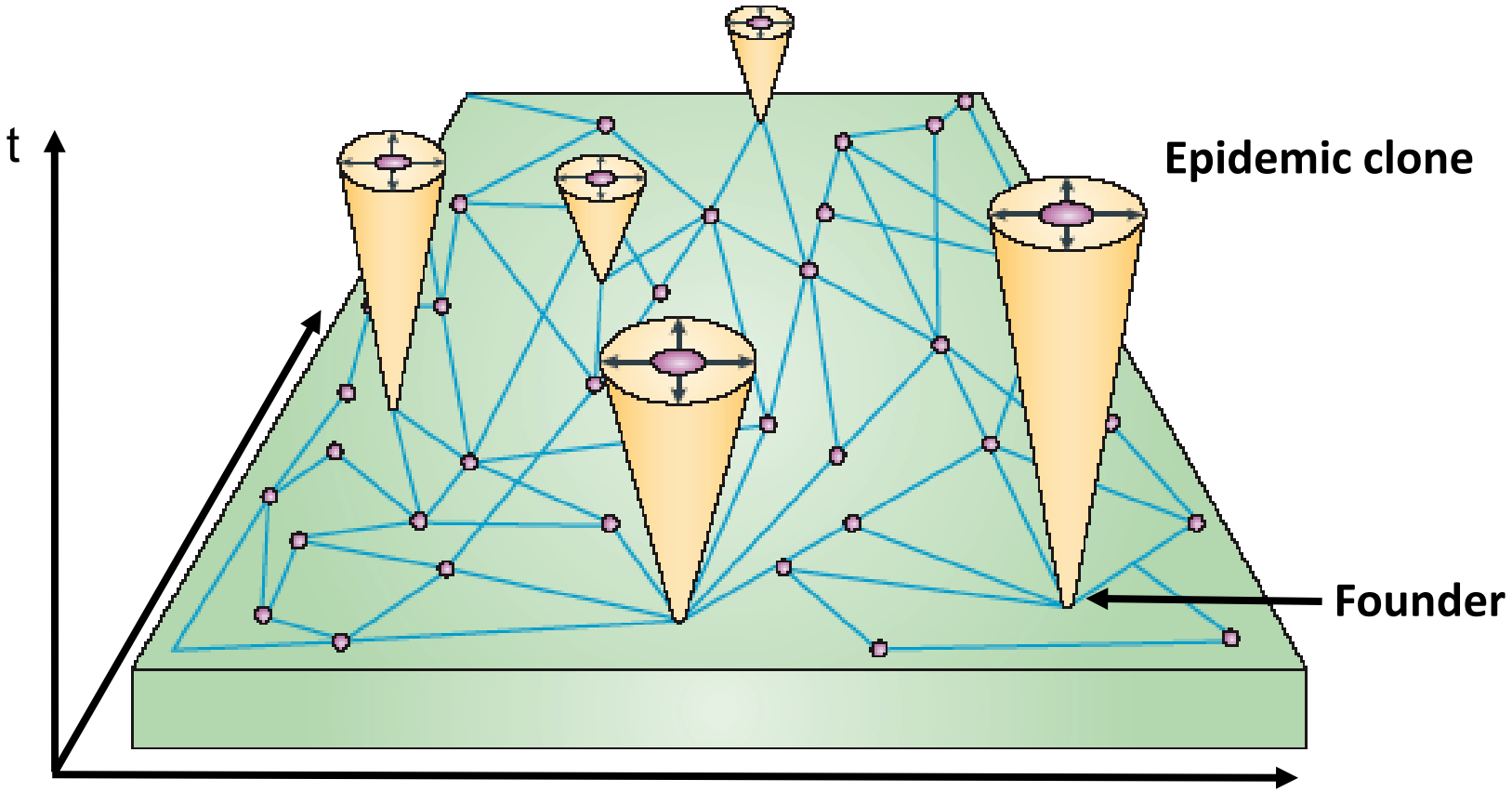
Clone in bacteria

- A relative category which depends on time scale/number of bacterial generations
- Defined by a founder



Epidemic clone

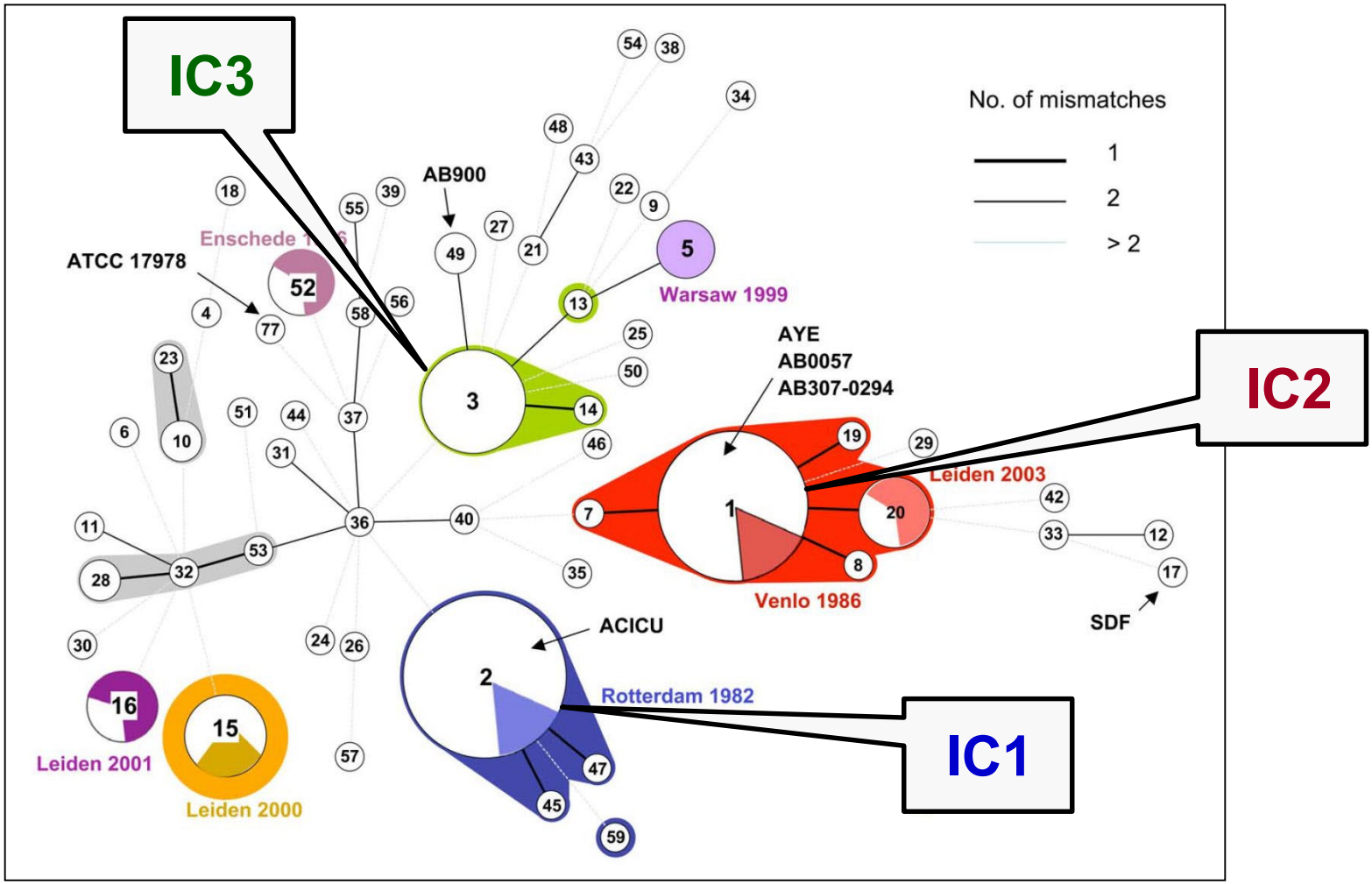
- **A group of organisms having the same ancestor, which is in terms of epidemic spread more successful compared with other lineages(strains) of a given species**



Maynard Smith et al. Bioassays 2000; 22: 1115

International clones (IC) of *A. baumannii*

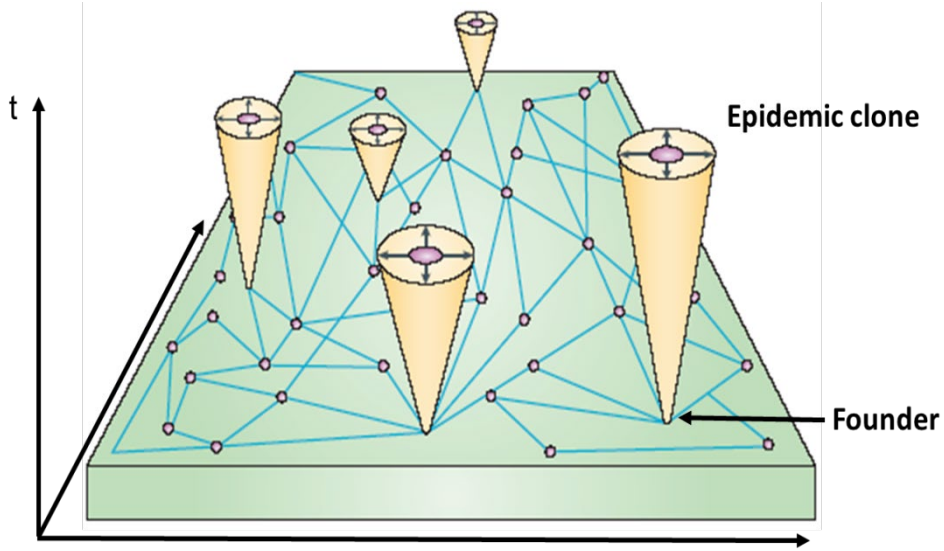
The population structure of *Acinetobacter baumannii*: expanding MDR clones from an ancestral susceptible genetic pool (Diancourt *et al*. 2010).



Diancourt et al. PLoS One 2010

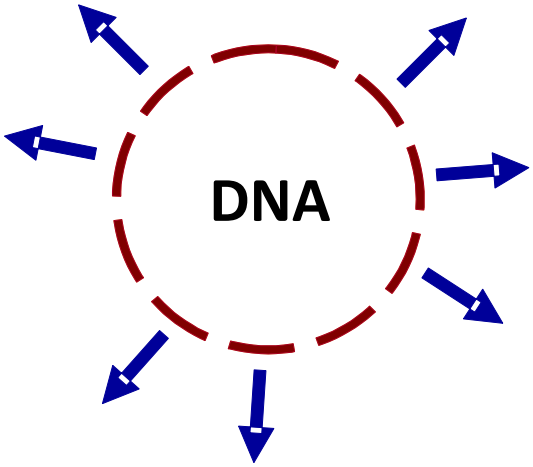
Assessment of clonality

- **Analysis of core genome**
  Multilocus sequence typing (MLST)
  Whole (core) genome sequencing (cgMLST)
- **Genomic DNA fingerprinting**
  Macrorestriction analysis (Pulsed-field gel electrophoresis, PFGE)
  AFLP fingerprinting
- **Analysis of accessory genes** (mobile genetic elements)
  PCR mapping and sequencing



Multilocus sequence typing (MLST)

7 housekeeping genes → PCR → Sequencing



Comparison of sequences with a MLST database

Assignation of allelic codes

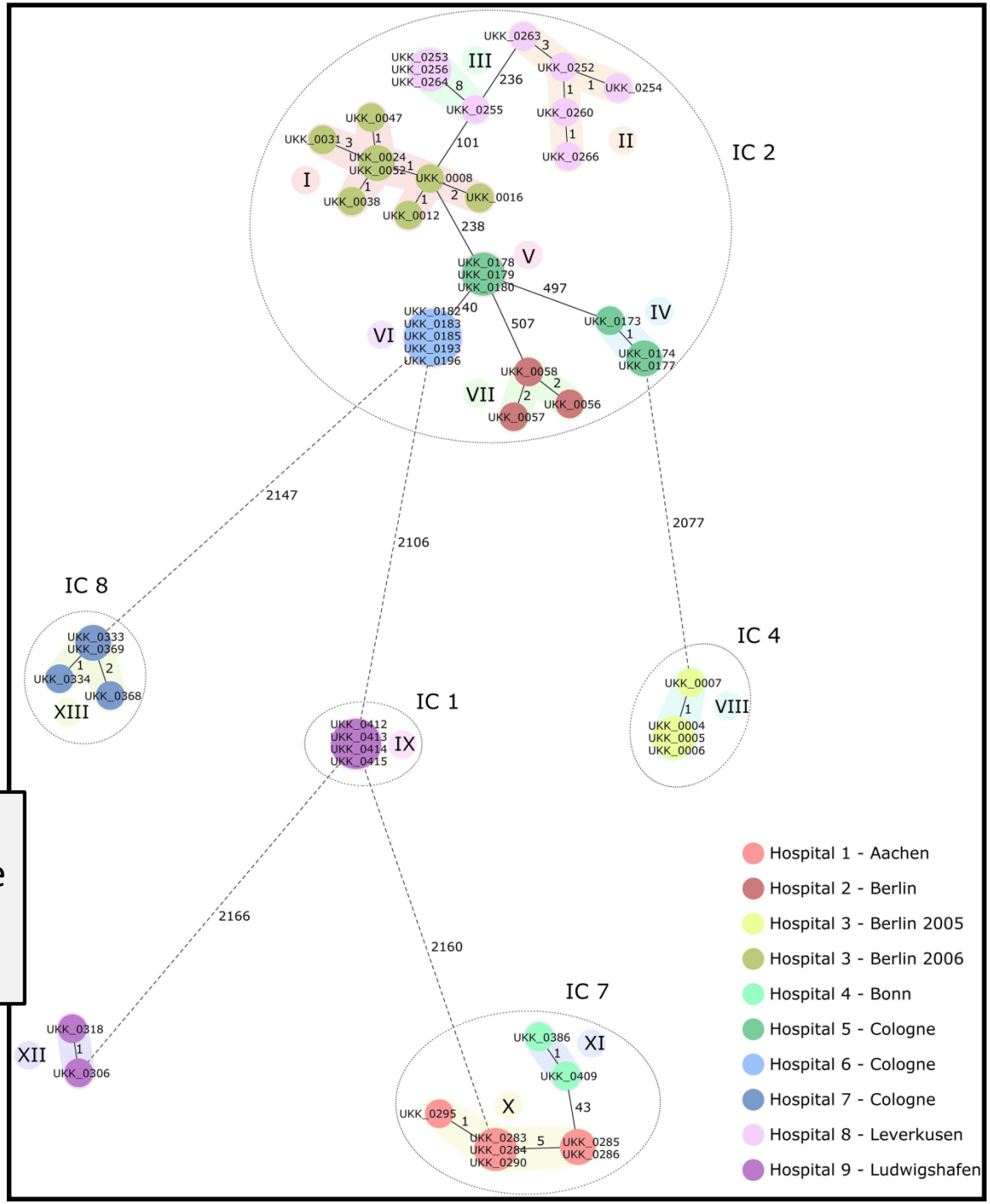
Determination of MLST genotype (sequence type - ST)

ST	*acsA*	*aroE*	*guaA*	*mutL*	*nuoD*	*ppsA*	*trpE*
235	38	11	3	13	1	2	4
175	28	22	5	3	3	14	19
132	6	20	1	3	4	4	2
244	17	5	12	3	14	4	7
357	2	4	5	3	1	6	11

Core genome (cg) MLST

- **Next generation sequencing**
- **1,000–3,000 housekeeping (core) genes**

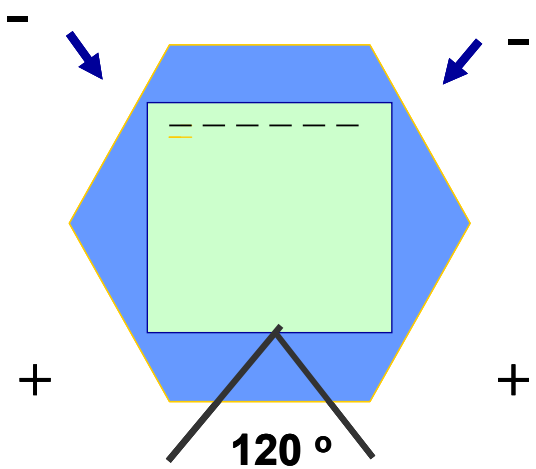
Dendrogram (*minimum spanning tree*) according to the cgMLST profiles of 53 isolates of *A. baumannii* (2390 genes).

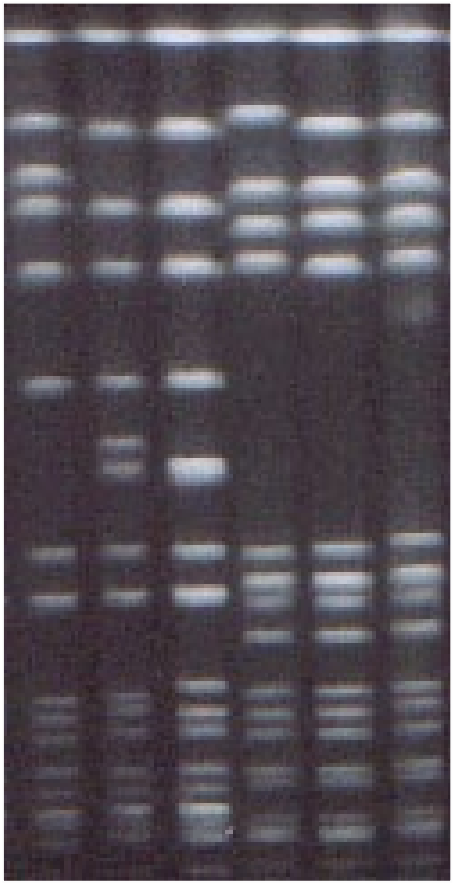


Higgins et al. PLoS ONE 2017

Macrorestriction analysis (PFGE)

- Isolation of intact genomic DNA
- Using a rare-cutting restriction enzyme
- Electrophoretic separation of DNA fragments (10–1000 kb) using PFGE





Surveillance in Europe

European Antimicrobial Resistance Surveillance Network (EARS-Net)

- *www.ecdc.europa.eu/en/about-us/partnerships-and-networks/disease-and-laboratory-networks/ears-net*
- **European Centre for Disease Prevention and Control**
- **The largest publicly funded system for antimicrobial resistance (AMR) surveillance in Europe**
- **EARS-Net is based on routine clinical antimicrobial susceptibility data from local and clinical laboratories reported to ECDC by appointed representatives from the member states**
- **The data originate form national AMR surveillance initiatives and/or laboratory networks**
- **Only data from invasive isolates (i.e. from blood and cerebrospinal fluid) are included in EARS-Net**

European Antimicrobial Resistance Surveillance Network (EARS-Net)

Surveillance of antimicrobial susceptibility of eight bacterial pathogens commonly causing infections in humans:

- ***Escherichia coli***
- ***Klebsiella pneumoniae***
- ***Pseudomonas aeruginosa***
- ***Acinetobacter* spp.**
- ***Streptococcus pneumoniae***
- ***Staphylococcus aureus***
- ***Enterococcus faecalis***
- ***Enterococcus faecium***

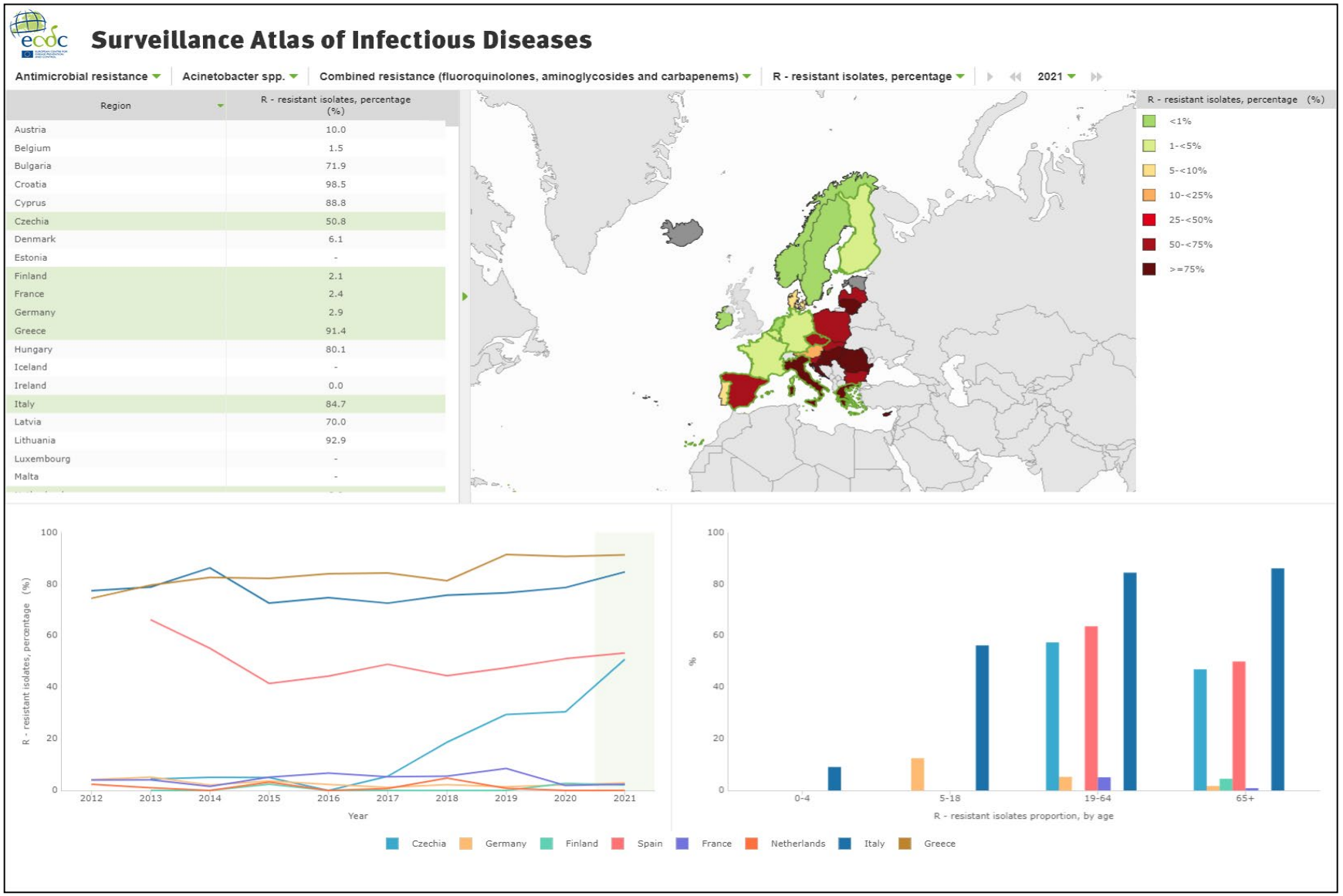
European Antimicrobial Resistance Surveillance Network (EARS-Net)

Surveillance of antimicrobial susceptibility of eight bacterial pathogens commonly causing infections in humans:

- ***Escherichia coli***
- ***Klebsiella pneumoniae***
- ***Pseudomonas aeruginosa***
- ***Acinetobacter* spp.**
- ***Streptococcus pneumoniae***
- ***Staphylococcus aureus***
- ***Enterococcus faecalis***
- ***Enterococcus faecium***

EARS-Net *Acinetobacter* 2021

Combined resistance to carbapenems, fluoroquinolones and aminoglycosides

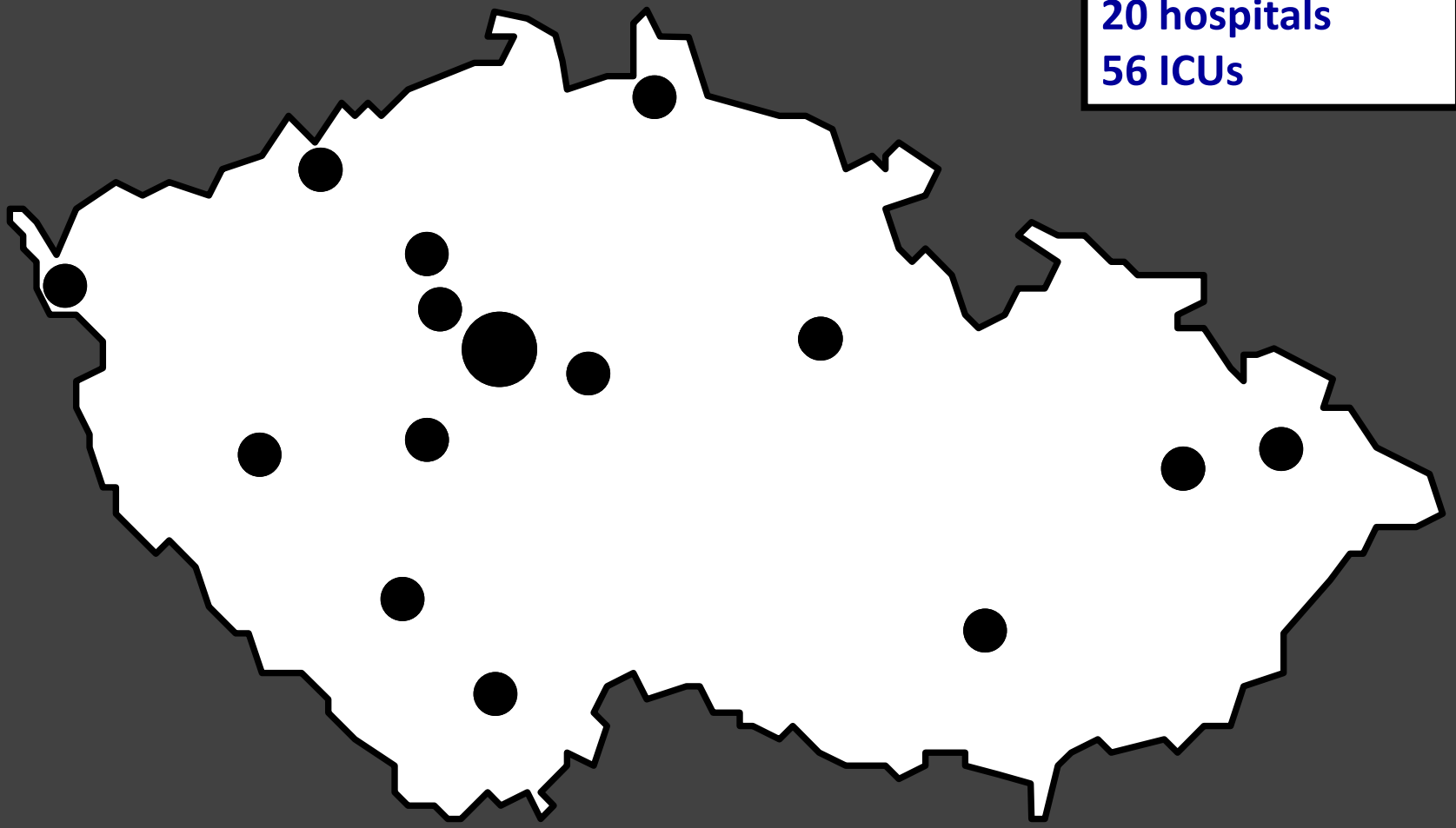


Evolution of MDR/XDR *A. baumannii* populations in Czechia

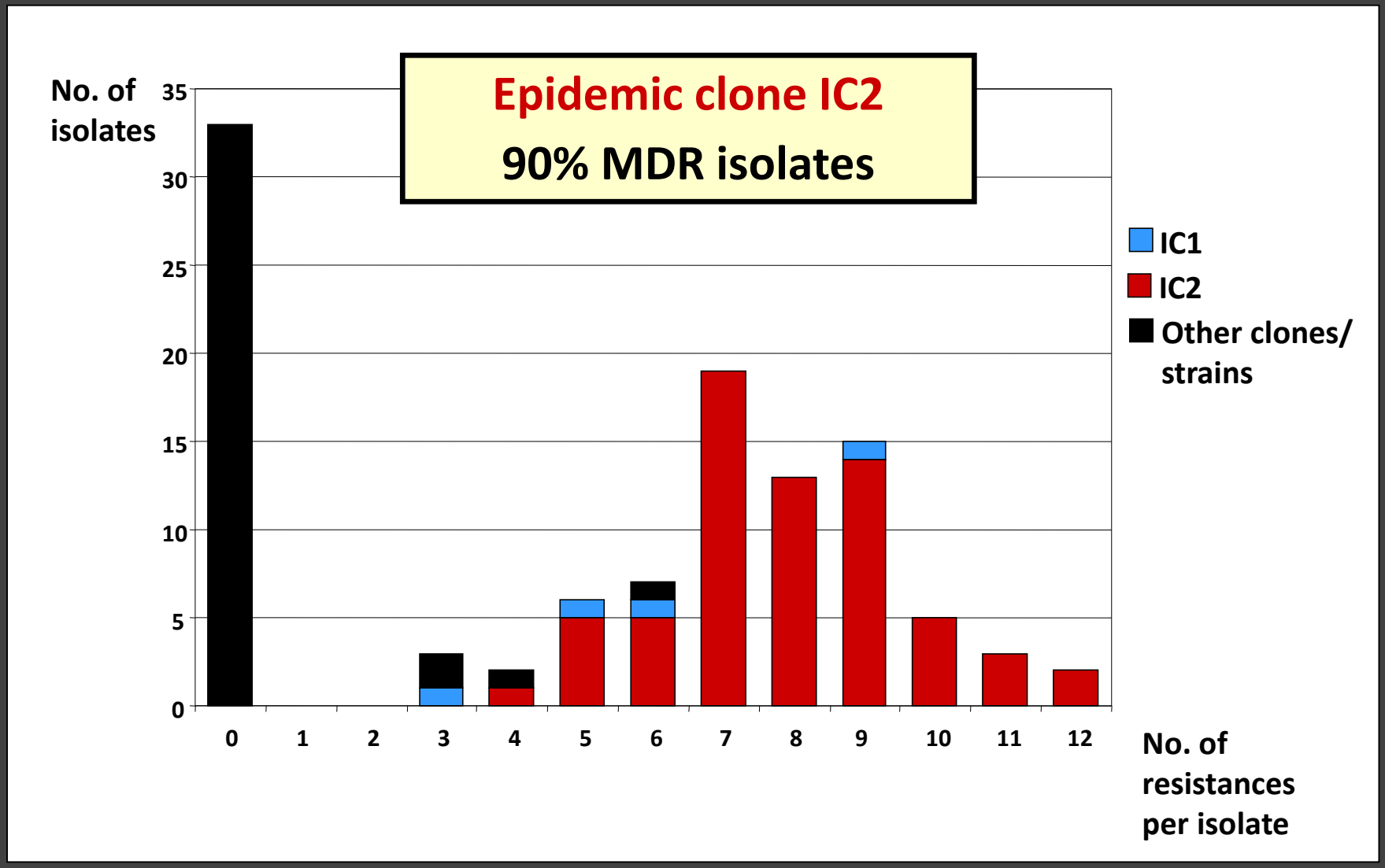
A. baumannii in Czechia (2005–2006)

108 clinical isolates

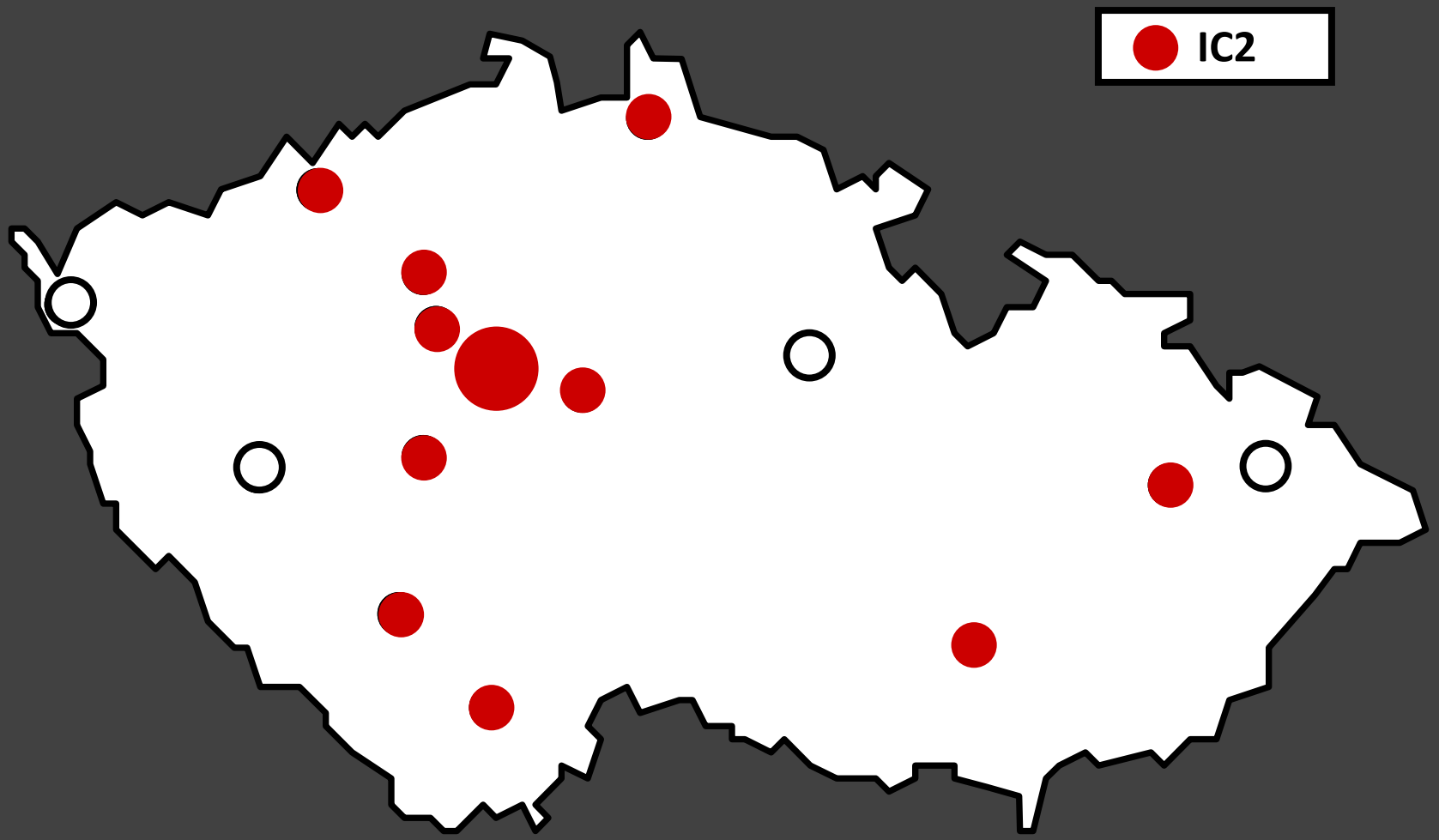
15 cities
20 hospitals
56 ICUs



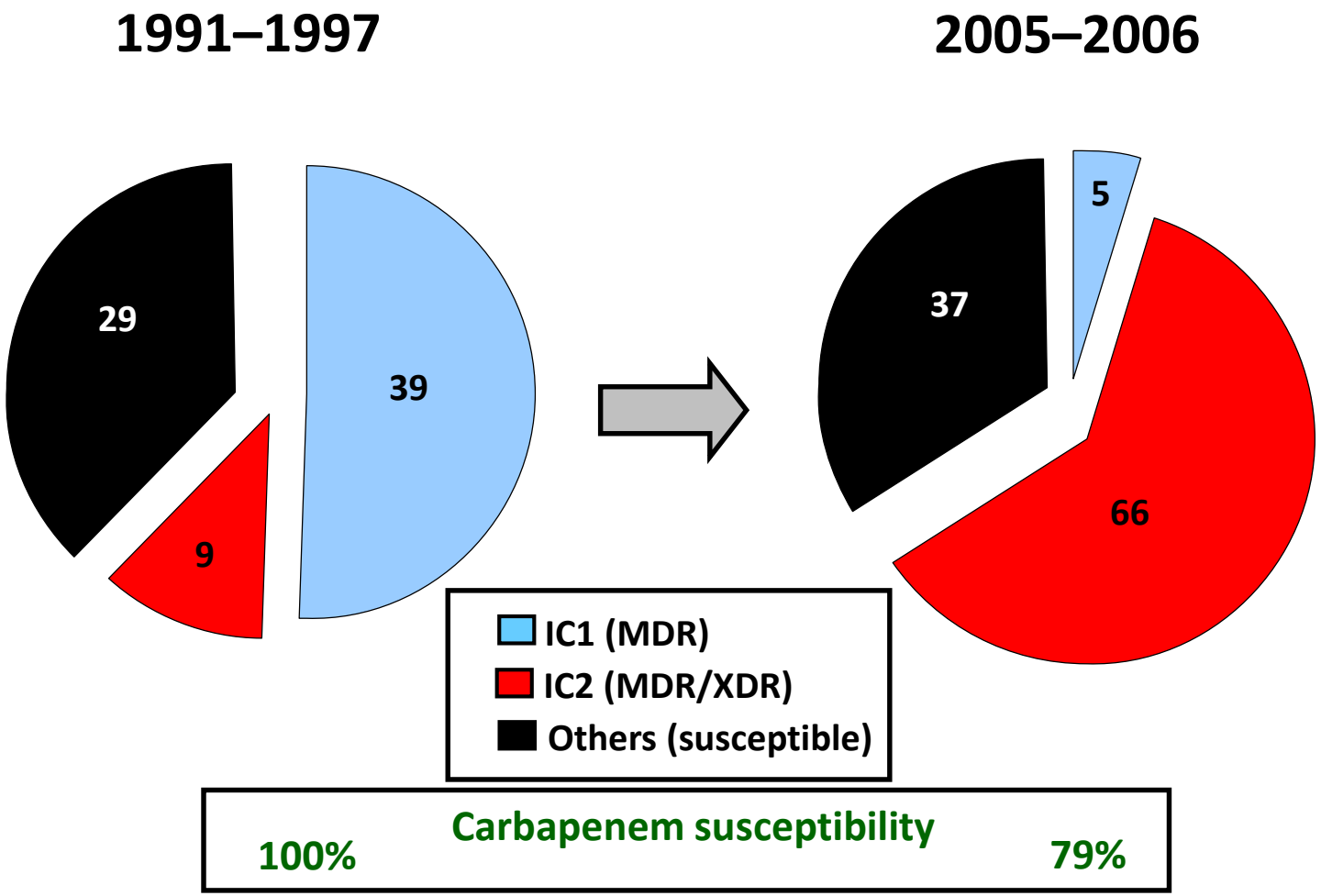
Relationship between clonal type and multidrug resistance



Spread of *A. baumannii* ECII (2005–2006)

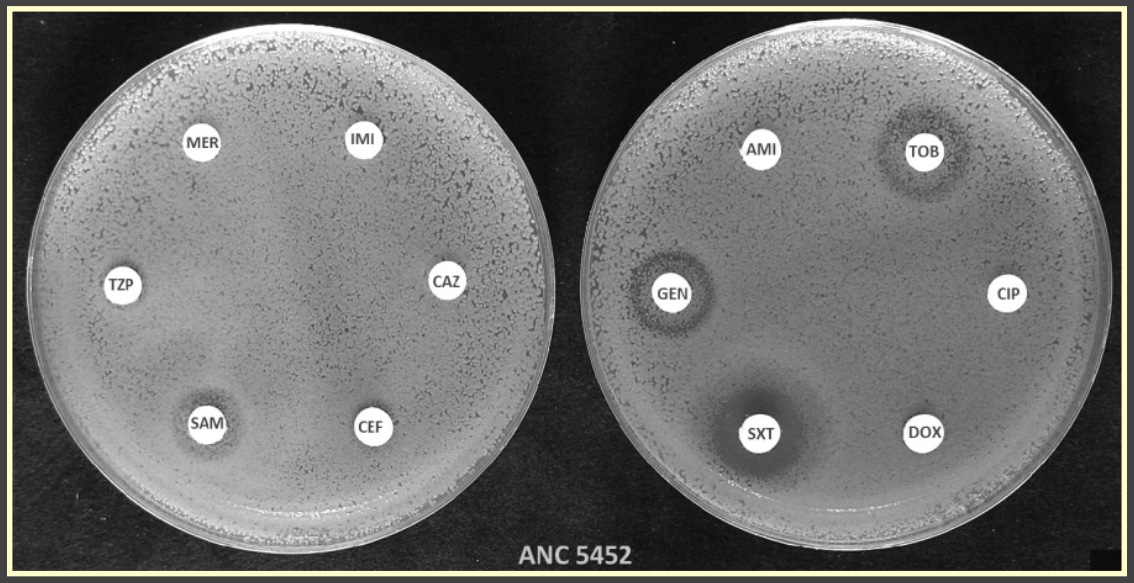


A. baumannii populations in Czechia 1991–1997/2005–2006



A. baumannii in Czechia since 2015

EC2 subclone carrying the carbapenemase OXA-23 and methylase ArmA, susceptible only to colistin

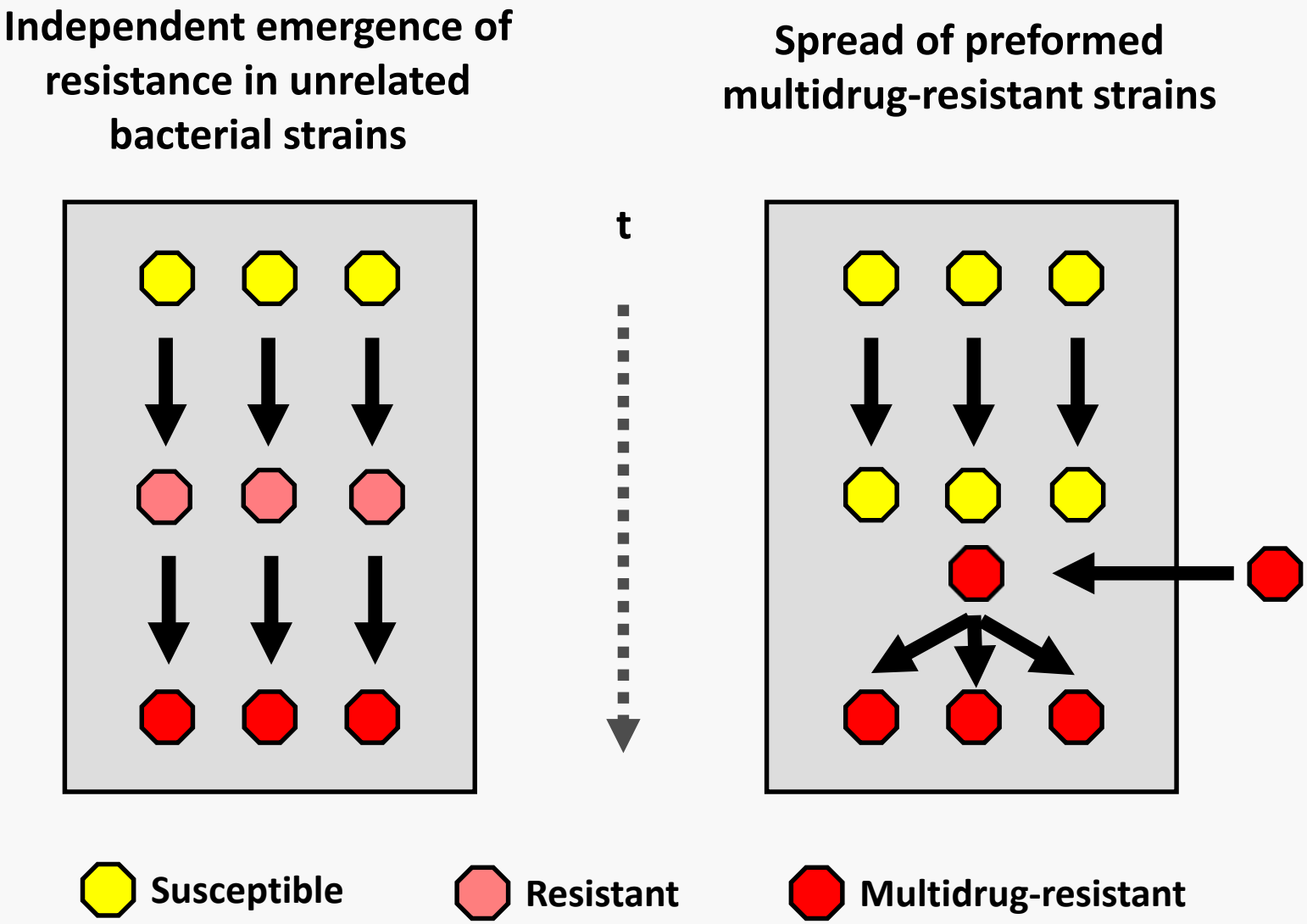


996 MDR/XDR/PDR isolates (2015–2022)

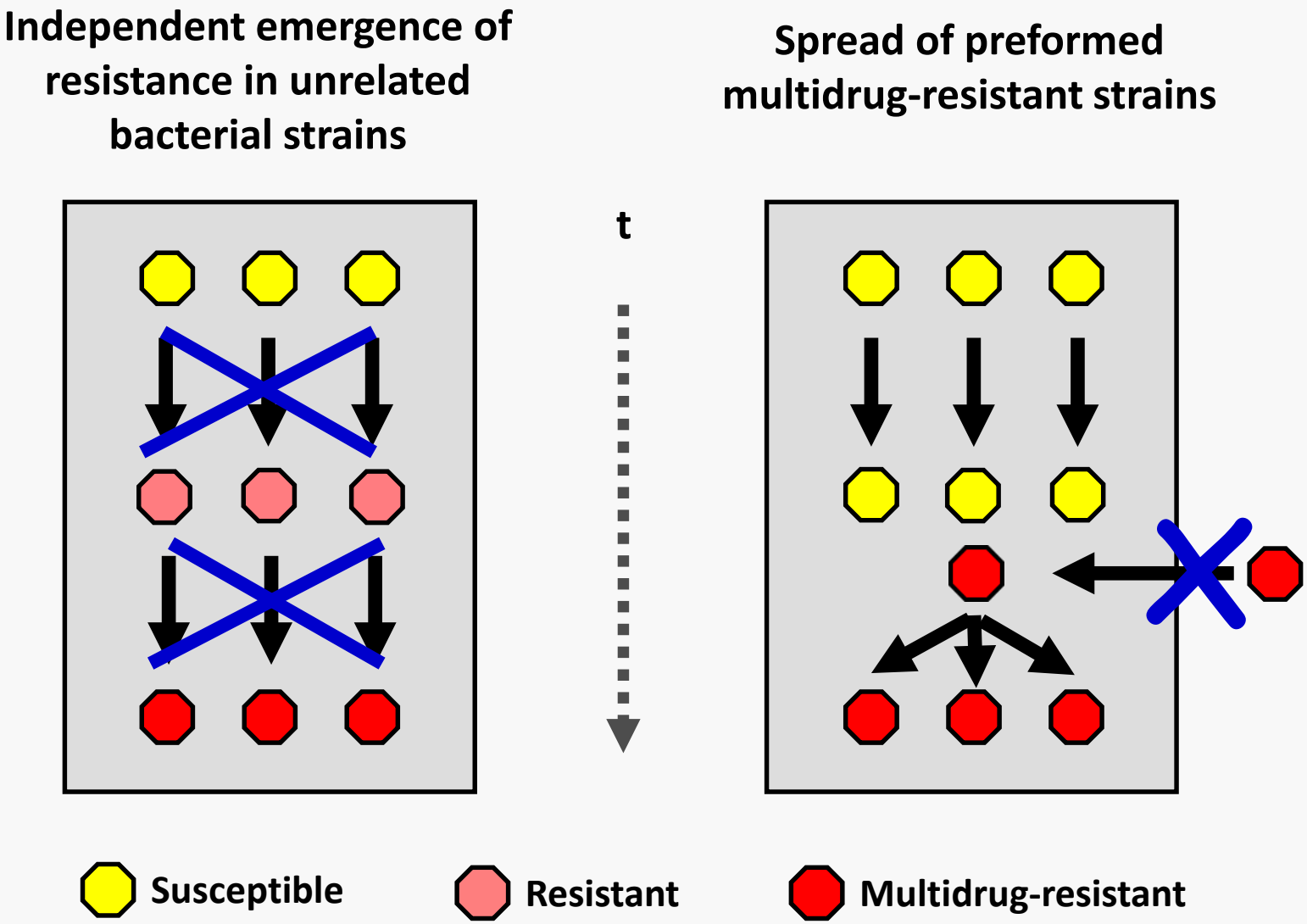
- **761 (76%) XDR/PDR (ArmA+OXA-23) from 38 hospitals of 25 cities**

Hospital outbreaks caused by MDR/XDR *A. baumannii*

Origin and spread of resistance



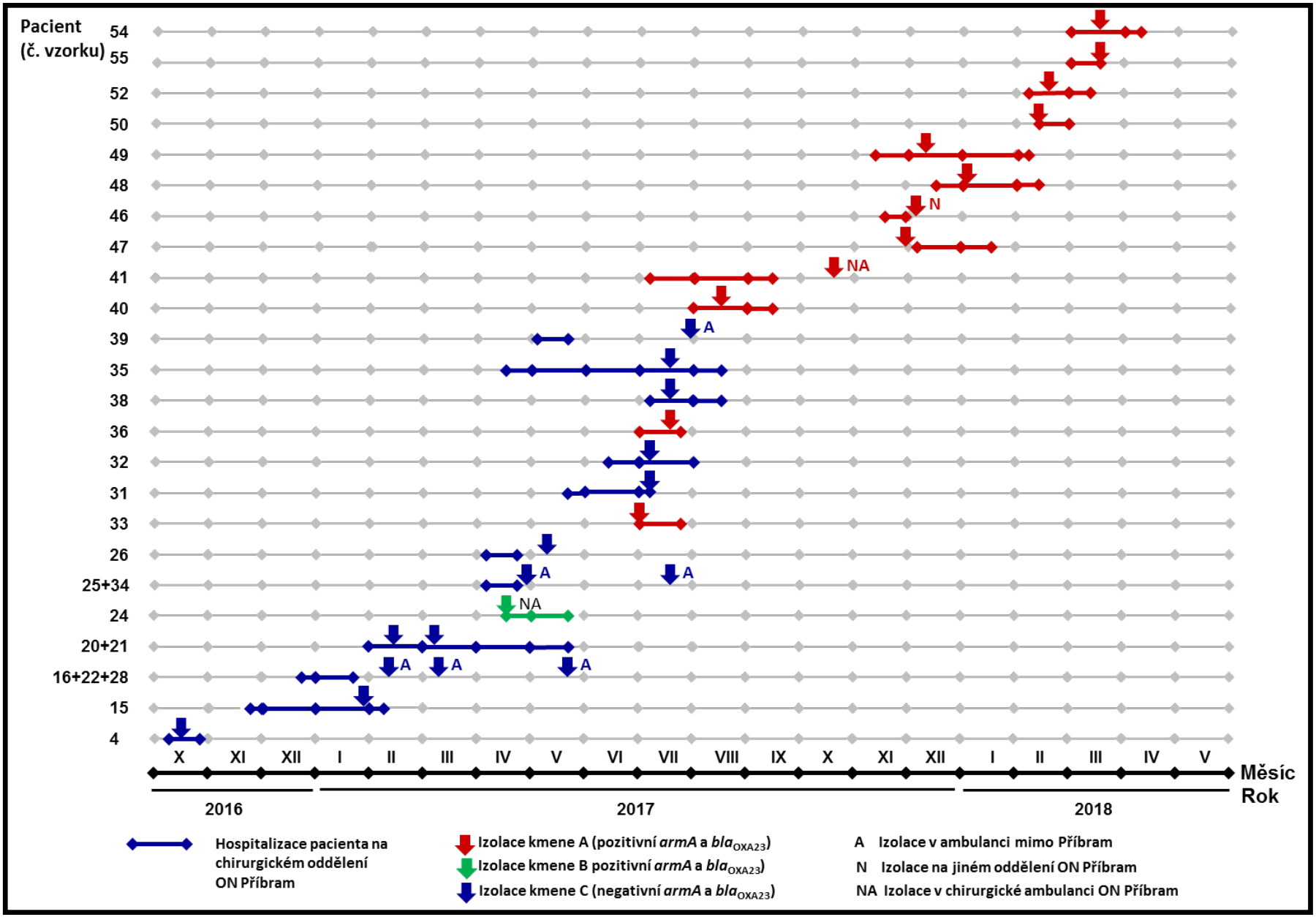
Origin and spread of resistance



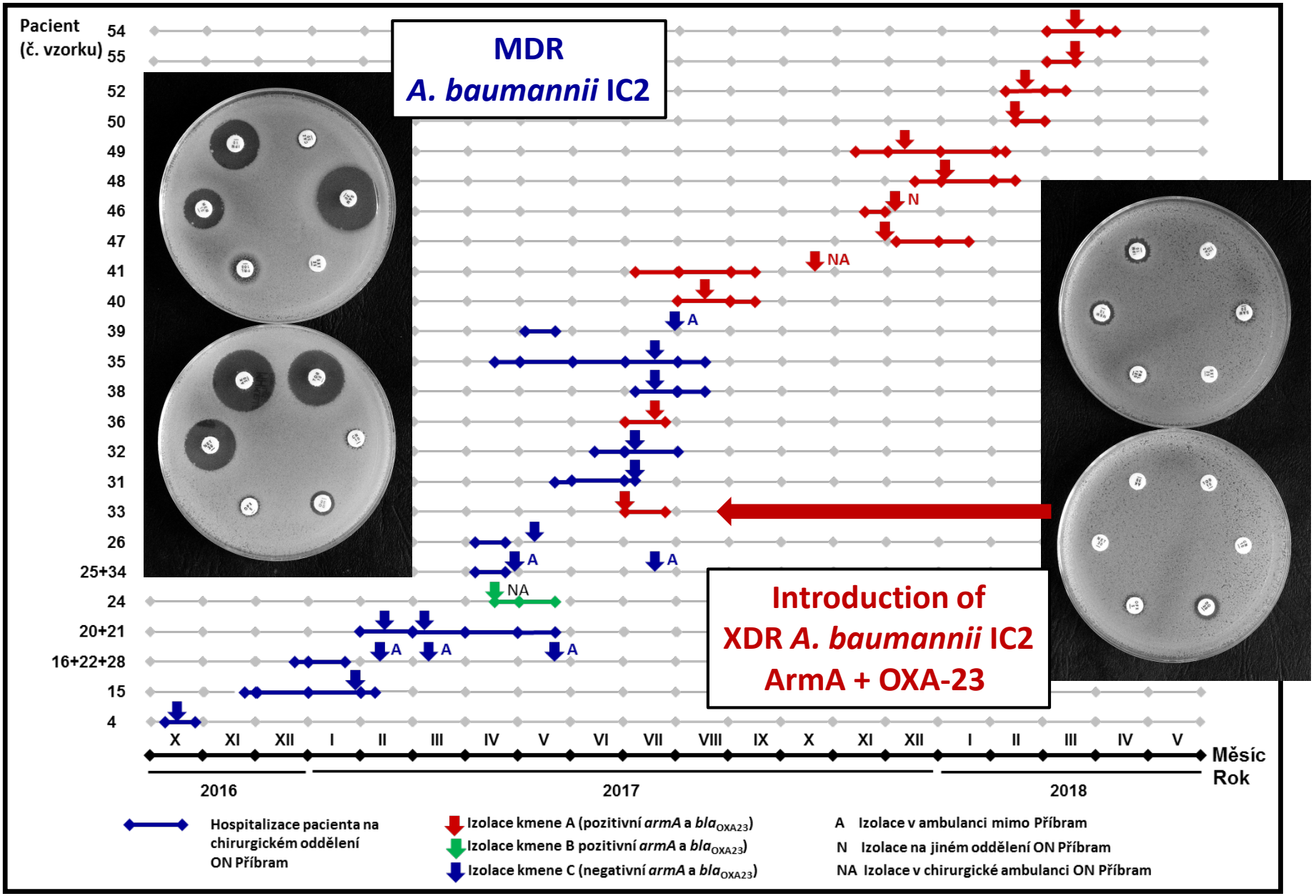
Example of a hospital outbreak

- **In 2016–2018, multiple isolates of MDR *A. baumannii* were recovered from patients hospitalized in a surgical unit of a regional hospital**
- **The isolates had different resistance profiles which were found in isolates from hospitalized patients or during their subsequent examinations at outpatients' departments**
- **Objective: To untangle the epidemiological basis of the problem**

Colonized/infected patients



Colonized/infected patients



Hospital outbreak - Conclusions

- **The abundance of MDR *A. baumannii* isolates resulted from partially overlapping monoclonal outbreaks caused by two different MDR strains**
- **The latter (OXA-23/ArmA) strain was introduced in the surgical unit via a patient transferred from another hospital**
- **Both MDR strains persisted in patients for months after their release from hospital care**
- **An example of the (i) population replacement of an original outbreak strain with a more resistant one and (ii) dissemination of MDR strains owing to long-term colonization of patients**

HAI - final remarks

- WHO reports that millions more across the globe suffer each year from infections acquired in the health care setting, estimating the pooled HAI prevalence among hospitalized patients worldwide to be 10%
- Every health care facility should have an effective infection prevention program charged with monitoring, preventing, and controlling the spread of infections in the health care environment
- As infection prevention requires the detection of both infections and colonization with potential pathogens
- The clinical microbiology laboratory plays a critical role in infection prevention program

Wash your hands!

www.cdc.gov/handwashing/when-how-handwashing.html