

**Nonfermentative  
gram-negative bacilli  
&  
enterobacteria**

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2nd Faculty of Medicine UK (April 17, 2024)

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### Focus on

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

# Lecture structure

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- **General features**
- **Nonfermentative Gram-negative bacilli (NFGNB)**
- **Enterobacteria**

# Lecture structure - General features

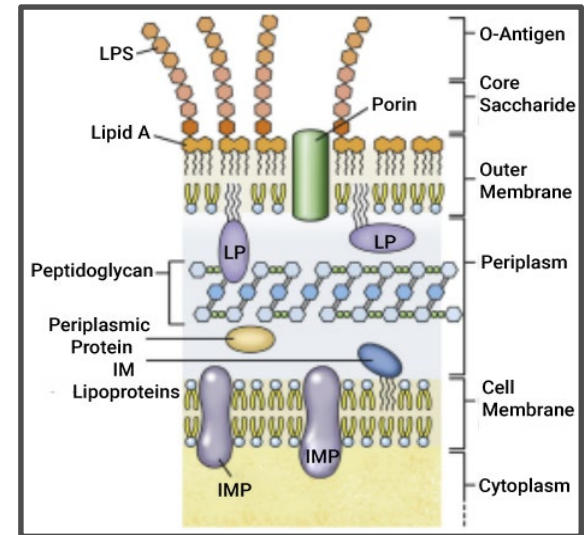
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- **General features**
  - **Shared and opposite features**
  - **Identification**
  - **Taxonomic position**
  - **Pathogenicity**
  - **Resistance to antibiotics**
  - **Health care-associated infections**
- **Nonfermentative Gram-negative bacilli (NFGNB)**
- **Enterobacteria**

# NFGNB *versus* enterobacteria

## ■ Characteristics in common

- Gram-negative (GN) rods/coccobacilli
- Aerobic
- Non-fastidious growth requirements
- Endotoxin (lipid A of lipopolysaccharide)
- Acquired resistance to antibiotics (ATB)



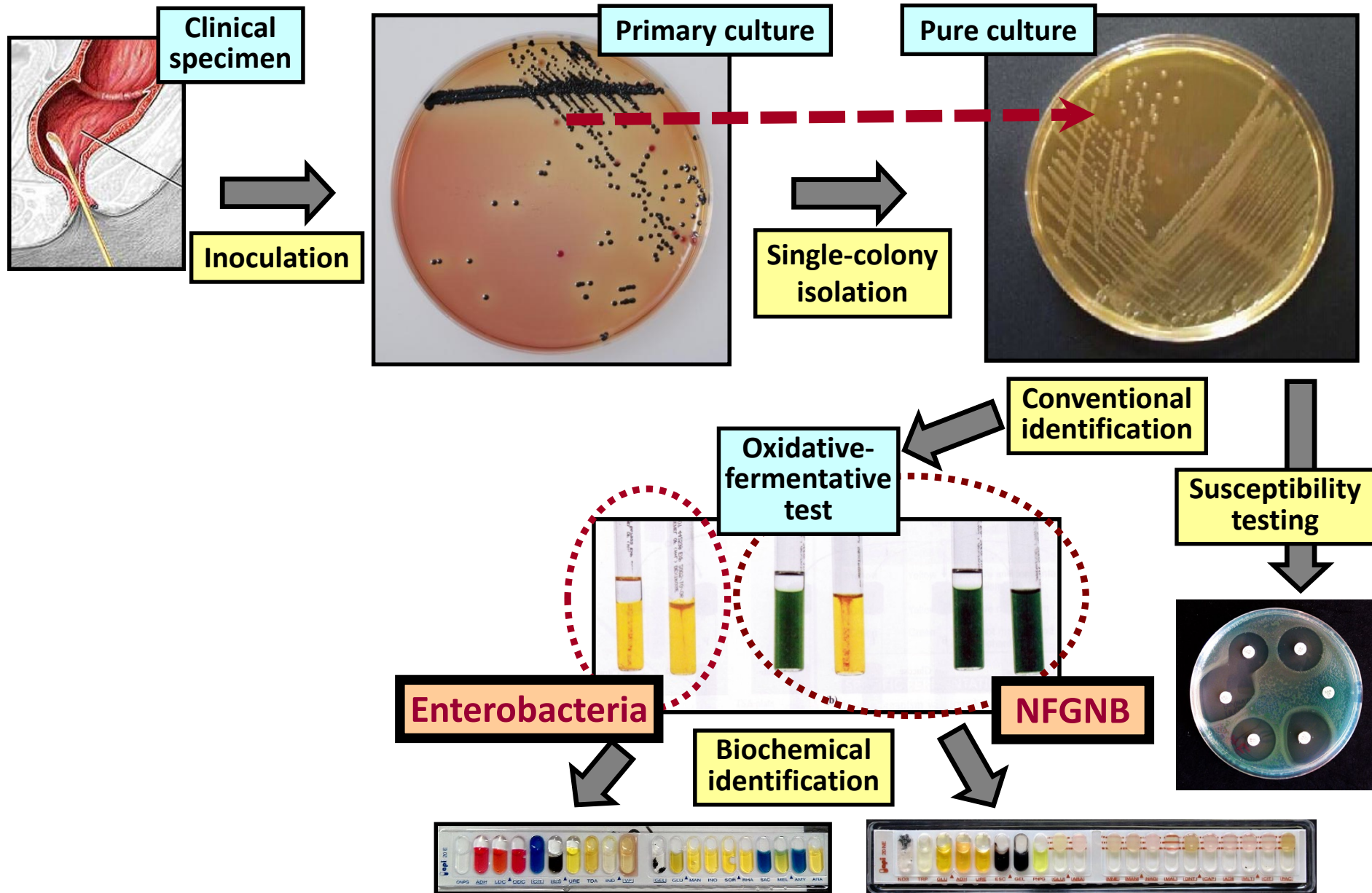
## ■ Differences

- **Glucose fermentation**
- Taxonomic coherence
- Primary pathogenicity
- Opportunistic pathogenicity
- Primary resistance to ATB
- Restricted to the human host
- Ecological ubiquity

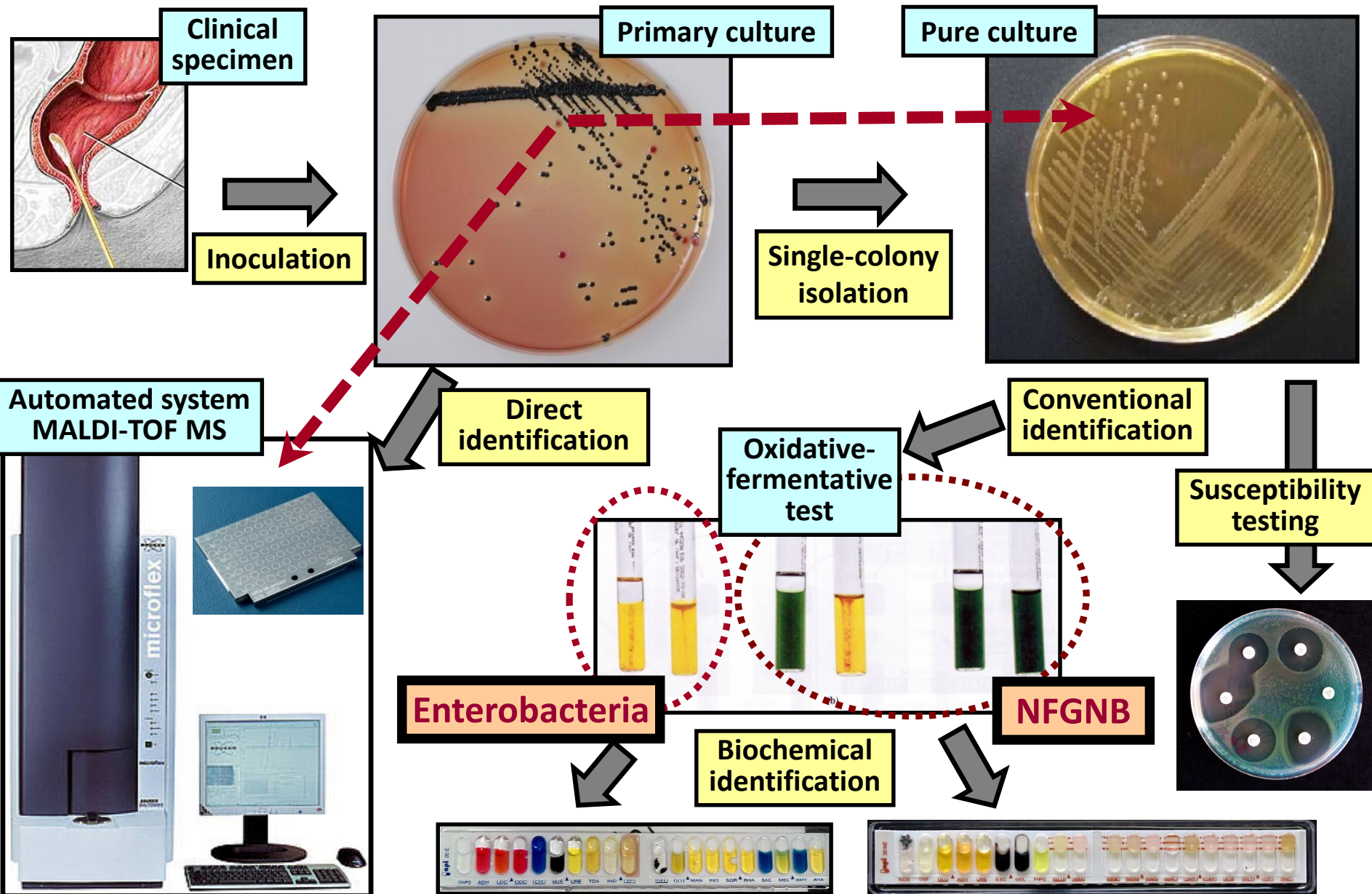
## NFGNB × enterobacteria

no	yes
no	yes
no	various
yes	various
yes	no
no	various
yes	various

# Identification of aerobic GN



# Identification of aerobic GN





# Taxonomic position

## ■ NFGNB

- Heterogeneous
- Different classes and phyla

<p><b>PSEUDOMONADOTA</b></p> <p><b>ALPHAPROTEOBACTERIA</b></p> <p><b>CAULOBACTERALES</b></p> <p>Caulobacteraceae</p> <p><i>Brevundimonas (B. vesicularis)</i></p> <p><b>RHIZOBIALES</b></p> <p>Brucellaceae</p> <p><i>Ochrobactrum (O. antropii)</i></p> <p><b>RHODOSPIRILLALES</b></p> <p>Acetobacteraceae</p> <p><i>Roseomonas</i></p> <p>Rhodospirillaceae</p> <p><i>Inquilius (I. limosus)</i></p> <p><b>BETAPROTEOBACTERIA</b></p> <p><b>BURKHOLDERIALES</b></p> <p>Burkholderiaceae</p> <p><i>Burkholderia (B. cenocepacia)</i></p> <p><i>Cupriavidus</i></p> <p><i>Pandoraea</i></p> <p><i>Ralstonia (R. pickettii)</i></p> <p><b>Alcaligenaceae</b></p> <p><i>Alcaligenes (A. faecalis)</i></p> <p><i>Oligella (O. urethralis)</i></p> <p><b>Comamonadaceae</b></p> <p><i>Acidovorax</i></p> <p><i>Comamonas (C. testosteroni)</i></p> <p><i>Delftia (D. acidovorans)</i></p>	<p><b>PSEUDOMONADOTA</b></p> <p><b>GAMMAPROTEOBACTERIA</b></p> <p><b>PSEUDOMONADALES</b></p> <p>Pseudomonadaceae</p> <p><i>Pseudomonas (P. aeruginosa)</i></p> <p>Moraxellaceae</p> <p><i>Acinetobacter (A. baumannii)</i></p> <p><i>Moraxella (M. catarrhalis)</i></p> <p><i>Psychrobacter</i></p> <p><b>XANTHOMONADALES</b></p> <p>Xanthomonadaceae</p> <p><i>Stenotrophomonas (S. maltophilia)</i></p> <p><b>ALTEROMONADALES</b></p> <p>Shewanellaceae</p> <p><i>Shewanella (S. putrefaciens)</i></p> <p><b>BACTEROIDOTA</b></p> <p><b>FLAVOBACTERIA</b></p> <p><b>FLAVOBACTERIALES</b></p> <p>Flavobacteriaceae</p> <p><i>Chryseobacterium (C. indologenes)</i></p> <p><i>Elizabethkingia (E. meningoseptica)</i></p> <p><i>Weeksella (W. virosa)</i></p> <p><b>SPHINGOBACTERIA</b></p> <p><b>SPHINGOBACTERIALES</b></p> <p>Sphingobacteriaceae</p> <p><i>Sphingobacterium (S. multivorum)</i></p>
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## ■ Enterobacteria

- Originally family *Enterobacteriaceae*
- Reclassified in 2016: order *Enterobacterales* with 7 families



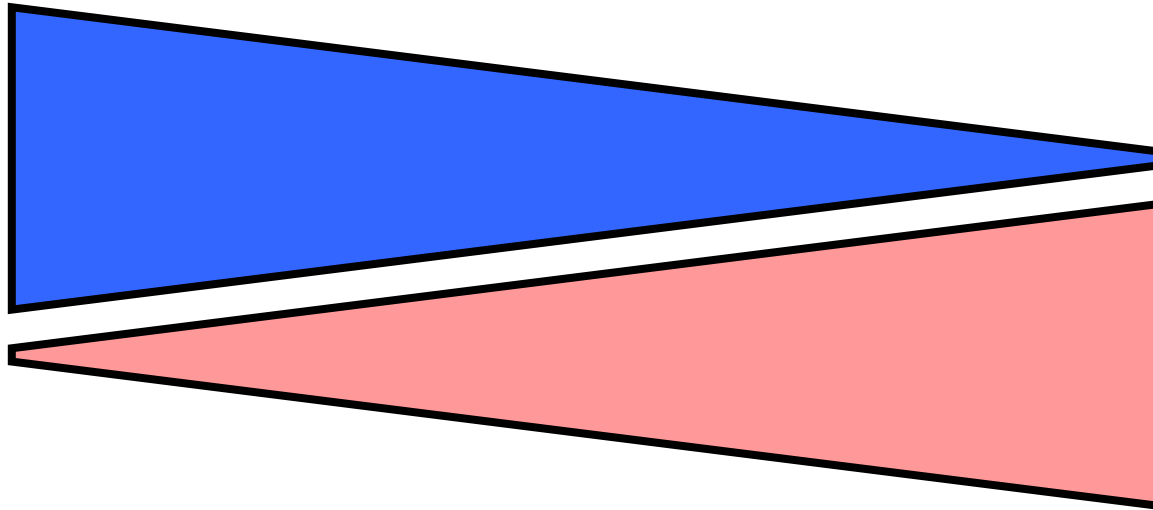
# Pathogenicity

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Decrease of host defense



Opportunistic  
pathogen



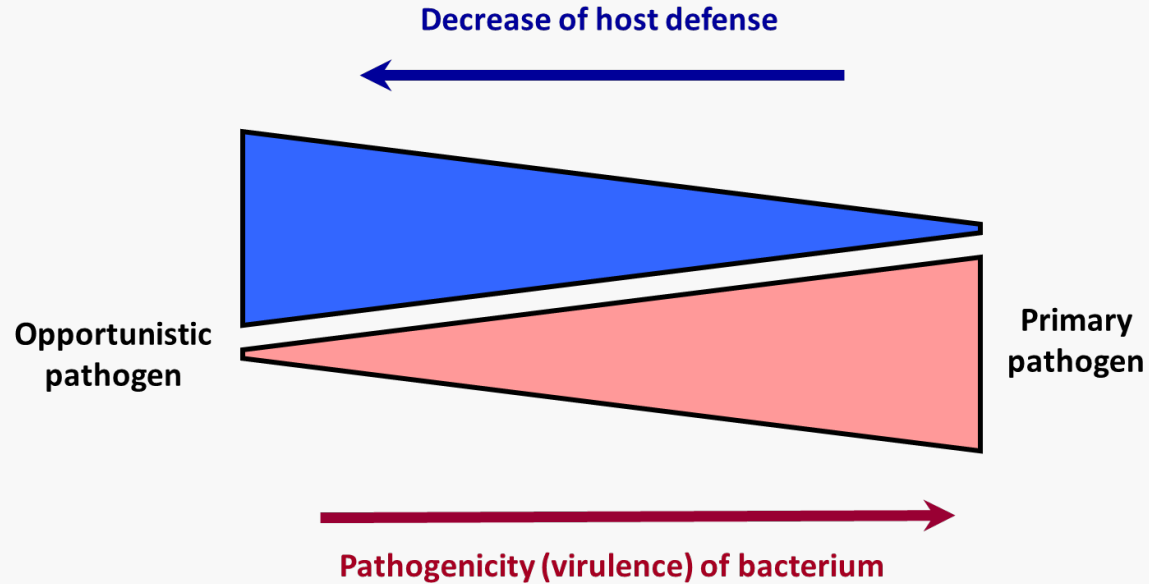
Primary  
pathogen



Pathogenicity (virulence) of bacterium

# Pathogenicity

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**Healthcare-associated  
infections**

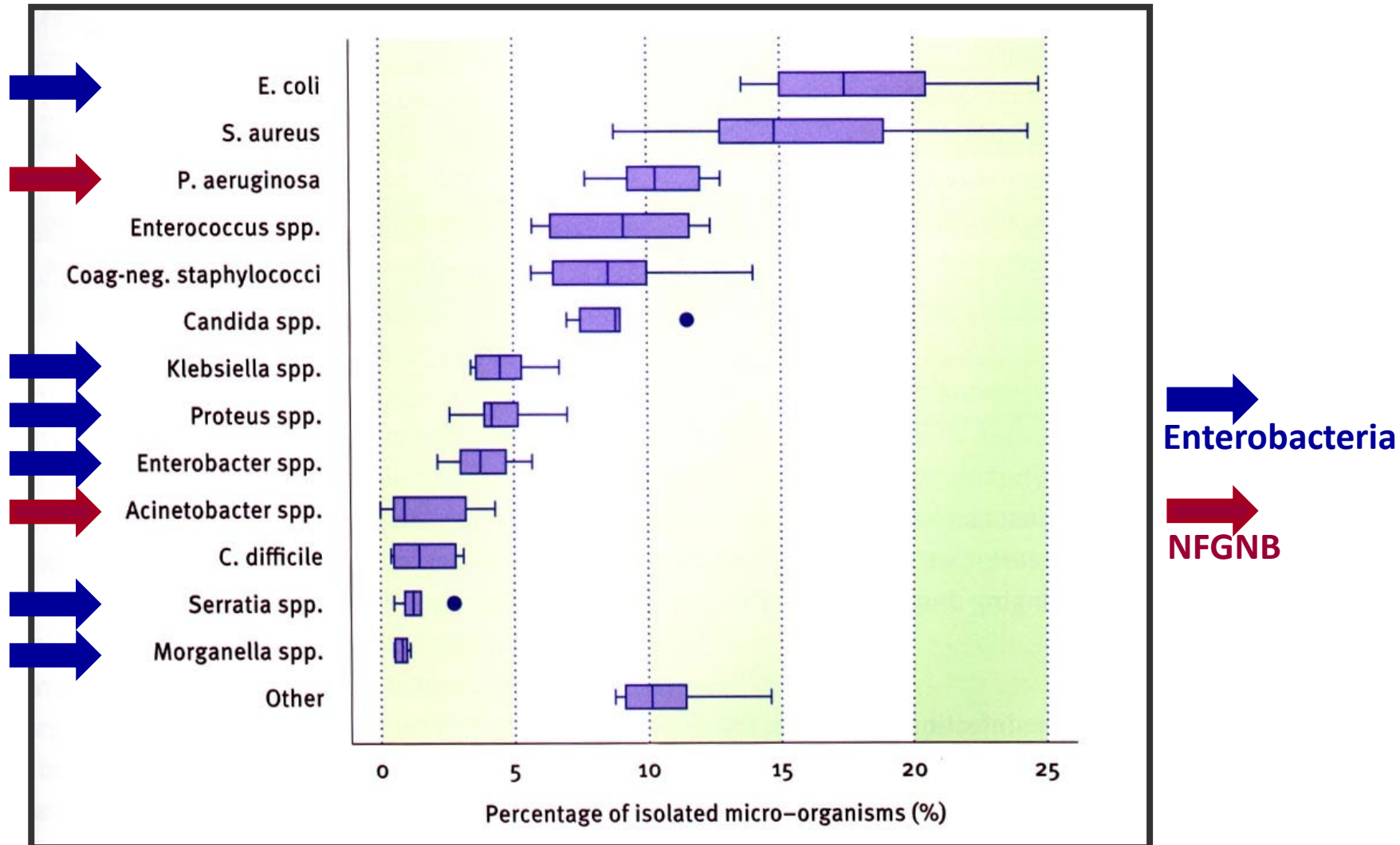
**Plague  
Enteric fever  
Bacterial dysentery  
Hemolytic uremic syndrome**

# Healthcare-associated infections (HAI)

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- **Diseases or pathologies related to the presence of an infectious agent or its products in association with exposure to healthcare facilities or healthcare procedures or treatments**
- **Impact of HAI in Europe (2009)**
  - **Incidence of HAI: 5.1%**
  - **No. of deaths (directly related): 37,179**
  - **No. of deaths (indirect): 111,537**
  - **Extra costs: 4,480,000,000 €**
- **Worldwide HAI prevalence among inpatients 10%**
- **Main HAI types (≈85% of total cases)**
  - **Pneumonia and other lower respiratory tract infections**
  - **Surgical site infections**
  - **Urinary tract infections**
  - **Bloodstream infections**

# Etiological agents of HAI

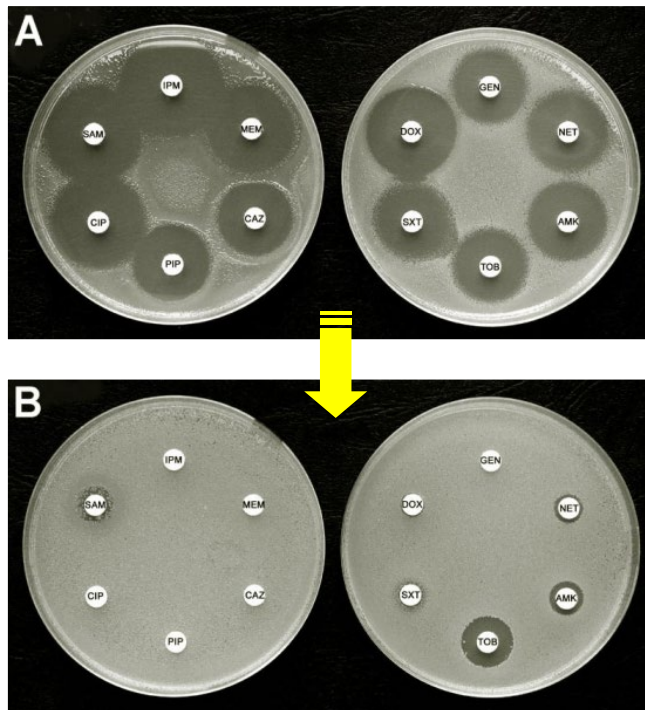


# Multidrug-resistant HAI agents - ESKAPE

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,<sup>1</sup> George H. Talbot,<sup>2</sup> John S. Bradley,<sup>3,4</sup> John Edwards, Jr.,<sup>5,6,7</sup> David Gilbert,<sup>8</sup> Louis B. Rice,<sup>9,10</sup> Michael Scheld,<sup>11</sup> Brad Spellberg,<sup>5,6,7</sup> and John Bartlett<sup>12</sup>



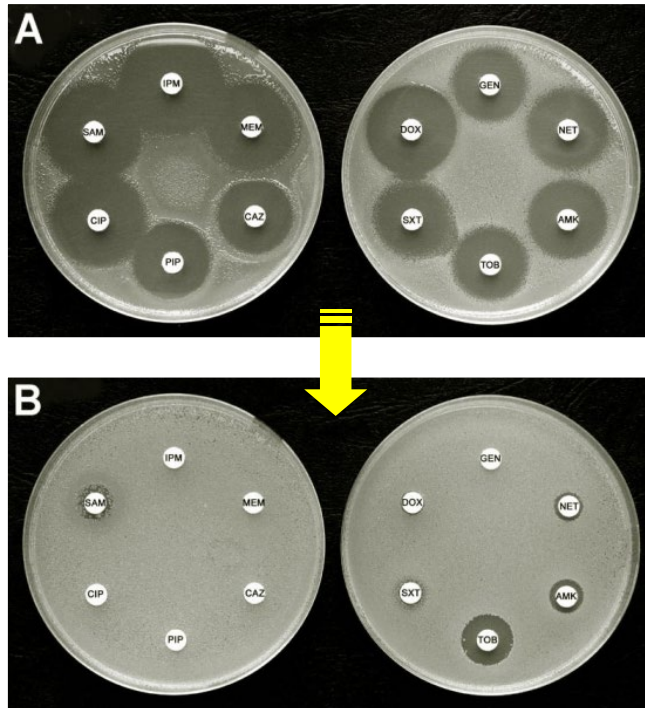
Pathogens that cause the majority of hospital infections and effectively “escape” the effects of antibacterial drugs.

# Multidrug-resistant HAI agents - ESKAPE

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Michael Scheld,<sup>11</sup> Brad Spellberg,<sup>5,6,7</sup> and John Bartlett<sup>12</sup>



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

# WHO 2017 Priority Pathogens List



## WHO PRIORITY PATHOGENS LIST FOR R&D OF NEW ANTIBIOTICS

### Priority 1: CRITICAL<sup>#</sup>

*Acinetobacter baumannii*, carbapenem-resistant

*Pseudomonas aeruginosa*, carbapenem-resistant

*Enterobacteriaceae*\*, carbapenem-resistant, 3<sup>rd</sup> 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*, 3<sup>rd</sup> generation cephalosporin-resistant, fluoroquinolone-resistant

### Priority 3: MEDIUM

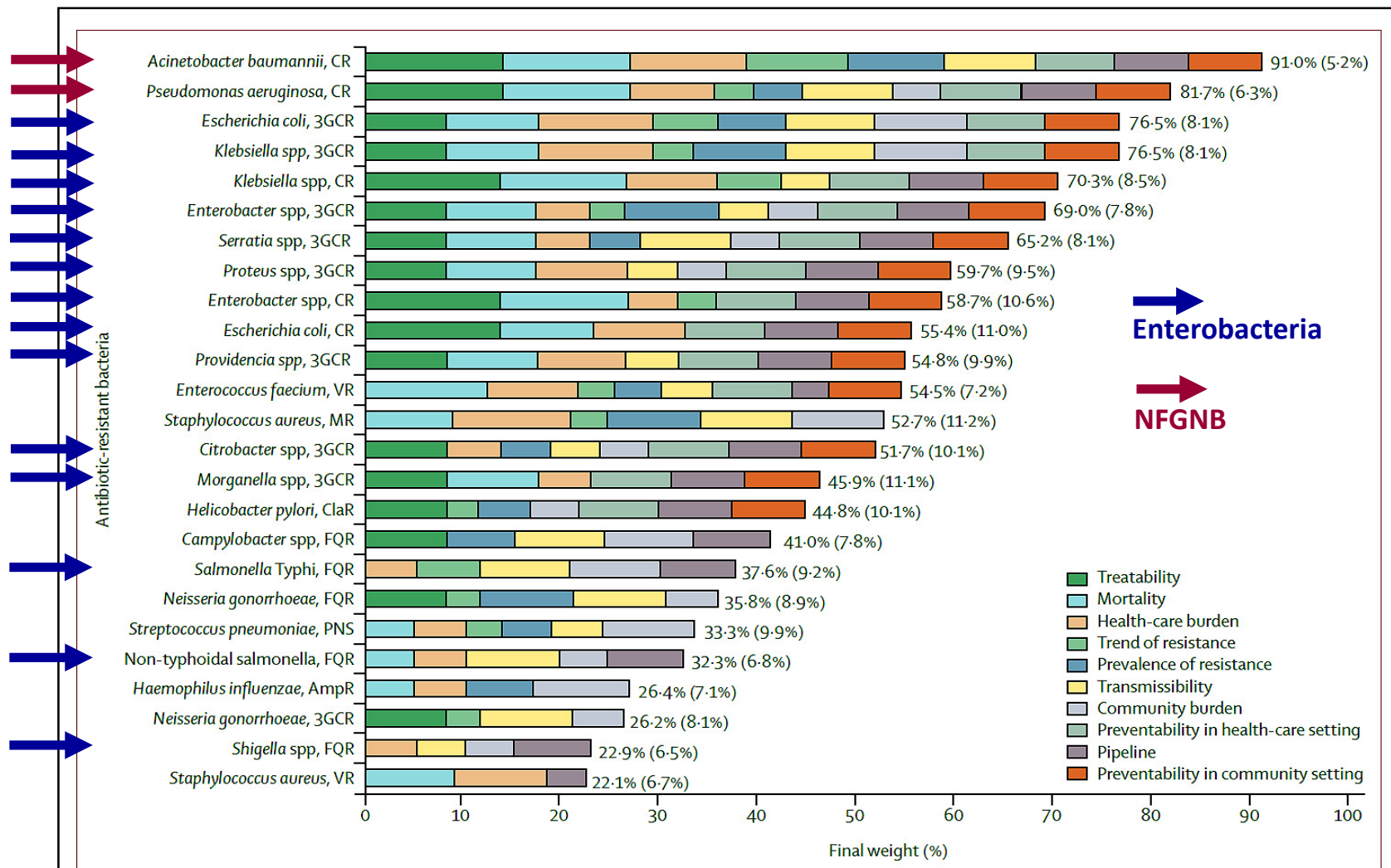
*Streptococcus pneumoniae*, penicillin-non-susceptible

*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=meticcillin resistant. ClaR=clarithromycin resistant. FQR=fluoroquinolone resistant. PNS=penicillin non-susceptible. AmpR=ampicillin resistant.

# Lecture structure - NFGNB

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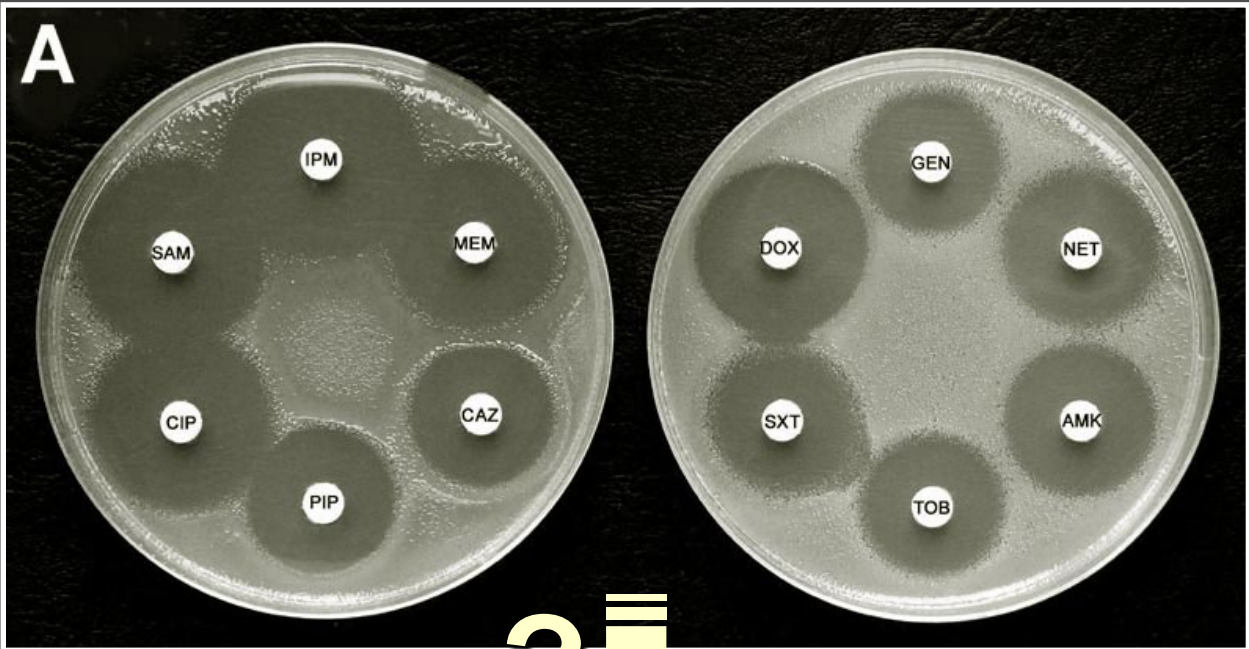
- General characteristics
- Nonfermentative Gram-negative bacilli (NFGNB)
  - *Acinetobacter baumannii*
    - ✓ Resistance to antibiotics
    - ✓ Epidemiology
  - *Pseudomonas aeruginosa*
  - *Burholderia cenocepacia*
  - *Stenotrophomonas maltophilia*
- Enterobacteria

# *Acinetobacter baumannii*

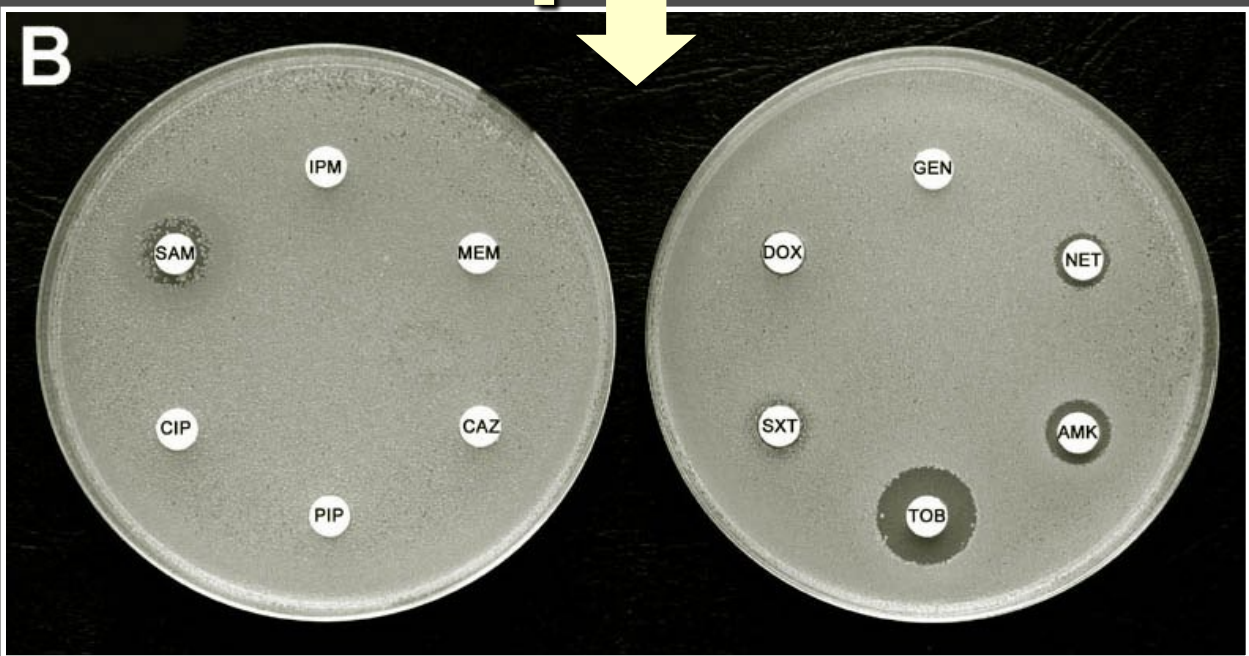
- **Taxonomy:** *Moraxellaceae* < *Pseudomonadales* < *Pseudomonadota*
- **Features:** strictly aerobic (capable of neither fermentation nor anaerobic respiration), oxidase-negative, catalase-positive, nonmotile (no flagella)
- **Habitat:** humans, animals, environment
- **Pathogenicity:** opport. pathogenic (rare infections in community); HAI in critically ill patients; colonization more common than infection
- **Resistance:** primary resistance to desiccation and other physical/chemical external factors; acquired resistance to virtually all primarily effective antibiotics
- **Epidemiology:** clonal spread at various geographic scales
- **Prototype of an HAI pathogen**



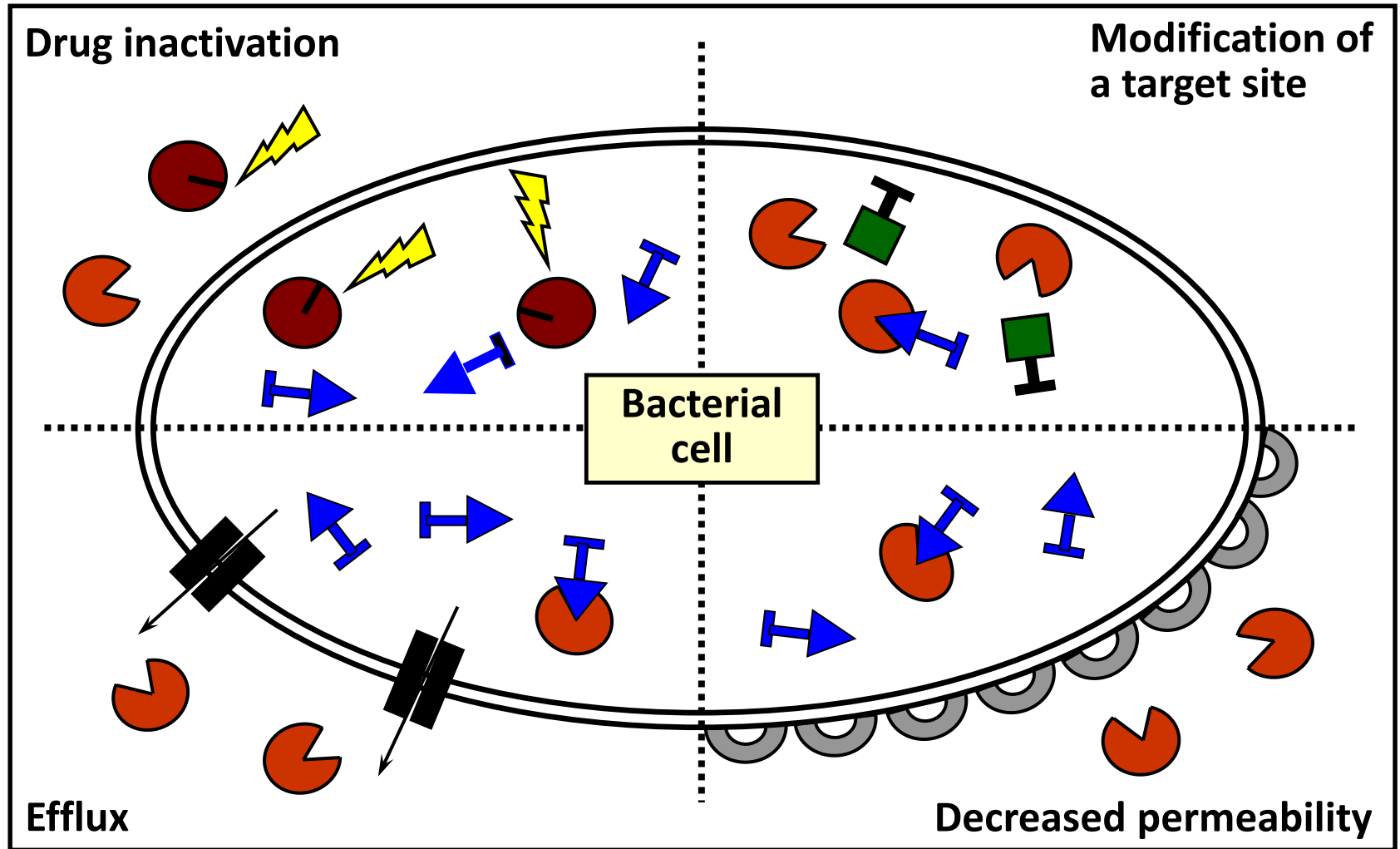
Fully (wild-type)  
susceptible  
*A. baumannii*



Multidrug-  
resistant  
*A. baumannii*



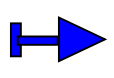
# Bacterial resistance mechanisms



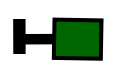
Active drug



Inactive drug



Sensitive target site



Modified target site

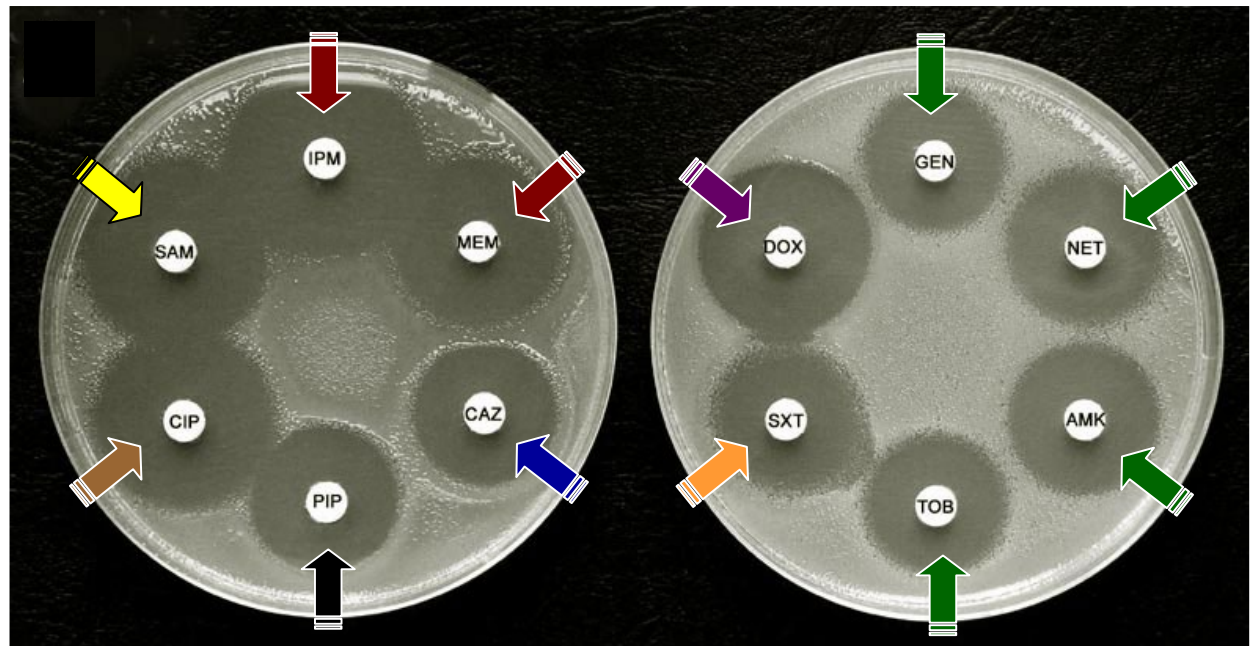


Modifying/lytic enzyme



# Antibiotics against *A. baumannii*

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



Disk diffusion test

**Novum: Sulbactam + Durlobactam** (approved by FDA in May 2023)  
a new treatment for hospital-acquired/ventilator-associated bacterial pneumonia  
caused by *A. baumannii*

# Acquired antibiotic resistance

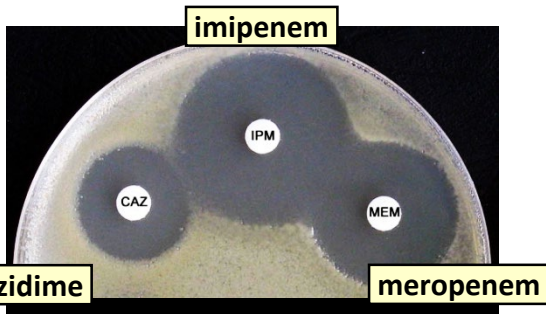
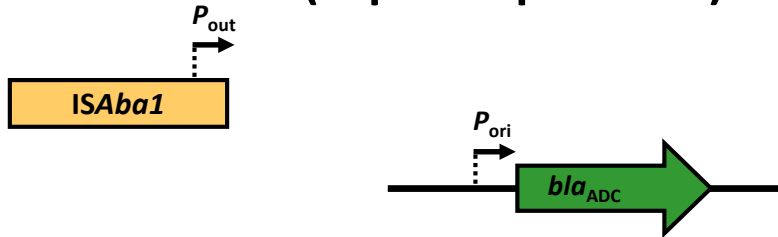
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- **Intrinsic origin - genetic changes of already present systems**
  - Regulatory genes > upregulation (activity)
  - Structural genes > decreased affinity to a target
- **Acquisition of resistance genes via horizontal gene transfer**
  - Conjugation
  - Transformation
  - Transduction



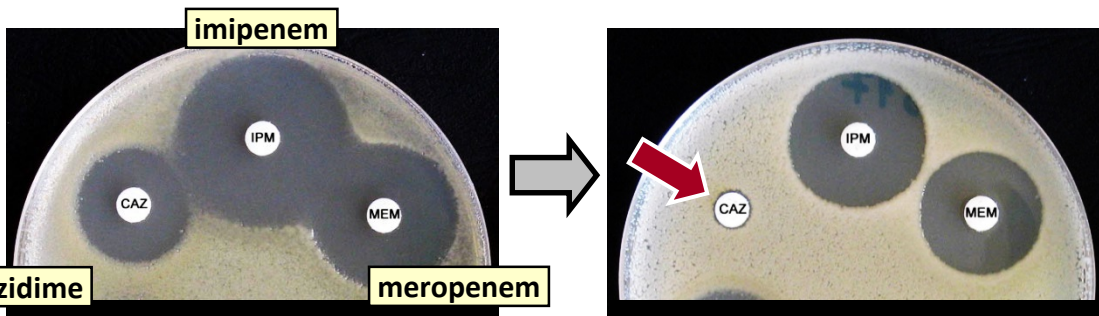
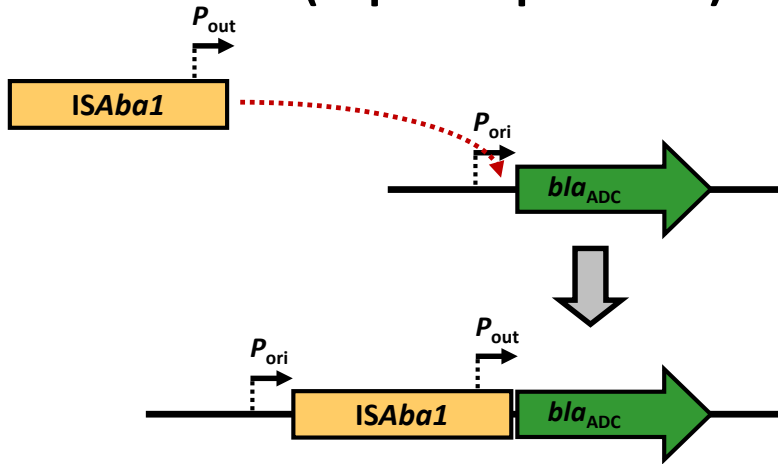
# Overexpression of intrinsic $\beta$ -lactamases

**ADC**  
(cephalosporinase)



# Overexpression of intrinsic $\beta$ -lactamases

**ADC**  
(cephalosporinase)

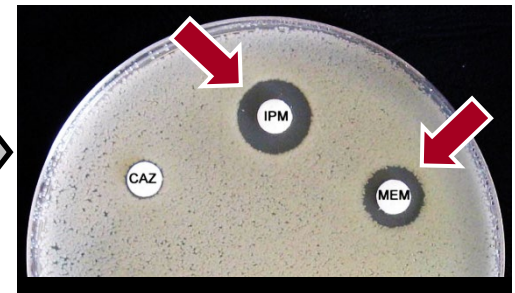
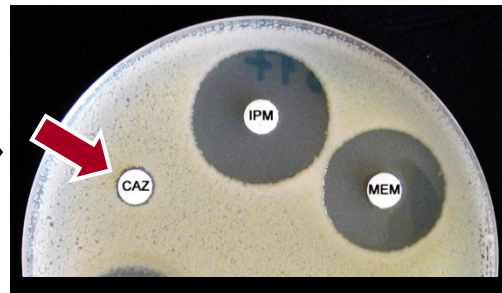
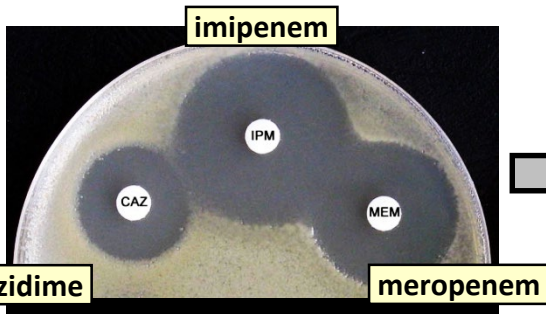
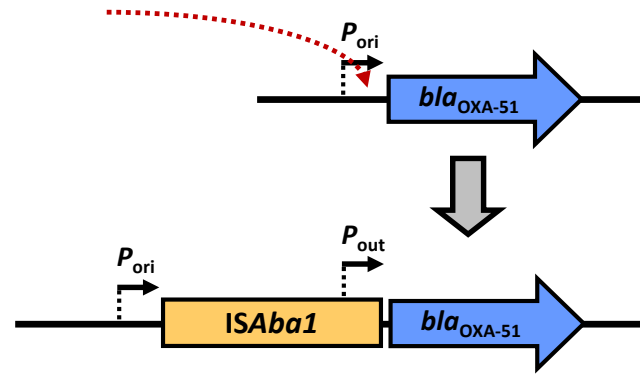
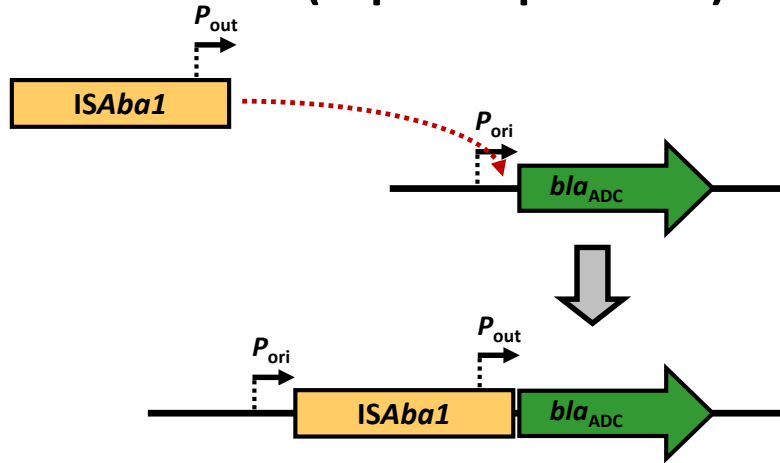


Resistance to  
3rd generation cephalosporins

# Overexpression of intrinsic $\beta$ -lactamases

**ADC**  
(cephalosporinase)

**OXA-51**  
(carbapenemase)

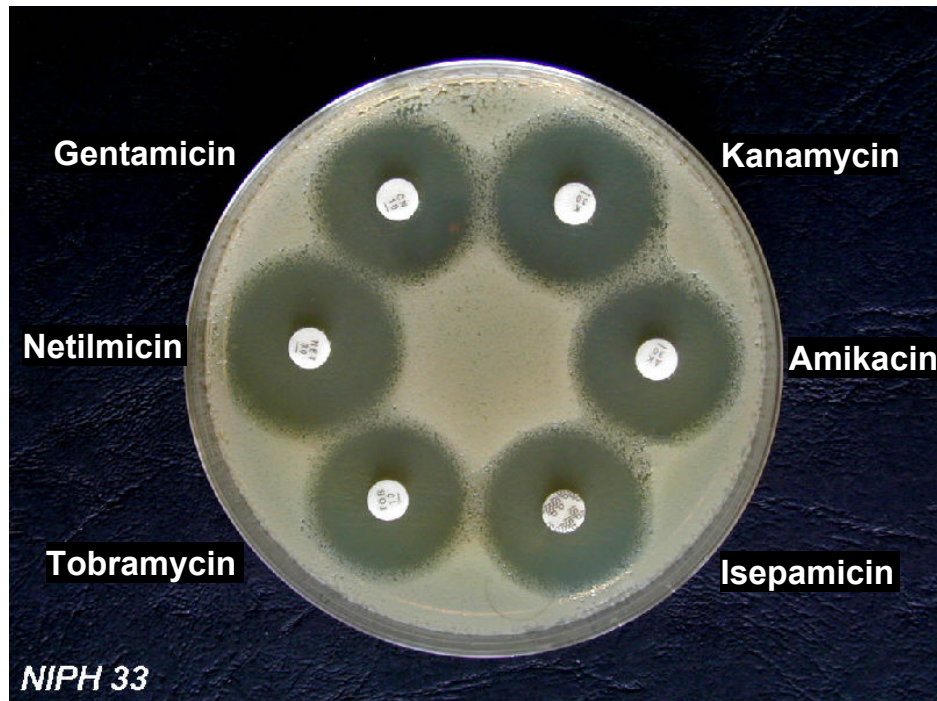


Resistance to  
3rd generation cephalosporins

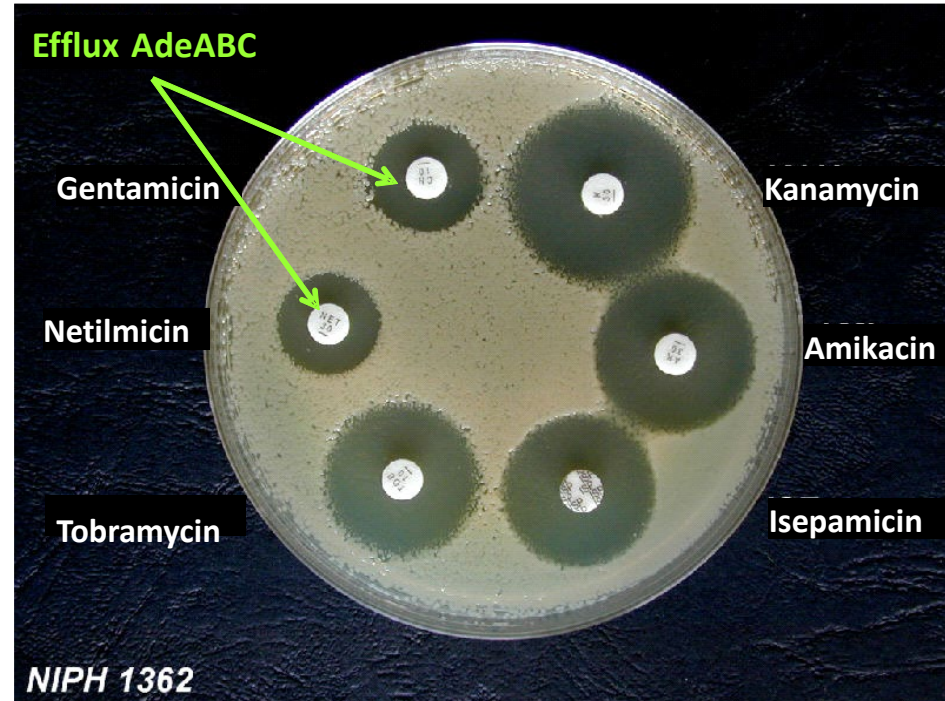
Resistance to  
carbapenems

# Successive acquisition of genes: resistance to aminoglycosides

## 1. Wild-type susceptible



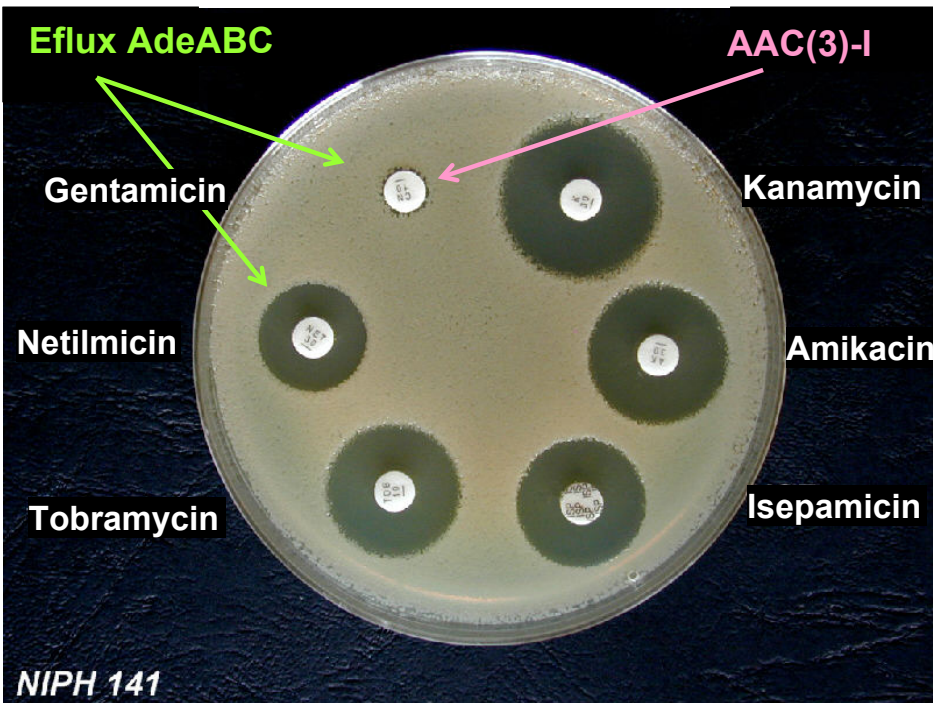
## 2. Overexpression of the AdeABC efflux



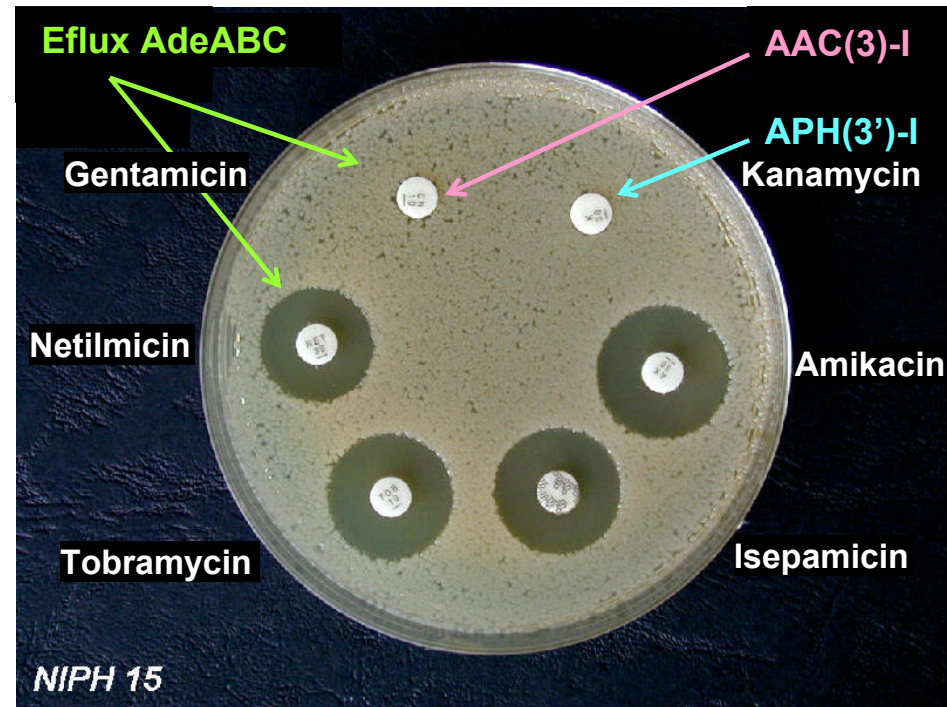


# Successive acquisition of genes: resistance to aminoglycosides

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

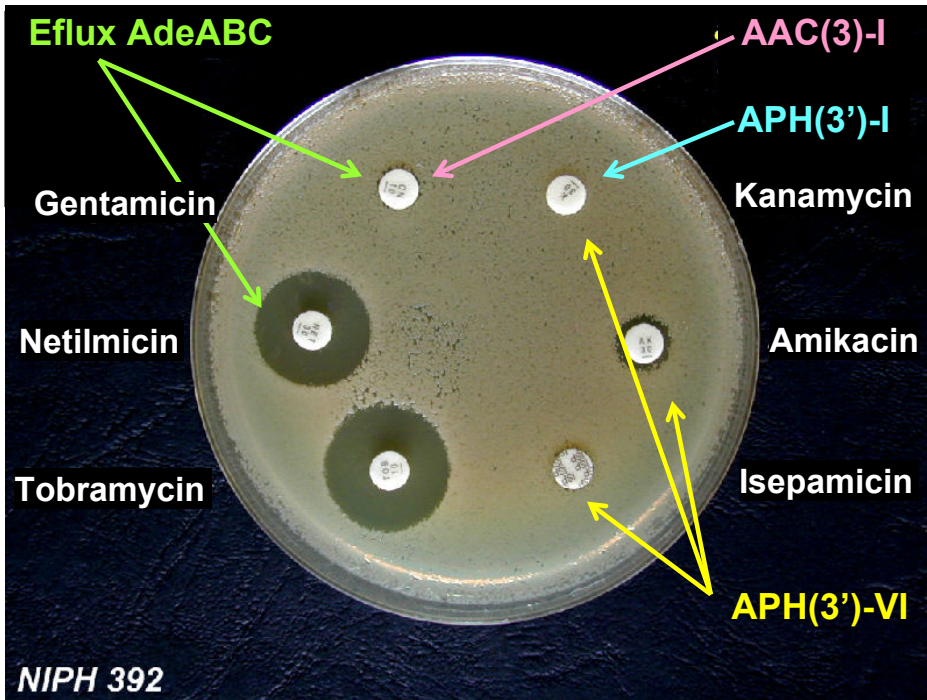


## 4. Kanamycin resistance: gene for phosphotransferase APH(3')-I

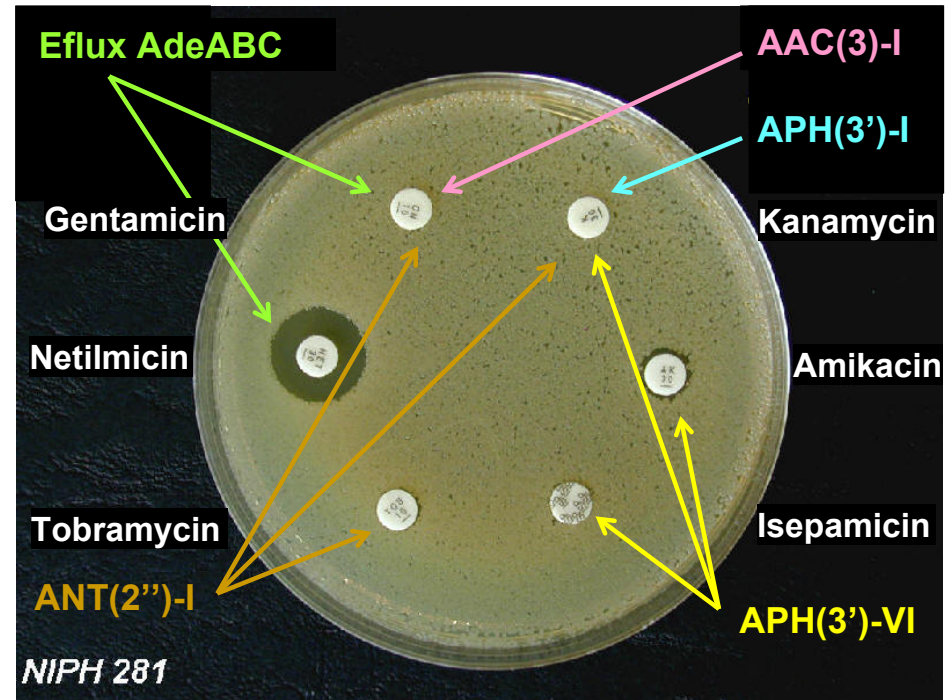


# Successive acquisition of genes: resistance to aminoglycosides

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



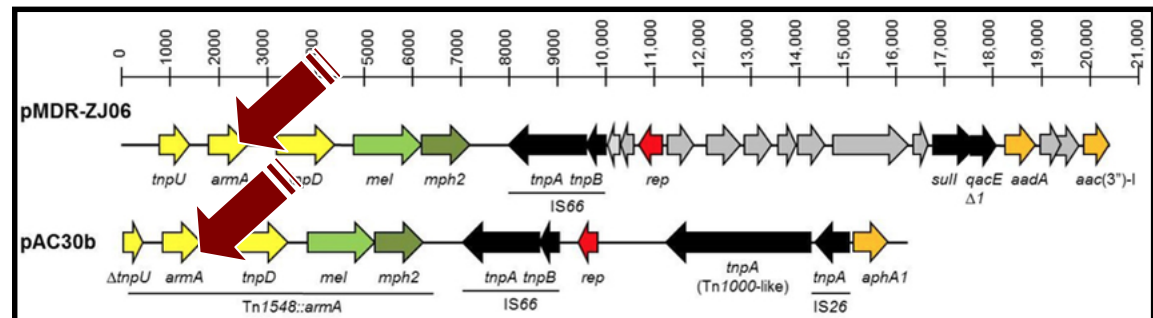
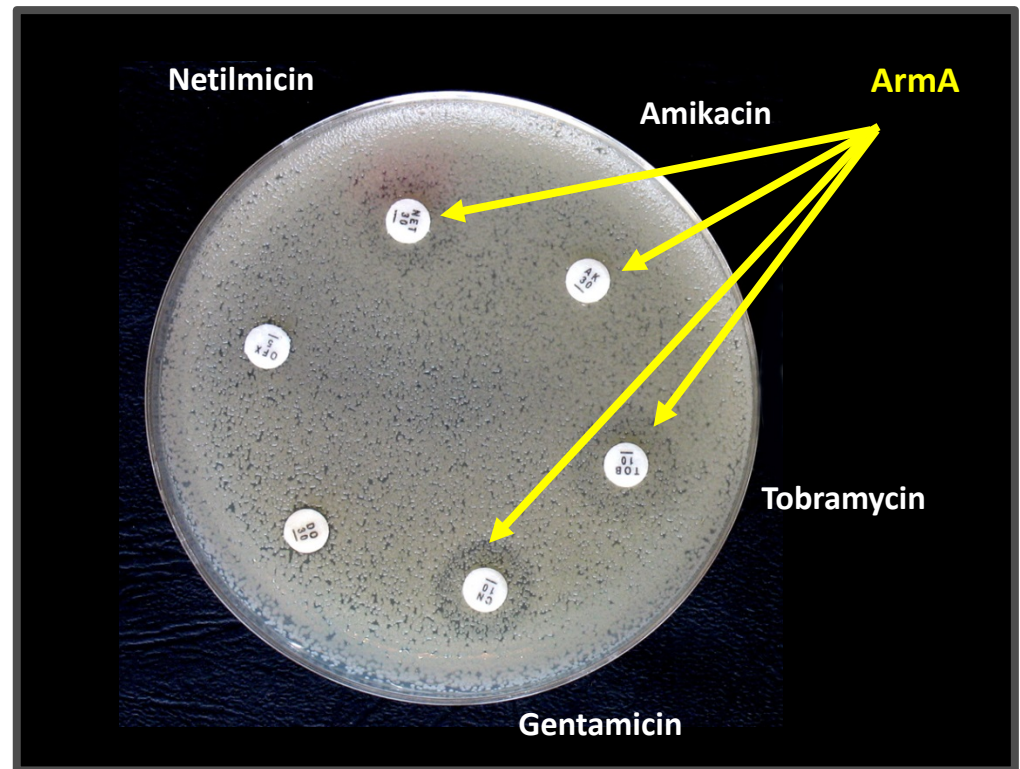
## 6. Tobramycin resistance: gene for nucleotidyltransferase ANT(2'')-I





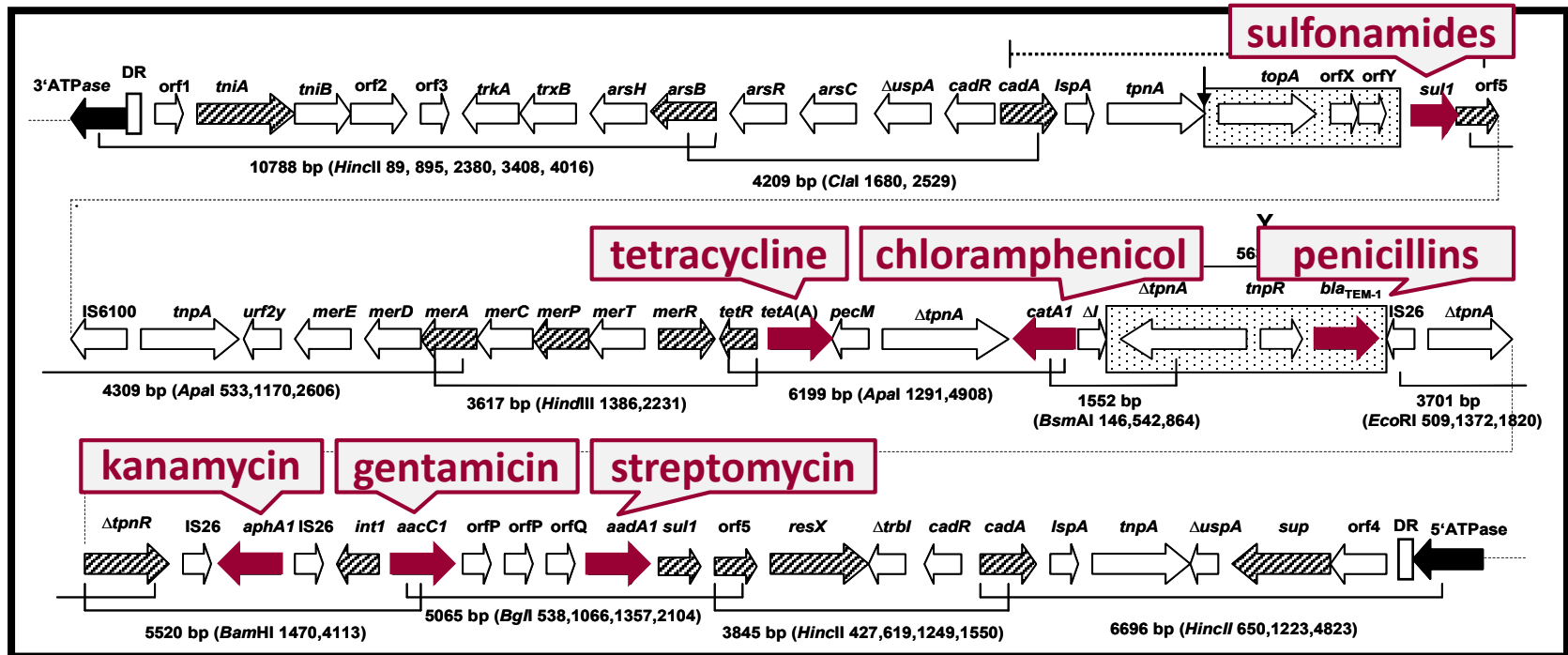
# One-step acquisition of pandrug resistance to aminoglycosides

- **ArmA** (16S rRNA m<sup>7</sup>G-methyltransferase) - **posttranscriptional methylation of rRNA** (modification of a target site)
- **Resistance to kanamycin, amikacin, gentamicin, netilmicin and tobramycin**
- **Carried by transposon Tn1548**





# Resistance genomic island

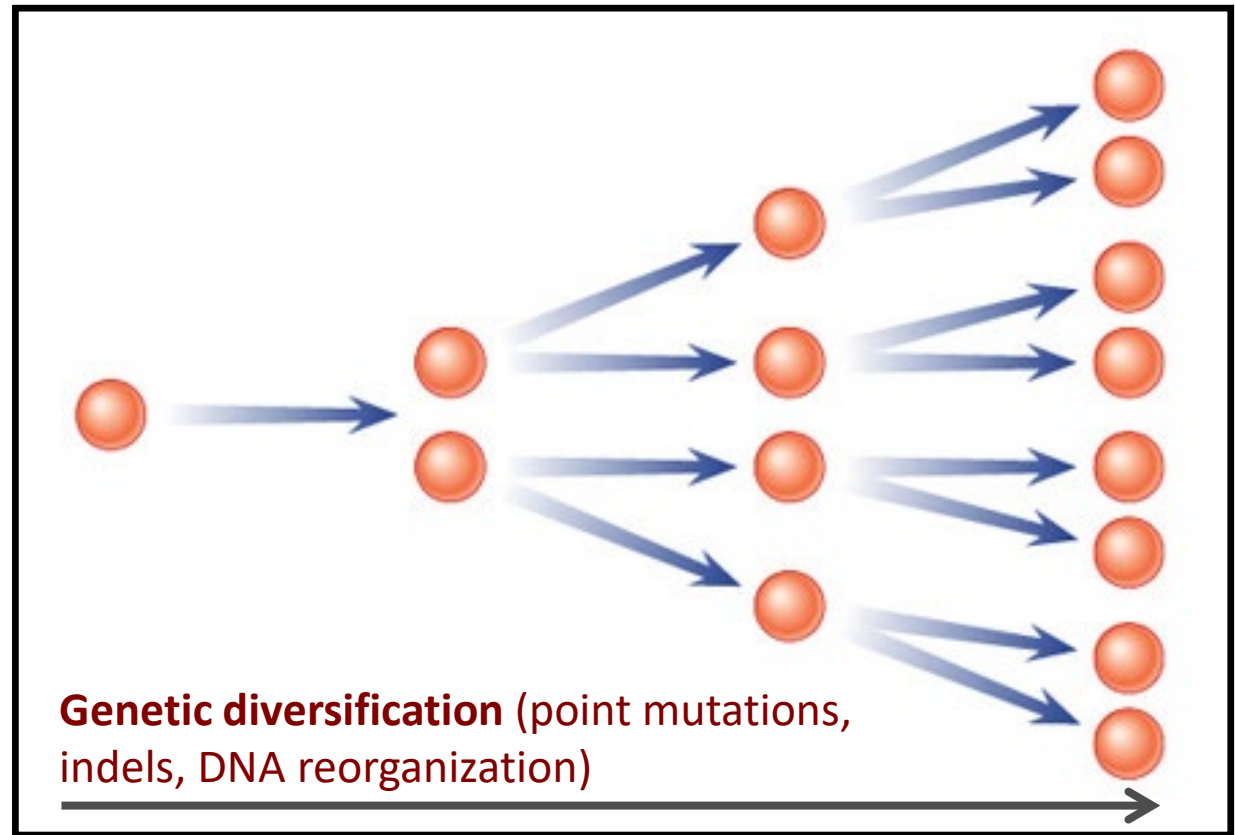
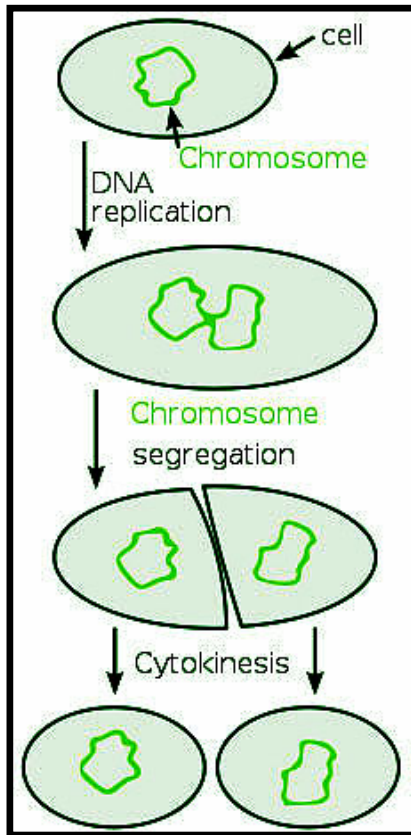


Krizova & Nemeč JAC 2010; 65: 1915

- Resistance genomic island **AbaR3** (63 kb) present in isolates of epidemic clone IC1 predominating in Europe in 1980–1990s
- Resistance to antibiotics widely used in 1970–1980s

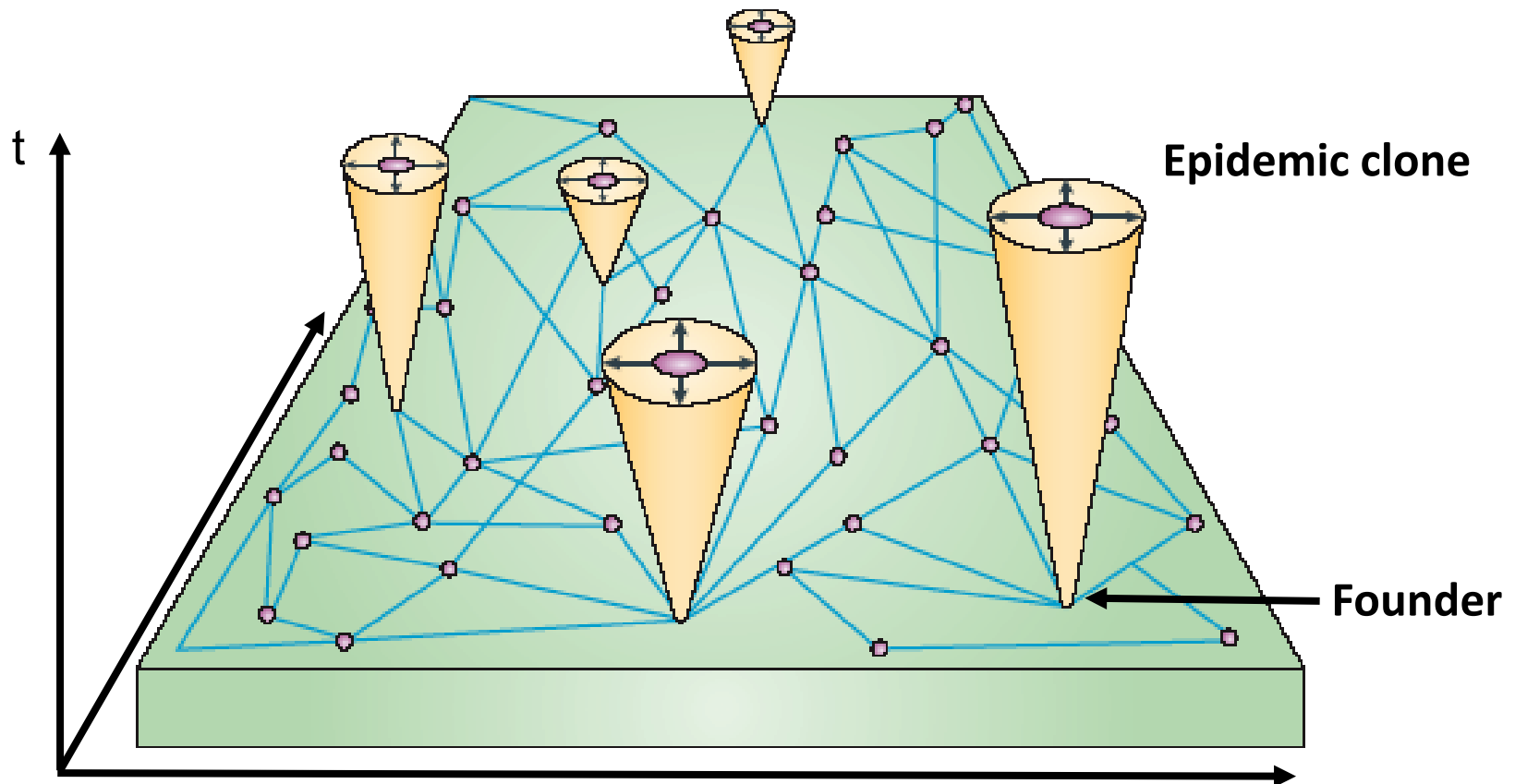
# Bacteria are haploid & clonal

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



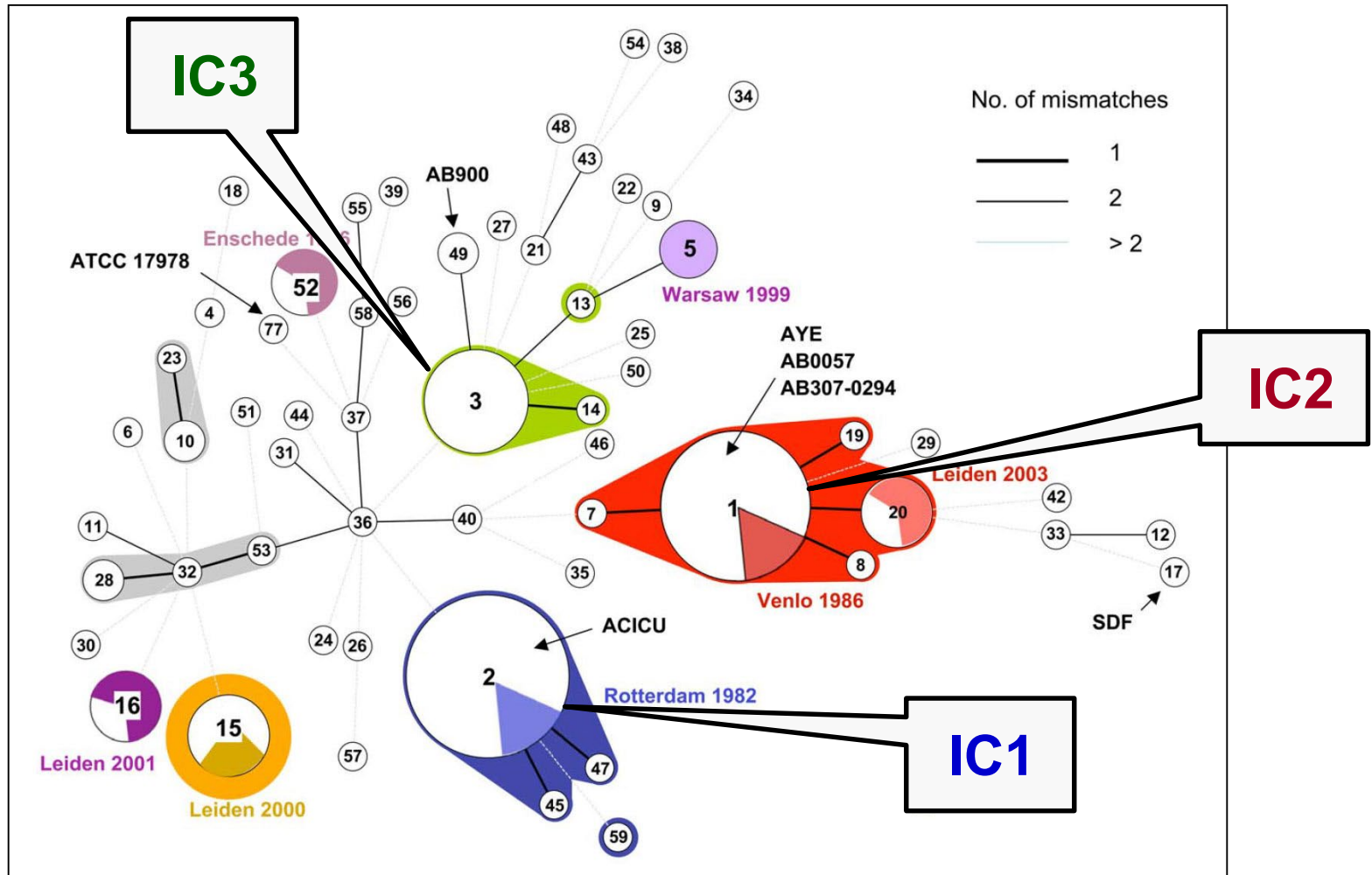
# Epidemic clone

- 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



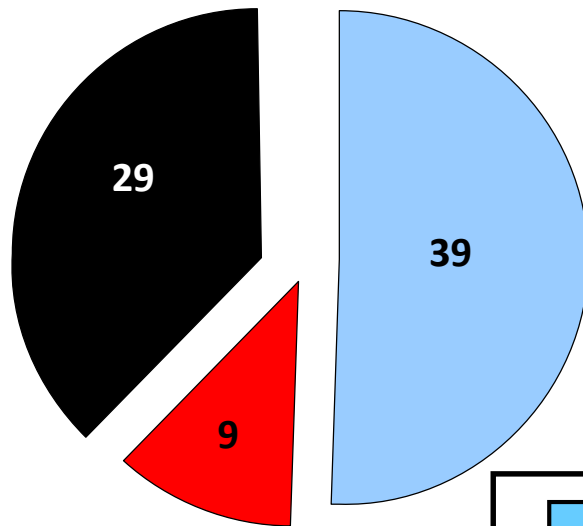
# International clones (IC) of *A. baumannii*

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

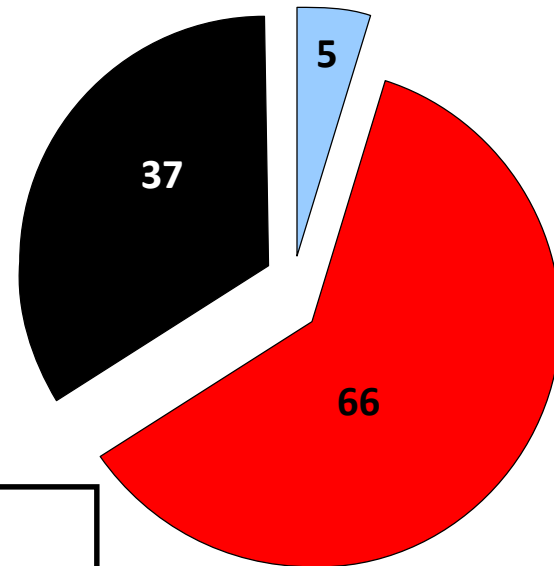


# *A. baumannii* populations in Czechia 1991–1997/2005–2006

1991–1997



2005–2006



■ IC1 (MDR)  
■ IC2 (MDR/XDR)  
■ Others (susceptible)

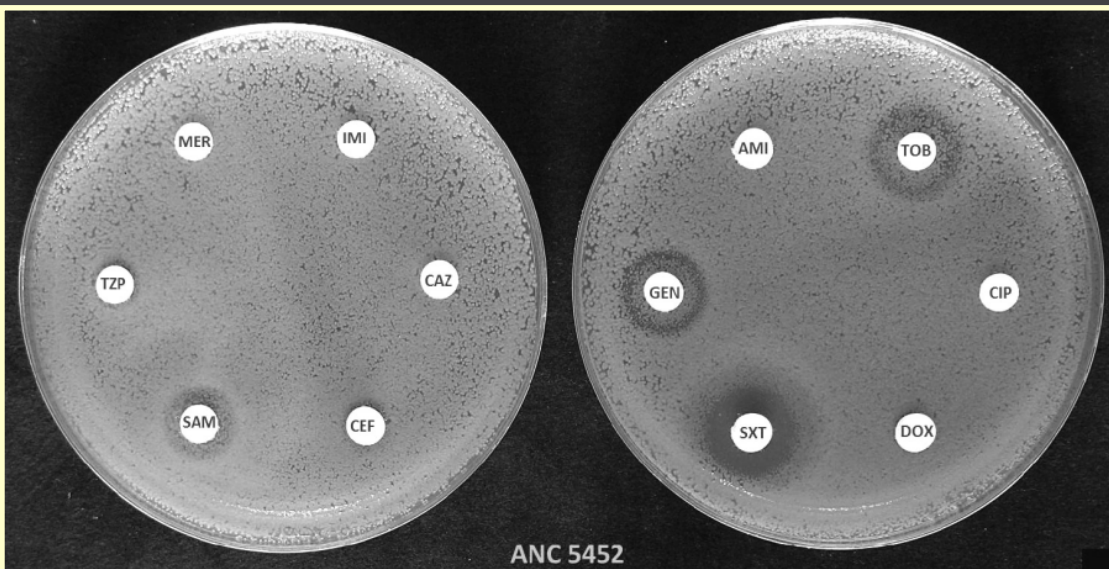
100%

Carbapenem susceptibility

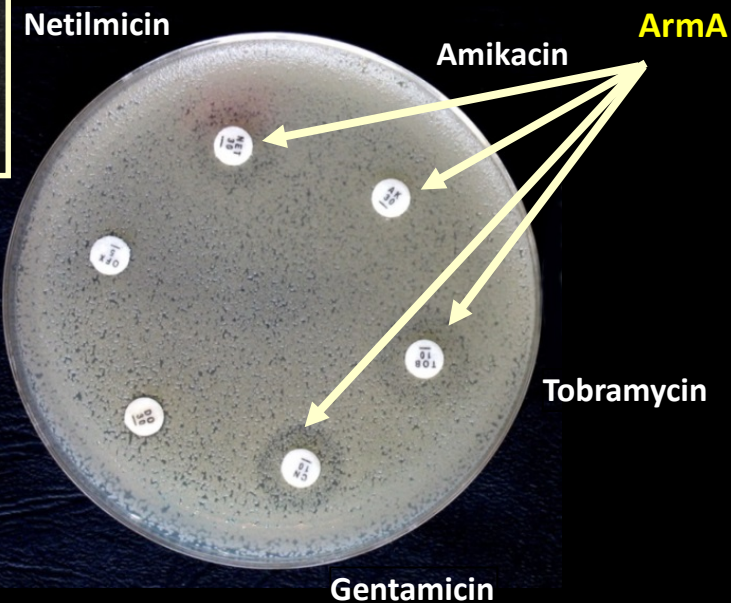
79%

# A. baumannii in Czechia since 2015

**IC2 subpopulaion** carrying the carbapenemase **OXA-23** and methylase **ArmA**, susceptible only to colistin



**Czechia 2015–2022:**  
**761 isolates from:**  
**25 cities**  
**38 hospitals**



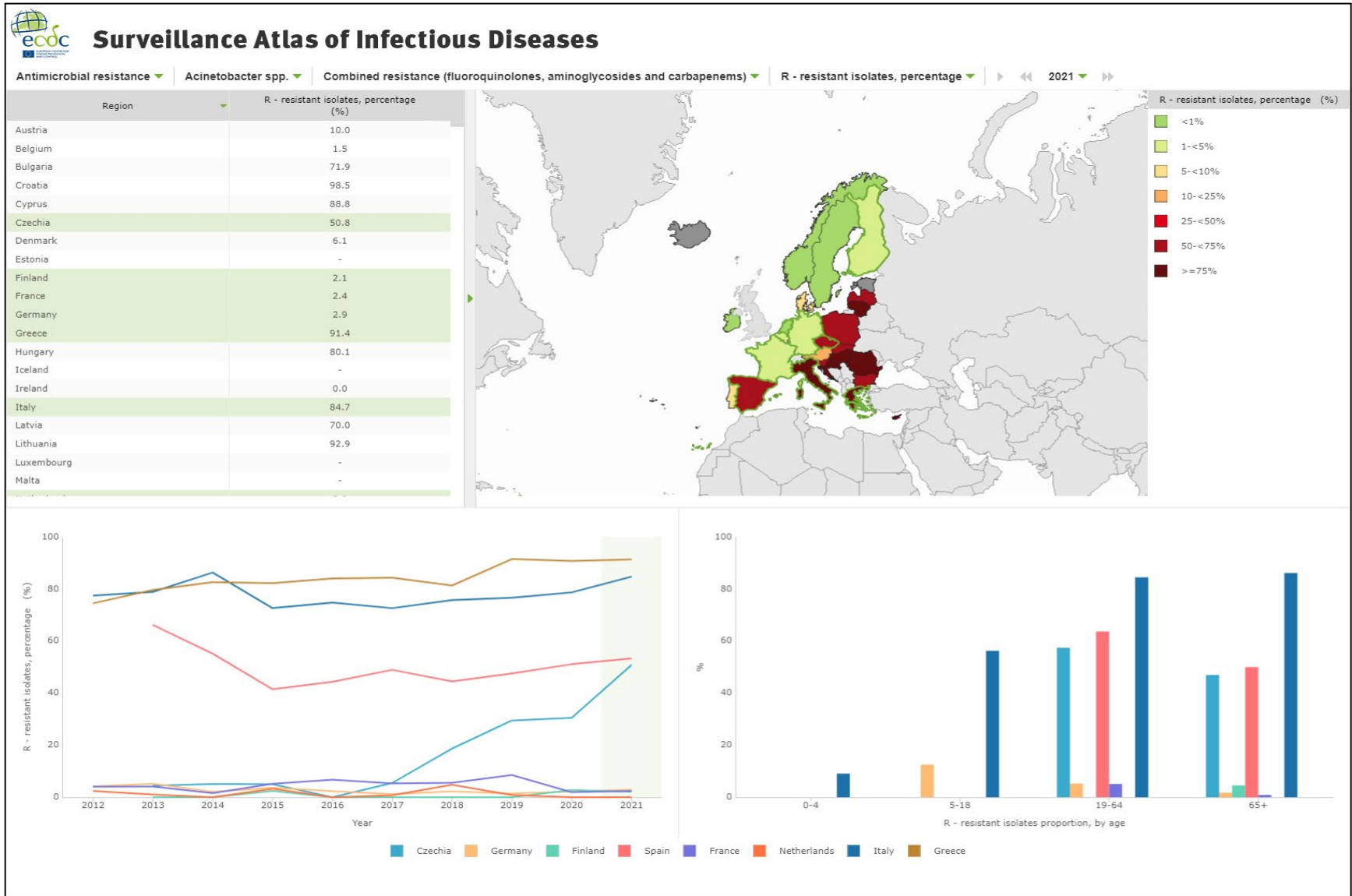
Extenzivně rezistentní kmeny *Acinetobacter baumannii* nesoucí geny pro karbapenemázu OXA-23 a metylázu ArmA v nemocnicích České republiky

Extensively drug-resistant *Acinetobacter baumannii* strains carrying genes encoding carbapenemase OXA-23 and methylase ArmA in hospitals of the Czech Republic



# EARS-Net *Acinetobacter* 2021

## Combined resistance to carbapenems, fluoroquinolones and aminoglycosides



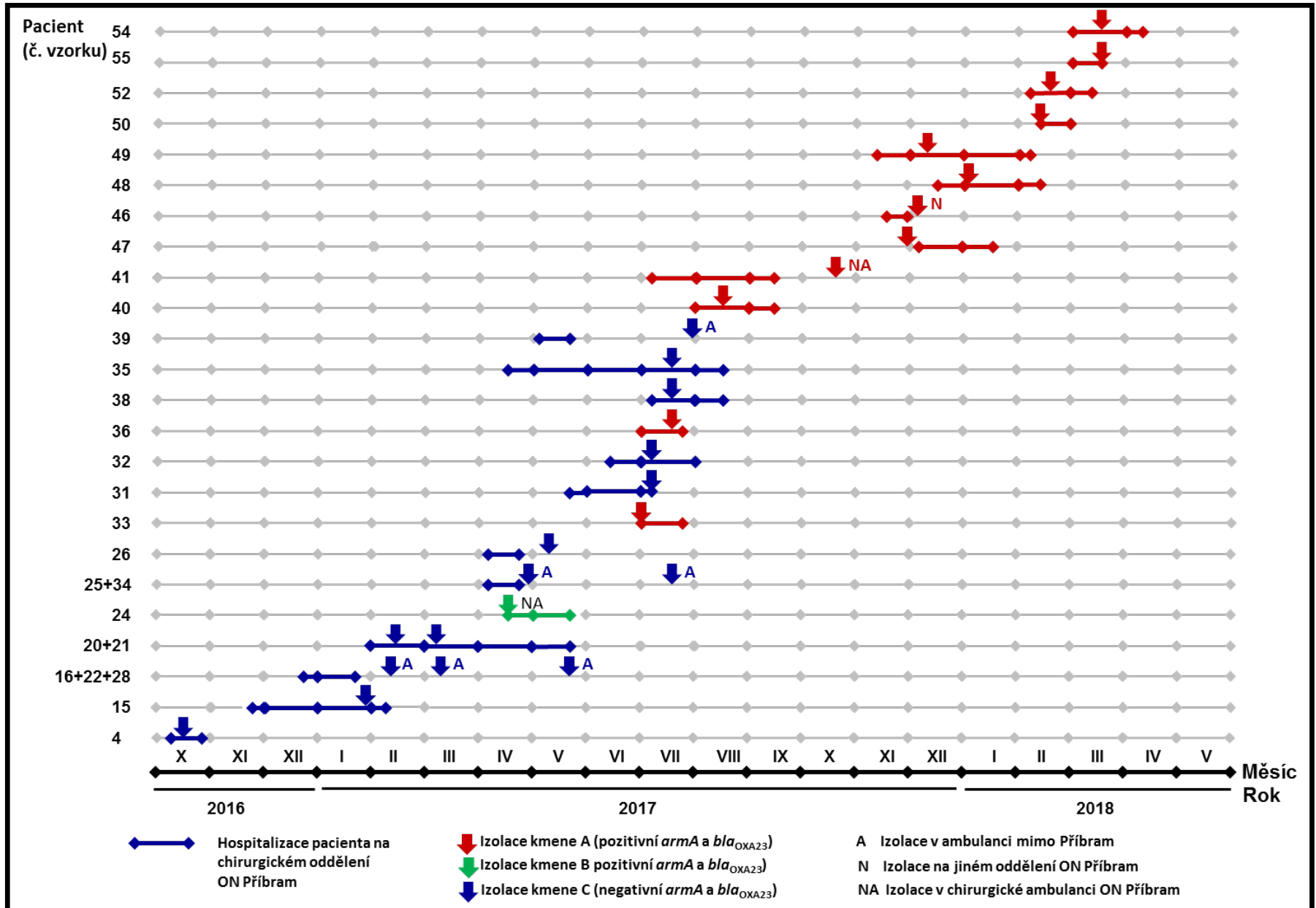


# Example of a hospital outbreak

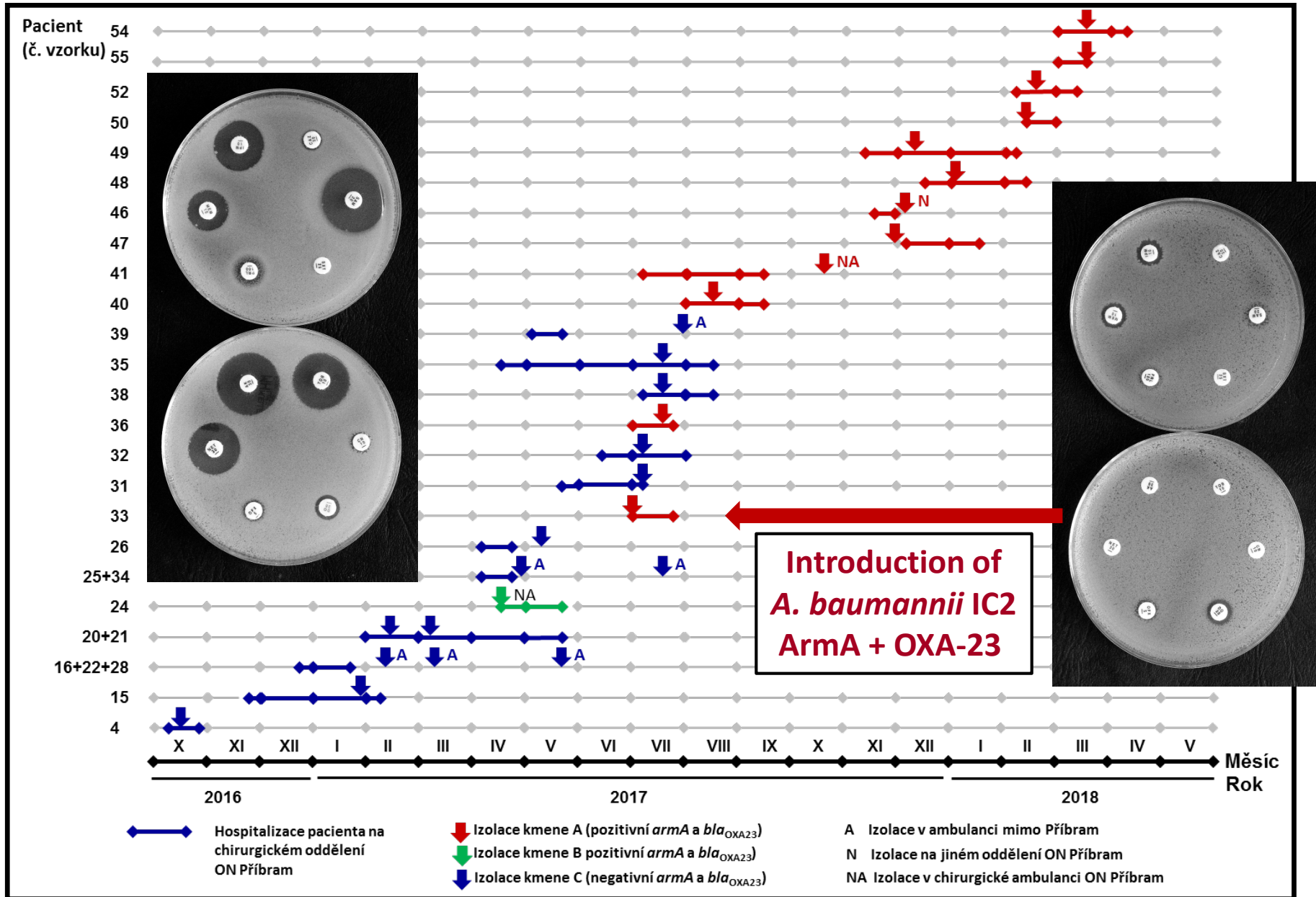
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- In 2016–2018, multiple isolates of MDR *A. baumannii* were recovered from patients hospitalized in a surgical unit of a regional hospital
- The isolates had different resistance profiles which were found in isolates from hospitalized patients or during their subsequent examinations at outpatients' departments
- Question: What is the genetic structure of the bacterial population? Were there one or more epidemic strains involved? Was it a monoclonal outbreak or more complex situation?

# Colonized/infected patients over time

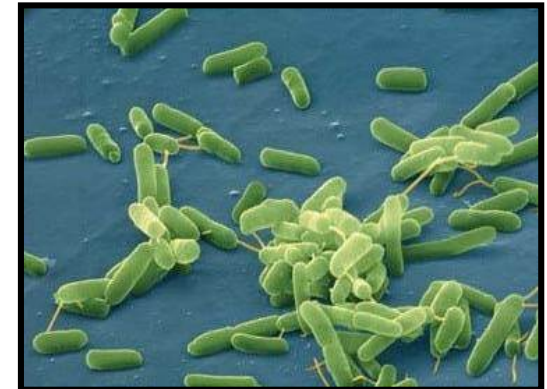
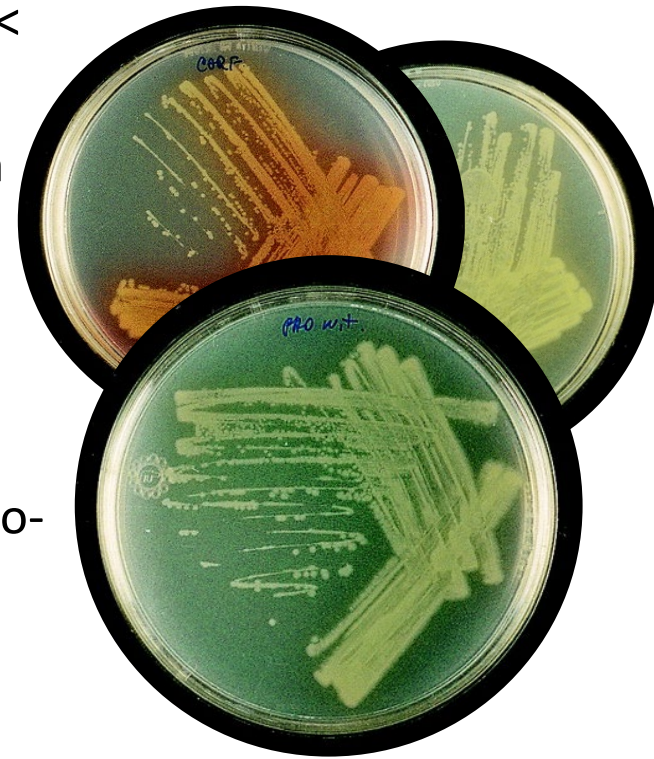


# Colonized/infected patients over time



# *Pseudomonas aeruginosa*

- **Taxonomy:** *Pseudomonadaceae* < *Pseudomonadales* < *Pseudomonadota*
- **Features:** aerobic/facultatively anaerobic (respiration of nitrate and fermentation of amino acids), oxidase- and catalase-positive, motile, pigments (pyocyanine, fluoresceine)
- **Habitat:** ubiquitous
- **Pathogenicity:** opport. pathogenic for immunocompromised/severely ill patients; rare community infections
- **Pathogenicity factors:**
  - Polysaccharidic capsule (alginate)
  - Exotoxin A (diphtheria toxin-like)
  - Pyocyanin (→ superoxide, peroxide, ciliary inhibition)
  - Exoenzymes S & T (→ epithelial actin)
  - Elastases LasA & LasB (→ elastin, IgG etc.)
  - Phospholipase C (hemolysin, → lecithin)
  - Alkaline protease
- **Epidemiology:** clonal spread/sporadic



# *P. aeruginosa* - HAI

- **Late ventilator-associated pneumonia**  
a major pathogen (also *A. baumannii* and enterobacteria)
- **Chronic pulmonary infections in cystic fibrosis (CF) patients**
- **Wound/burn infections**
- **Catheter-associated sepsis**  
often central venous catheters
- **Urinary tract infections**
- **Osteomyelitis**
- **Systemic infections in neutropenic patients**  
prognostically serious
- **Endoarteritis**
- **Ecthyma gangrenosum**  
disseminated infection leading to skin lesions (perivascular invasion)



Infected burn wound

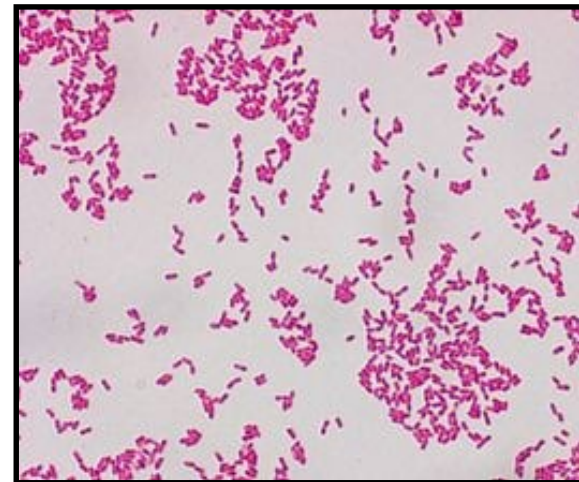


Ecthyma gangrenosum



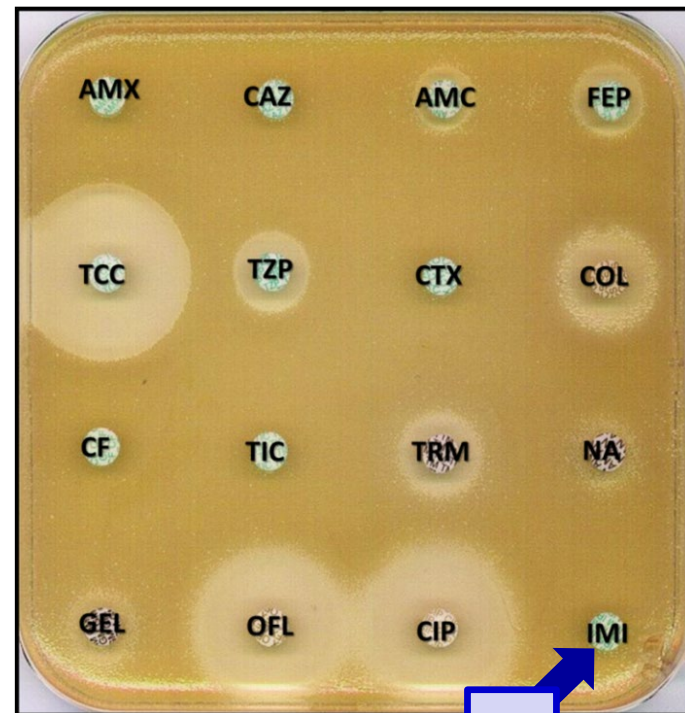
# *Burkholderia cenocepacia*

- **Taxonomy:** *Burkholderiaceae* < *Burkholderiales* < *Pseudomonadota*  
Belongs to the ***B. cepacia* complex** (≈20 species)
- **Features:** aerobic (microaerophilic), oxidase- and catalase-positive, motile with polar flagella
- **Genome:** 3 chromosomes + 1 plasmid
- **Habitat:** rhizosphere, plants (endophyte), soil, water, animals
- **Pathogenicity:** opport. pathogenic for immunocompromised patients - with CF, chronic granulomatous disease or mechanical ventilation  
**Cepacia syndrom** - necrotizing form of pneumonia/fulminant septicemia in ≈10% of CF patients
- **Primary resistance:** multidrug incl. aminoglycosides, colistin, 1st/2nd gen. cephalosporins, carboxypenicillins
- **Therapy:** co-trimoxazole, ceftazidime, meropenem,
- **Epidemiology:** possible clonal spread between patients



# *Stenotrophomonas maltophilia*

- **Taxonomy:** *Lysobacteraceae* < *Lysobacterales* < *Pseudomonadota*
- **Features:** strictly aerobic, oxidase-negative/weak, catalase-positive, motile with polar flagella
- **Habitat:** widespread in the environment
- **Pathogenicity:** opport. pathogenic for immunocompromised patients e.g. those requiring ventilatory support and **prolonged therapy with broad-spectrum antibiotics**
- **Primary resistance:** multidrug incl. carbapenems intrinsic metallo- $\beta$ -lactamase **L1** and cephalosporinase **L2**
- **Therapy:** co-trimoxazole, fluoroquinolones, minocycline, ceftazidime, ticarcillin+clavulanate
- **Epidemiology:** typically **non-clonal spread** (selection by broad-spectrum antibiotics)



L1

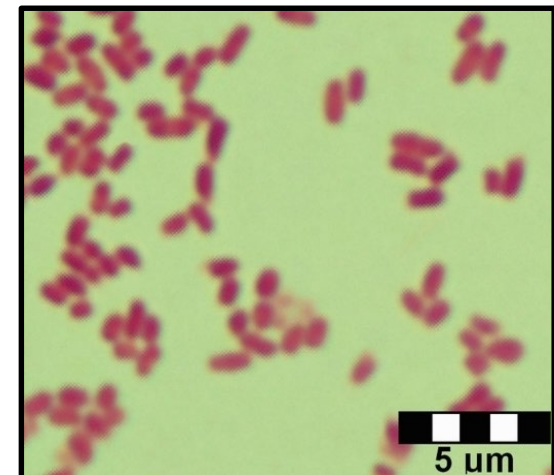
# Lecture structure - Enterobacteria

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- General features
- Nonfermentative Gram-negative bacilli (NFGNB)
- **Enterobacteria**
  - Common characteristics
  - Cellular components and pathogenicity factors
  - *Escherichia coli* & *Shigella*
  - *Salmonella*
  - Others

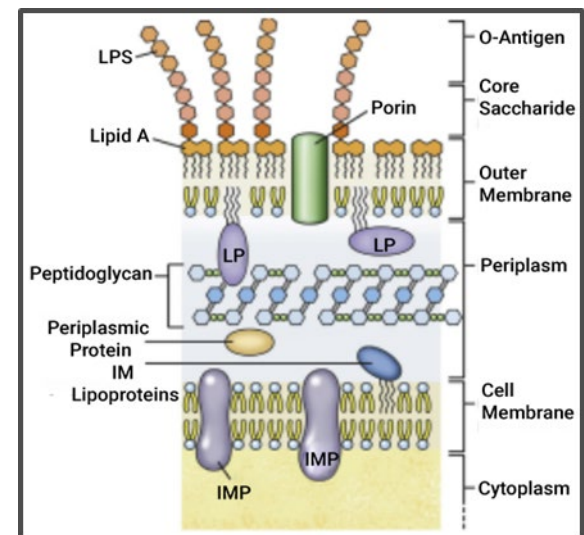
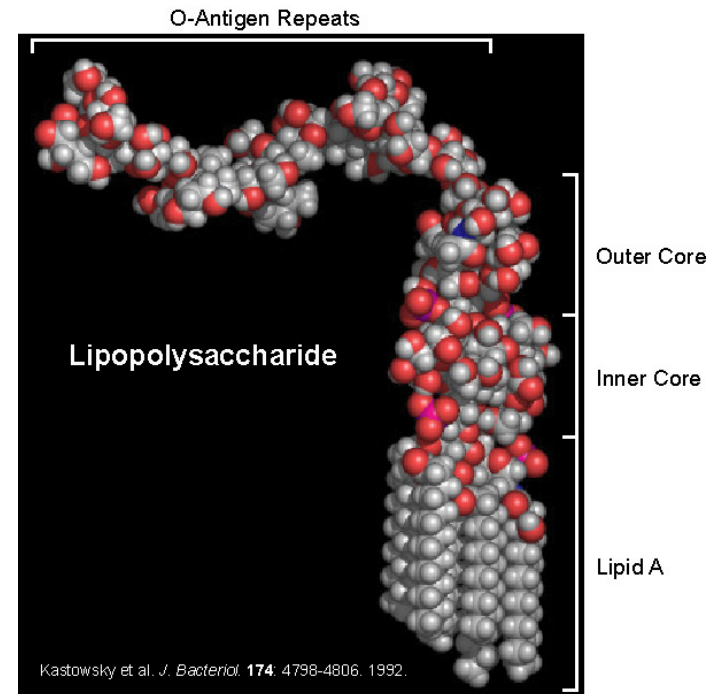
# Enterobacteria (order *Enterobacteriales*)

- **Taxonomy:** *Enterobacteriales* < *Gamaproteobacteria*  
the largest group of medically important Bacteria  
with **7 families, 77 genera** and **>300 species**
  - *Enterobacteriaceae* (*Enterobacter*, *Escherichia*, *Klebsiella*, *Salmonella*, *Shigella*)
  - *Morganellaceae* (*Proteus*, *Morganella*)
  - *Yersiniaceae* (*Yersinia*, *Serratia*)
- **Features:**
  - facultatively anaerobic (glycolysis, aerobic and anaerobic respiration)
  - oxidase-negative, catalase-positive
  - mostly motile by peritrichous flagella
- **Antibiotic susceptibility:**
  - primarily well susceptible
  - acquired resistance to multiple drugs of most main antimicrobial classes



# Cell components & virulence factors

- **Lipopolysaccharide (LPS)** is the major cell wall antigen with **3 components**:
  - **O polysaccharide** (somatic **O antigen**) strain-dependent, useful for epidemiologic classification of strains
  - **Core polysaccharide** common antigen of enterobacteria
  - **Lipid A (endotoxin)** **major pathogenicity factor** released by cell lysis and responsible for **systemic manifestations** initiated by complement activation - release of cytokines, leukocytosis, thrombocytopenia, disseminated intravascular coagulation, fever, decreased peripheral circulation, shock
- **Polysaccharide capsule (K antigen)** protection from phagocytosis







# Habitat and epidemiology

## ■ Habitat

- widespread in nature (opport. pathogenic/non-pathogenic spp.): soil, water, and plants;
- normal intestinal flora of animals and humans
- a few (primary pathogenic) are restricted to humans
- extraintestinal colonization (infections) in hospitalized patients

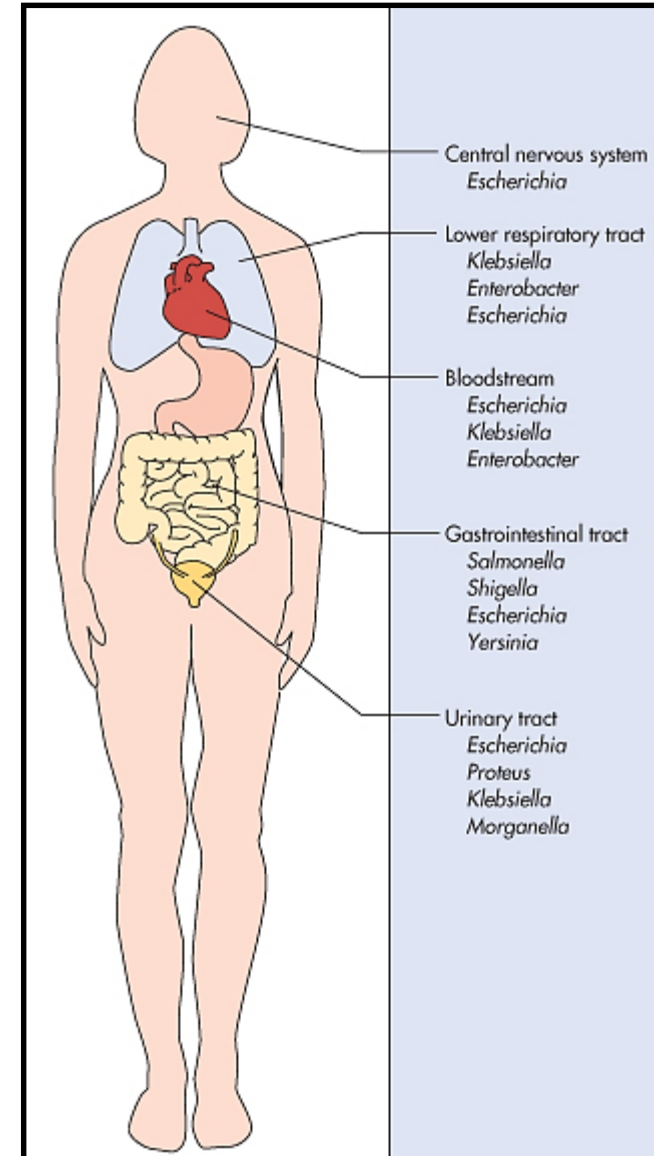
■ **Pathogenicity:** opportunistic/primary pathogenic, non-pathogenic

## ■ Infections

### • Community infections

- urinary tract infections
- gastrointestinal tract infections
- hemolytic uremic syndrome

### • HAI

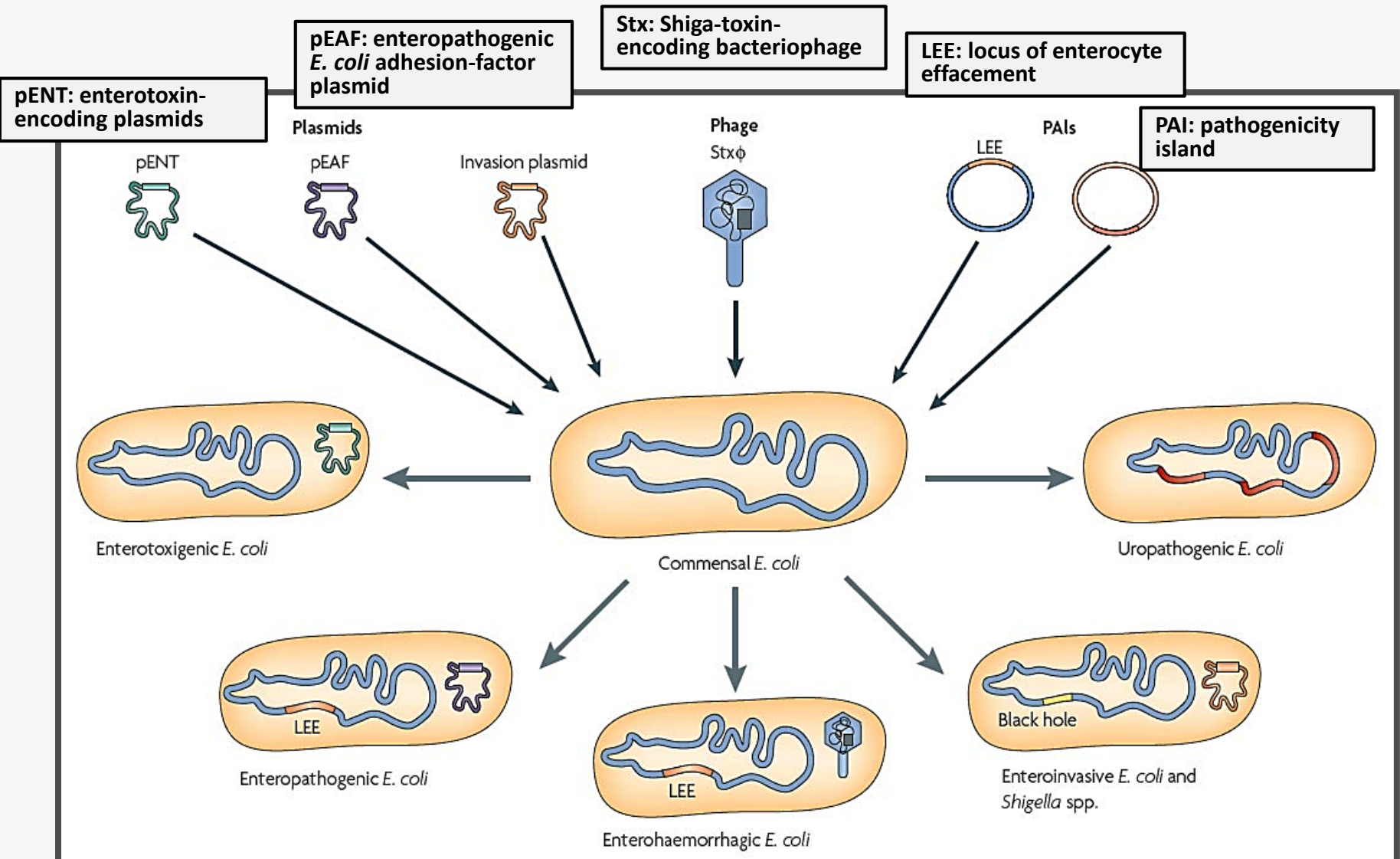


# *Escherichia coli*

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- **One of the most studied microorganisms**
- Discovered by T. Escherich in the feces of healthy individuals in 1885
- **Natural habitat:** intestine of humans and warm-blooded animals (a commensal)
- **Gastrointestinal infections** caused by various pathovars of *E. coli* with acquired pathogenicity factors:
  - **enterotoxigenic (ETEC)**      watery diarrhea (infants, travelers)
  - **enteropathogenic (EPEC)**      watery diarrhea (infants)
  - **enteroaggregative (EAEC)**      watery diarrhea (infants, travelers)
  - **enteroinvasive (EIEC)**      watery diarrhea > dysentery
  - **enterohemorrhagic (EHEC)**      watery diarrhea > hemorrhagic colitis >  
> **hemolytic uremic syndrome**
- **Community extraintestinal infections**
  - **uropathogenic (UPEC)**      80% of all community urinary tract infections
  - *E. coli* K1      neonatal meningitis
- **HAI**

# Pathovars of *E. coli*



# Shigella

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- **Taxonomy:** conspecific with *E. coli* according to the current classification criteria, but four *Shigella* species names have been conserved (*nomina conservanda*)
- **Infections:**
  - *S. sonnei* (predominates in developed countries), *S. flexneri* (in developing countries), and *S. boydii* cause gastroenteritis (**shigellosis**), an initial watery diarrhea progressing within 1-2 days to abdominal cramps and tenesmus (possible bloody stools)  
pathogenicity corresponding to EIEC
  - *S. dysenteriae* produces **Shiga toxin** (like in EHEC) > severe form of disease (**bacterial dysentery**)
- **Epidemiology:** humans - the only reservoir; spread person-to-person by fecal-oral route; relatively few organisms (~200) produce disease
- **Treatment:** empiric therapy with fluoroquinolones or co-trimoxazole shortens the course of symptomatic disease and fecal shedding



# Salmonella

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- **Taxonomy:** single species *Salmonella enterica* with >2500 serovars (serotypes)
- **Nomenclature (example):** *Salmonella enterica* subspecies *enterica* serovar Typhi (abbreviated as *Salmonella* Typhi)
- **Infections:**
  - **S. Typhi: enteric fever** (typhoid fever) – clinically the most serious, systemic disease; bacteria pass through the cells lining the intestines being engulfed by macrophages and transported to the liver, spleen and bone marrow; 10–14 days after ingestion of the bacteria, gradually increasing fever, with nonspecific complaints of headache, myalgias, malaise, and anorexia, followed by gastrointestinal symptoms
  - **S. Paratyphi A, S. Schottmuelleri** (Paratyphi B), and **S. Hirschfeldii** (Paratyphi C): a milder form of enteric fever („para-typhoid fever“)
  - **Other serovars: enteritis** (fever, nausea, vomiting, bloody or nonbloody diarrhea, abdominal cramps), 6–48 hours after consumption of contaminated food or water. Fever, myalgias and headache are common. Symptoms persist 2–7 days before spontaneous resolution.

# Salmonella

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- **Infections:**

- **All salmonellae:** can cause **septicemia** (most commonly associated with *S. Typhi*, *S. Paratyphi*, and *S. Choleraesuis*)
- ***S. Typhi* and *S. Paratyphi*:** chronic **asymptomatic colonization** after symptomatic disease develops in 1–5% of patients (gallbladder as a reservoir)

- **Treatment:** **antibiotic treatment not recommended for enteritis** (may prolong the duration of disease);  
**infections with *S. Typhi* and *S. Paratyphi* or disseminated infections with other serovars should be treated** with fluoroquinolones, chloramphenicol, cotrimoxazole or broad-spectrum cephalosporins

- **Epidemiology:** mostly acquired by eating contaminated food products;  
***S. Typhi* and *S. Paratyphi* are strict human pathogens** (no other reservoirs); these infections are passed person-to-person; asymptomatic long-term colonization occurs

# Other important enterobacteria

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## ■ *Yersinia*:

- *Y. pestis*: causes **bubonic** (most common) and **pulmonary plague**, with a high mortality rate; a zoonosis with rodents as natural reservoirs and humans as accidental hosts; the disease is spread by flea bites or direct contact with infected tissues or person to person by inhalation of infectious aerosols from a patient with pulmonary disease
- Taxonomically, *Y. pestis* is a pathovar of *Y. pseudotuberculosis*
- *Y. pseudotuberculosis* and *Y. enterocolitica*: **gastroenteritis** (acute watery or chronic diarrhea)

## ■ *Klebsiella*: capsule responsible for mucoid colonies and virulence

- *K. pneumoniae*: one of the most important HAI pathogens associated with extensive antimicrobial resistance (**pneumonia**, wound, soft-tissue or urinary tract infections)
- Community- or hospital-acquired primary lobar pneumonia (necrotic destruction of alveoli, formation of cavities, production of bloody sputum)

## ■ *Proteus*, *Morganella*, *Enterobacter*, *Citrobacter*, *Serratia* (HAI, UTIs etc.)