

Komerčiālo slimību novērtējums  
Latvijas zivjaudzētavās  
**Antimikrobiālā rezistence**



Olga Revina  
olga.revina@bior.lv  
BIOR, Zivju audzētava Pelči,  
Veterinārārste/pētniece

# Antimikrobiālā rezistence (AMR)

ir baktēriju noturība pret tādiem antimikrobiālajiem līdzekļiem, pret kuriem tās iepriekš bija jutīgas.

- Antimikrobiālā rezistence (AMR) 2020. gadā Eiropā izraisīja aptuveni **100 nāves gadījumus dienā** (>35 000 gadā).
- Bez efektīviem ierobežošanas pasākumiem līdz **2050. gadam** AMR varētu izraisīt līdz **10 miljoniem nāves gadījumu gadā pasaulē**.

## Fatal sepsis due to community-associated methicillin-resistant *Staphylococcus aureus* – a case report

Sepsis fatal datorat infecției cu *Staphylococcus aureus* metilicilino - rezistent comunitar - prezentare de caz

Edit Székely<sup>1,2</sup>, Liviu Sorin Enache<sup>1</sup>, Simona Marinescu<sup>2</sup>, Erika Ungvári<sup>3</sup>, Ákos Tóth<sup>3</sup>, Judit Pászti<sup>3</sup>

1. University of Medicine and Pharmacy Tg Mures, Romania  
2. Tg Mures County Emergency Clinical Hospital, Romania  
3. National Center for Epidemiology, Budapest, Hungary

### Abstract

We present the case of a community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infection, which led to a rapidly evolving fatal sepsis with necrotizing pneumonia in a four-year-old girl. The patient was admitted to the Mures County Emergency Clinical Hospital at 7:50 a.m. on the 15<sup>th</sup> of March 2007. A few days before presentation the girl had suffered a minor trauma of her left heel. According to clinical, biochemical and radiological findings, septic shock with cutaneous origin, cellulitis of the left heel and bilateral pneumonia were diagnosed. She received intravenous fluid resuscitation and large spectrum antibiotic therapy was started. Later that day, the patient's condition deteriorated and she went on a cardiorespiratory stop and died at 03:25 p.m. On autopsy, bilateral necrotizing pneumonia was documented. MRSA was isolated from blood cultures. Based on epidemiological data and on phenotypical and molecular characterization, the strain was found to be a CA-MRSA harboring SCCmec type IV and Panton-Valentine leukocidin genes which belonged to spa type t044. This was the first and so far only case of fatal sepsis occurring in our hospital due to CA-MRSA strain confirmed by means of molecular techniques. The dramatic rapidity of its evolution represents a major concern and demonstrates the extreme virulence and harming capacity of this type of CA-MRSA.

**Keywords:** pneumonia, Panton-Valentine leukocidin, bacterial typing

## Four Pediatric Deaths from Community-Acquired Methicillin-Resistant *Staphylococcus aureus* -- Minnesota and North Dakota, 1997-1999

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an emerging community-acquired pathogen among patients without established risk factors for MRSA infection (e.g., recent hospitalization, recent surgery, residence in a long-term-care facility [LTCF], or injecting-drug use [IDU]) (1). Since 1996, the Minnesota Department of Health (MDH) and the Indian Health Service (IHS) have investigated cases of community-acquired MRSA infection in patients without established risk factors. This report describes four fatal cases among children with community-acquired MRSA; the MRSA strains isolated from these patients appear to be different from nosocomial MRSA strains in antimicrobial susceptibility patterns and pulsed-field gel electrophoresis (PFGE) characteristics.

### Case Reports

**Case 1.** In July 1997, a 7-year-old black girl from urban Minnesota was admitted to a tertiary-care hospital with a temperature of 103 F (39.5 C) and right groin pain. An infected right hip joint was diagnosed; she underwent surgical drainage and was treated with cefazolin. On the third day of her hospital stay, antimicrobial therapy was changed to vancomycin when cultures of blood and joint fluid grew MRSA. The same day patient had another hip drainage procedure, but had respiratory failure and was placed on mechanical ventilation. Her course was complicated by acute respiratory distress syndrome, pneumonia, and an empyema that required chest tube drainage. She died from a pulmonary hemorrhage after 5 weeks of hospitalization.

MRSA isolated from her blood, hip joint, and sputum was susceptible to multiple antibiotic classes (Table 1). An autopsy revealed bilateral bronchopneumonia with abscesses. The patient was previously healthy without recent hospitalizations. No family members resided in LTCFs or worked in health-care settings.

**Case 2.** In January 1998, a 16-month-old American Indian girl from rural North Dakota was taken to a local hospital in shock and with a temperature of 105.2 F (40.6 C), seizures, a diffuse petechial rash, and irritability. She was treated with ceftriaxone but developed respiratory failure and cardiac arrest and died within 2 hours of arriving at the hospital. Blood and cerebrospinal fluid cultures drawn immediately postmortem grew MRSA that was susceptible to multiple antibiotic classes (Table 1). An autopsy revealed multiple small abscesses of the brain, heart, liver, and kidneys; autopsy cultures of meninges, blood, and lung tissue grew MRSA. One year earlier, the patient had been treated with amoxicillin for otitis media. Neither the patient nor family members had been hospitalized during the previous year; no family members resided in LTCFs or worked in health-care settings.

**Case 3.** In January 1999, a 13-year-old white girl from rural Minnesota was brought to a local hospital with fever, hemoptysis, and respiratory distress. The day before admission she had a productive cough and a 2-cm papule on her lower lip. A chest radiograph revealed a left lower lobe infiltrate and a pleural effusion. She was treated with ceftriaxone and nafcillin. Within 5 hours of arriving at the hospital, she became hypotensive and was transferred to a pediatric hospital, intubated, and treated with vancomycin and cefotaxime. Despite pulmonary and hemodynamic support, the patient's respiratory status deteriorated, and she died on the seventh day from progressive cerebral edema and multiorgan failure.

The patient's blood, sputum, and pleural fluid grew MRSA that was multidrug susceptible (Table 1). An autopsy revealed consolidated hemorrhagic necrosis of the left lung. The patient had no chronic medical conditions and no recent hospitalizations; no family members were health-care workers or employees of an LTCF or had a history of IDU.

### The case

In October 2004 a young mother with mastitis suffering from high fevers (> 39°C), general malaise, and pleural effusions, was admitted to our hospital. Cultures taken at her GP's office unexpectedly revealed MRSA. The patient recovered quickly after treatment with teicoplanin. When repeated attempts to eradicate her MRSA carriage failed, her family was screened for MRSA. The father and the baby daughter were found to be MRSA positive. Six months later, the baby girl was admitted with an acute pneumococcal infection. Due to the history of MRSA, the baby was isolated and screened on admission. While initial screening cultures were negative, follow-up cultures during antibiotic treatment revealed MRSA. At this point all family members were re-screened and the parents were found to still carry MRSA. The source of MRSA remained unclear. As animals have been described as a source of MRSA and the father was a pig-farmer, we decided to screen his pigs. Furthermore, three co-workers on the farm were screened.

# VIENA VESELĪBA

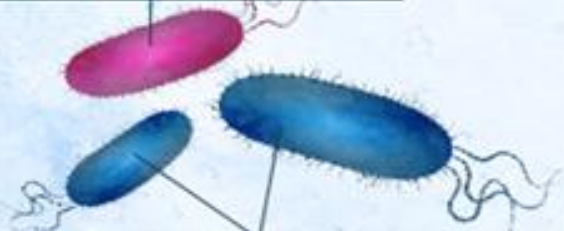


- Antimikrobiālā rezistence nav tikai cilvēku veselības problēma.
- Rezistences gēni cirkulē vidē, dzīvniekos un pārtikas ķēdē, un var nonākt arī pie cilvēka.
- Tādēļ AMR ir jāvērtē **Vienas veselības (One Health) pieejā**, kur cilvēka, dzīvnieku un vides veselība ir cieši savstarpēji saistīta.

# Kādā veidā baktērijas to panāc

Rezistentā baktērija

Mutācija



Jutīgas (uzņēmīgas) baktērijas

Antibiotikas

Replīcējoties, dažas baktērijas mutē, kā rezultātā tās kļūst nejutīgas pret AB

Pēc mutācijas rezistentas baktērijas spēj izdzīvot

Rezistentas baktērijas turpina vairoties, neskatoties uz AB lietošanu

Horizontālā gēnu nodošana = gēnu apmaiņu starp baktērijām



Nodod AB rezistences gēnu

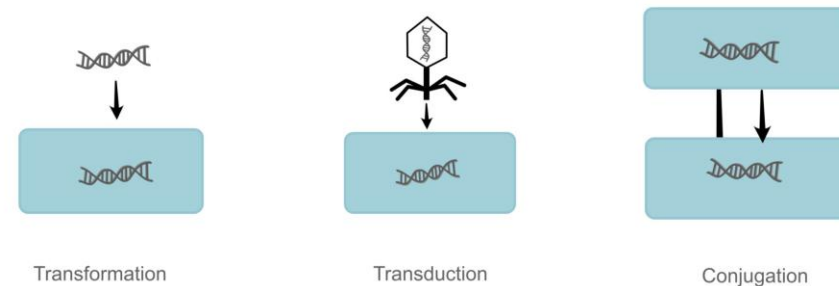
AB rezistences ģenētiskā informācija tiek nodota arī citām baktēriju sugām, ģintīm

Transformācija – DNS uzņemšana no vides (retāk, atkarīga no apstākļiem).

Transdukcija – pārnese ar bakteriofāgiem (mazāk prognozējama).

Konjugācija –  galvenais AMR izplatības mehānisms.

## Horizontal Gene Transfer



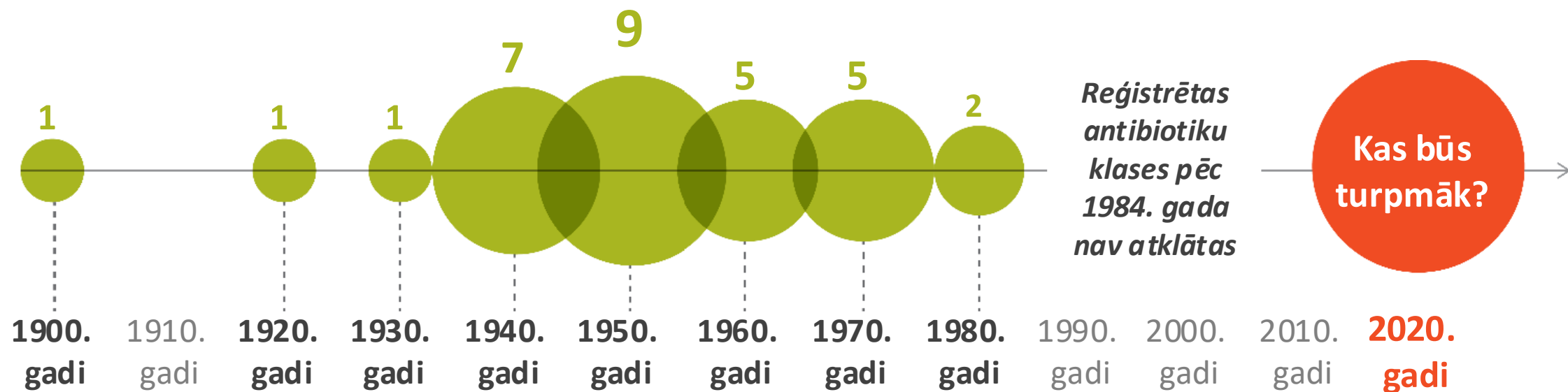
Transformation

Transduction

Conjugation

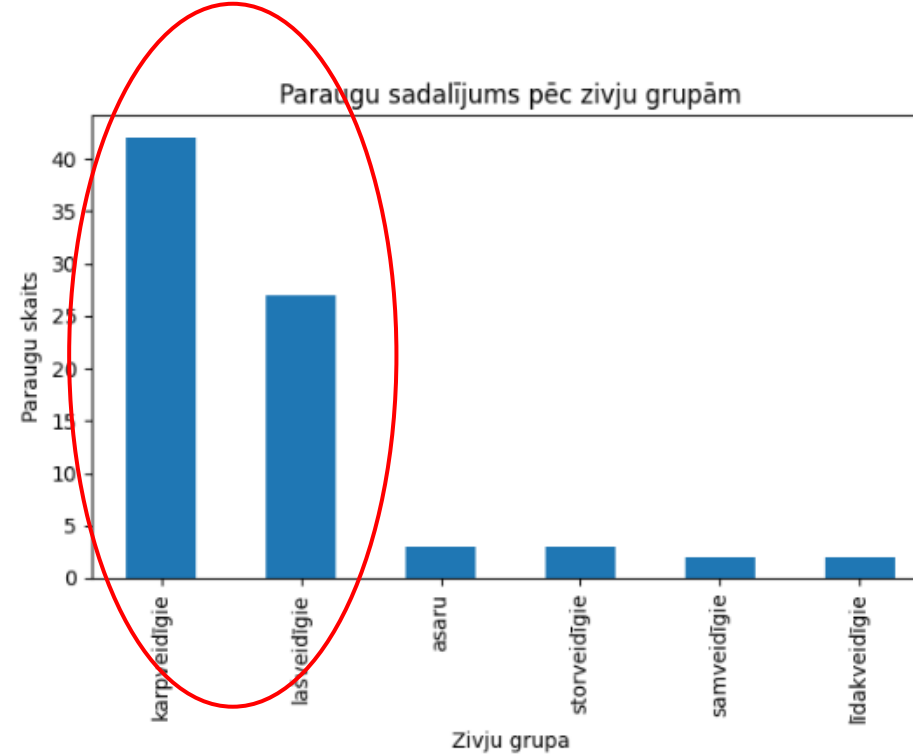
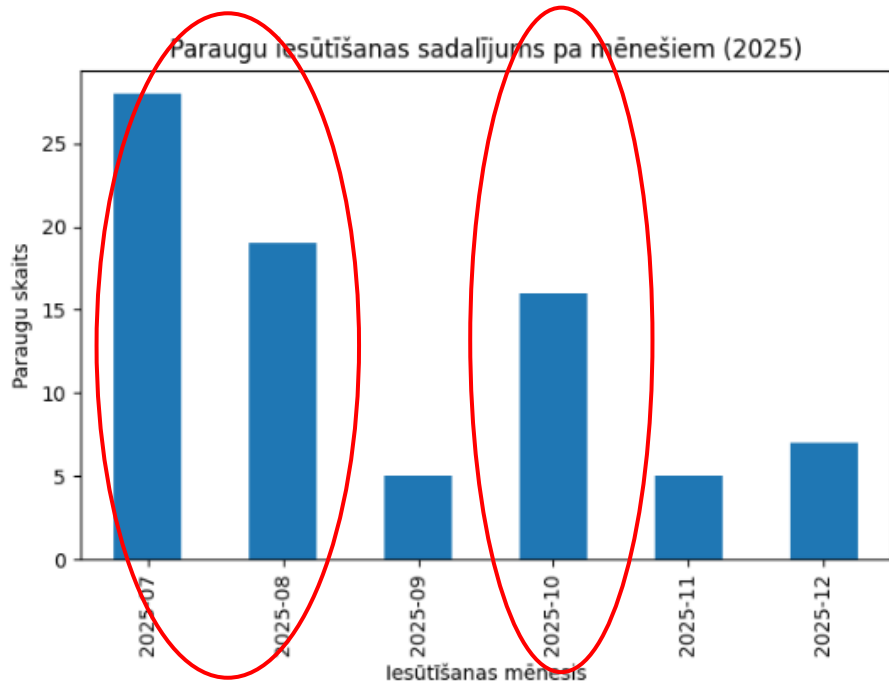
## Jauni antibiotiku veidi nav atklāti vairāk nekā 30 gadus

(Atklāto vai patentēto antibiotiku klašu skaits)



# Pētījuma rezultāti

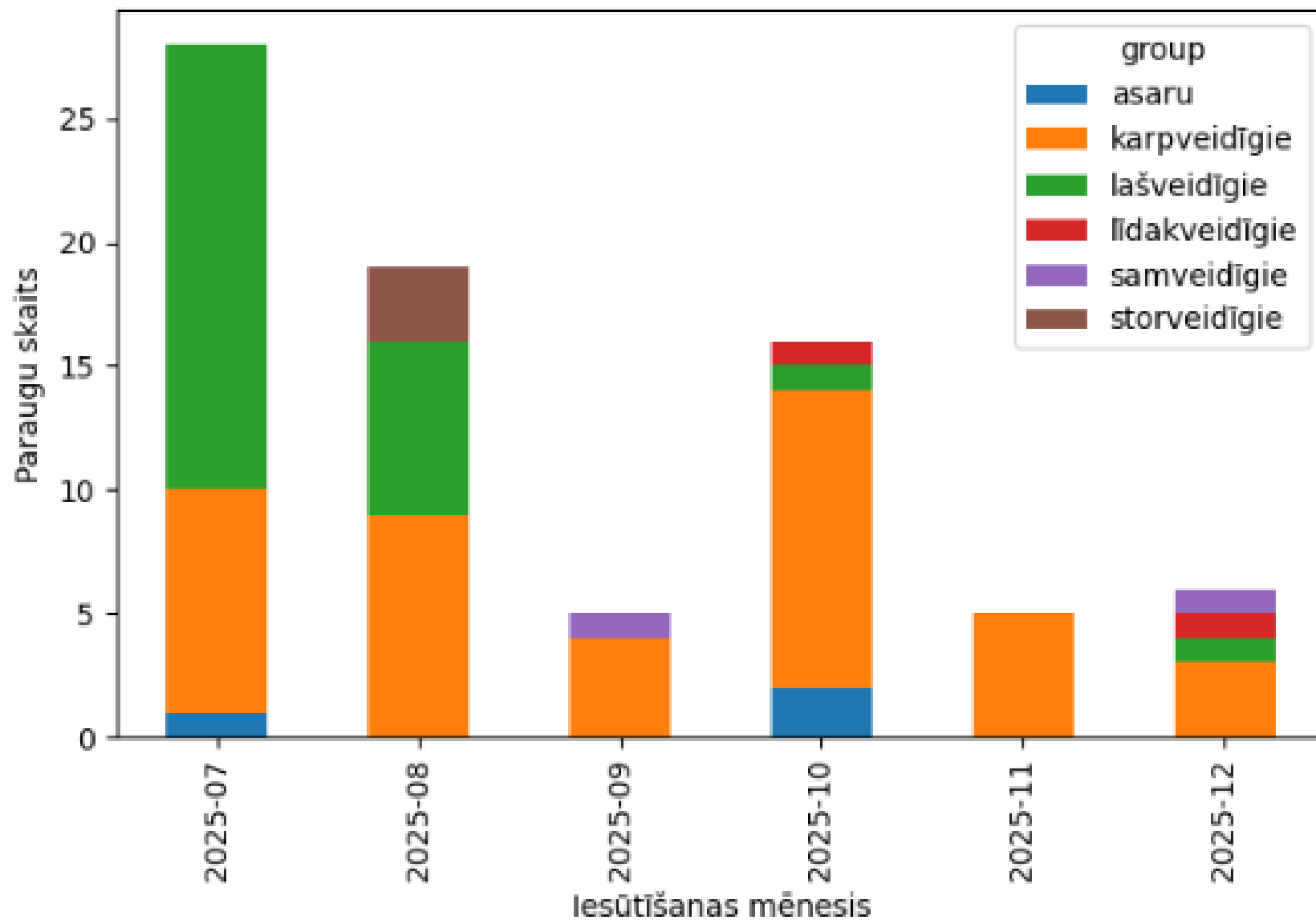
# Paraugi



## Novadi

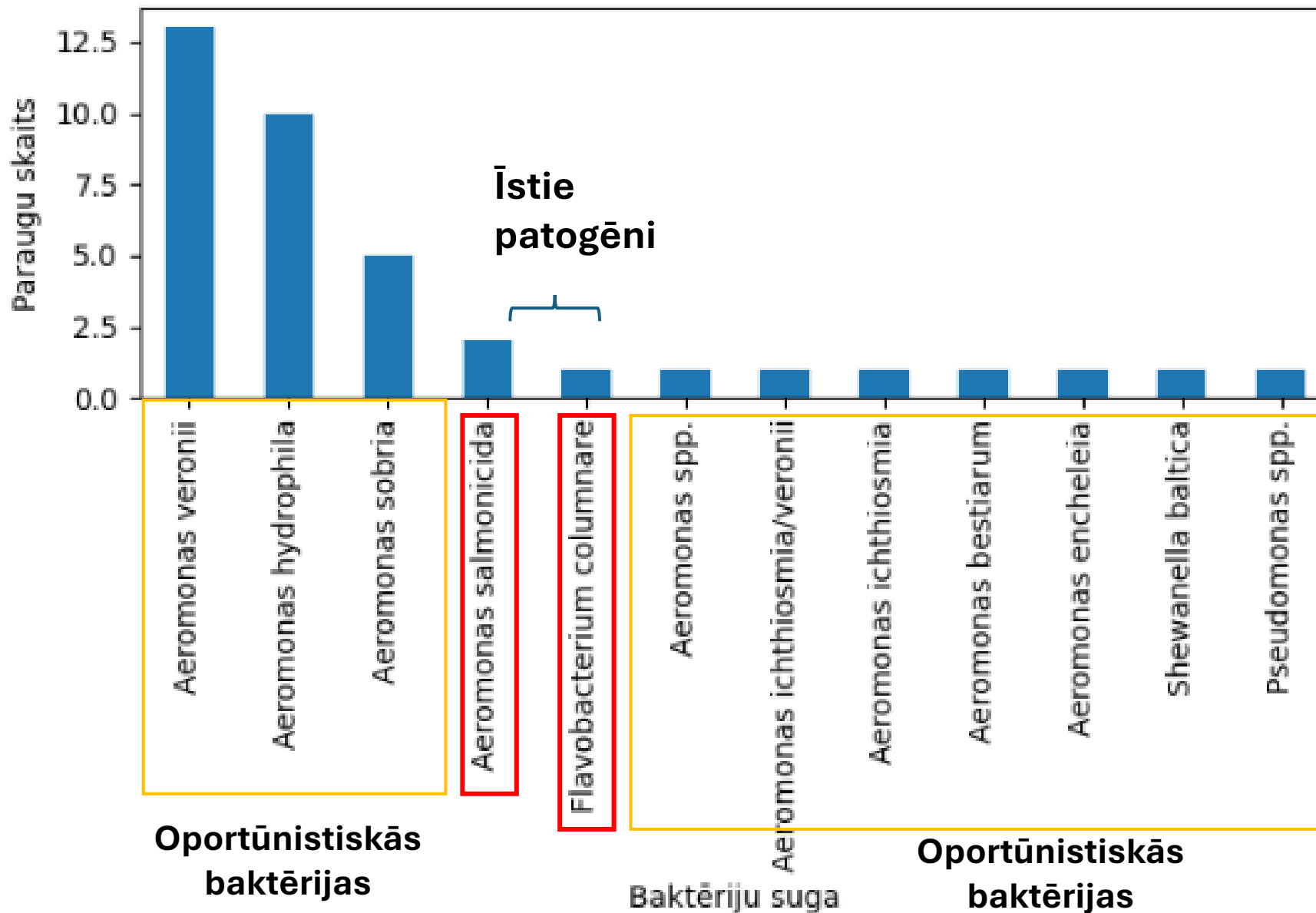
- Aizkraukles nov.
- Cēsu nov.
- Dienvidkurzemes nov.
- Jēkabpils nov.
- Kuldīgas nov.
- Limbažu nov.
- Ogres novads
- Rēzeknes nov.
- Salaspils novads
- Smiltenes nov.
- Talsu nov.
- Valmieras nov.

Paraugu iesūtīšana pa mēnešiem un zivju grupām (stacked)



## Konstatēto baktēriju sastopamība

Lielākā daļa zivju bija bez klīniskām pazīmēm, un dominēja oportūnistiskā baktērija; savukārt primārie patogēni (*Flavobacterium spp.*) tika konstatēti paraugos ar klīniskām slimības pazīmēm.



Oportūnistiskās baktērijas

Baktēriju suga

Oportūnistiskās baktērijas



# Pētījumā tika analizēta rezistence pret 5 antibiotikām:

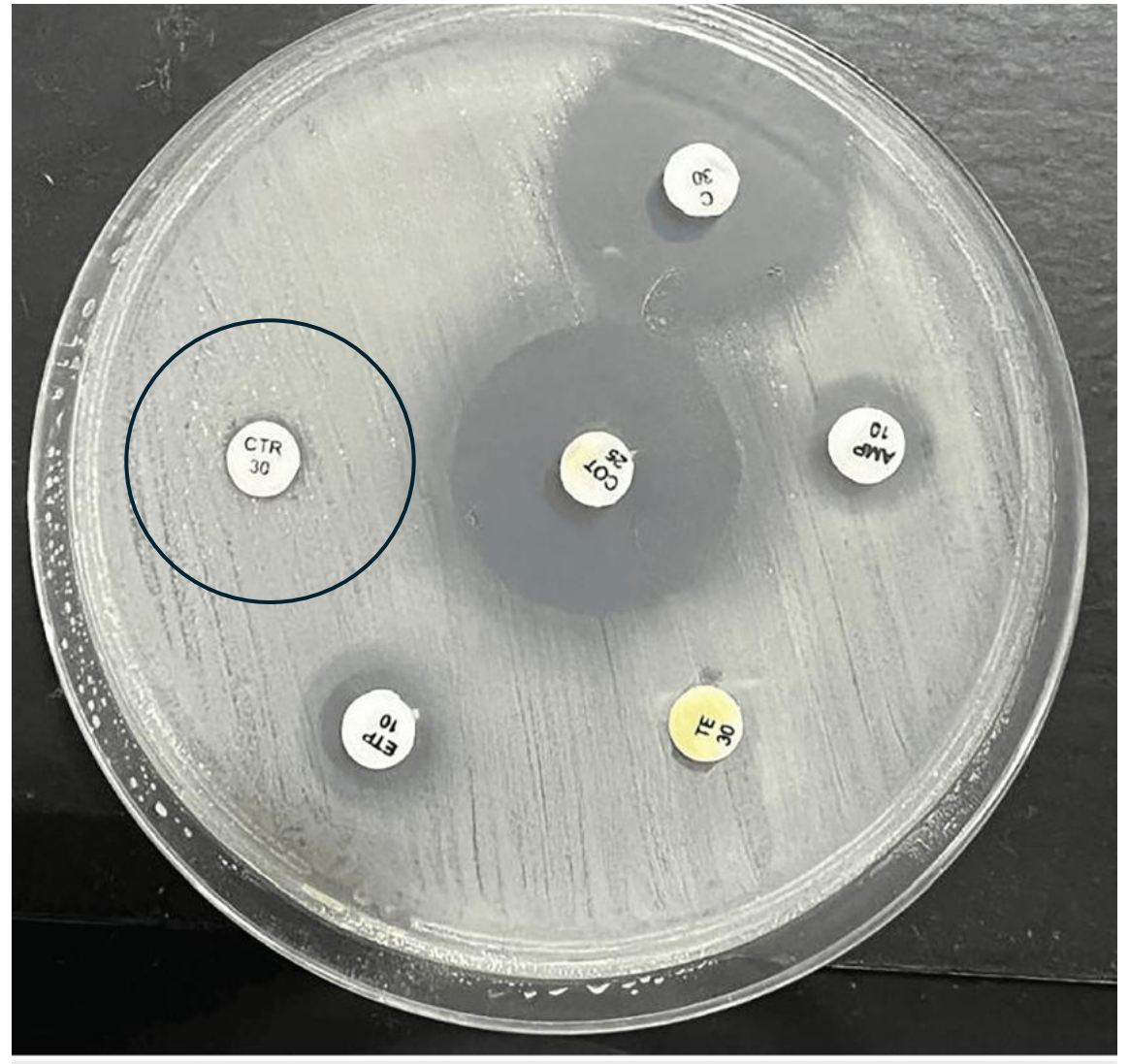
- Doksiciklīns (Doxycycline);
  - Oksitetraciklīns (Oxytetracycline);
  - Enrofloksacīns (Enrofloxacin);
  - Eritromicīns (Erythromycin);
  - Florfenikols (Florfenicol).
-

# Secinājumi – *Aeromonas* spp.

- **Karpveidīgajām** zivīm AMR bija **mazāk** izteikta, savukārt **lašveidīgajām** zivīm – **augstāka**, kas saistīta ar intensīvāku audzēšanu baseinos un lielāku saslimstību.
- Analizēti **62 *Aeromonas* spp. izolāti**.
- 19% (12/62) uzrādīja rezistenci vai vidēju jutību pret vismaz vienu antibiotiku.
- ~80% izolātu bija jutīgi → **kopumā labvēlīga situācija**.
- Rezistence visbiežāk pret tetraciklīniem.
- Florfenikols un enrofloksacīns saglabāja augstu efektivitāti.
- Rezistenti izolāti (klīniski veselām zivīm) → AMR cirkulācija vidē.

# Secinājumi

- Vairākiem *Aeromonas spp.* izolātiem netika vispār novērota inhibīcijas zona (0 mm), kas liecina par pilnīgu rezistenci un baktēriju augšanu arī antibiotikas klātbūtnē.



# Secinājumi- *Pseudomonas* spp.

- Analizēti 3 *Pseudomonas* spp. izolāti.
- Visi izolāti uzrādīja rezistenci pret vismaz vienu no testētajām antibiotikām.
- Izteikta rezistence pret eritromicīnu un florfenikolu tika konstatēta visos izolātos.
- **Vienam izolātam netika novērota inhibīcijas zona nevienam no izmantotajiem antibiotiku diskiem, kas liecina par ļoti augstu rezistences līmeni.**

# Secinājumi – *Shewanella* spp, *Plesiomonas* spp.

- Kopumā analizēti 9 izolāti.
- Vairums izolātu bija jutīgi pret enrofloksacīnu un florfenikolu, kas norāda uz šo antibiotiku saglabātu efektivitāti.
- Rezistence un vidēja jutība tika konstatēta galvenokārt pret doksiciklīnu un oksitetraciklīnu.
- Atsevišķiem izolātiem novērota pilnīga rezistence (0 mm inhibīcijas zona), kas norāda uz augstu adaptācijas potenciālu un rezistences gēnu klātbūtni pat oportūnistiskās mikrofloras pārstāvjos.

# Secinājumi – *Flavobacterium* spp,

- Analizēti 4 *Flavobacterium* spp. izolāti.
- Visi izolāti uzrādīja jutību pret florfenikolu, kas norāda uz šīs antibiotikas saglabātu efektivitāti.
- Enrofloksacīna efektivitāte bija augsta, tomēr atsevišķiem izolātiem novērota robežvērtību (I) zona, kas liecina par potenciālu rezistences attīstības risku.
- Rezistence vai samazināta jutība pret oksitetraciklīnu tika konstatēta atsevišķiem izolātiem.

# Izteiktas antimikrobiālās rezistences riski

- Izteikta rezistence konstatēta audzētavās, kur antibiotikas tika lietotas ilgstoši.
- Pastāv pamatots risks, ka ārstēšana vairs nebūs efektīva un var attīstīties smagas infekcijas (superinfekcijas).
- Notiek rezistences gēnu uzturēšana un izplatīšanās vidē un baktēriju populācijās, radot riskus gan zivīm un citiem dzīvniekiem, gan videi, gan cilvēku veselībai.



# Ieteikumi zivju audzētājiem

- Ievērot biodrošību ikdienas darbā.
- Savlaicīgi iesaistīt kompetento veterinārārstu pie pirmajām slimības pazīmēm.
- Nelietot antibiotikas bez diagnozes.
- Izvēlēties terapiju, balstoties uz jutības testiem, nevis profilaktiski.

•AB lietošana

**eVETIS**

- Samazināt stresu zivīm, ievērot labturības normas (blīvums, ūdens kvalitāte, manipulācijas).
- Stiprināt zivju imunitāti.

	Pīles
	Zosis
	Aitas
	Kazas
	Zivis (laši, varavīksnes foreles, zeltainās jūras karūsas, Eiropas labraki, karpas)
	Zirgi
	Truši

**Paldies par uzmanību!**