

Resistance trends in anaerobes

- NordicAST 2024

Ulrik Stenz Justesen

Department of Clinical Microbiology

Odense University Hospital

Odense - Denmark

Outline

- Resistance in *Bacteroides* spp. – the Danish and European perspective
- Resistance in other species with EUCAST breakpoints – the Nordic perspective
- What is in the pipeline – new species and what to expect?
- Trend wrap up



Resistance genes and mechanisms

Antimicrobial agent	Resistance gene: mechanism
Ampicillin	cepA/cfxA – cfiA: beta-lactamases
Amoxicillin-clavulanic acid	
Cefoxitin	
Imipenem	cfiA: beta-lactamase
Clindamycin	ermF: modified target
Moxifloxacin	gyrA(?): modified target
Metronidazole	nim A-? enzyme modification of drug
Tetracycline	tetQ: modified target
Tigecycline	
Chloramphenicol	

IMPORTANT:
 EUCAST clinical breakpoints are calibrated
 to detect these resistance mechanisms

Sóki et al. Anaerobe. 2020.

... and also just remember the expected resistant phenotypes (don't panic)

“The metronidazole resistant gang”:

- *Actinomyces* spp.
- *Lactobacillus* spp.
- *Propionibacterium/Cutibacterium* spp.

... fine, but how much resistance is there?

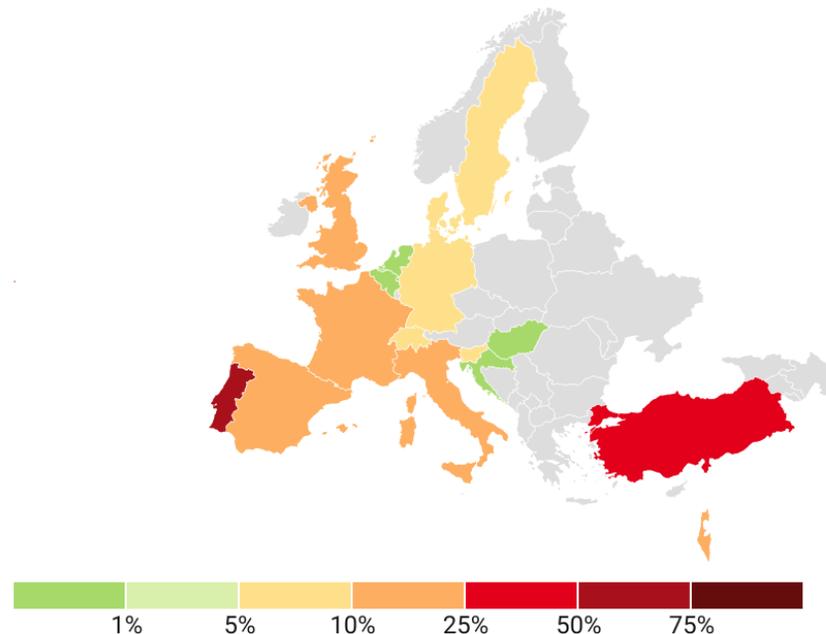
Bacteroides spp. – the Danish perspective



Bacteroides fragilis – the European perspective

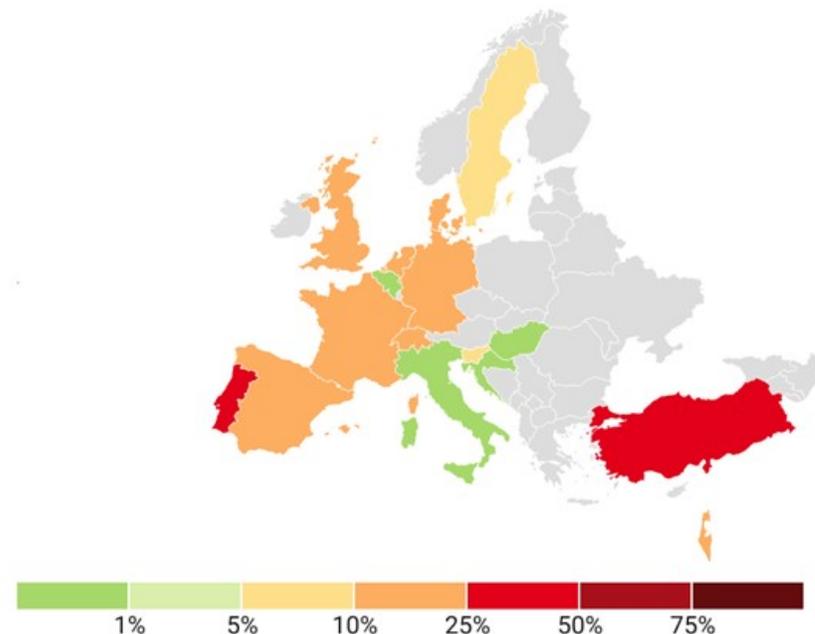
European antimicrobial resistance surveillance of *Bacteroides fragilis* from blood cultures 2022 (ReSuBacfrag)

Piperacillin-tazobactam resistance (%)



Mean 11.1 % (range 0 - 54.5%)

Meropenem resistance (%)



Mean 13.4% (range 0 - 45.5%)

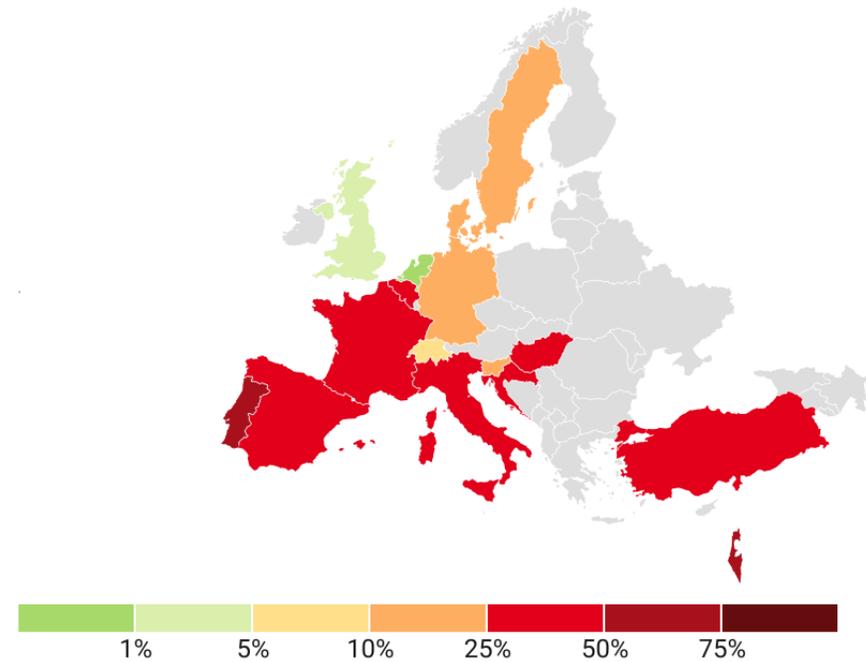
A total of **16 European countries** reported **449 unique isolates** of *Bacteroides fragilis* from blood for which AST had been performed (EUCAST disk diffusion)

ReSuBacfrag 2024
+60 laboratories from +25 European countries

Buhl M et al. ESCMID Global 2024. P0938

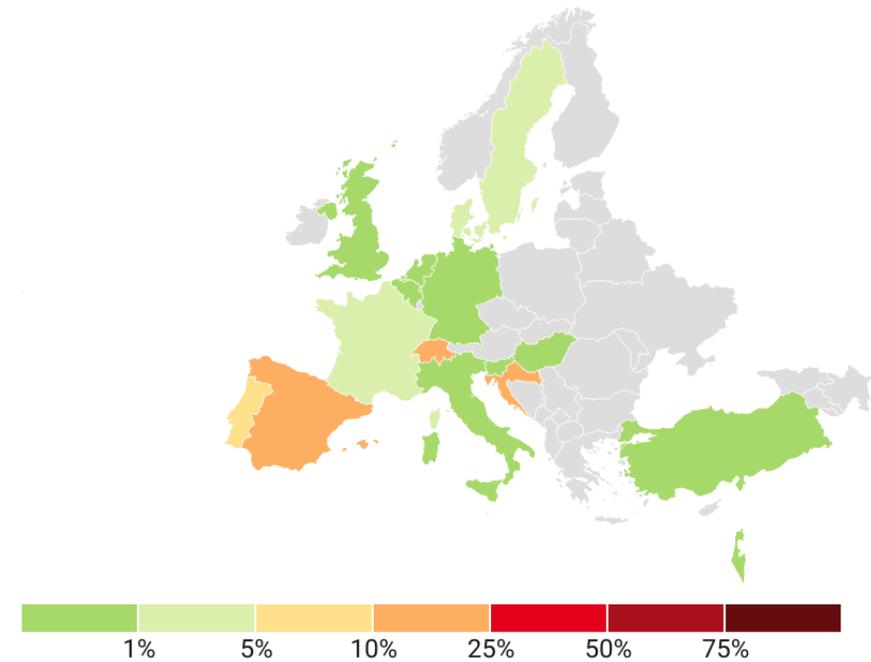
Bacteroides fragilis – the European perspective

Clindamycin resistance (%)



Mean 20.9% (Range 0 - 63.6%)

Metronidazole resistance rates (%)



Mean 1.8% (Range 0 – 20.0%!!!)

Buhl M et al. ESCMID Global 2024. P0938

Bacteroides fragilis – the European perspective

Previous European studies: piperacillin-tazobactam (?), meropenem (?), clindamycin (28.5%)¹, metronidazole almost no resistance in *B. fragilis* (up to 0.5%)¹⁻³

Do we need to worry about metronidazole resistance?

Anaerobe 69 (2021) 102357



Antimicrobial susceptibility of anaerobic bacteria

Molecular characterization of metronidazole resistant *Bacteroides* strains from Kuwait

Zain Baaity ^{a,b}, Wafaa Jamal ^c, Vincent O. Rotimi ^c, Katalin Burián ^{a,b}, David Leitsch ^d, Ferenc Somogyvári ^b, Elisabeth Nagy ^a, József Sóki ^{a,*}

^a Institute of Clinical Microbiology, Faculty of Medicine, University of Szeged, Szeged, Hungary

^b Department of Medical Microbiology and Immunobiology, Faculty of Medicine, University of Szeged, Szeged, Hungary

^c Department of Microbiology, Faculty of Medicine, University of Kuwait, Safat, Kuwait

^d Institute for Specific Prophylaxis and Tropical Medicine, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria

Twelve isolates, 10 *B. fragilis*, all with *nim* genes on plasmids!

Metronidazole resistance in European *Bacteroides fragilis* - a ReSuBacfrag 2024 substudy

Panic!

1. Nagy E et al. Clin Microbiol Infect. 2011.
2. Eitel Z et al. Anaerobe. 2013.
3. Sóki J et al. Anaerobe. 2020.

The Nordic(AST) perspective (non *Bacteroides* spp.)

Data from

- Clinical microbiology and infection control, Region Skåne Office for Medical Services, **Lund, Sweden** (1.4 mil. people) courtesy of **Lealdina Rebihic** and **Torgny Sunnerhagen** and Department of Clinical Microbiology Odense University Hospital, **Odense, Denmark** (0.5 mil. people)
- All isolates with EUCAST disk diffusion breakpoints from 2023
- Disk diffusion results

Prevotella spp.

<i>Prevotella</i> spp.	SE (Lund)		DK (Odense)	
Antimicrobial agent	% resistant	n	% resistant	n*
Benzylopenicillin	55.6	27	56.6	327
Piperacillin-tazobactam	0	27	0.6	327
Clindamycin	28.6	35	25.4	327
Metronidazole	2.9	35	0.9	346

Penicillin resistance in *Prevotella* spp. mainly involves beta-lactamase production

*We did a lot of vaginal cultures in 2023?

Fusobacterium necrophorum

<i>Fusobacterium necrophorum</i>	SE (Lund)		DK (Odense)	
Antimicrobial agent	% resistant	n	% resistant	n
Benzylopenicillin	0	12	0	23
Piperacillin-tazobactam	-	-	0	23
Clindamycin	0	14	4.3	23
Metronidazole	0	14	0	23

Penicillin resistance in *Fusobacterium* spp. mainly involves beta-lactamase production (RARE)

Clostridium perfringens

<i>Clostridium perfringens</i>	SE (Lund)		DK (Odense)	
Antimicrobial agent	% resistant	n	% resistant	n
Benzylopenicillin	2.3	43	10	20
Piperacillin-tazobactam	-	-	10	20
Meropenem	-	-	0	20
Clindamycin	56.9	109	65	20
Metronidazole	0	109	0	20

Penicillin resistance in *C. perfringens* mainly involves PBP changes – also affects piperacillin-tazobactam

Cutibacterium acnes

<i>Cutibacterium acnes</i>	SE (Lund)		DK (Odense)	
Antimicrobial agent	% resistant	n	% resistant	n
Benzylopenicillin	0	110	0	162
Clindamycin	3.6	112	4.3	162

Anaerobic bacteria – antimicrobial resistance

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

Organization
Public consultations
EUCAST News
New definitions of S, I and R
Clinical breakpoints and dosing
Rapid AST in blood cultures
Expert rules and expected phenotypes
Resistance mechanisms
Guidance documents
SOP
MIC and zone distributions and ECOFFs
AST of bacteria
AST of mycobacteria
AST of fungi
AST of veterinary pathogens
AST of phages
Frequently Asked Questions (FAQ)
Meetings
Rationale documents and publications
Presentations and statistics
Videos and online seminars
Warnings!
Translations
Information for industry

search term

QUICK NAVIGATION

The European Committee on Antimicrobial Susceptibility Testing - EUCAST

EUCAST is a standing committee jointly organized by ESCMID, ECDC and European national breakpoint committees. EUCAST was formed in 1997. It has been chaired by Ian Phillips (1997 - 2001), Gunnar Kahlmeter (2001 - 2012), Rafael Canton (2012 - 2016) and Christian Giske (2016 - 2024), Sören Gatermann (2024 -). Its scientific secretary is Derek Brown (1997 - 2016), John Turnidge (2016 - 2023) and Mandy Wootton (2023 -).

The EUCAST webmaster is Gunnar Kahlmeter (2001 -), the clinical data coordinator Rafael Canton (2016-), the technical data coordinator Gunnar Kahlmeter (2012 -), the head of the EDL for bacteria Gunnar Kahlmeter (2010 - 2024) and Erika Matuschek (2024 -), the head of the EDL for fungi Maiken Cavling-Arendrup (2010 -).

EUCAST projects for 2024:

- addressing breakpoint criteria and disk diffusion for new agents,
- reviewing criteria for pathogens frequently involved in endocarditis,
- developing disk diffusion methodology for *Neisseria gonorrhoeae*,
- extending the panel of agents with breakpoints and disk diffusion criteria for anaerobic bacteria (*Clostridium ramosum*, *Clostridium innocuum*, *Clostridium tertium*, *Clostridium septicum*, *Cutibacterium avidum*, *Fusobacterium nucleatum*, *Finnegoldia magna*, *Parvimonas micra*, *Peptostreptococcus anaerobius*, *Peptoniphilus* spp.)
- evaluating alternative (alternative to MH-F with horse-blood) media for fastidious microorganisms,
- developing RAST criteria for *Salmonella enterica*,
- developing reference methods and criteria for mycobacteria and for veterinary purposes, participate in the development of reference methodology for *Mycobacterium* spp and several veterinary agents and pathogens.

EUCAST News

11.05.2024
General Committee 2024 meeting - minutes published

07.05.2024
Proposed change of breakpoints for aminopenicillins in enterococci

03.05.2024
Consultation: benzylpenicillin breakpoints for *S.pneumoniae* and *Viridans* group streptococci

03.05.2024
Aztreonam-avibactam and cefepime-enmetazobactam now available.

24.04.2024
***Salmonella enterica* - multinational zone diameter distributions uploaded**

About Newsfeeds

EUCAST projects for 2024:

- extending the panel of agents with breakpoints and disk diffusion criteria for anaerobic bacteria (*Clostridium ramosum*, *Clostridium innocuum*, *Clostridium tertium*, *Clostridium septicum*, *Cutibacterium avidum*, *Fusobacterium nucleatum*, *Finnegoldia magna*, *Parvimonas micra*, *Peptostreptococcus anaerobius*, *Peptoniphilus* spp.)

What can we expect from these new species?

Anaerobic bacteria – antimicrobial resistance

- *Clostridium ramosum* and metronidazole resistance -> **not nim-mediated** (OUH 5%)
- *Clostridium innocuum* (*Clostridium ramosum*) is very often **vancomycin resistant** (change of binding site)
- *Clostridium tertium* **can grow in a normal atmosphere** -> metronidazole resistant
- *Clostridium septicum* **SWARMS** – difficult to test

- *Fusobacterium nucleatum*, **even more sensitive** than *F. necrophorum*

Gram-positive anaerobic cocci (the **GPACs**):

- *Finegoldia magna*, *Parvimonas micra* (*Micromonas micros*) *Peptostreptococcus anaerobius* and *Peptoniphilus* spp.
 - > Resistance: Clindamycin (OUH **5-50%**) and penicillin (OUH **0-7%**) species dependent

Trend wrap up

- Anaerobic bacteria are clinically significant and should be considered when choosing empirical and prophylactic antibiotic therapy (ab. surgery)
- We need to know whether anaerobic bacteria are susceptible to our antibiotic therapy -> especially clindamycin!
- Usually susceptible to metronidazole, but this might be changing(!), so -> AST

The end