ESBL & plasmid-mediert AmpC (tidligere $ESBL_A$ & $ESBL_{M-C}$)

AFA-kurset
Rikshospitalet, Oslo
15.01.2026

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Nasjonalt senter for påvisning av antibiotikaresistens (K-res)
Universitetssykehuset Nord-Norge
Avd. for mikrobiologi og smittevern
&
Institutt for farmasi
UiT Norges Arktiske Universitet

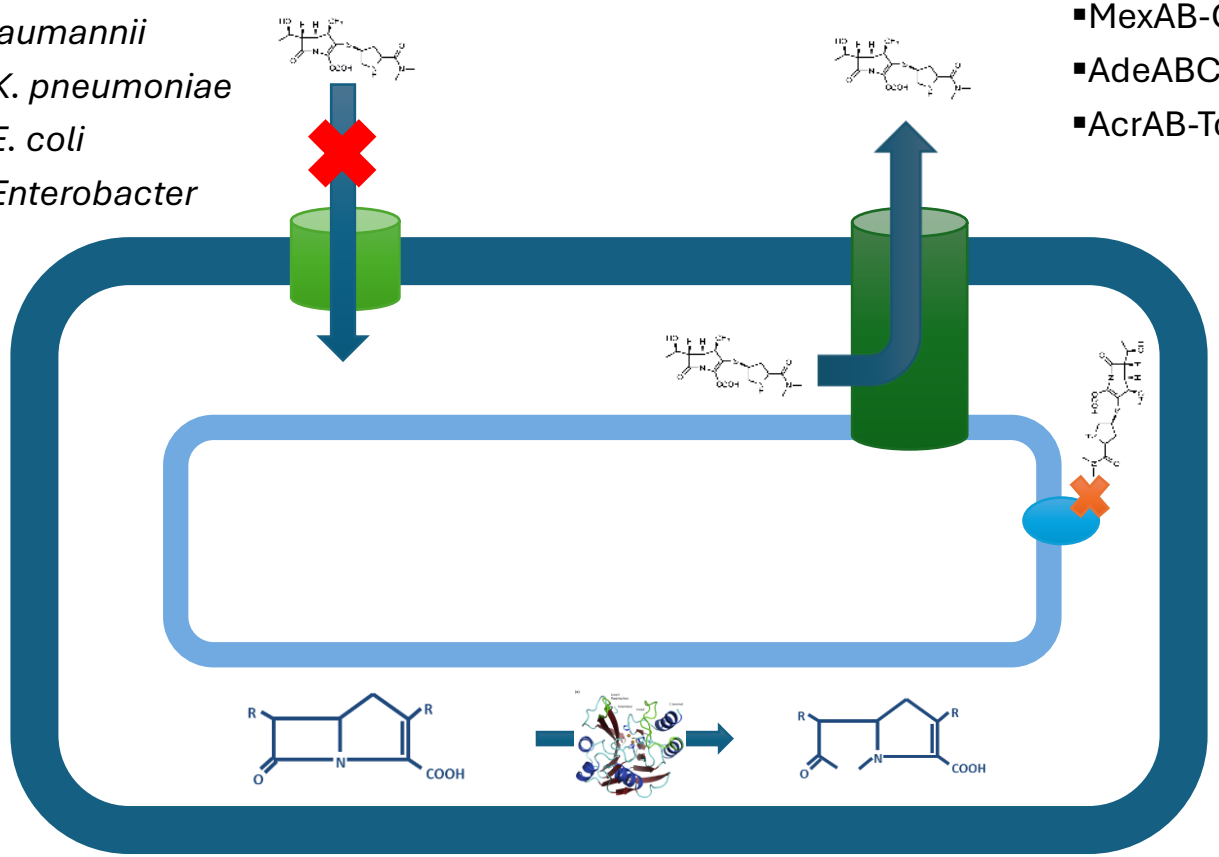
Agenda

- Del 1:
  - β-laktam resistens
  - β-laktamaser
  - ESBL og plasmid-mediert AmpC
    - Egenskaper og epidemiologi
    - Påvisning av ESBL og plasmid-mediert AmpC
- Del 2:
  - Karbapenemaser
    - Egenskaper og epidemiologi
    - Påvisning

β-laktam resistens – Gram-negative

- **Nedsatt permeabilitet**
  - OprD – *P. aeruginosa*
  - CarO – *A. baumannii*
  - OmpK36 – *K. pneumoniae*
  - OmpC/F – *E. coli*
  - OmpC/F – *Enterobacter*

- **Effluks:**
  - MexAB-OprM – *P. aeruginosa*
  - AdeABC – *A. baumannii*
  - AcrAB-TolC – *Enterobacteriaceae*



- **PBP:**
  - Mutasjoner -> ↓ affinitet
  - ↓ transkripsjon

NB: kombinasjoner av resistensmekanismer kan være nødvendig for klinisk resistens

Resistensmekanismer påvirker forskjellige β-laktamer ulikt

- **β-laktamaser – iboende, ervervede (ESBL, pAmpC, karbapenemaser)**

«An enzyme from bacteria able to destroy penicillin»

No. 3713, DEC. 28, 1940 NATURE 837

LETTERS TO THE EDITORS

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IN THE PRESENT CIRCUMSTANCES, PROOFS OF "LETTERS" WILL NOT BE SUBMITTED TO CORRESPONDENTS OUTSIDE GREAT BRITAIN.

An Enzyme from Bacteria able to Destroy Penicillin

FLEMING[1] noted that the growth of *B. coli* and a number of other bacteria belonging to the coli-typhoid group was not inhibited by penicillin. This observation has been confirmed. Further work has been done to find the cause of the resistance of these organisms to the action of penicillin.

An extract of *B. coli* was made by crushing a suspension of the organisms in the bacterial crushing mill of Booth and Green[2]. This extract was found to contain a substance destroying the growth-inhibiting property of penicillin. The destruction took place on incubating the penicillin preparation with the bacterial extract at 37°, or at room temperature for a longer time. The following is a typical experiment showing the penicillin-destroying effect of *B. coli* extracts. A solution of 1 mgm. penicillin in 0·8 c.c. of water was incubated with 0·2 c.c. of centrifuged and dialysed bacterial extract at 37° for 3 hours, in the presence of ether, and a control solution of penicillin of equal concentration was incubated without enzyme for the same time. (The penicillin used was extracted from cultures of *Penicillium notatum* by a method to be described in detail later. It possessed a degree of purity similar to that of the samples used in the chemotherapeutic experiments recorded in a preliminary report[3].) The growth-inhibiting activity of the solutions was then tested quantitatively on agar plates against *Staphylococcus aureus*. The penicillin solution incubated with the enzyme had entirely lost its growth-inhibiting activity, whereas the control solution had retained its full strength.

The conclusion that the active substance is an enzyme is drawn from the fact that it is destroyed by heating at 90° for 5 minutes and by incubation with papain activated with potassium cyanide at *p*H 6, and that it is non-dialysable through 'Cellophane' membranes. It can be precipitated by 2 volumes of alcohol, but much of its activity is lost during this operation. The activity of the enzyme, which we term penicillinase, is slight at *p*H 5, but increases considerably towards the alkaline range of *p*H. It is very active at *p*H 8 and 9. Higher *p*H's could not be tested as penicillin is unstable above *p*H 9.

The mechanism of the enzymatic inactivation of penicillin is being studied. No oxygen uptake occurs during the reaction, and the inactivation proceeds with equal facility under aerobic and anaerobic conditions. No appearance of acid groups could be detected by *p*H measurement with the hydrogen electrode. Extracts of a number of other micro-organisms, made by crushing the bacteria in the bacterial grinding mill, were tested for penicillinase. The enzyme was absent from extracts of the penicillin-sensitive *Staphylococcus aureus*, of yeast and of *Penicillium notatum*. It was present in a Gram-negative rod, insensitive to penicillin, found as a contaminant of some Penicillium cultures. Unlike *B. coli*, it was not necessary to crush the organism in the bacterial mill in order to obtain the enzyme from it; the latter appeared in the culture fluid. The enzyme was also found in *M. lysodeikticus*, an organism sensitive to the action of penicillin, though less so than *Staphylococcus aureus*. Thus, the presence or absence of the enzyme in a bacterium may not be the sole factor determining its insensitivity or sensitivity to penicillin.

The tissue extracts and tissue autolysates that have been tested were found to be without action on the growth-inhibiting power of penicillin. Prof. A. D. Gardner has found staphylococcal pus to be devoid of inhibiting action, but has demonstrated a slight inhibition by the pus from a case of *B. coli* cystitis. The bacteriostatic action of the sulphonamide drugs is known to be inhibited in the presence of tissue constituents and pus.[4] That the anti-bacterial activity of penicillin is not affected under these conditions gives this substance a definite advantage over the sulphonamide drugs from the chemotherapeutic point of view. The fact that a number of bacteria contain an enzyme acting on penicillin points to the possibility that this substance may have a function in their metabolism.

E. P. ABRAHAM.
E. CHAIN.

Sir William Dunn School of Pathology,
Oxford.
Dec. 5.

[1] Fleming, A., *Brit. J. Exp. Path.*, **10**, 226 (1929).
[2] Booth, V. H., and Green, D. E., *Biochem. J.*, **32**, 853 (1938).
[3] Chain, E., Florey, H. W., Gardner, A. D., Heatley, N. G., Jennings, M. A., Orr-Ewing, J., and Sanders, A. G., *Lancet*, 226 (1940).
[4] MacLeod, C., *J. Exp. Med.*, **72**, 217 (1940).

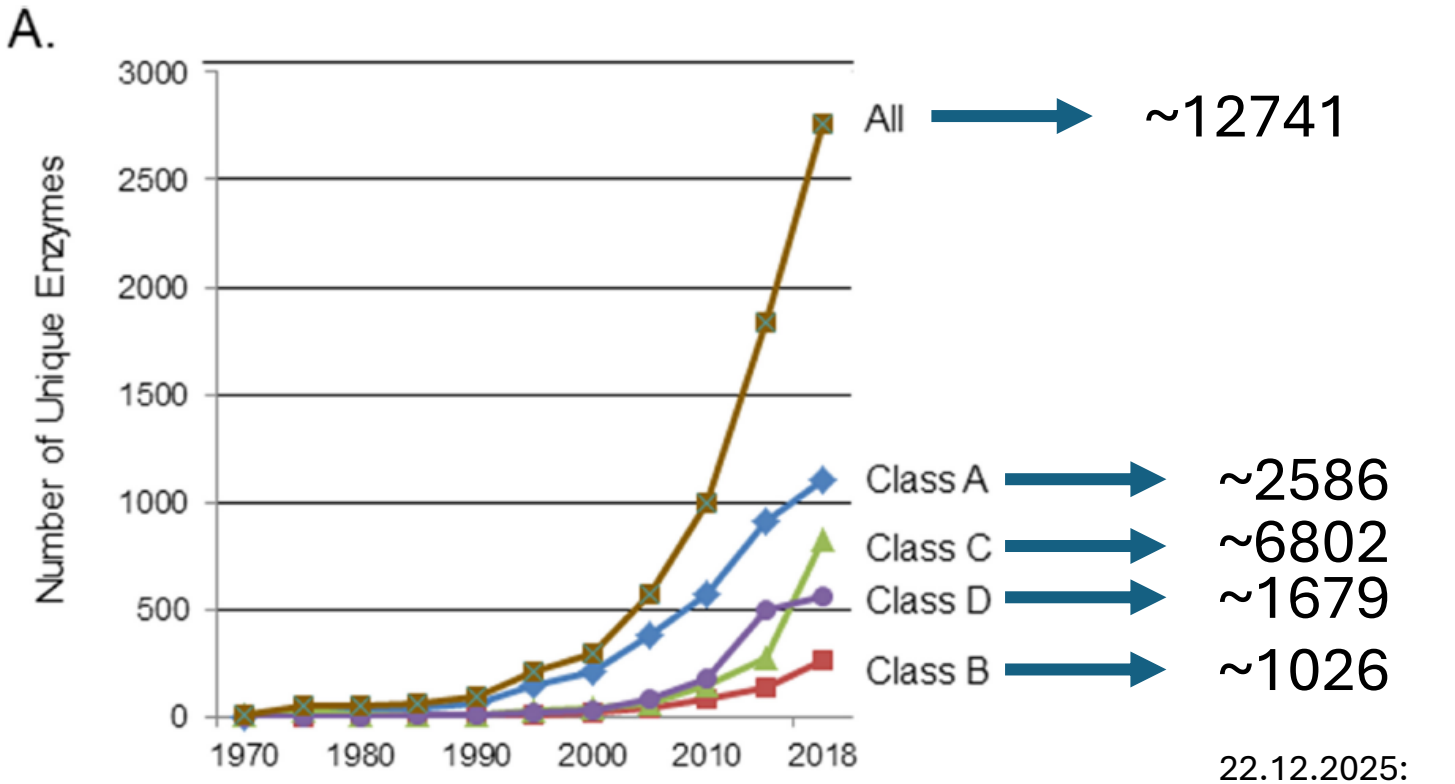
Morphological Effects of Penicillin on Bacteria

WHILE working with Chain, Florey and others on the inhibition of bacterial growth by penicillin[1], I noticed that concentrations of less than full inhibiting power caused a change in the appearance of the growth of *Cl. welchii* in fluid media. The normal uniform turbidity was replaced by a flocculent growth with a heavy deposit. Microscopical examination showed an extreme elongation of the majority of the cells, which took the form of unsegmented filaments ten or more times longer than the average normal cell.

I have now examined a number of bacteria grown in broth or serum broth with penicillin, and I have found similar microscopical changes in all the rod-shaped organisms that have shown any inhibition. These changes may be traceable, in the form of a distinct average lengthening of the cells, to a dilution eight or ten times, and even sometimes thirty times, higher than that which completely inhibits growth.

The Gram-negative rods, which are relatively resistant to penicillin, show the effect very well. Thus

Abraham and Chain, *Nature* **1940**

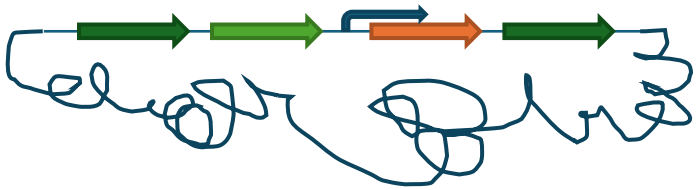


Bush K. *Antimicrob. Agents Chemother.* 2018

22.12.2025:
http://bldb.eu/

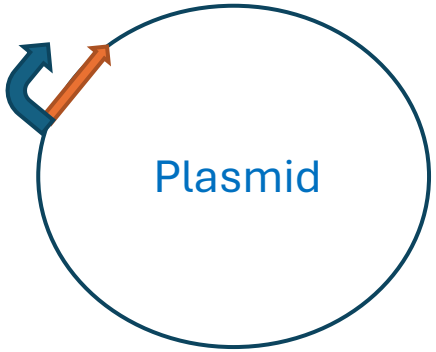
1 aminosyre endring = ny variant

Iboende vs. ervervede β-laktamaser

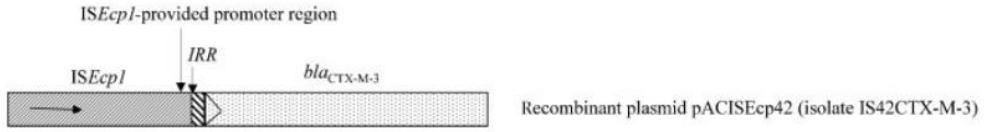


- Gen-uttrykk:
  - Ofte regulert –> lavgradig uttrykk
  - Kan være induserbart
  - IS-elementer/promoter mutasjoner kan øke uttrykk

β-laktamase	**Species**
bla_{EC}	*E. coli*
bla_{SHV}	*K. pneumoniae*
$bla_{...}$	*Enterobacter* spp.
$bla_{OXA-50-lik}$, bla_{PDC}	*P. aeruginosa*
bla_{ADC}, $bla_{OXA-51-lik}$	*Aci. baumannii*
bla_{DHA}	*M. morganii*
$bla_{OXY/K1}$	*K. oxytoca*
bla_{CTX-M}	*Kluyvera* spp.
$bla_{OXA-48-lik}$	*Shewanella* spp.
$bla_{OXA-23-lik}$	*Aci. radioresistens*
...	



- Gen-uttrykk:
  - Regulering av uttrykk ofte fjernet -> høygradig uttrykk
  - IS-elementer kan gi ny promotor



Ma L et al. *Int. J. Med. Microbiol.* 2011

- Flere kopier av plasmidet

β-laktamase «Nomenklatur»

- TEM: navngitt etter pasienten – Temoniera
- PER: Pseudomonas extended resistant / initialene til forfatterne: Patrice, Esthel, and Roger
- SFC: *Serratia fonticola* resistant to carbapenem
- NDM: New-Delhi metallo-β-lactamase
- Etc.

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

COMMENTARY

Consensus on β-Lactamase Nomenclature

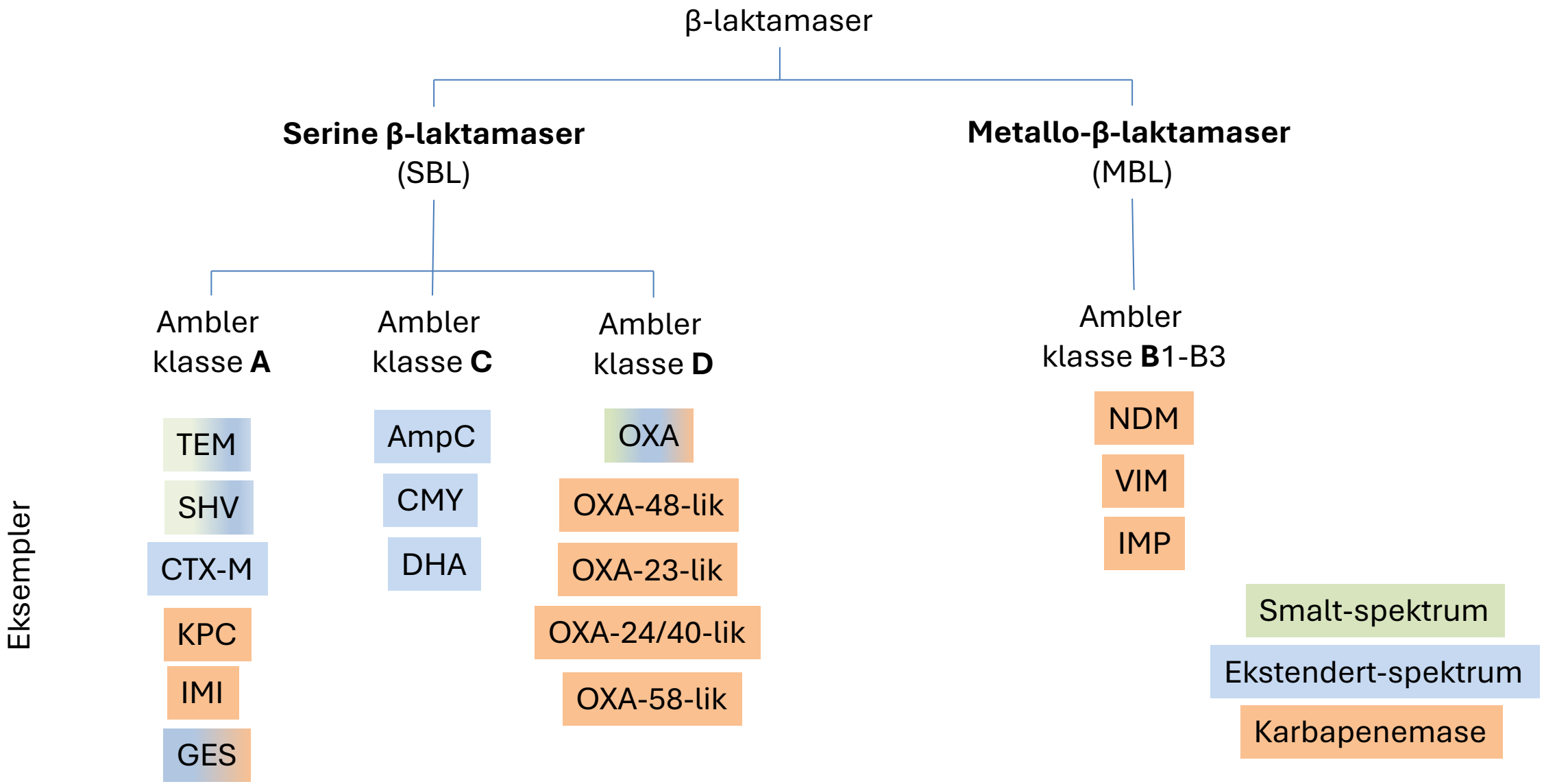
Patricia A. Bradford,[a] Robert A. Bonomo,[b] Karen Bush,[c] Alessandra Carattoli,[d] Michael Feldgarden,[e] Daniel H. Haft,[e] Yoshikazu Ishii,[f] George A. Jacoby,[g] William Klimke,[e] Timothy Palzkill,[h] Laurent Poirel,[i,j,k] Gian Maria Rossolini,[l,m] Pranita D. Tamma,[n] Cesar A. Arias[o,p]

IMPORTANT RULES GOING FORWARD

- New β-lactamase numbers will continue to be assigned based on predicted amino acid sequences that differ by at least one amino acid substitution from previously designated sequences.
  - New allele requests can be based on predicted amino acid changes in the leader sequence.
  - DNA sequences that differ by a single nucleotide that does not encode a different amino acid (synonymous change) will not be given a new allele number.
  - Only β-lactamases from natural sources will be numbered, not laboratory constructs.
- Allele numbering for most β-lactamase families is designated and tracked by NCBI and new allele numbers of these gene families will be assigned by NCBI if necessary (if a submitted but not yet published allele number exists, and it matches the new submitted sequence, that allele number will be assigned). The list of families for which NCBI assigns alleles can be found on this page: https://www.ncbi.nlm.nih.gov/pathogens/submit-beta-lactamase/.
- Allele requests should be made only when constructive, that is, where single amino acid changes likely will have functional or epidemiological significance, and where citing allele numbers provides greater clarity than simply citing protein accession numbers.
- For large families of chromosomal class C β-lactamases (*ampC*) that so far have not received extensive allele assignments, allele numbers may not be assigned. The bla_{ADC}, bla_{ACT}, and bla_{PDC} families are exceptions for which allele assignments are well-established and new requests are welcome.
- The nomenclature for OXA-type β-lactamases is in evolution and efforts are underway to meet this challenge in a subsequent publication.
- New β-lactamases should not be named based on geographical location.
- The proper format for citations of β-lactamase genes should be written following the convention for bla_{TEM-1} (italicized *bla*, followed by subscript allele designation).
- Functional categorization of β-lactamases will not be assigned based upon sequence similarity (i.e. ESBL phenotype cannot be based on sequence alone).

Bradford PA. et al. *Antimicrob. Agents Chemother,* 2022

Overordnet klassifisering



Ambler RP. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* 1980; Bush K. *Expert Rev. Anti-Infect. Ther.* 2023

NB: Variabelt aktivitetsspektrum innad i hver klasse

2026 Endring i terminologi – tilbake til start

Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

Endring i terminologi av betalaktamaser med ekstendert spektrum

Fra 1. januar 2026 innføres ny terminologi for β-laktamaser med ekstendert spektrum. Endringen

Harmonisering med internasjonal litteratur og rådgivende organisasjoner

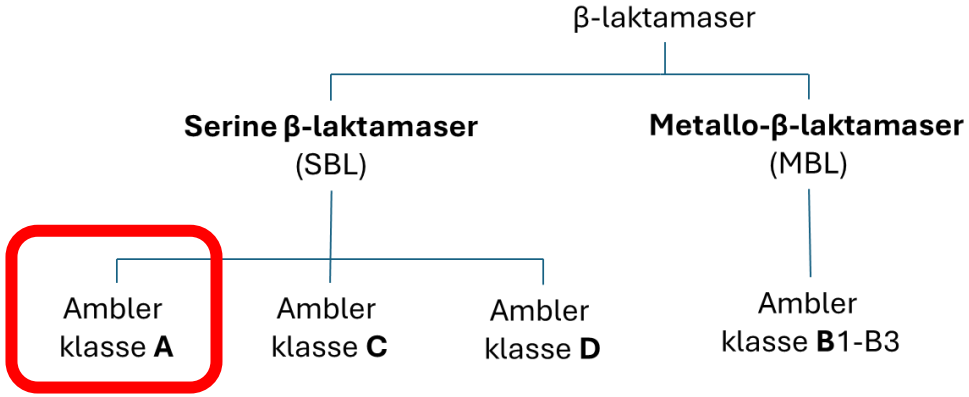
- Giske et al. 2009:
  - Alle **mobile/ervervede** β-laktamaser med **ekstendert spektrum** (cefalosporiner og/eller karbapenemer) = **ESBL**

Acquired β-lactamases with hydrolytic activity against extended-spectrum cephalosporins and/or carbapenems			
	$ESBL_A$	$ESBL_M$	$ESBL_{CARBA}$
β-Lactamase classes	High prevalent $ESBL_A$ CTX-M TEM-ESBLs SHV-ESBLs VEB PER	$ESBL_{M-C}$ (Plasmid-mediated AmpC) CMY FOX MIR MOX DHA LAT BIL ACT ACC	$ESBL_{CARBA-A}$ KPC GES-2, -4, -5, -6, -8 NMC SME IMI-1, -2
	Low prevalent $ESBL_A$ GES-1, -3, -7, -9 SFO-1 BES-1 BEL-1 TLA IBC CMT[a]	$ESBL_{M-D}$ (OXA-ESBL) OXA-10-group OXA-13-group OXA-2-group OXA-18 OXA-45	$ESBL_{CARBA-B}$ (MBL) IMP VIM SPM-1 GIM-1 SIM-1 AIM-1
			$ESBL_{CARBA-D}$ (OXA-carbapenemases) OXA-23-group OXA-24-group OXA-48[b] OXA-58-group
Operational definition	Non-susceptibility to extended-spectrum cephalosporins AND clavulanate synergy	Non-susceptibility to extended-spectrum cephalosporins AND phenotypic detection ($ESBL_{M-C}$) OR genotypic detection ($ESBL_{M-D}$)	Non-susceptibility to extended-spectrum cephalosporins and at least one carbapenem AND $ESBL_{CARBA}$ detected with phenotypic and/or genotypic methods

Giske CG. et al. *J. Antimicrob. Chemother.* 2009

Giske et al. 2009	**Nå**
ESBL-A	ESBL
ESBL-M-C	Plasmidmediert AmpC (pAmpC)
ESBL-CARBA	Karbapenemase

ESBL



- Serin Ambler klasse A β-laktamase
- Vanligste enzymer: **CTX-M**, SHV-ESBL, TEM-ESBL
- Sjeldne: VEB, PER, GES-ESBL, BEL, TLA,

Aktivitetsspektrum ESBL

β-laktamgruppe	**ESBL (CTX-M)**
Penicilliner (Ampicillin, Piperacillin)	●
1-3. gen. cefalosporiner (Cefotaxim, Ceftazidim)	●
4. gen. cefalosporiner (Cefepim)	●
Cefamyciner (Cefoxitin, Cefotetan)	○
Monobaktamer (Aztreonam)	●
Karbapenemer (Meropenem, Imipenem, Ertapenem)	○
β-laktamase inhibitorer	**ESBL (CTX-M)**
Klavulansyre, Tazobaktam, Avibaktam, Vaborbaktam, Relebaktam	●

● hydrolyseres
○ hydrolyseres ikke
● inhiberes

NB: Iboende klasse A β-laktamaser hos f.eks. *K. oxytoca, P. vulgaris, C. koseri, C. sedlakii, C. farmeri, S. fonticola* kan ha samme fenotypiske profil

Epidemiologi 3. gen. cefalosporin-resistens (ESBL)

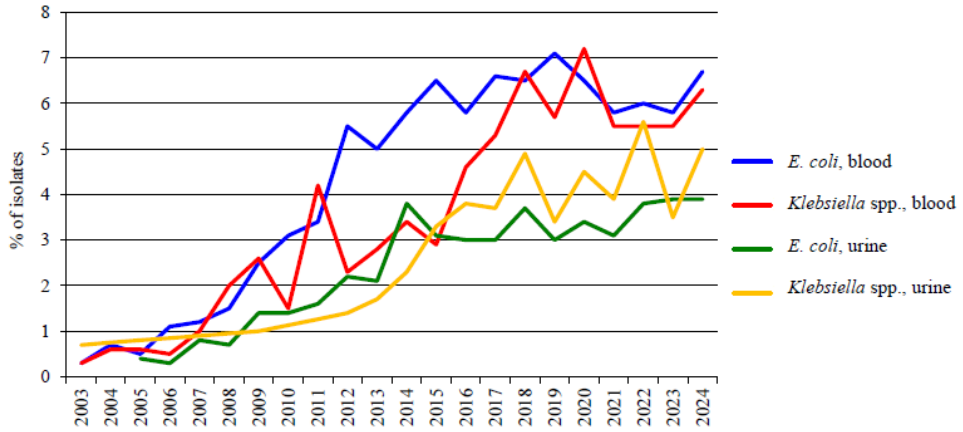
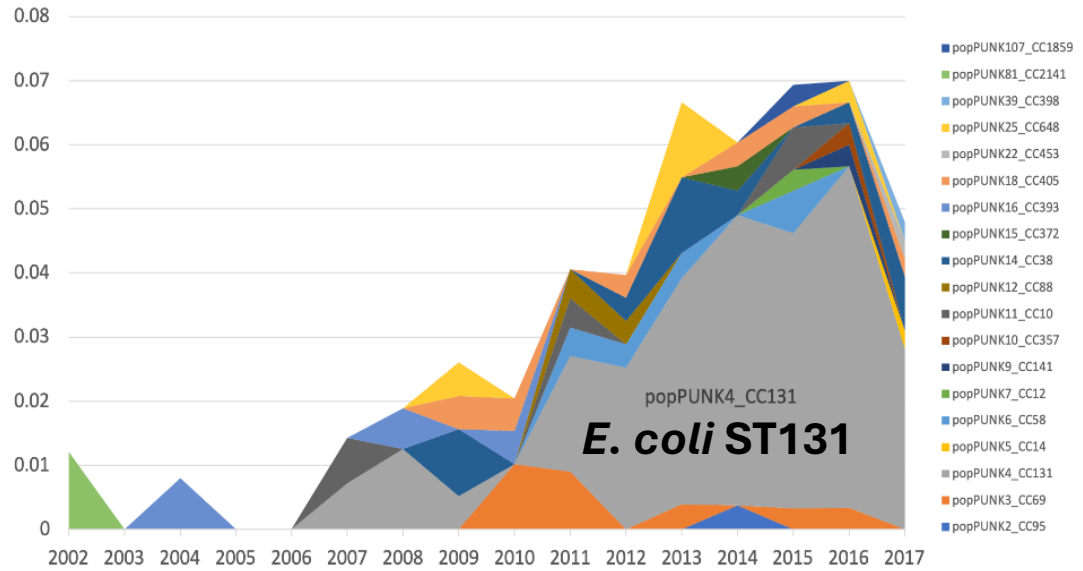


FIGURE 87. Prevalence of ESBL production among *Escherichia coli* and *Klebsiella* spp. isolates from blood and urine 2003-2024.

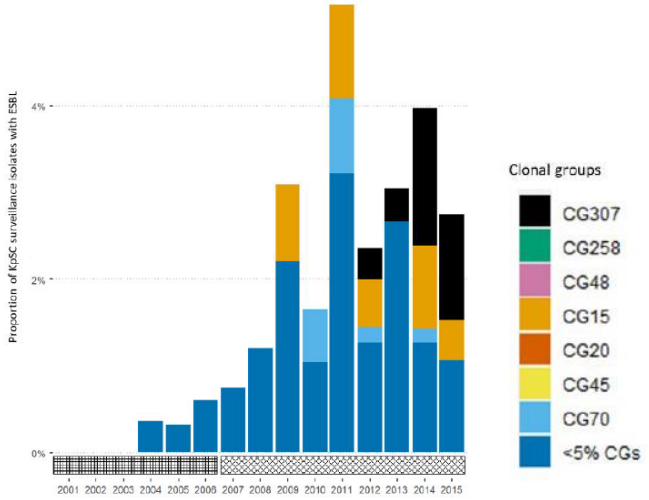
NORM/NORM-VET 2024 report (2025)



Gladstone RA. et al. *Lancet Microbe* 2021

- Ko-resistens (NORM/NORM-VET 2023)
  ESBL-positive *E. coli* blodkultur:
  - 61% R ciprofloxacin (10 %)
  - 29% R gentamicin (5 %)
  - 57% R trim-sulfa (22 %)

NORM/NORM-VET 2023 report (2024)



***K. pneumoniae* ST307**

Fostervold A. et al. *J. Antimicrob. Chemother.* 2022

Påvisning ESBL

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases

3. Extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae

Importance of detection of resistance mechanism	
Required for clinical antimicrobial susceptibility categorization	No
Infection control purposes	Yes
Public health purposes	Yes

EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological value. v. 2.0 July 2017

Fenotypiske metoder ESBL

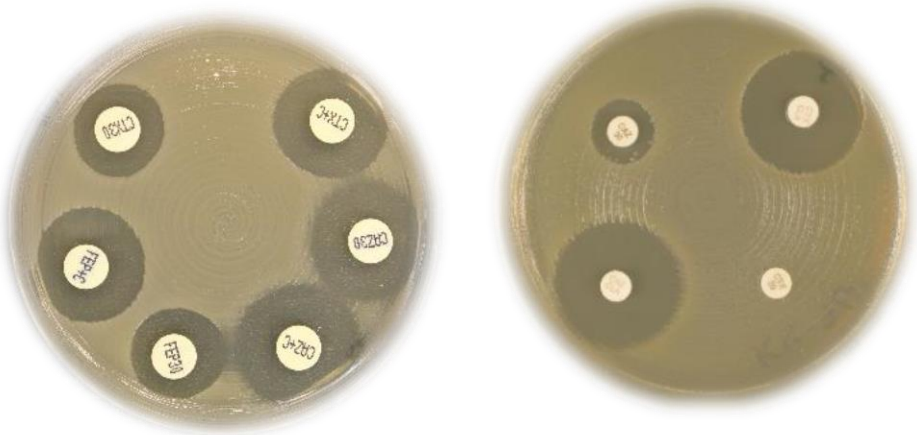
Basert på synergi mellom cefalosporiner og **klavulansyre**

Kombinasjons gradient-tester:

- Ceftazidim/ceftazidim+klavulansyre
- Cefotaxim/cefotaxim+klavulansyre
- Cefepim/cefepim+klavulansyre

- Positiv test:
  - ✓ Ratio ≥8
  - ✓ Fantomsone

Kombinasjons lapper/tabletter:



- Ceftazidim/ceftazidim+klavulansyre
- Cefotaxim/cefotaxim+klavulansyre
- Cefepim/cefepim+klavulansyre

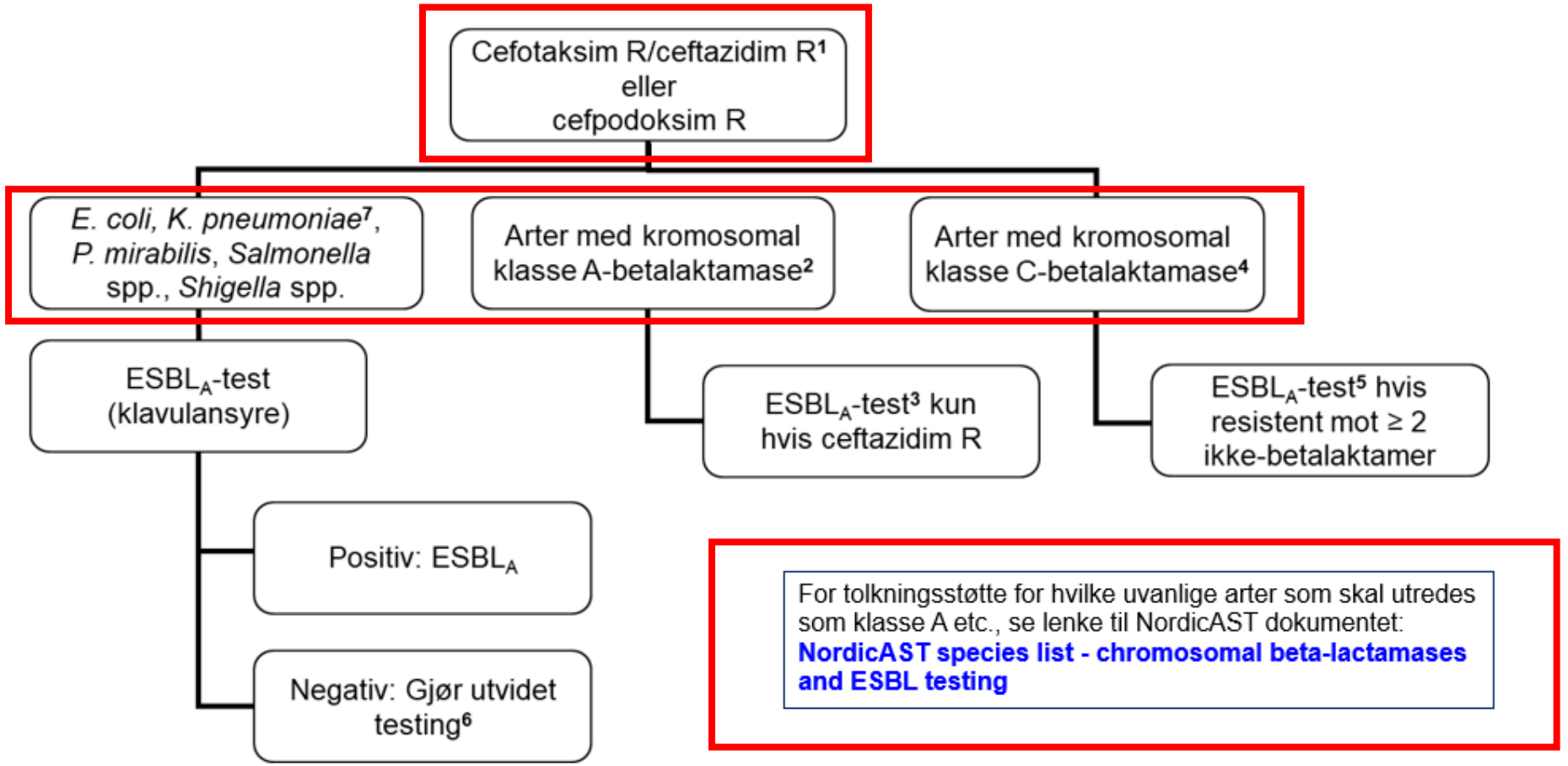
- Positiv test:
  - ✓ Ratio ≥5

NB: Synergi med en av kombinasjonene nok!

Bilder: Nasjonalt senter for påvisning av antibiotikaresistens (K-res)

Enterobacterales

ALGORITME FOR PÅVISNING AV KLASSISK ESBL ($ESBL_A$)



[1] Lappediffusjon: Test kun isolater som er cefotaksim eller ceftazidim R. Automatisert resistensbestemmelse: Test også isolater som er cefotaksim eller ceftazidim I.

[2] Vanligste arter er *K. oxytoca*, *P. vulgaris*, *C. koseri*, *C. sedlakii*, *C. farmeri*, *S. fonticola*. Disse er vanligvis resistente mot cefotaxim grunnet kromosomal betalaktamase som hemmes av klavulansyre.

[3] $ESBL_A$-test med ceftazidim anbefales.

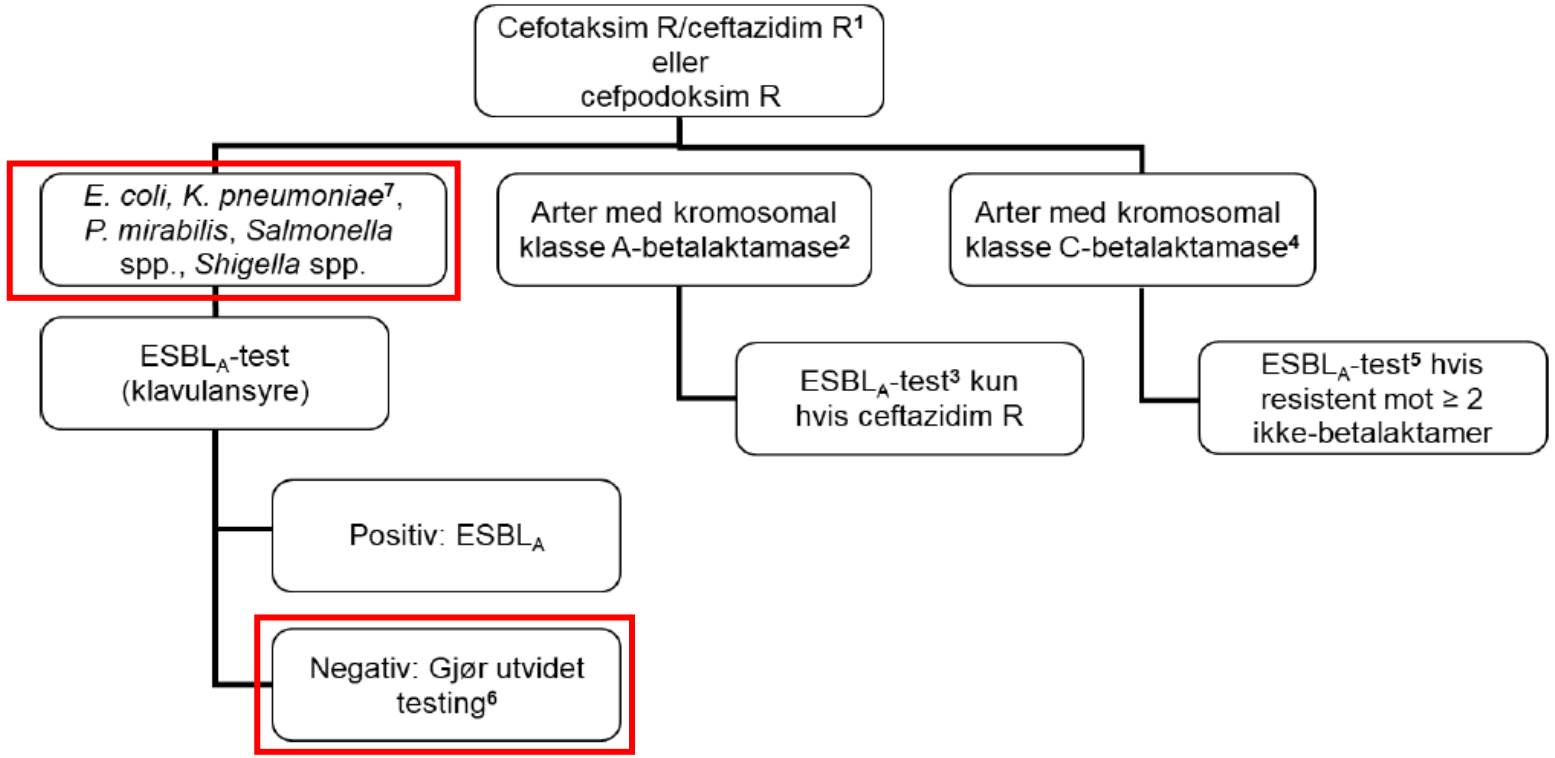
[4] Vanligste arter er *Enterobacter* spp., *C. freundii*, *Morganella* spp., *Serratia* spp. (untatt *fonticola*), *Providencia* spp., *Hafnia* spp., *K. aerogenes*.

[5] $ESBL_A$-test med cefepim/cefpirom anbefales, alternativt kombinasjonslapp med både kloxacillin og klavulansyre.

[6] Manglende synergi kan skyldes forekomst av $ESBL_M$ (eller kromosomal AmpC) alene eller i kombinasjon med $ESBL_A$, eller andre mer sjeldne kromosomale resistensmekanismer.

[7] *Klebsiella pneumoniae*-komplekset består av 7 underarter: de vanligste er *K. pneumoniae* (sensu stricto), *K. quasipneumoniae* og *K. variicola*.

E. coli, K. pneumoniae, P. mirabilis, Salmonella, Shigella



NordicAST Breakpoint table v. 16.0

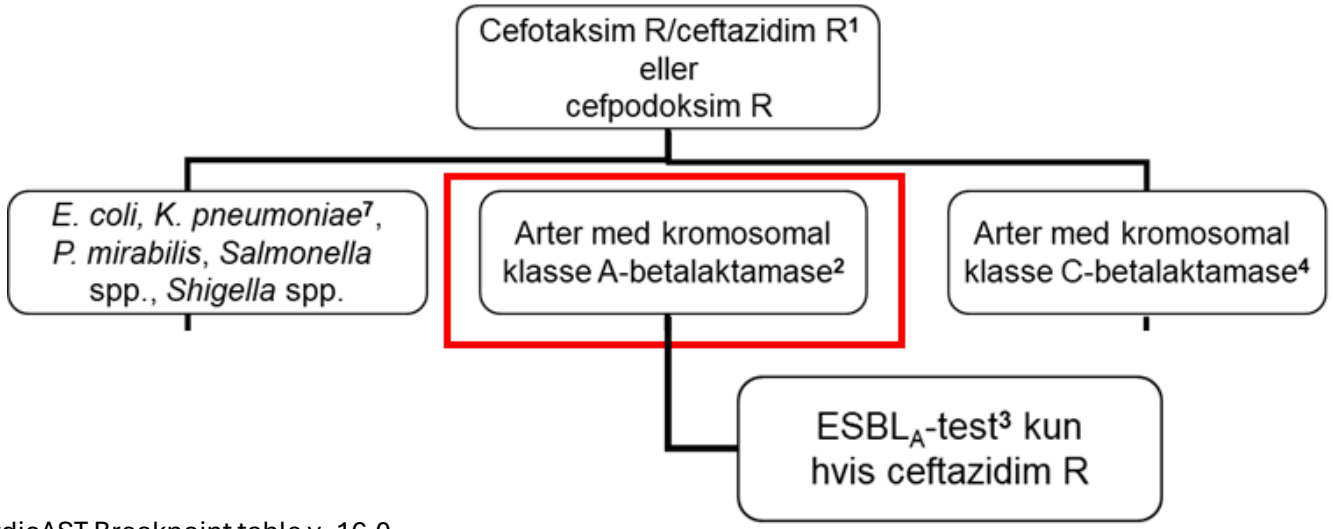
Species mostly absent of beta-lactamases interfering with ESBL-testing	
Main species	**Related species**
Escherichia coli	*E. hermannii* *E. albertii* *E. fergusonii* *E. marmotae* *Leclercia adecarboxylata*
Klebsiella pneumoniae	*K. quasipneumoniae* *K. variicola* *K. quasivariicola* *K. africana*
Proteus mirabilis	
Salmonella spp.	
Shigella spp.	

https://s3-eu-west-1.amazonaws.com/hl-intranet/files/753c6ba0696ba6b67a230a71a11cdd6674e61ba2/copy_of_nordicast_synonymlista_2024_002.pdf

[6]Manglende synergi kan skyldes forekomst av plasmid-mediert AmpC (eller kromosomal AmpC) alene eller i kombinasjon med ESBL, eller andre mer sjeldne kromosomale resistensmekanismer

↳ Cefoxitin R -> test også for plasmid-mediert AmpC (NB: bruk da også cefepim/cefepim-klavulansyre)

Arter med kromosomal klasse A β-laktamase



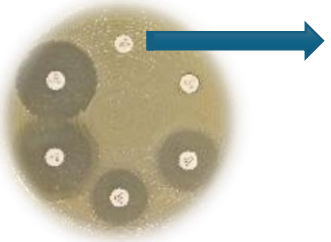
NordicAST Breakpoint table v. 16.0

Species featuring class A chromosomal beta-lactamases that can interfere with ESBL-testing	
Main species	**Related species**
Klebsiella oxytoca	*K. michiganensis* *K. spallanzanii* *K. pasteurii* *K. grimontii* *K. huaxensis* *Raoultella* spp.
Proteus vulgaris	*P. hauseri* *P. penneri*
Citrobacter koseri	*C. sedlakii* *C. farmeri* *C. amalonaticus* *C. gillenii*
Serratia fonticola	
Kluyvera ascorbata	*Kluyvera* spp.

https://s3-eu-west-1.amazonaws.com/hl-intranet/files/753c6ba0696ba6b67a230a71a11cdd6674e61ba2/copy_of_nordicast_synonymlista_2024_002.pdf

- ² ***K. oxytoca, P. vulgaris, C. koseri, C. sedlakii, C. farmeri, S. fonticola*…..:**
  - ✓Kromosomale klasse A β-laktamaser – noen har lignende substratprofil som ESBL og hemmes av klavulansyre
  - ✓Gir vanligvis resistens mot cefotaxim
  - ✓Oftest lavgradig uttrykt
  - ✓Falsk positive ESBL tester (cefotaxim/cefepime)
  - **ESBL test kun hvis ceftazidim R!!**

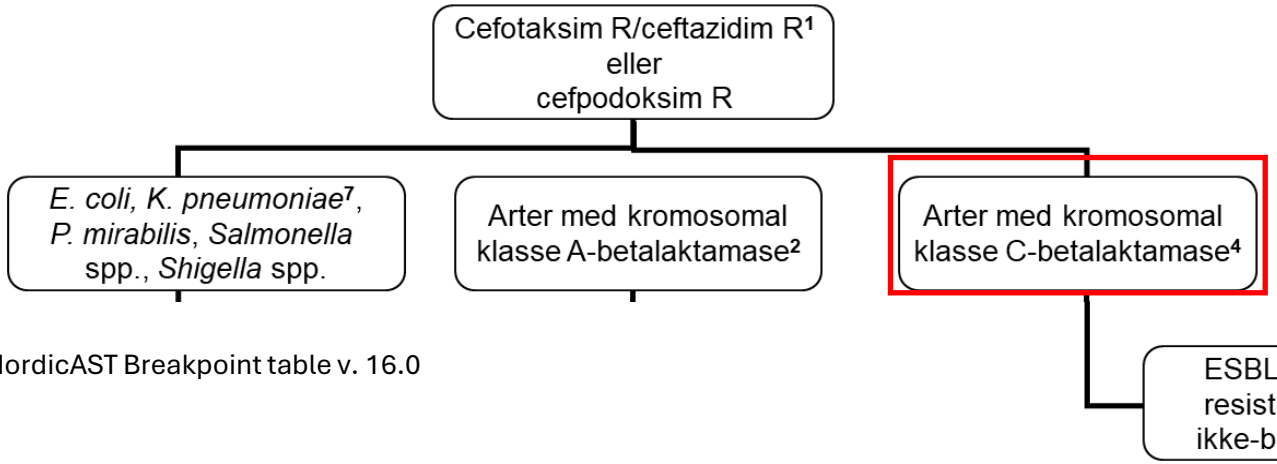
³ ESBL$_A$-test med ceftazidim anbefales.



- høygradig R pip-tazo (+ resistens aztreonam og cefuroxim) -> indikator for økt uttrykk av kromosomal β-laktamase

Bilde: Nasjonalt senter for påvisning av antibiotikaresistens (K-res)

Arter med kromosomal klasse C β-laktamase



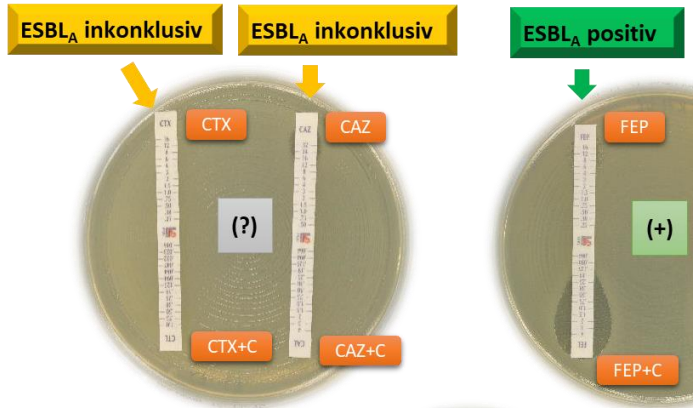
NordicAST Breakpoint table v. 16.0

Species featuring class C chromosomal beta-lactamases that can interfere with ESBL-testing when derep	
Main species	**Related species**
Enterobacter cloacae	*E. asburiae* *E. bugandensis* *E. cancerogenus* *E. hormaechei* *E. kobei* *E. ludwigii* *E. roggenkampii* *Lelliottia (Erwinia) nimipressuralis*
Citrobacter freundii	*C. braakii* *C. werkmanii* *C. youngae* *C. murliniae* *C. portucalensis*
Morganella morganii	*Morganella* spp.
Serratia marcescens	*Serratia* spp. (except *fonticola*)
Providencia stuartii	*Providencia* spp.
Hafnia alvei	*Hafnia* spp.
Klebsiella aerogenes	
Pantoea agglomerans	*Pantoea* spp.

https://s3-eu-west-1.amazonaws.com/hl-intranet/files/753c6ba0696ba6b67a230a71a11cdd6674e61ba2/copy_of_nordicast_synonymlista_2024_002.pdf

➢ [2] Vanligste arter er ***Enterobacter* spp.**, ***C. freundii*, *Morganella* spp.**, ***Serratia* spp. (unntatt *fonticola*)**, ***Providencia* spp.**, ***Hafnia* spp.**, ***K. aerogenes*:**

- ✓**Induserbar kromosomal AmpC**
- ✓**Klavulansyre-synergi med ceftazidim/cefotaxim kan bli maskert**



Bilder: Nasjonalt senter for påvisning av antibiotikaresistens (K-res)

[5] ESBL-test med cefepim/cefpirom anbefales, alternativt kombinasjonslapp med både kloxacillin og klavulansyre.

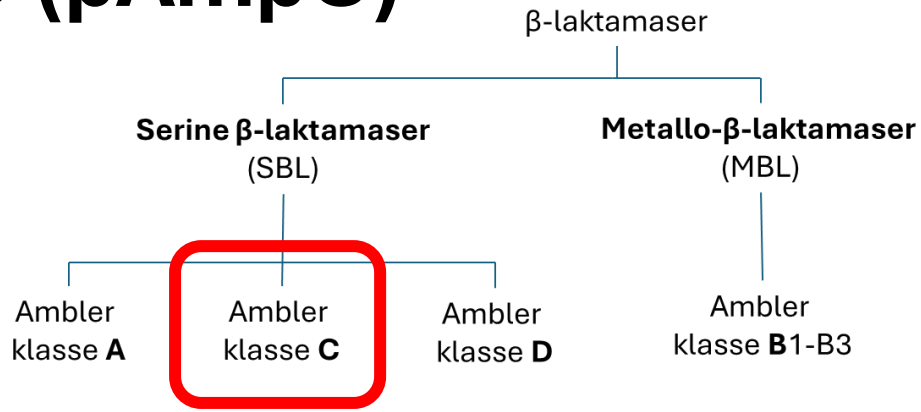
Plasmid-mediert AmpC (pAmpC)

- Serin Ambler klasse C β-laktamase

TABLE 5. Chronology and homology of plasmid-mediated AmpC β-lactamases

AmpC β-lactamase	Country of origin	Publication yr	Species of first isolate	Likely source of AmpC gene	Similarity (%)	Reference(s)
CMY-1	South Korea	1989	*K. pneumoniae*	*A. hydrophila*	82	20, 23
CMY-2	Greece	1996	*K. pneumoniae*	*C. freundii*	96	22
MIR-1	United States	1990	*K. pneumoniae*	*E. cloacae*	99	142, 248
MOX-1	Japan	1993	*K. pneumoniae*	*A. hydrophila*	80	134
LAT-1	Greece	1993	*K. pneumoniae*	*C. freundii*	95	326
FOX-1	Argentina	1994	*K. pneumoniae*	*A. caviae*	99	95, 109
DHA-1	Saudi Arabia	1997	*S. enteriditis*	*M. morganii*	99	98
ACT-1	United States	1997	*K. pneumoniae*	*E. asburiae*	98	41, 279
ACC-1	Germany	1999	*K. pneumoniae*	*H. alvei*	99	21, 106
CFE-1	Japan	2004	*E. coli*	*C. freundii*	99	229

Jacoby GA. *Clin. Microbiol. Rev.* 2009

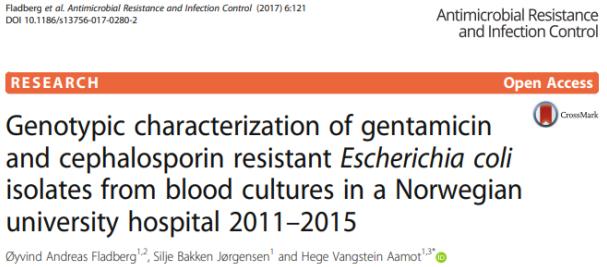


- Vanligste enzymer: **CMY**, **DHA**
- Sjeldne: FOX, MIR, MOX, LAT, BIL, ACT, ACC, CFE..

E. coli NORM 2010-2012:

Prøvemateriale	År	pAmpC	cAmpC
Urin	2010-12	0-0,4 %	0-0,3 %
Blodkultur	2010-12	0,1-0,2 %	0,4-0,6 %

Data: Nasjonalt senter for påvisning av antibiotikaresistens


Fladberg *et al. Antimicrobial Resistance and Infection Control* (2017) 6:121
DOI 10.1186/s13756-017-0280-2

Antimicrobial Resistance and Infection Control

RESEARCH Open Access

Genotypic characterization of gentamicin and cephalosporin resistant *Escherichia coli* isolates from blood cultures in a Norwegian university hospital 2011–2015

Øyvind Andreas Fladberg[1,2], Silje Bakken Jørgensen[1] and Hege Vangstein Aamot[1,3*]

Fladberg ØA et al. *Antimicrob. Resist. Infect. Control* 2017

101 cefalosporin resistente *E. coli:*

- 84 % ESBL
- 3 % pAmpC

Aktivitetsprofil pAmpC (& cAmpC)

β-laktamgruppe	**pAmpC**
Penicilliner (Ampicillin, Piperacillin)	●
1-3. gen. cefalosporiner (Cefotaxim, Ceftazidim)	●
4. gen. cefalosporiner (Cefepim)	○
Cefamyciner (Cefoxitin, Cefotetan)	●
Monobaktamer (Aztreonam)	○/●
Karbapenemer (Meropenem, Imipenem, Ertapenem)	○
β-laktamase inhibitorer	**pAmpC**
Klavulansyre, Tazobaktam, Enmetazobaktam	○
Avibaktam, Vaborbaktam, Relebaktam	●
Kloxacillin	●

● hydrolyseres
○ hydrolyseres ikke

← NB
← NB
← NB
← NB

● inhiberes
○ Inhiberes ikke

Påvisning av pAmpC

4. Acquired AmpC β-lactamase-producing Enterobacteriaceae

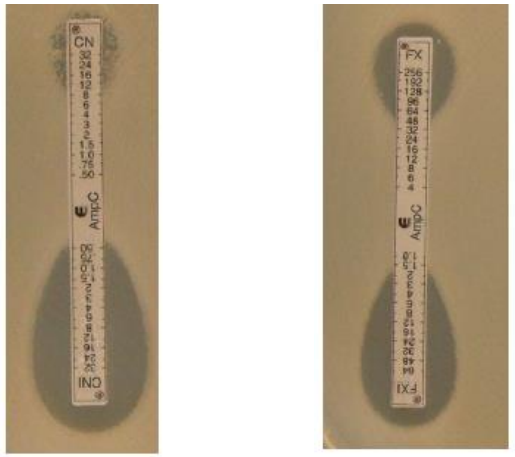
Importance of detection of resistance mechanism	
Required for clinical antimicrobial susceptibility categorization	No
Infection control purposes	Yes
Public health purposes	Yes

EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological value. v. 2.0 July 2017

Fenotypiske metoder for påvisning av pAmpC

Basert på synergi mellom cefamyciner/3. gen. cefalosporiner og **kloxacillin**

Kombinasjons gradient-test:



- Cefotetan/cefotetan+kloxacillin
- Cefoxitin/cefoxitin+kloxacillin

- Positiv test:
  - ✓ Ratio ≥8
  - ✓ Fantomsone

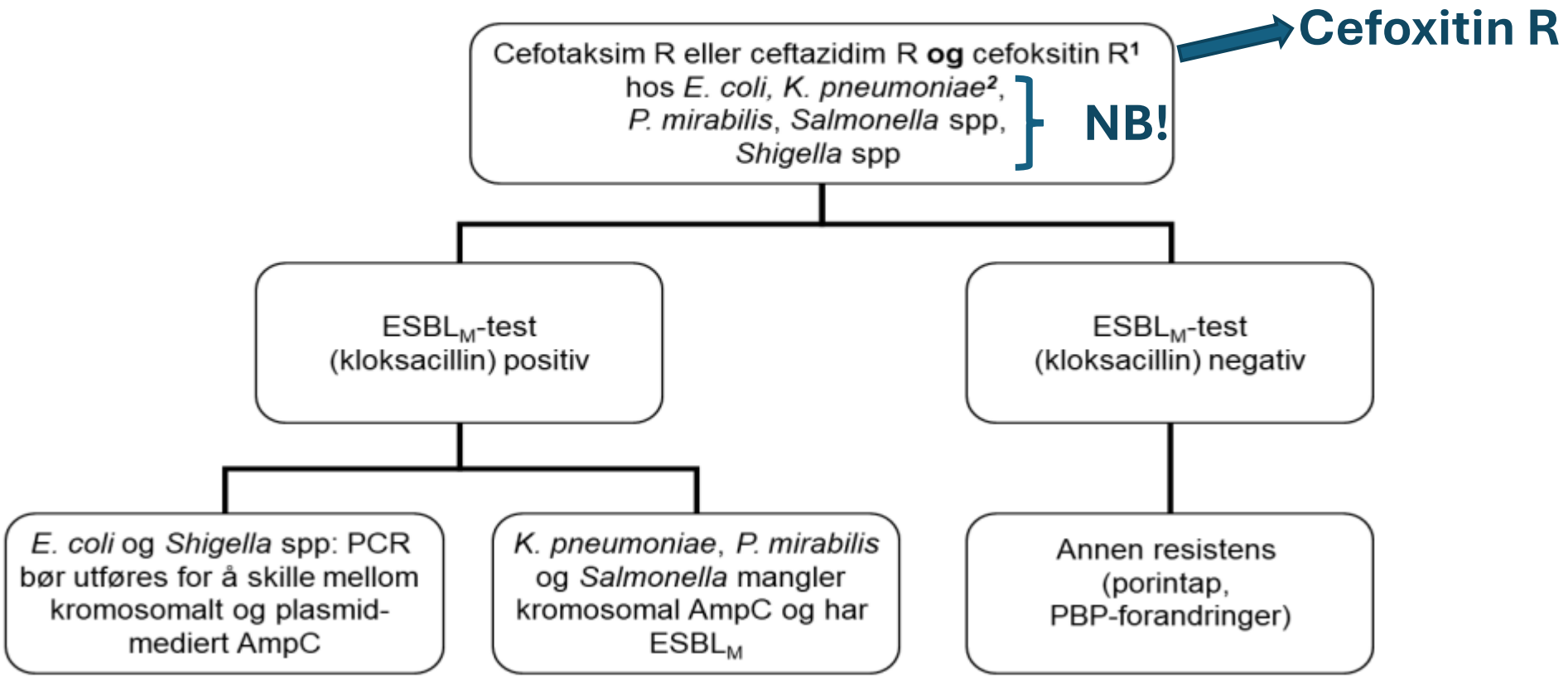
Kombinasjons tabletter:

- Ceftazidim/ceftazidim+kloxacillin
- Cefotaxim/cefotaxim+kloxacillin

- Positiv test:
  - ✓ Ratio ≥5 (1 kombinasjon nok!)

Bilder: Nasjonalt senter for påvisning av antibiotikaresistens (K-res)

Enterobacterales
ALGORITME FOR PÅVISNING AV PLASMIDMEDIERT AmpC ($ESBL_M$)



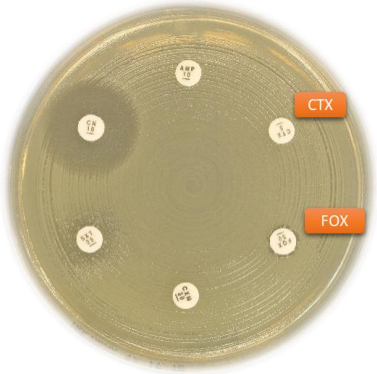
[1] Test isolater med cefotaksim R eller ceftazidim R (ved automatisert resistensbestemmelse: test også isolater som er cefotaksim eller ceftazidim I) i kombinasjon med cefoksitin R. Merk at $ESBL_A$-positive isolater også kan være $ESBL_M$-positive. $ESBL_M$-test bør derfor utføres uansett resultat ved $ESBL_A$-testing.

[2] *Klebsiella pneumoniae*-komplekset består av 7 underarter: de vanligste er *K. pneumoniae* (sensu stricto), *K. quasipneumoniae* og *K. variicola*.

Både ESBL & pAmpC/(cAmpC)?

ESBL

Cefotaksim R/ceftazidim R[1]
eller
cefpodoxim R



pAmpC

Cefotaksim R eller ceftazidim R **og** cefoksitin R[1]
hos *E. coli, K. pneumoniae*,
P. mirabilis, *Salmonella* spp,
Shigella spp

β-laktamgruppe	**ESBL**	**pAmpC**
Penicilliner (Ampicillin, Piperacillin)	●	●
1-3. gen. cefalosporiner (Cefotaxim, Ceftazidim)	●	●
4. gen. cefalosporiner (Cefepim)	●	○
Cefamyciner (Cefoxitin, Cefotetan)	○	●
Monobaktamer (Aztreonam)	●	○ / ●
Karbapenemer (Meropenem, Imipenem, Ertapenem)	○	○
β-laktamase inhibitorer	**ESBL**	**pAmpC**
Klavulansyre, Tazobaktam, Enmetazobaktam	●	○
Avibaktam, Vaborbaktam, Relebaktam	●	●
Kloxacillin	○	●

Bilder: Nasjonalt senter for påvisning av antibiotikaresistens (K-res)

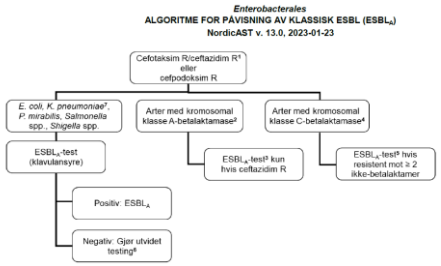
pAmpC/cAmpC – aktivitet mot 3GC og hemmes ikke av klavulansyre -> maskere tilstedeværelse av ESBL

ESBL testing må inkludere cefepim/cefepim-klavulansyre!!

Andre tester

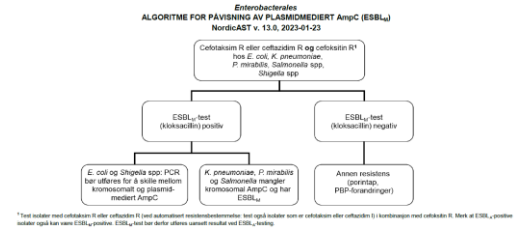
- Lateral flow tester
  - NG-TEST CTX-M Multi
  - RESIST CTX-M
- NAATs
  - eazyplex SuperBug AmpC
  - eazyplex SuperBug CRE
- Biokjemiske tester
  - MBT STAR-BL Assays
  - β-LACTA test
  - Rapid ESBL NP test
- ++++++

Oppsummering

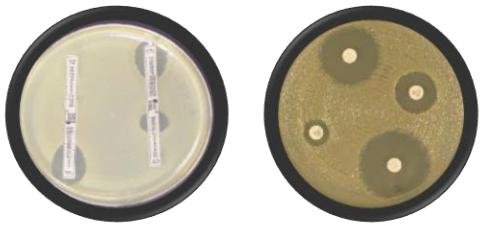


NordicAST Breakpoint table v. 16.0

β-laktamgruppe	ESBL	pAmpC
Penicilliner (Ampicillin, Piperacillin)	●	●
1-3. gen. cefalosporiner (Cefotaxim, Ceftazidim)	●	●
4. gen. cefalosporiner (Cefepim)	●	○
Cefamyciner (Cefoxitin, Cefotetan)	○	●
Monobaktamer (Aztreonam)	●	○ / ●
Karbapenemer (Meropenem, Imipenem, Ertapenem)	○	○
β-laktamase inhibitorer	**ESBL**	**pAmpC**
Klavulansyre, Tazobaktam, Enmetazobaktam	●	○
Avibaktam, Vaborbaktam, Relebaktam	●	●
Kloxacillin	○	●



NordicAST Breakpoint table v. 16.0



- ESBL: synergi 3GC & klavulansyre
- pAmpC: synergi 3GC/cefamyciner & kloxacillin

- Lateral-flow, NAATs etc.:
  - ESBL: CTX-M gr. 1 og gr. 9
  - pAmpC: CMY, DHA

Bilder: Nasjonalt senter for påvisning av antibiotikaresistens (K-res)