Vorgehen bei gramnegativen Erregern mit induzierbarer chromosomaler AmpC-Beta-Laktamase

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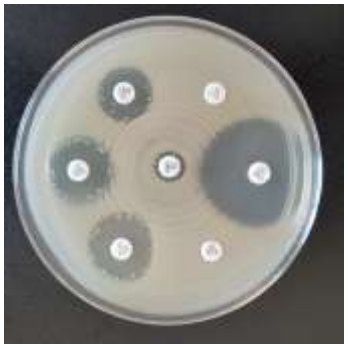
AmpC Betalaktamasen

- AmpC-Enzyme (Cephalosporinasen) sind β-Laktamasen der Ambler-Klasse C (Bush Jacoby Medeiros Klasse 1 und 1e)

- Hydrolytisches Profil: Penicilline, Cephalosporine (I–III) und Monobactame
- Inhibitoren: Cloxacillin oder Boronsäurederivate, die durch klassische ESBL-Inhibitoren nur schwach gehemmt werden

- **Natürlich vorkommend (chromosomale AmpCs**)

- Mehrere erworbene AmpC-Gene bekannt (meist von natürlichen Produzenten stammend)
  - am häufigsten bei: E. coli (schwierig), K. pneumoniae, K. oxytoca, Salmonella enterica und P. mirabilis



Darstellung am Antibiogramm?

CMR 2009 22:161-82

EUCAST Expected Resistant Phenotypes

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Rule	Organisms	Ampicillin/Amoxicillin	Amoxicillin-clavulanic acid	Ampicillin-sulbactam	Ticarcillin	Cefazolin, Cephalothin Cefalexin, Cefadroxil	Cefoxitin[2]	Cefuroxime	Tetracyclines	Tigecycline	Polymyxin B, Colistin	Fosfomycin	Nitrofurantoin
1.1	*Citrobacter koseri, Citrobacter amalonaticus*[3]	R			R								
1.2	*Citrobacter freundii*[4]	R	R	R		R	R						
1.3	*Enterobacter cloacae* complex	R	R	R		R	R						
1.4	*Escherichia hermannii*	R			R								
1.5	*Hafnia alvei*	R	R								R		
1.6	*Klebsiella aerogenes*	R	R	R		R	R						
1.7	*Klebsiella pneumoniae* complex	R			R								
1.8	*Klebsiella oxytoca*	R			R								
1.9	*Leclercia adecarboxylata*											R	
1.10	*Morganella morganii*	R	R	R		R			R		R		R
1.11	*Plesiomonas shigelloides*	R	R	R									
1.12	*Proteus mirabilis*								R		R		R
1.13	*Proteus penneri*	R				R		R	R		R		R
1.14	*Proteus vulgaris*	R				R		R	R		R		R
1.15	*Providencia rettgeri*	R	R	R		R			R		R		R

Rule	Organisms	Ampicillin/Amoxicillin	Amoxicillin-clavulanic acid	Ampicillin-sulbactam	Ticarcillin	Cefazolin, Cephalothin Cefalexin, Cefadroxil	Cefoxitin[2]	Cefuroxime	Tetracyclines	Tigecycline	Polymyxin B, Colistin	Fosfomycin	Nitrofurantoin
1.16	*Providencia stuartii*	R	R	R		R			R		R		R
1.17	*Raoultella* spp.	R			R								
1.18	*Serratia marcescens*	R	R	R		R	R	R			R		R
1.19	*Yersinia enterocolitica*	R	R	R	R	R	R						
1.20	*Yersinia pseudotuberculosis*										R		

[2] Clinical breakpoints for cefoxitin have not been defined. *Enterobacterales* species expected to be resistant to this antibiotic produce a chromosomal inducible AmpC β-lactamase (AmpC) that is responsible for higher cefoxitin MIC values when compared with those from *Enterobacterales* species lacking production of this beta-lactamase.

EUCAST Expert Rules v 3.3 Enterobacterales

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Rule No.	Organisms	Indicator Agent*	Agents affected*	Rule	Remarks	Grade	References
Beta-Lactams							
3	*Enterobacter* spp., *K. aerogenes*, *Citrobacter freundii*[r], *Hafnia alvei*	cefotaxime, ceftriaxone, ceftazidime	cefotaxime, ceftriaxone, ceftazidime, piperacillin±tazobactam	IF susceptible in vitro to cefotaxime, ceftriaxone, ceftazidime, or piperacillin±tazobactam THEN EITHER add a note that monotherapy with cefotaxime, ceftriaxone, ceftazidime or piperacillin±tazobactam as well as combination therapy of these agents with an aminoglycoside should be discouraged owing to risk of selecting resistance, OR suppress the susceptibility testing results for these agents	Selection of AmpC de-repressed cephalosporin-resistant mutants may occur during therapy. The risk is relatively high in *Enterobacter* spp, *K. aerogenes* and *C. freundii* and low in *M, morganni* and *S, macescens*. For *Hafnia alvei in-vitro* mutation rates are similar to *Enterobacter* spp. or *C. freundii*. The use of a 3rd generation cephalosporin in combination with an aminoglycoside may also lead to failure by selection of resistant mutants. The combination with a quinolone, however, has found to be protective, although the clinical utility of this combination is not known The selection risk is absent or much diminished for cefepime	A	Sanders & Sanders, 1988; Choi et al., 2008; Harris & Ferguson, 2012; Kohlmann, Bähr, & Gatermann, 2018 Maillard et al 2023

Hinweistext oder Ergebnis unterdrücken

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Rule No	Organisms	Indicator Agent*	Agents affected*	Rule	Remarks	Grade	References
4	*Serratia* spp., *Morganella morganii*, *Providencia* spp	cefotaxime, ceftriaxone, ceftazidime	cefotaxime, ceftriaxone and ceftazidime	IF susceptible to cefotaxime, ceftriaxone or ceftazidime, THEN note that monotherapy with cefotaxime, ceftriaxone or ceftazidime may infrequently select resistant mutants		A	Sanders & Sanders, 1988; Choi et al [illegible] Kohlmann, Bähr, & Gatermann, 2018
5	*Enterobacter* spp., *K. aerogenes*, *Citrobacter freundii*, *Serratia* spp., *Morganella morganii*, *Hafnia alvei*, *Providencia* spp.	cefuroxime	cefuroxime other 2nd generation cephalosporins	IF susceptible to cefuroxime, THEN report cefuroxime and/or any other 2nd generation cephalosporin as resistant	Although the breakpoint table does not list cefuroxime breakpoints for species other than *E. coli*, *P. mirabilis*, *Klebsiella* spp. (except *K. aerogenes*) and *Raoultella* spp., isolates may ap[illegible] susceptible in vitro b[illegible] tend to be higher tha[illegible] mentioned species a[illegible] with cefuroxime is not recommended. In addition, de-repressed mutants may be selected as with a third-generation cephalosporin.	C	

Hinweistext

Ceph 2: R

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Vielen Dank für die Aufmerksamkeit