

Intrinsic Resistance and Expert Rules

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Expert rules and intrinsic resistance

EUCAST expert rules are a tabulated collection of expert knowledge on intrinsic resistances, exceptional resistance phenotypes and interpretive rules that may be applied to antimicrobial susceptibility testing in order to reduce errors and make appropriate recommendations for reporting particular resistances.

EUCAST Expert rules, intrinsic resistance and exceptional phenotypes v 3.1 (Sept 27, 2016)

There are parts of the original document which is not yet covered by the revision. For these the original document ([EUCAST Expert rules v 2.0](#)) is valid until the review has been completed.

Expert rules are under revision. The next version will be available as separate tables for each species/species group. The revision is expected to be finalised during 2018. One example is given below for Staphylococcus.

Enterobacteriaceae

Pseudomonas aeruginosa

Stenotrophomonas maltophilia

Acinetobacter spp.

Staphylococcus spp.

Enterococcus spp.

Streptococcus A, B, C and G

Streptococcus pneumoniae

Viridans Group Streptococci

New Documents

- Intrinsic resistance and unusual phenotypes
- expert rules
 - one file per species (group)

First Question

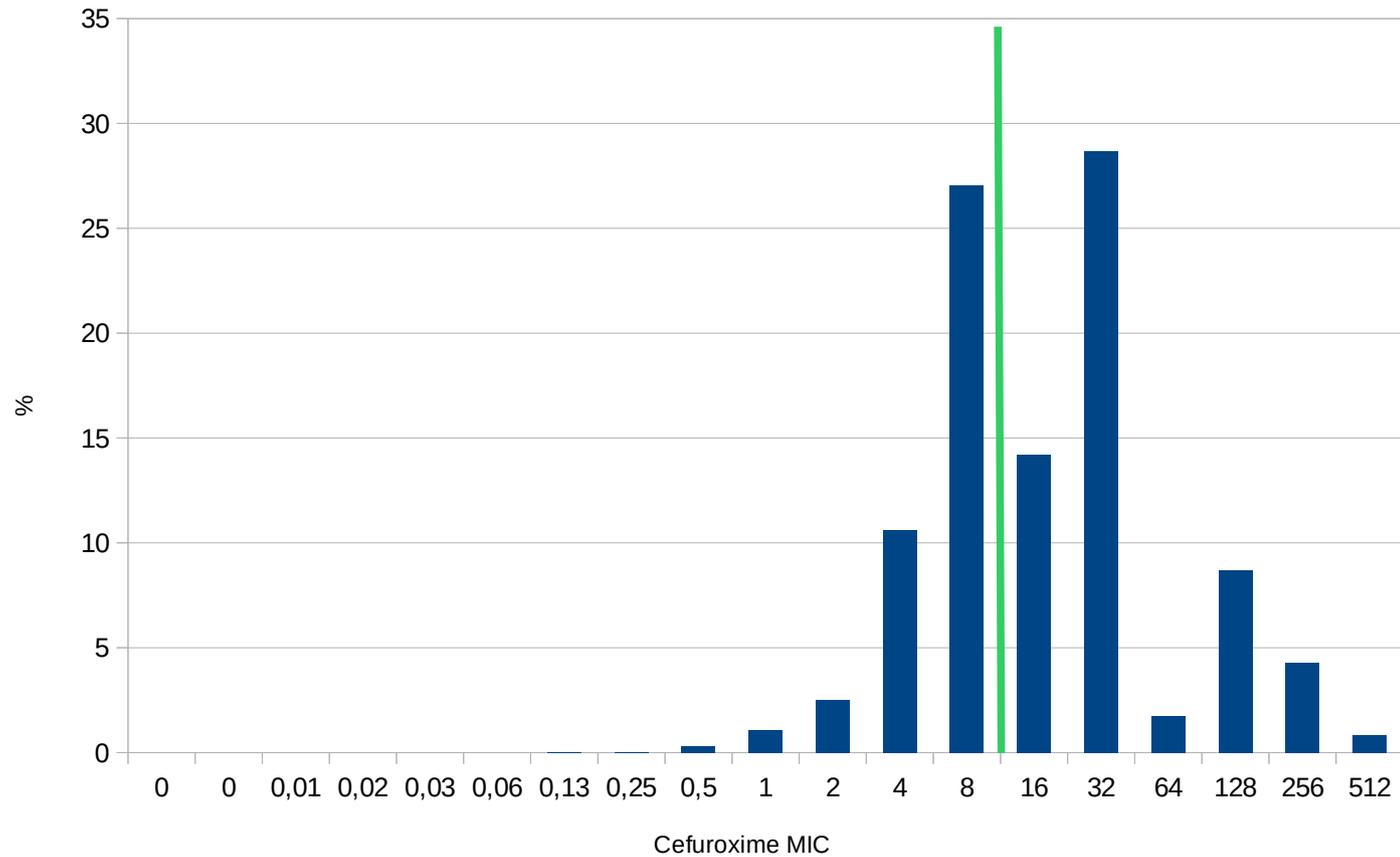
Which is intrinsic resistance?
(more than one may be correct)

- A) Cefuroxime in *Enterobacter cloacae*
- B) Tigecycline/Doxycycline in *Proteus mirabilis*
- C) Ampicillin in *Klebsiella pneumoniae*
- D) Gentamicin in *Salmonella* spp.
- E) Cefotaxime in *Enterococcus faecalis*

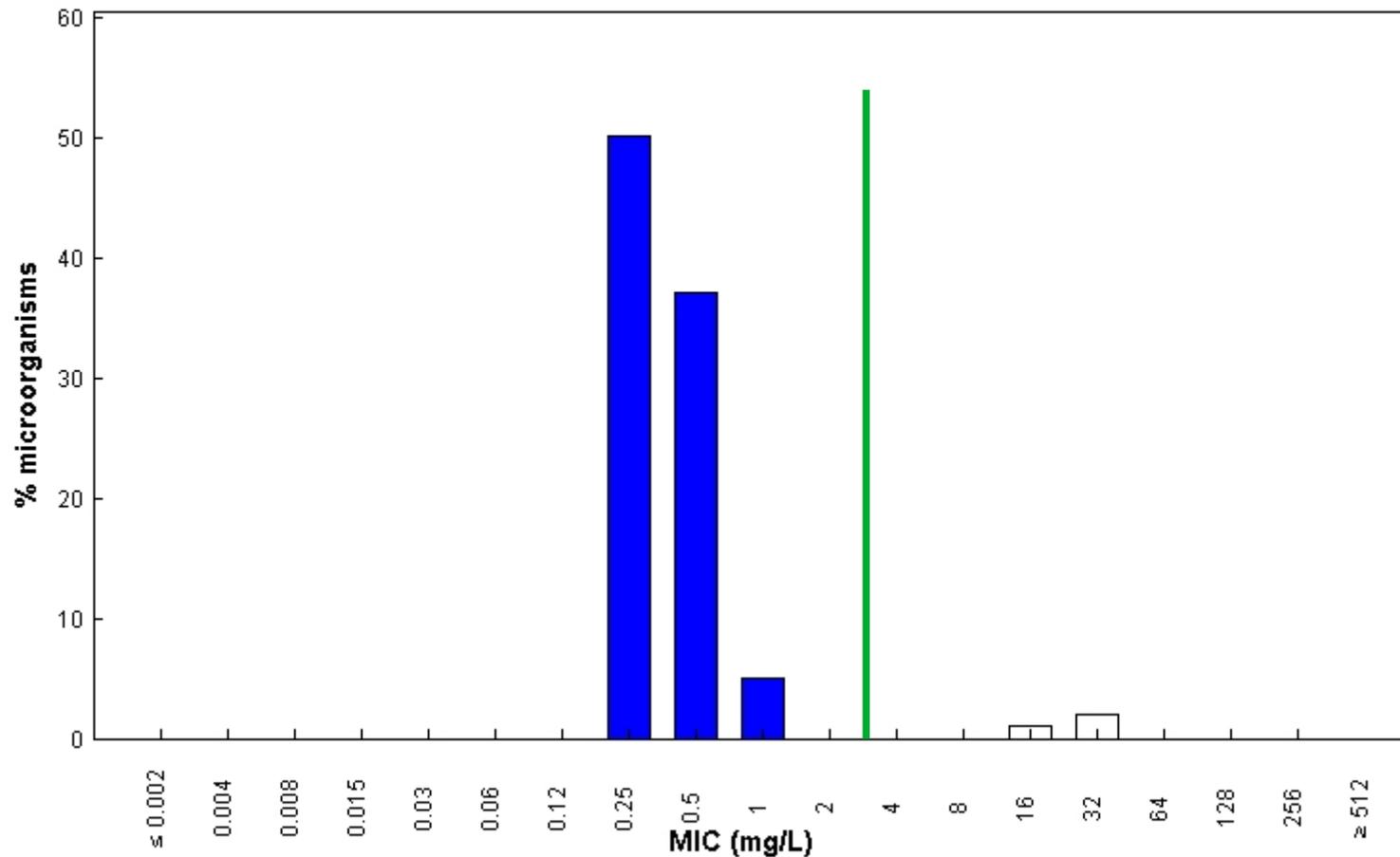
Definitions

- Intrinsic Resistance
 - is found *in vitro* in (almost) every isolate of a certain species
- Unusual Phenotypes
 - resistance is typically not found in a certain species

Cefuroxime in Enterobacter



Gentamicin in Salmonella



MIC
Epidemiological cut-off (ECOFF): 2 mg/L
Wildtype (WT) organisms: ≤ 2 mg/L

46664 observations (14 data sources)

Answer to First Question

- *Enterobacter cloacae* may appear susceptible to cefuroxime *in vitro* in about 40%
- Salmonella usually are susceptible against gentamicin *in vitro*
- *Proteus mirabilis* tests resistant towards tetracyclines
- *Klebsiella pneumoniae* test resistant to ampicillin
- Cefotaxime tests resistant against *E. faecalis*

Intrinsic Resistance, Unusual Phenotypes

- are used to validate identification and susceptibility tests
 - a susceptible gentamicin result does not argue against the identification as *Salmonella*
 - susceptibility to cefuroxime is no argument against the identification as *E. cloacae*
 - ampicillin susceptibility would argue against identification as *K. pneumoniae*
 - cefotaxime susceptibility is very unusual in *E. faecalis*
 - penicillin resistance in group A streptococci strongly argues against the identification (or the susceptibility test)

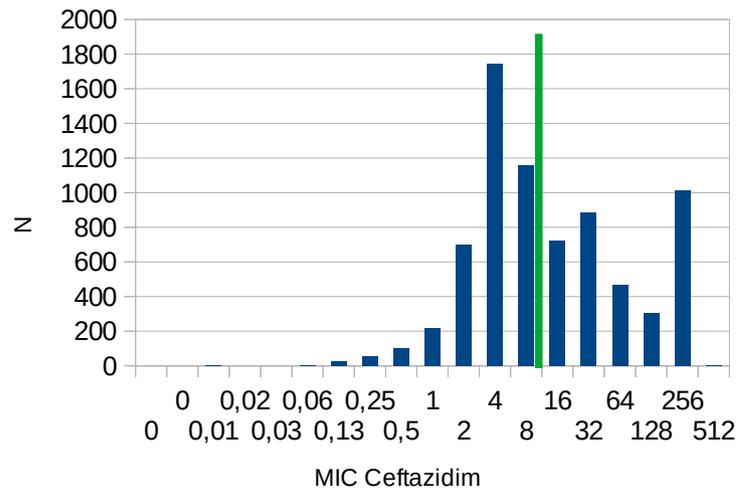
Expert Rules

- although cefuroxime may test susceptible in *E. cloacae*, it is not recommended for therapy
 - there are no breakpoints for cefuroxime and *E. cloacae*
- in *Salmonella* spp. gentamicin always appears susceptible *in vitro*, but is not active *in vivo*
 - gentamicin breakpoints apply to Enterobacterales, so there has to be an extra rule for Salmonella

The Dash '-' is an Implicit Expert Rule

Cephalosporins in *Acinetobacter* spp.

Cefpodoxime	-	-			-	-	
Ceftaroline	=	=			=	=	
Ceftazidime	-	-			-	-	
Ceftazidime-avibactam	=	=			=	=	
Ceftibuten	-	-			-	-	
Ceftahinrole	-	-			-	-	



A '-' says:
 „Inappropriate agent for this
 organism“, regardless of test
 result.

The Dash '—': an Implicit Expert Rule

- the dash means „do not use this antibiotic on this organism“
- a dash does not mean that resistance will always be detected
- if there is intrinsic resistance, there is always a dash

Utility of Intrinsic Resistance and Unusual Phenotypes

IF intrinsic resistance is absent **OR** an unusual phenotype (usually resistance when the species is typically susceptible) is detected

THEN

check identification and/or susceptibility test

Utility of Expert Rules

- avoid reporting a susceptible result if there is data indicating that therapy will fail
 - MRSA and most β -lactams
 - piperacillin and ampicillin-resistant *E. coli*
- alert that therapy may need modification

An Expert Rule for ESBL

E. coli, *Klebsiella* spp.(except *K. aerogenes*), *Raoultella* spp.

IF resistant to any 3rd generation (cefotaxime, ceftriaxone, ceftazidime) or 4th generation (cefepime) cephalosporin **AND** susceptible to piperacillin-tazobactam or amoxicillin-clavulanic acid,

THEN report as tested.

The comment

This phenotype is most often caused by ESBL production. ESBL producers sometimes test as susceptible to beta-lactam-beta-lactamase-inhibitor combinations. The use of these combinations in infections caused by ESBL- producers has historically been a matter of controversy. A number of studies have shown that they may be safe provided appropriate dosing is used. One publication indicates that carbapenem therapy may be superior to piperacillin-tazobactam, as measured by 30-day mortality and primarily in patients with terminal cancer.

How to Implement that Rule?

- the clinician should be informed about the problems with that phenotype
- as mortality increases with piperacillin-tazobactam MIC ≥ 16 , a measured „I“ should probably be reported as an „R“ (16 is the ATU)
- „provided appropriate dosing is used“ may be translated into reporting an „I“

No Rule for Carbapenems

- prevalence (of enzymes) differs
- studies are contradictory
- many different opinions
- possible solutions
 - report as tested
 - use comment that is adapted to your situation

Question two

There is a dash '-' for ceftazidime in *Acinetobacter*; if someone asks for a result for ceftazidime, what do you do?

- A. Use the breakpoints for *Pseudomonas* spp.
- B. Use the Pk-Pd breakpoints
- C. Use the CLSI breakpoints
- D. Report the MIC
- E. Report an 'R'

Answer

The dash means „inappropriate agent“, using another system does not change the biology.

The Pk-Pd breakpoints only apply if there are no recommendations against its use, i.e., implicit or explicit expert rules, only in those cases an MIC may be reported.

