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BIA
British Infection Association

Gram positive bacteria: some key antimicrobial resistance mechanisms

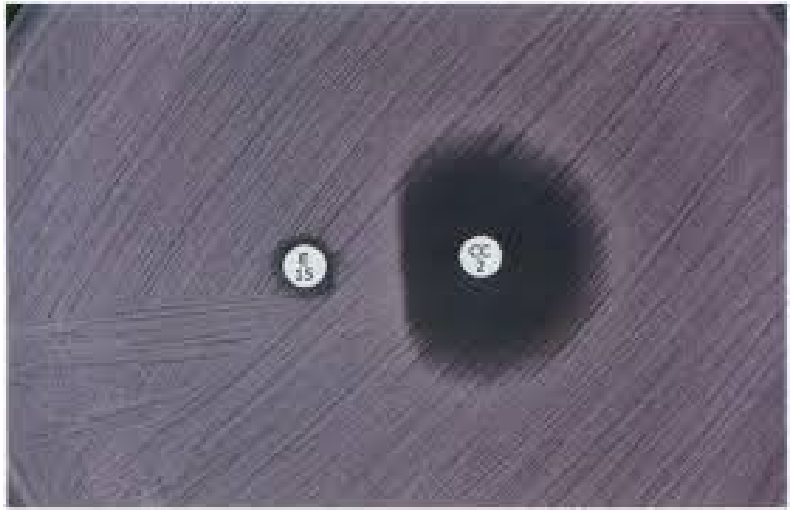
March 2022

Inducible clindamycin resistance

- Erythromycin (macrolide)
- Clindamycin (lincosamide)
- Both act on 50S ribosomal subunit

MLSB Resistance = by methylation of the ribosomal target, mediated by *erm* gene

- May be constitutive
- May be inducible
  - This is the trip-you-up one!
  - Appears ery R clind S in routine testing but…..if you tx with clinda, you select for *erm* mutants and may get treatment failure.



A positive D-zone test result for detection of inducible clindamycin resistance. From: Lewis JS and Jorgensen JH. CID 2005; 40 (2):280-285. Fig 1.

Staph spp, pneumo and β haem strep

2µg clinda and 15µg ery 15mm apart (from disc edge)

Flattening of clinda zone- D zone = inducible resistance.

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Penicillin-resistant pneumococci

- Pneumo have 6 PBPs.
- 2x is the primary penicillin target.
- Horizontal gene transfer from viridans strep confers mosaic genes encoding low affinity PBPs.
- This confers low level pen non-susceptibility - which is an issue in meningitis. Associated with higher mortality. Other infections ok as long as high doses used.

So MIC interpretation depends on clinical scenario:

- If 0.12 – 2mg/L
- R if meningitis
- S if elsewhere.

Screen with 1µg oxa disc

- If R (zone ≤20mm) must do an etest to determine MIC.
- Oxa zone size also determines how amox / cephs are reported (S ≥8mm)

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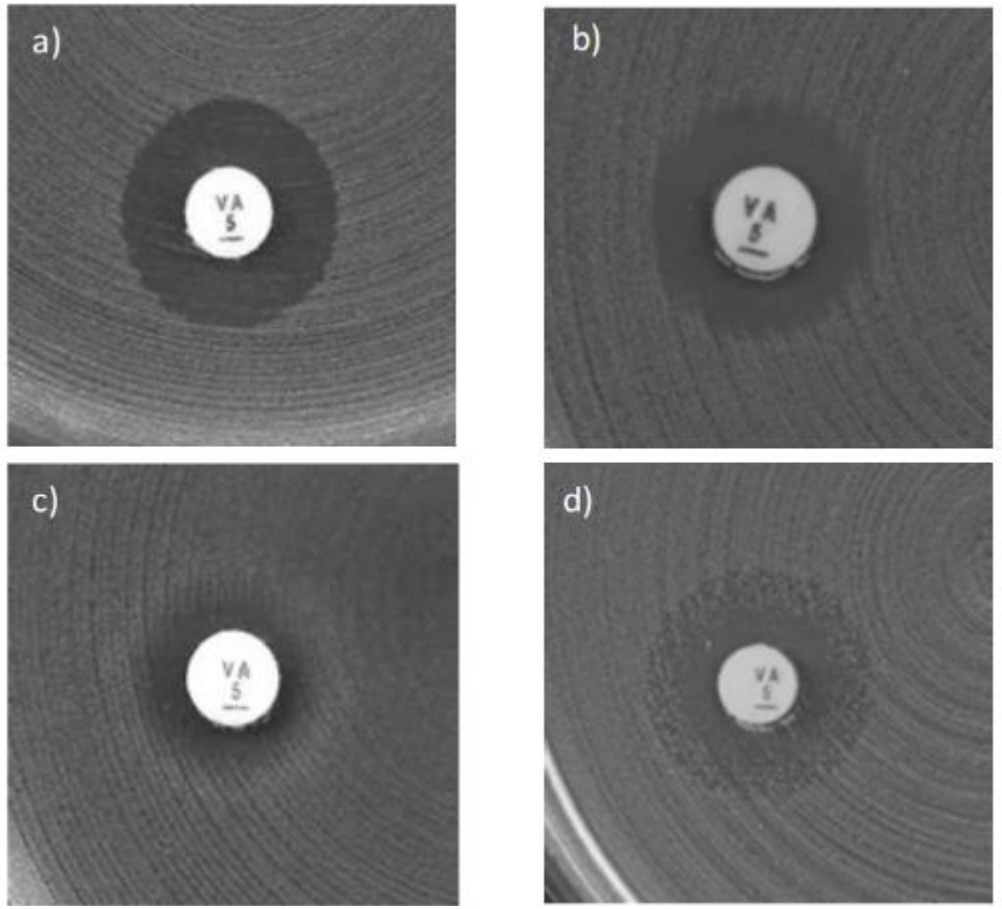
VRE

= *Enterococcus faecium* or *Enterococcus faecalis* with resistance to vancomycin (MIC >4 mg/L).

- Plasmid-encoded VanA and VanB ligases replace the terminal D-Ala(nine) in the peptidoglycan with D-Lac(tate).
- This reduces the binding of glycopeptides to the target.
- VanA = R to vanc and teic
- VanB = R to vanc, S to teic (lack of induction of the resistance operon



Hegstad K et al. JCM 2014; 52(5) 1582-1589. https://doi.org/10.1128/JCM.03544-13

a) Sharp zone edges and zone diameter ≥12 mm. Report as susceptible.

b-d) Fuzzy zone edges and/or colonies within the zone. Report as resistant regardless of zone diameter.

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MRSA

Classical resistance is due to *mecA* gene, coding for an alternative PBP2' (or PBP2a), characterised by a low affinity for most βlactams and which takes over.

The *mecA* gene is part of a mobile genetic element, the SCC*mec*, which is incorporated in the chromosome.

12 distinct types described.

Healthcare ass^{d} mostly = I, II or III

Community ass^{d} mostly = IV or V

Can also get mecC

Can also get borderline resistance from hyperproduction of β lactamases.

Disc testing:

- Oxa testing markedly affected by test conditions = DON'T USE

- Cefoxitin = more reliable
  - Better inducer of *mecA* gene.
  - More reproducible and accurate results
  - 30µg disc
  - S ≥ 22 mm; R ≤ 21 mm

MRSA screening:

- overnight chromogenic selective MRSA agar
- selective broth culture (containing 2.5% NaCl and cefoxitin)

CDC MRSA laboratory testing
EUCAST Clinical breakpoints
PHE MRSA screening SMI

VISA / VRSA

- VISA (MIC 3-8µg/mL) first detected 1997 -> some vanc tx failure

BUT

- no data demonstrate superior outcomes with alternative antimicrobials agents

- VRSA (MIC ≥ 32µg/mL) mediated by *vanA* (stolen from enterococci)
  - Very rare, probably due to fitness cost
  - Usually arises in diabetic wounds co-infected with SA and VRE.

Vancomycin-resistant Gram positives?

- VRE
- Erysipelothrix
- Pediococcus
- Lactobacillus
- Leuconostoc