Routine methods for susceptibility testing of staphylococci to beta-lactam antibiotics

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Aim:

To harmonize test methods and interpretation
Beta-lactam resistance in Staphylococci
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Routine methods for testing beta-lactam antibiotics for staphylococci

You only need to test 3 things:

(1) Susceptibility to penicillin (blaZ)
(2) Production of beta-lactamases (blaZ)
(3) Susceptibility to cefoxitin (mecA)
Susceptibility to penicillin

- **Susceptible to penicillin:**
  - Always test for production of beta-lactamases! (especially with borderline MICs or inhibition zone diameters).

- **Resistant against penicillin (cefoxitin S):**
  - Resistant against all “penicillinase-labile” penicillins such as penicillin, amoxicillin and ampicillin.
  - Susceptible to:
    - (A) semi-synthetic (“penicillinase-stabile”) penicillins such as nafcillin and oxacillin
    - (B) inhibitor combinations such as amox/clavulanic acid
    - (C) first generation cephalosporins such as cefalexin and cefaperine.
Testing of β-lactamase production

Test for induced beta-lactamase production by using bacterial growth from the border of the inhibition zone of a penicillin disk.

- **Beta-lactamase negative**: bacteria penS, amoxS and ampiS
- **Beta-lactamase positive**: bacteria penR, amoxR and ampiR, but susceptible to semi-synthetic penicillins, inhibitor combinations and cephalosporins.
Susceptibility to cefoxitin

• Susceptible to cefoxitin (disk test) or oxacillin (MIC-test): *meca*-gene not present

• Resistant against cefoxitin (or oxacillin): *meca* probably present (should be confirmed by PCR)

• Resistant against cefoxitin or oxacillin: resistant against all beta-lactam antibiotics, including all semi-synthetic penicillins, inhibitor combinations and all cephalosporins.
  — Except for ceftobiprole and ceftaroline (anti-MRSA cephalosporins)
Summarizing

3 possibilities

• Penicillin S, β-lactamase negative and cefoxitin S:
  – Bacteria susceptible to all beta-lactam antibiotics
  – *blaZ* and *meca* negative

• Penicillin R and or β-lactamase positive and cefoxitin S:
  – Bacteria resistant to penicillins, but susceptible to semi-synthetic penicillins, inhibitor combinations and all cephalosporins.
  – *blaZ* positive and *meca* negative

• Cefoxitin R (regardless of *in vitro* penicillin resistance):
  – Bacteria resistant to all beta-lactam antibiotics, except for anti-MRSA cephalosporins.
  – *meca* positive (and *blaZ* positive or negative)
Advise for routine testing

• Use **penicillin**, a test for β-lactamase production and **cefoxitin** (or oxacillin) for routine testing of staphylococci.

• No other beta-lactam antibiotics need to be tested
Questions?