Detection of carbapenemases in Enterobacterales: presentation of the new German guideline

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Background

- Rapid identification of carbapenemases is indispensable for initiation of an effective therapy, epidemiological purposes, and infection control.
- Not all microbiology laboratories in Germany have established workflows for detection and differentiation of carbapenemase variants, likely as a result of the low frequency of carbapenemase-producing Enterobacterales (CPE) in Germany.
- Additionally, there is a high diversity of carbapenemases and isolates with low MICs prevail (e.g., OXA-48-like, VIM, NDM, IMI)
- Currently, there is no obligation to identify a carbapenemase beyond results of susceptibility testing.

Objectives

- The goal of the National Antimicrobial Susceptibilty Testing Committee (NAC) of Germany was to develop an algorithm which will allow all microbiology laboratories to rapidly identify carbapenemases.

Methods

- A selection of carbapenem-resistant clinical isolates which have undergone whole genome sequencing and MIC determination were used to develop the algorithm, taking into account the diversity of carbapenemases and the performance of different tests in the context of the German epidemiology.

Results

- An easy to follow two-step algorithm was developed
- To increase specificity, species-specific screening criteria are employed, taking into account common resistance mechanisms and MICs of carbapenems and ampicillin-sulbactam (FIG 1).
- Recommended testing: meropenem and ertapenem ±imipenem
- If ampicillin-sulbactam is susceptible, further work-up is not necessary.
- For confirmation of carbapenemase production, two different tests should be established in all laboratories
  1. **differentiation test** which can rapidly identify the major carbapenemase classes (e.g. OXA-48-like, VIM, NDM, KPC)
  2. **activity test** which detects the hydrolyzing activity irrespective of the type of carbapenemase and is suitable for rare carbapenemases not targeted by the differentiation test (e.g. GIM, IMI, OXA-23).

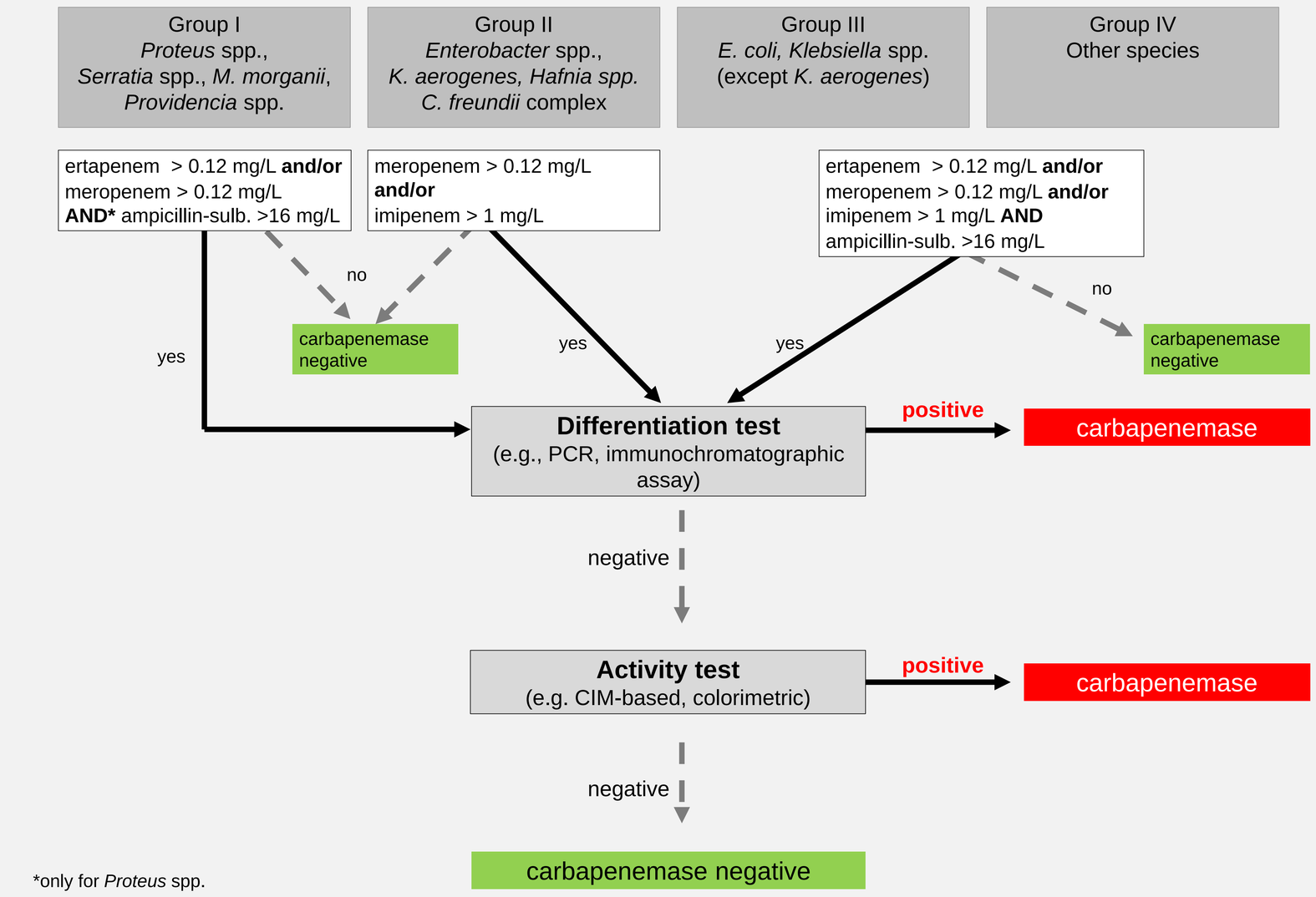

Figure 1 Diagnostic algorithm for the detection of carbapenemases in Enterobacterales

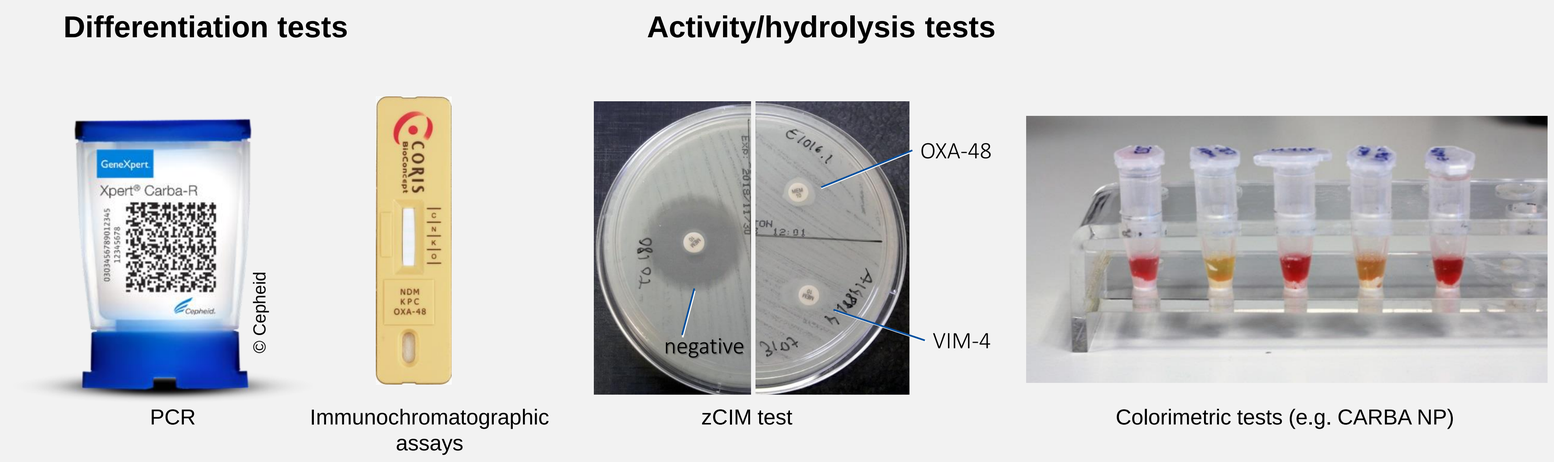

Figure 2 Examples of differentiation tests and activity tests

Algorithm

- If an isolates fulfills the criteria for further testing, a test which allows the differentiation of carbapenemases and rapid adjustment of therapy (e.g. ceftazidime-avibactam) is recommended. These tests include PCR/NAT assays or immunochromatographic tests. If the differentiation test is negative, in a second step an assay based on inactivation of carbapenems/activity assay (e.g. CIM based test, colorimetric test) is performed to identify rare carbapenemases which cannot be detected by the differentiation test.
- Recommended differentiation tests are PCR/NAT-based tests or immunochromatographic tests (targeting the major carbapenemases OXA-48-like, VIM, NDM, KPC); recommended activity tests are zCIM/mCIM or CARBA-NP test (FIG 2).

Conclusion

An easy to follow algorithm was developed which takes into account species-specific differences and allows the detection of common and rare carbapenemases.

The complete algorithm can be retrieved at https://www.nak-deutschland.org/nak-dokumente/detektion-von-resistenzmechanismen.html (in German).

N | A | K Nationales Antibiotika-Sensitivitätstest-Komitee

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