PUBLICATIONS ON OUR R·E·S·I·S·T RANGE

Performance evaluation of the newly developed In Vitro rapid diagnostic test for detecting OXA-48-like, KPC-, NDM-, VIM- and IMP- type carbapenemases: the RESIST-5 O.K.N.V.I. Multiplex Lateral Flow Assay - 2021 - *Antibiotics (Basel)*

Comparison of three lateral flow immunochromatographic assays for the rapid detection of KPC, NDM, IMP, VIM and OXA-48 carbapenemases in Enterobacterales - 2022 - *J Antimicrob Chemother.*

Assessing O.K.N.V.I. RESIST-5 performance for post-mortem biological samples: A prospective pilot study - 2023 - *Exp Ther Med.*

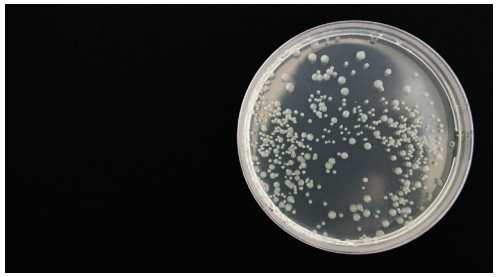
Carbapenem-resistant organismsisolated in surgical site infections in Benin: A public health problem - 2022 - *Trop Med Infect Dis.*

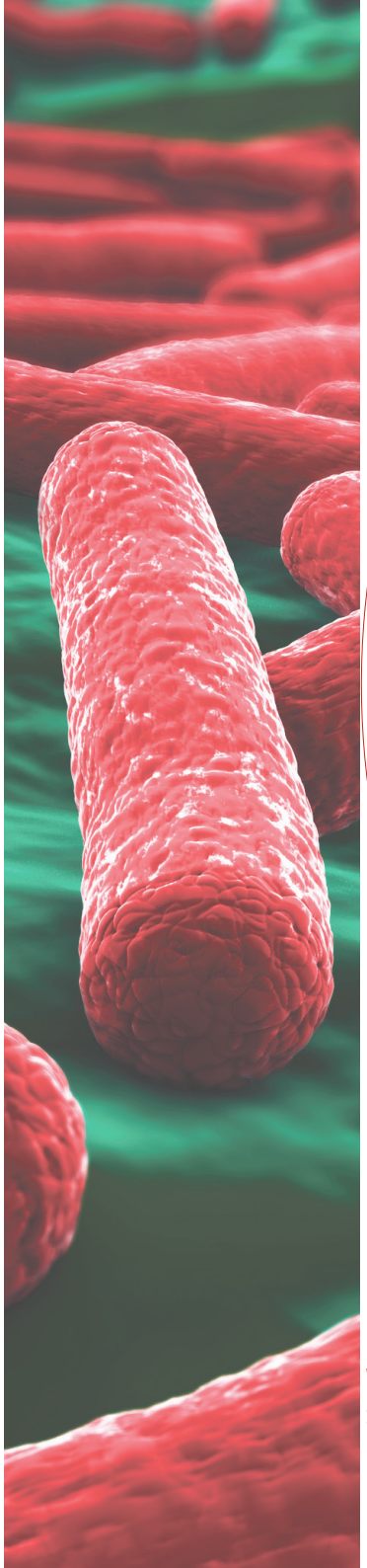
RESIST Acineto rapid immunological test for the detection of acquired carbapenemase producers among Acinetobacter spp - 2023 - *Diagn Microbiol Infect Dis.*

Evaluation of RESIST ACINETO immunochromatographic assay from positive blood cultures - 2023 - *J Antimicrob Chemother.*

Comparison of two immunochromatographic tests for the detection of CTX-M ESBL on clinical isolates at the Belgian National Reference Centre - 2023 - *ECCMID*

NEW **RESIST ACINETO test for the rapid detection of NDM and OXA acquired carbapenemases directly from blood culture in Acinetobacter species** - 2024 - *Microbiol Spectr.*





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A selection of the most recent publications on AMR

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HIGHLIGHTS

Global burden of bacterial AMR 1990-2021: a systematic analysis with forecasts to 2050 - 2024 - *Lancet*

◊ In 2021, bacterial AMR was linked to approximately 4.71 million deaths worldwide, with 1.14 million deaths directly attributed to AMR. These figures underline AMR's significant role in global mortality, particularly through drug-resistant bacterial infections.

◊ Resistance among *S. aureus* and Gram-negative bacteria, particularly to carbapenems, has increased. This rise poses challenges due to limited treatment options for carbapenem-resistant infections, especially in resource-limited settings

◊ Forecasts show an estimated 1.91 million deaths attributable to AMR and 8.22 million deaths associated with AMR by 2050. Super-regions with the highest all-age AMR mortality rate are forcasted to be South Asia, Latin America and the Caribbean

◊ Scenarios that could avert millions of deaths: improved healthcare (92 million lives potentially saved), minimisation of inappropriate antibiotic use in farming and humans, new Gram-negative targeted drugs (11.1 million AMR deaths averted) by 2050

Overview of Antimicrobial Resistant ESKAPEE pathogens in food sources and their implications from a One Health Perspective - 2024 - *microorganisms*

◊ ESKAPEE pathogens currently challenging commonly available treatment options: broad-spectrum β-lactams, carbapenems, glycopeptides, fluoroquinolones and aminoglycosides

◊ ESKAPEE increasingly identified within food production systems, (widespread antibiotic use in livestock & agriculture). Thus resistance in bacteria within animals, which can transfer to humans via food (raw meat, fish, dairy products, cooked foods ...)

◊ A coordinated, multi-sector strategy involving human health, veterinary practices, and environmental management is essential to monitor and mitigate AMR spread among ESKAPEE pathogens in food sources

◊ Enhanced surveillance and stricter regulations on antibiotic use in agriculture are recommended to curb the spread of AMR

Non-carbapenemase OXA-48 variants (OXA-163 and OXA-405) falsely detected as carbapenemases by the β-Carba test - 2017 - *J Clin Microbiol*

◊ Colorimetric assay designed to detect carbapenemase production by observing a color change. It claims high specificity and sensitivity in detecting carbapenemase-producing organisms

◊ Non-carbapenemase OXA-48 variants like OXA-163 and OXA-405 - despite not having carbapenemase activity - gave false-positive results with the β-Carba test due to structural similarities with true carbapenemases

◊ Limitations: distinguishing between carbapenemase-active & non-active OXA-48 variants, leading to misclassification & diagnostic inaccuracies

EPIDEMIOLOGY & MECHANISMS

Insertions sequences within oxacillinases genes as molecular determinants of *A. baumannii* resistance to carbapenems - 2024 - *microorganisms*

◊ Carbapenem-resistant *A. baumannii* is prevalent in hospital settings, especially in ICU patients. The pathogen's resistance is primarily due to carbapenem-hydrolyzing class D β-lactamases (CHDLs), notably the OXA-type enzymes

◊ Insertion sequences, particularly ISAba1, found upstream of the blaOXA-23 gene, enhance carbapenem resistance by boosting gene expression. Among resistant isolates, nearly all contained ISAba1 preceding blaOXA-23

◊ BlaOXA-23 is a major contributor to carbapenem resistance, but blaOXA-51 and blaOXA-40 genes. ISAba1-blaOXA-23 combination most strongly associated with extensive drug resistance

◊ Colistin remains one effective treatments against many resistant strains, despite some exhibiting resistance even to colistin

◊ Necessity of tracking genetic elements like insertion sequences, as they play a critical role in resistance emergence.

Insights into the rising threat of Carbapenem-resistant enterobacterales and *P. aeruginosa* epidemic infections in Eastern Europe: A systematic literature review - 2024 - *antibiotics*

◊ High incidence rates, particularly in countries like Greece, Romania, Serbia. Common carbapenem resistance mechanisms include KPC, VIM, NDM, and OXA-48

◊ Newer antimicrobials - imipenem/relebactam (IMI/REL) and ceftazidime/avibactam (CAZ/AVI) - show effectiveness against CRE, particularly KPC and OXA-48 producers. However, resistance remains high among MBL-producing strains

◊ Rapid diagnostics and molecular surveillance are essential for detecting CRE/CRPA and implementing timely control measures. Variations in diagnostic methods influence detection accuracy across regions

◊ High rates of carbapenem resistance call for coordinated infection control, antimicrobial stewardship, and policy interventions to limit the spread and manage outbreaks effectively in Eastern Europe

Prevalence, characterization and epidemiological relationships between ESBL and carbapenemase-producing *E. coli*, *K. pneumoniae* and *Acinetobacter* spp. isolated from humans and the kitchen environment of two Greek hospitals - 2024 - *antibiotics*

◊ Findings reveal that 4.5%, 1.5%, and 15% of environmental samples tested positive for *E. coli*, *K. pneumoniae*, and *Acinetobacter* spp., respectively. Chicken was a significant source, with high association between chicken and kitchen environment isolates

◊ All *E. coli* isolates were ESBL producers, while all *K. pneumoniae* and some *Acinetobacter* spp. isolates were carbapenemase producers demonstrating multi-drug resistance

◊ The majority of resistant *E. coli* isolates belonged to phylogenetic groups A and B1. Key β-lactamase genes, including blaCTX-M, blaSHV, and blaTEM, were commonly identified among ESBL-producing isolates

◊ Close genetic relationships between clinical, kitchen, and food-origin strains, suggesting possible cross-contamination within hospital settings. Need for stringent infection control practices & continuous monitoring

THERAPEUTICS

Ceftazidime-Avibactam vs Polymyxin-based combination therapies: a study on 30-day mortality in carbapenem-resistant enterobacteales bloodstream infections in an OXA-48 endemic region - 2024 - *antibiotics*

◊ CAZ-AVI showed a significantly lower 30-day mortality rate (20%) compared to PBCT (36.9%). Microbiological eradication rates were also higher in patients treated with CAZ-AVI, suggesting better infection clearance

◊ CAZ-AVI was linked to a significant reduction in mortality risk (hazard ratio of 0.16), underscoring its potential as a superior treatment for CRE infections in OXA-48-endemic settings

◊ CAZ-AVI's pharmacokinetic and pharmacodynamic properties provide faster and more reliable therapeutic outcomes than polymyxins, which are associated with limitations like a narrow therapeutic window and risk of resistance development

In vivo efficacy of enmetazobactam combines with cefepime in a murine pneumonia model induced by OXA-48-producing *K. pneumoniae* - 2024 - *Microbiol Spectr.*

◊ Enmetazobactam, when combined with cefepime, significantly reduced bacterial counts in lung tissues of infected mice. This effect was achieved even in strains with high resistance levels, where cefepime alone or meropenem were ineffective

◊ Enmetazobactam enhances cefepime's efficacy by inhibiting β-lactamase enzymes (including ESBL and carbapenemases like OXA-48), overcoming resistance that would render cefepime ineffective alone

◊ The combination therapy maintained optimal drug concentrations in lung tissues, which allowed sustained bacterial reduction over the 26-hour treatment period, achieving a 2-log reduction in bacterial load for strains with high resistance (MIC up to 8 µg/mL)

◊ Promising alternative for treating multidrug-resistant *K. pneumoniae*, potentially providing a carbapenem-sparing option for severe lung infections

Ceztazidime-Avibactam resistance in KPC-producing *K. pneumoniae* accompanied hypermucoviscosity acquisition - 2024 - *BMC Microbiol*

◊ Results indicate that CAZ-AVI-resistant *K. pneumoniae* isolates exhibit a significantly higher rate of hypermucoviscosity (46.7%) compared to CAZ-AVI-sensitive isolates (5.6%). This trait is associated with increased virulence, complicating infection control

◊ Mutations in the *wzc* gene, involved in capsular polysaccharide (CPS) synthesis, were frequently observed in CAZ-AVI-resistant strains displaying hypermucoviscosity. These mutations were experimentally shown to trigger mucus overproduction and elevate virulence

◊ In vitro experiments confirmed that some CAZ-AVI-sensitive strains developed resistance and acquired hypermucoviscosity during selective passaging. Additionally, clinical samples showed a similar trend, linking CAZ-AVI resistance with heightened virulence

◊ The study highlights the dual risk of CAZ-AVI resistance and hypermucoviscosity in KPC-producing *K. pneumoniae*, raising concerns about treatment challenges and the potential for severe infections