

Combination Of Modified Carbapenem
Inactivation Method (mCIM) And EDTA-CIM
(eCIM) For Phenotypic Detection Of
Carbapenemase-producing *Enterobacteriaceae*

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Introduction



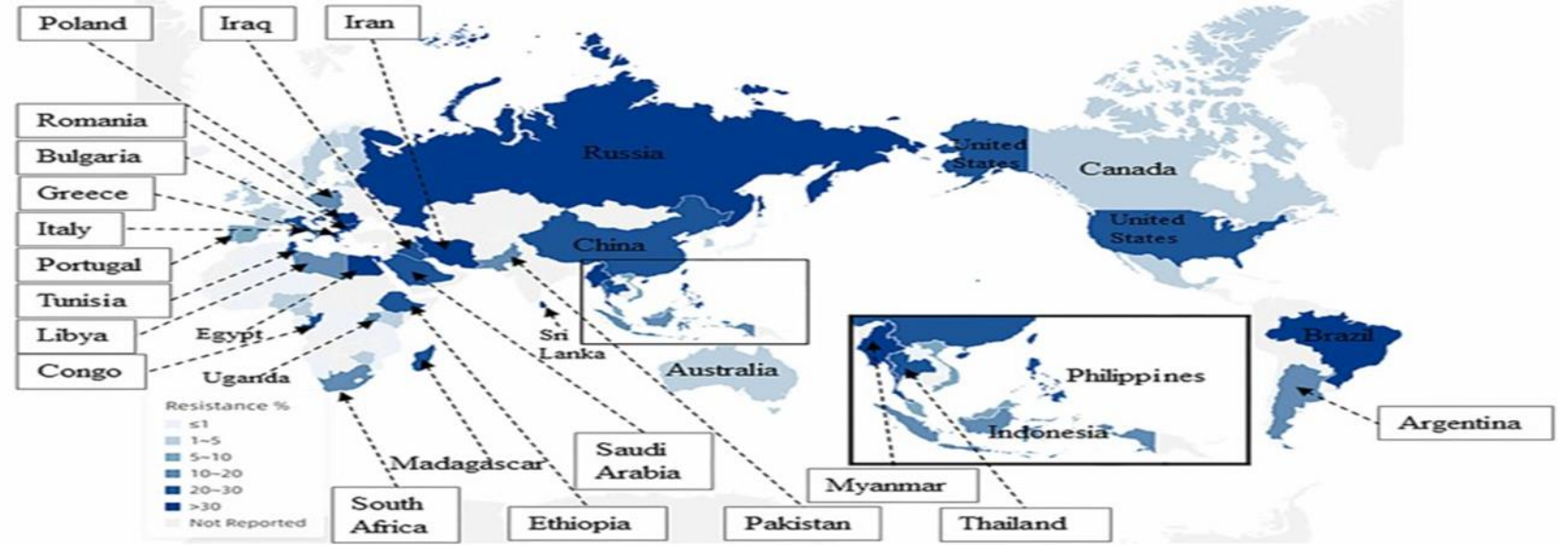
Carbapenem-Resistant *Enterobacteriaceae* (CRE)

Enterobacteriaceae, these gram negative rod bacteria have become resistant to most available antibiotics

Even
antibiotics of last-sort,
Carbapenems
(imipenem, ertapenem,
meropenem, and doripenem)
known as
Carbapenem-
resistant *Enterobacteriaceae*
(CRE)

Global distribution of CRE isolates

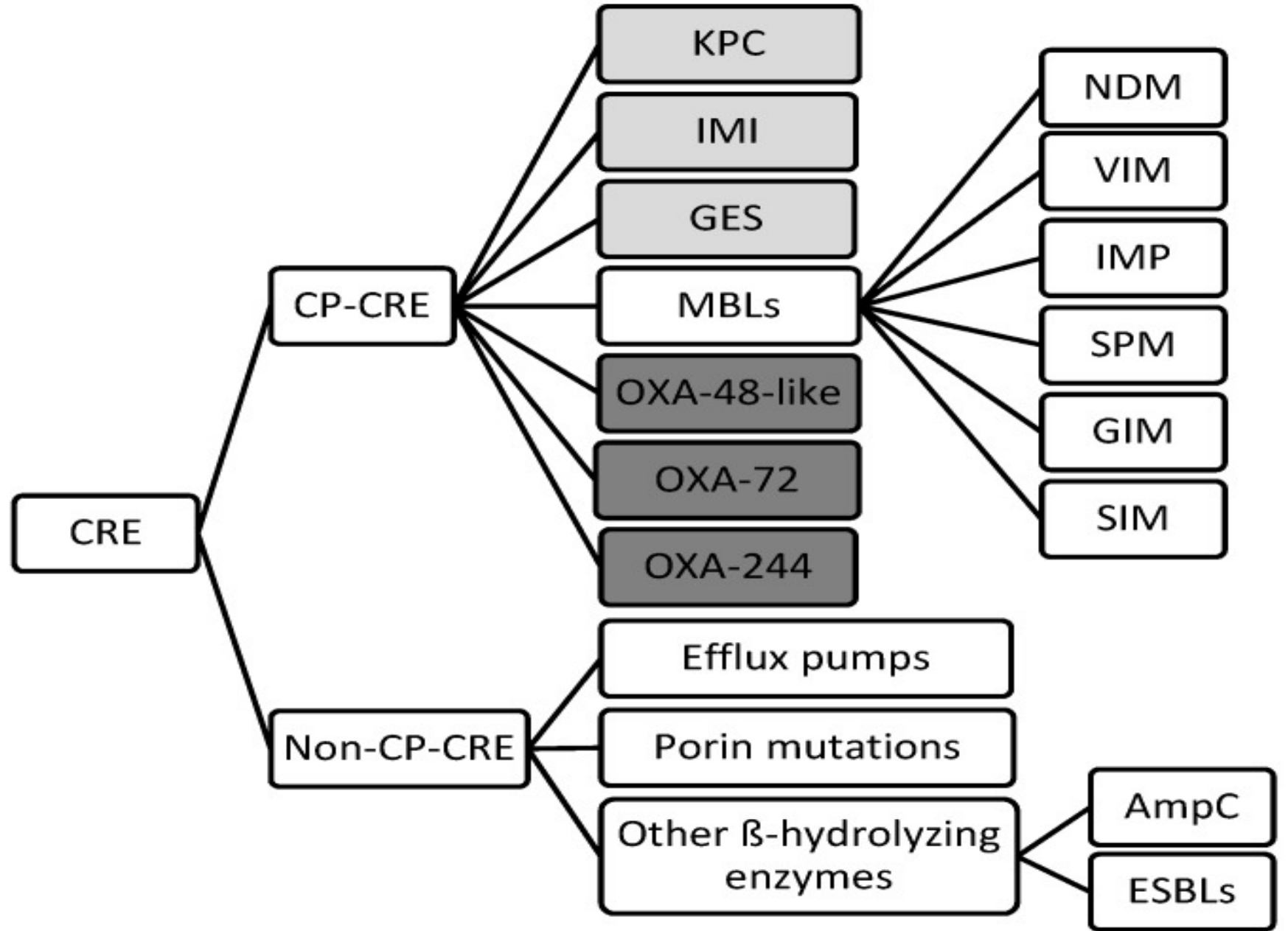
(a) *Klebsiella* spp.



(b) *Escherichia coli*

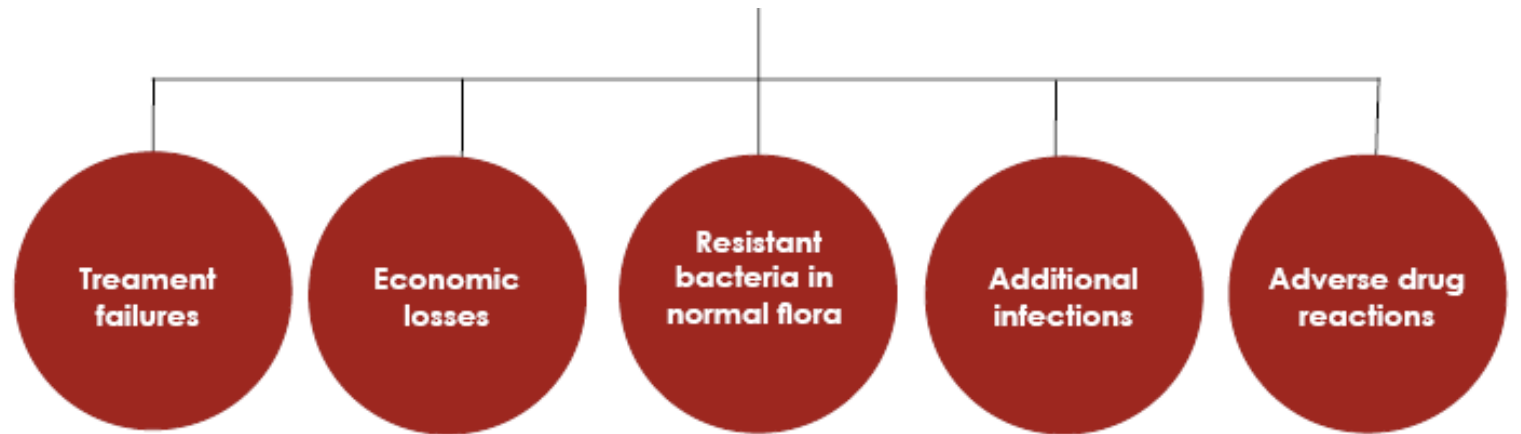


Mechanism of resistance to carbapenems





Consequences of CRE isolates emerge



Importance of diagnosis

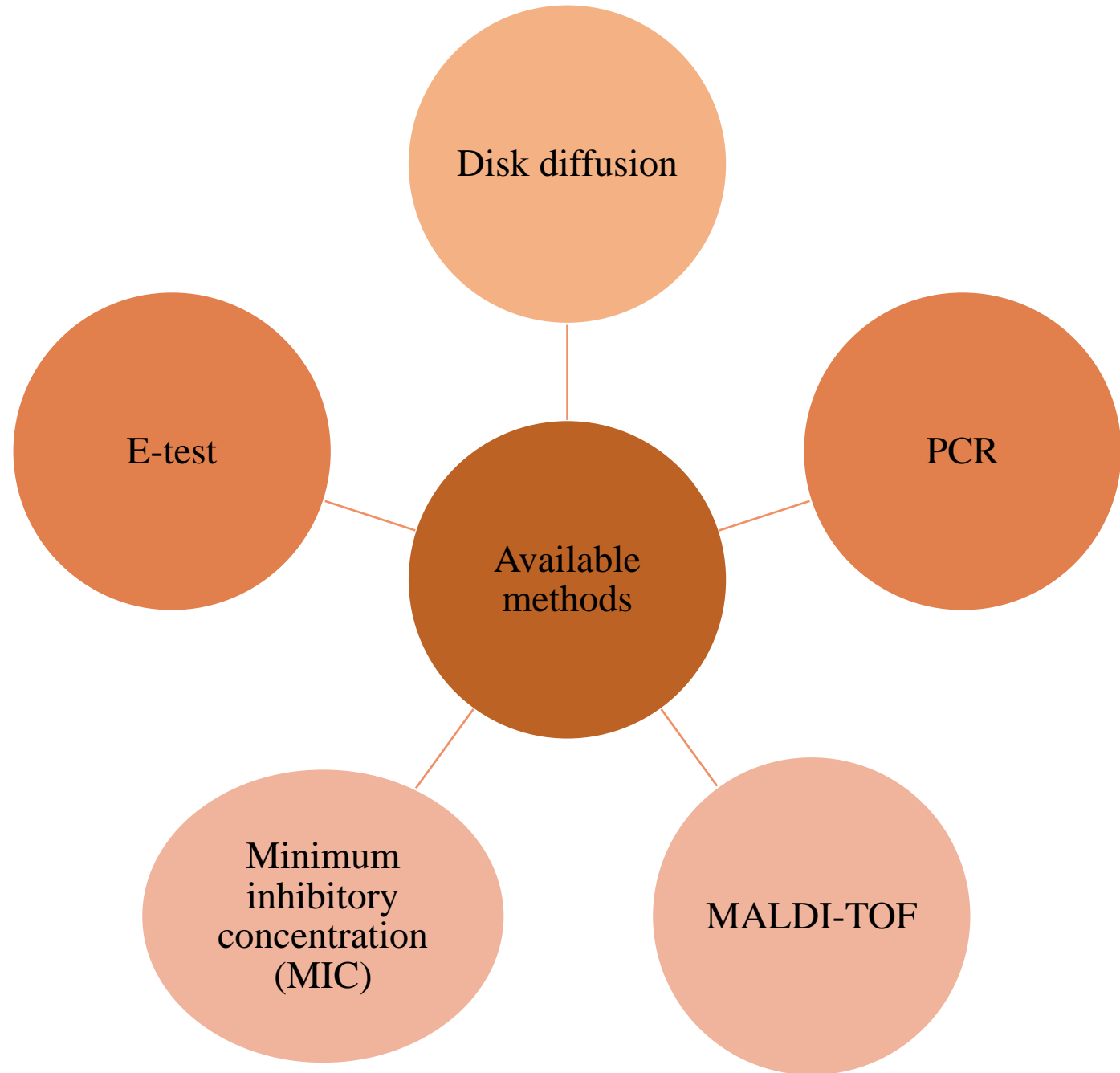
Early detection of CRE infections helps
to:

Narrow down the best treatments:
therapeutic management

Epidemiologic surveillance

Infection prevention and control purposes

Available Diagnosis methods for detecting CRE isolates



Limitations of available methods

Disk diffusion

Do not necessarily reflect other mechanisms
 : porin loss or increased efflux pump activity or chromosomally located genes

MIC

Do not necessarily reflect other mechanisms
 : porin loss or increased efflux pump activity or chromosomally located genes

PCR

only known targets are detected,
 Not mutations within targets
limited in their scope detection of carbapenemase genes

MALDI-TOF

High Cost, lack of access to MALDI-TOF units, and relative **newness** of this method are the most significant barriers to further utilization of this diagnostic modality

Presenting methods



Modified Hodge test (MHT)

- The first **CLSI** –recommended
- **Growth-based carbapenemase detection test (2009)**
- CRE detection and other suspected Gram-negative bacteria
- High level of sensitivity and specificity in detecting carbapenemases

Procedure of Modified Hodge test (MHT)

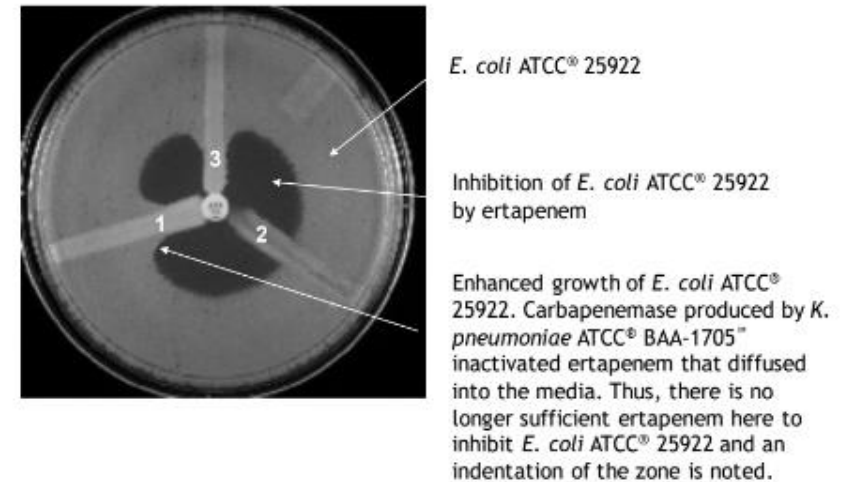
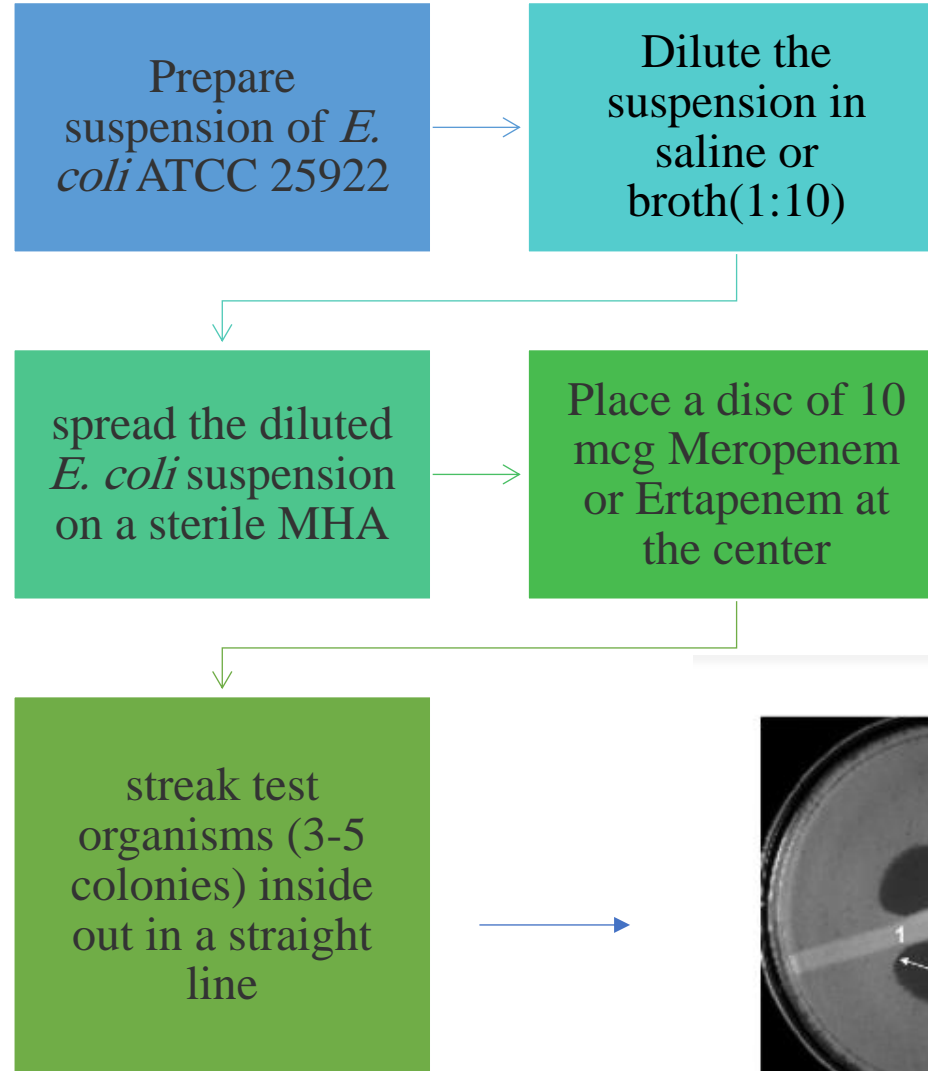
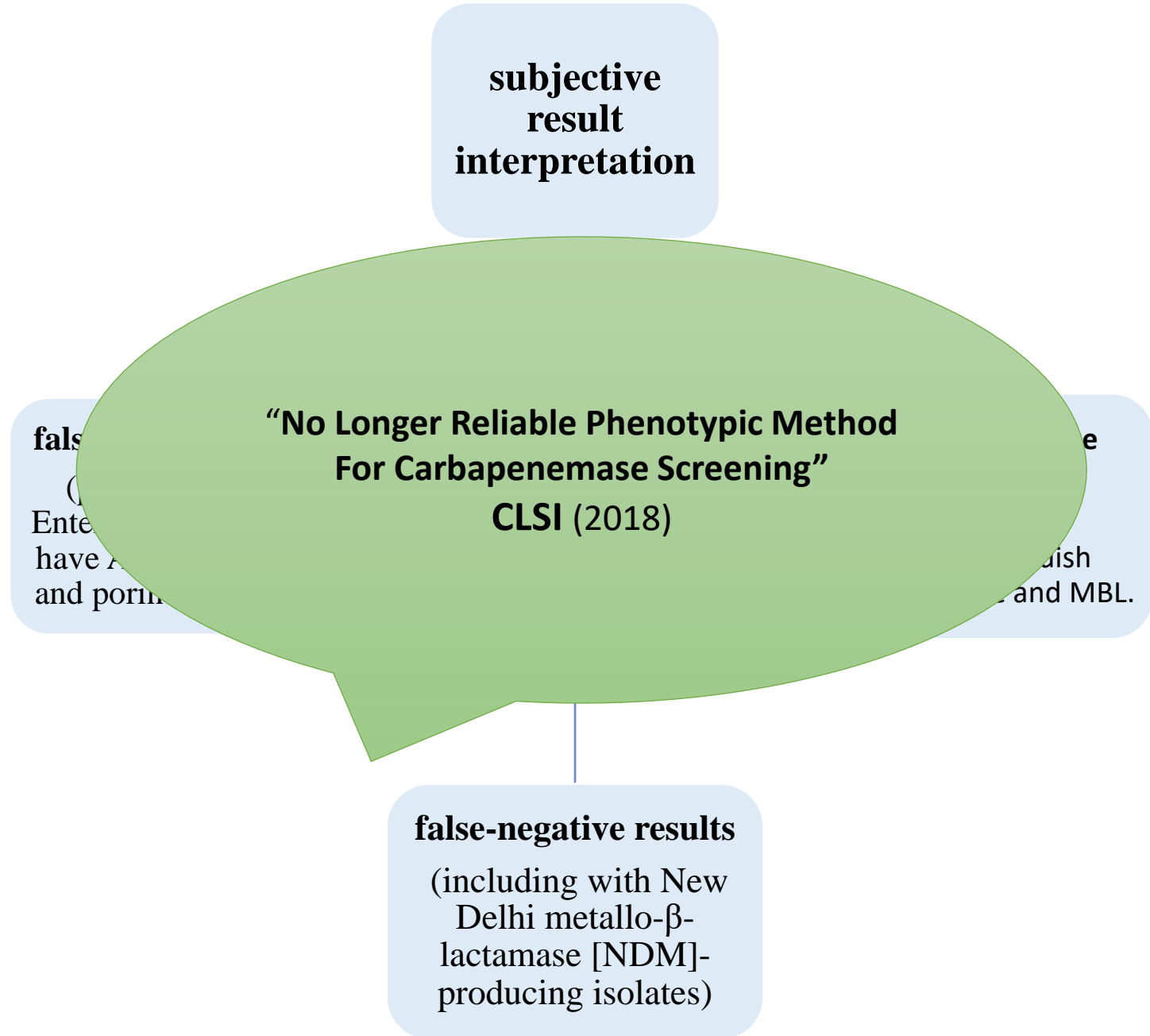


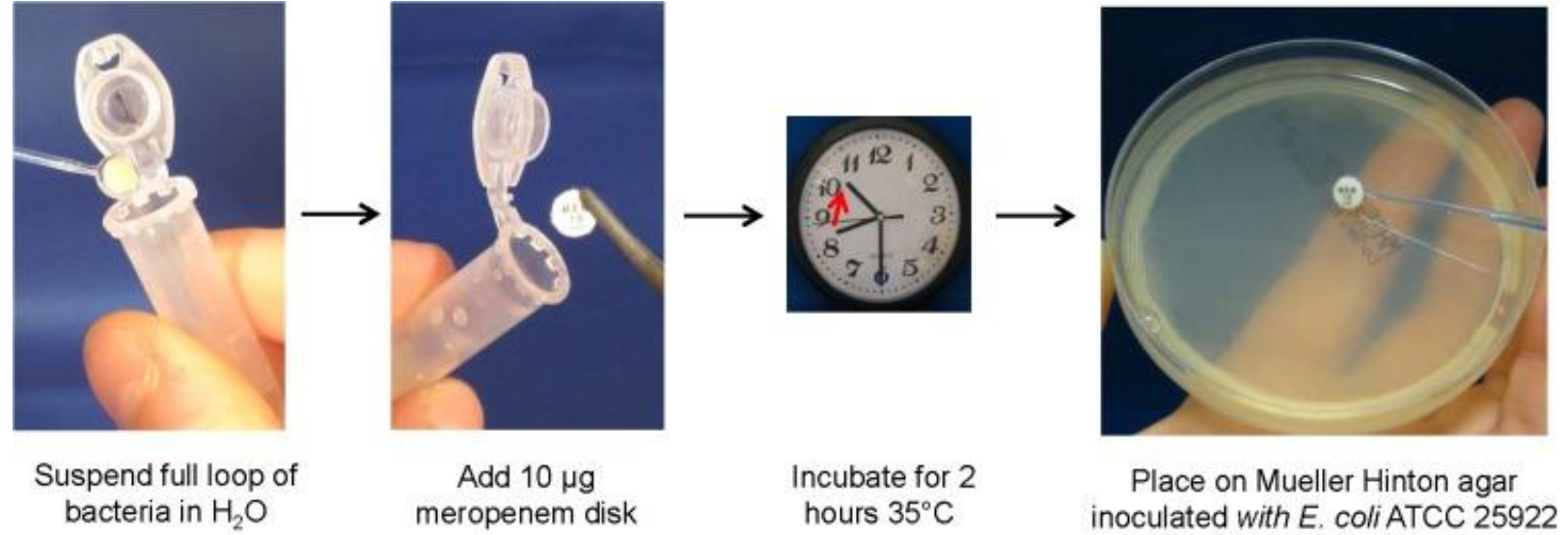
Figure 1. The MHT Performed on a Small MHA Plate.
 (1) *K. pneumoniae* ATCC® BAA-1705™, positive result;
 (2) *K. pneumoniae* ATCC® BAA-1706™, negative result;
 and (3) a clinical isolate, positive result.

Modified Hodge test (MHT)



Carbapenem inactivation method (CIM)

first described in
2015



Modified Carbapenem inactivation method (mCIM)

- Using TSB instead of water
- Extending the incubation time from 2 to 4 h
- Detection of :
 - carbapenemases with either weaker hydrolytic activities
 - lower levels of expression
 - metallo- β -lactamases that require divalent cations for activity
- **more sensitive** for the detection of OXA-48-type carbapenemases (reported as negative result in **CIM**)

Advantages and disadvantages of mCIM

Advantages

- Few false-positive mCIM results
- simple, inexpensive, accurate, and reproducible method

Limitations

- **overnight incubation with the indicator organism**
- Does not provide information about **the specific carbapenemase gene present in a given bacterial isolate**

EDTA- Carbapenem inactivation method (e CIM)

- CLSI: eCIM use in combination with the mCIM to detect MBL-producing *Enterobacteriaceae*
- EDTA or dipicolinic acid can serve as chelators to block class B carbapenemases activity by binding zinc
- **Sensitivity and specificity** → (EDTA) : 100 and 90%

Limitation of EDTA-CIM

- **Inability to differentiate between serine and MBL carbapenemase production in isolates that harbor both serine and MBL enzymes**

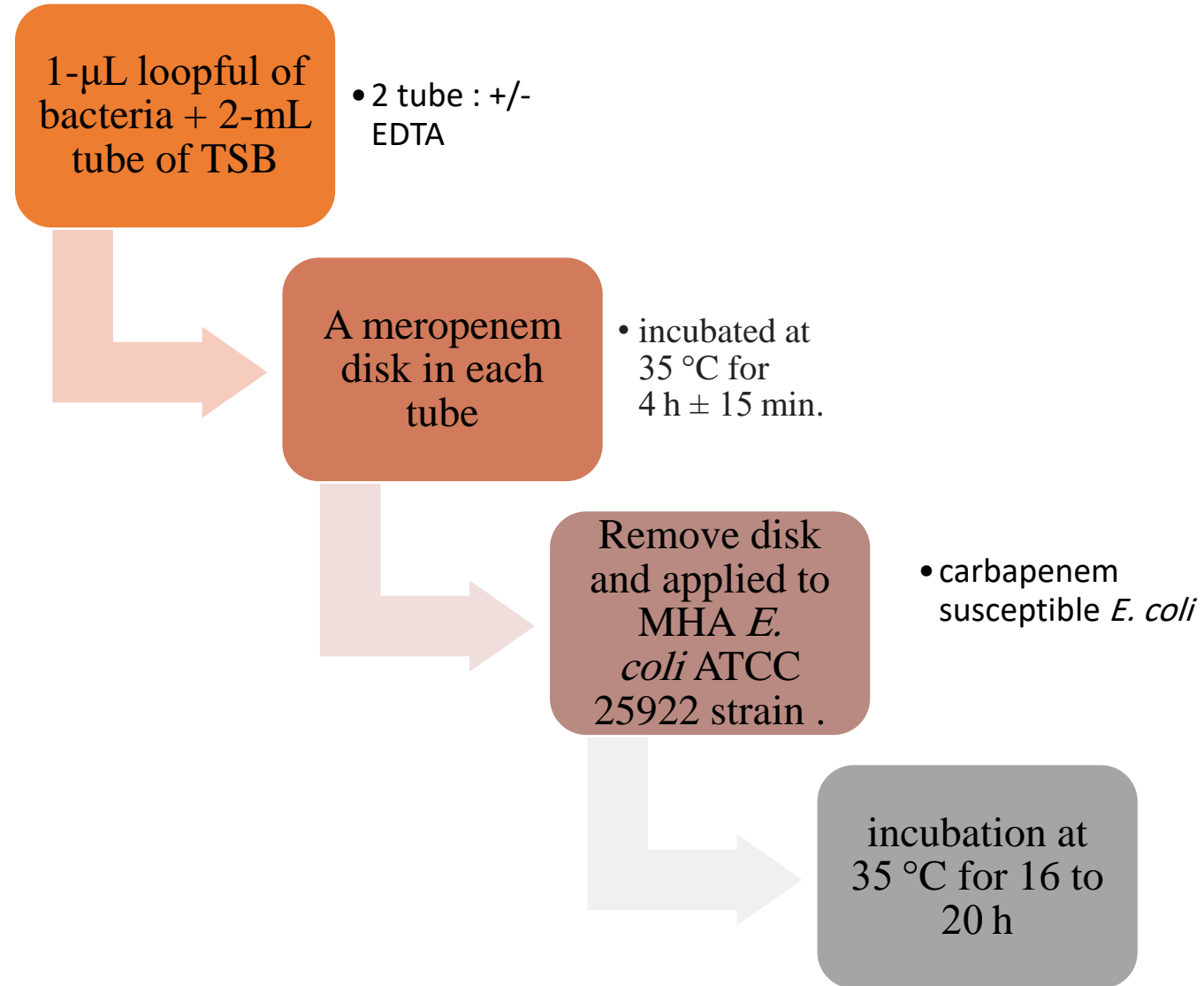
Note : the prevalence of isolates encoding both serine and MBL carbapenemases is low.

- Only 1% (2/202) of carbapenemase-producing Enterobacteriaceae from the United States, Europe, Latin America, and Asia-Pacific encoded both a serine and MBL carbapenemase (*OXA-48*-type and *VIM* in both instances)

Presenting method

Combination Of mCIM And
EDTA-CIM (eCIM)

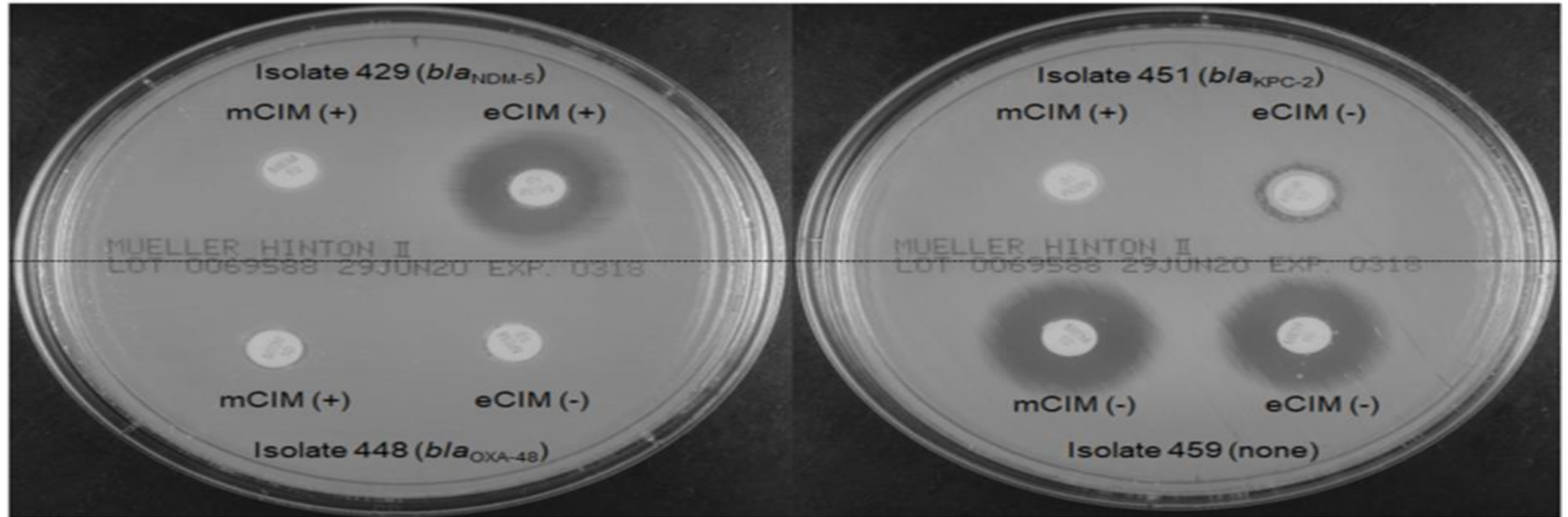
procedure



A



B





Interpretation

Test	Zone size	Interpretation
m CIM	≥ 19 mm 16–18 mm 6–15 mm	Negative Intermediate Positive
e CIM	≤ 4 -mm increase in zone size (compared to m CIM zone size)	negative
	≥ 5 -mm increase in zone size (compared to m CIM zone size)	positive

ADVANTAGES

Simultaneously detect and distinguish the types of carbapenemase

High sensitivity and specificity:
89.3 and 98.7%

Simple and easy to perform

Don't require expensive resources

Cost effective

DISAVANTAGES

Over night incubation

Need pure culture of clinical isolate

Disability to detect new or unexpressed carbapenemase genes

Conclusion

- importance of distinguish classes of carbapenemase
- molecular methods are **expensive, require special equipment and expertise** to perform, **and are not in widespread use.**
- Seeking reassurance The researchers stipulated that tests should be **affordable, sensitive, specific, user-friendly, rapid, equipment-free** and ...



Reference

Tsai et al. *BMC Microbiology* (2020) 20:315
<https://doi.org/10.1186/s12866-020-02010-3>

BMC Microbiology

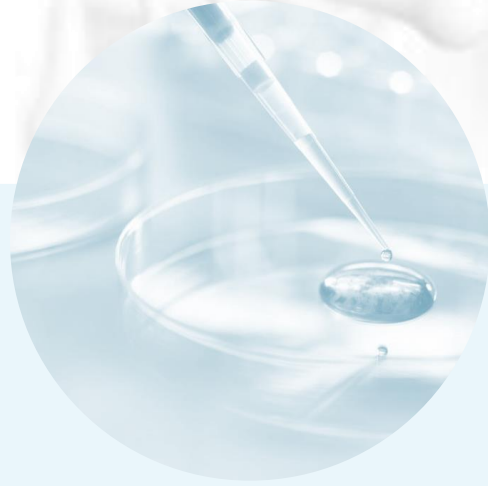
RESEARCH ARTICLE

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Combination of modified carbapenem inactivation method (mCIM) and EDTA-CIM (eCIM) for phenotypic detection of carbapenemase-producing *Enterobacteriaceae*



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THANK YOU

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Any question?