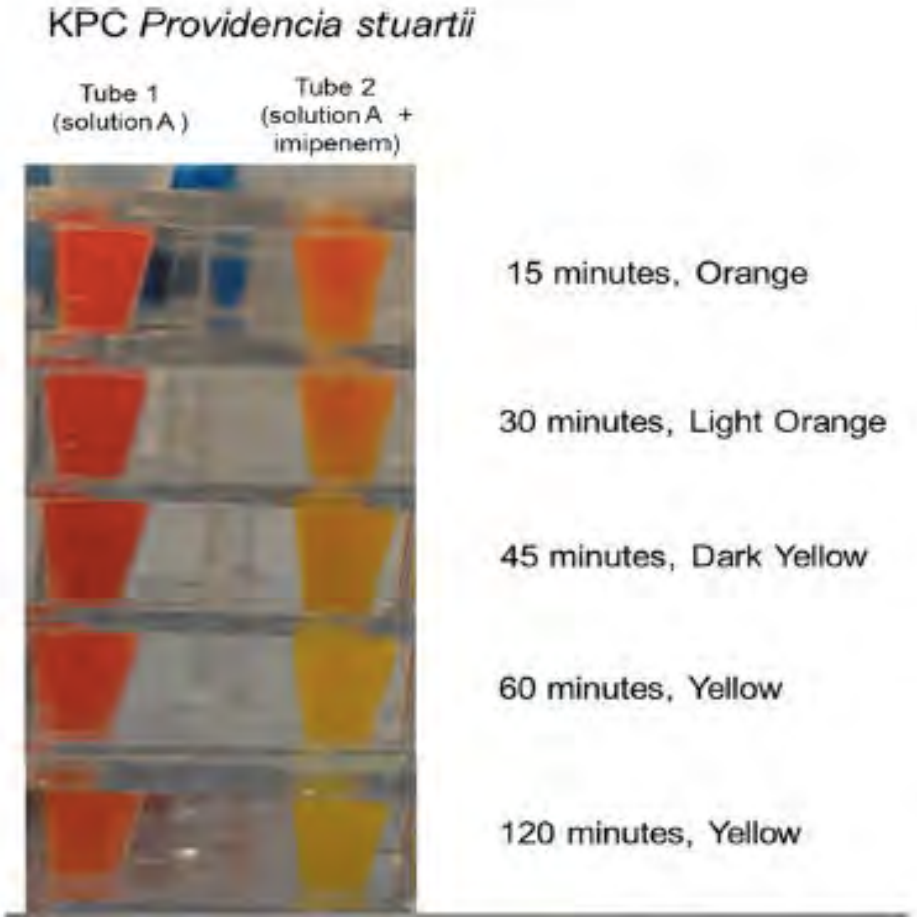

Comparison of a Novel, Rapid Chromogenic Biochemical Assay, the Carba NP Test, with the Modified Hodge Test for Detection of Carbapenemase-Producing Gram-Negative Bacilli

Shawn Vasoo,[a] Scott A. Cunningham,[a] Peggy C. Kohner,[a] Patricia J. Simner,[a] Jayawant N. Mandrekar,[b] Karen Lolans,[c] Mary K. Hayden,[c,d] Robin Patel[a,e]

JCM, Sep 2013

The CIM (Carbapenemase inactivation method) a new phenotypic Test to assess Carbapenemase activity

PLOS ONE | The CIM, a New Phenotypic Test to Assess Carbapenemase Activity

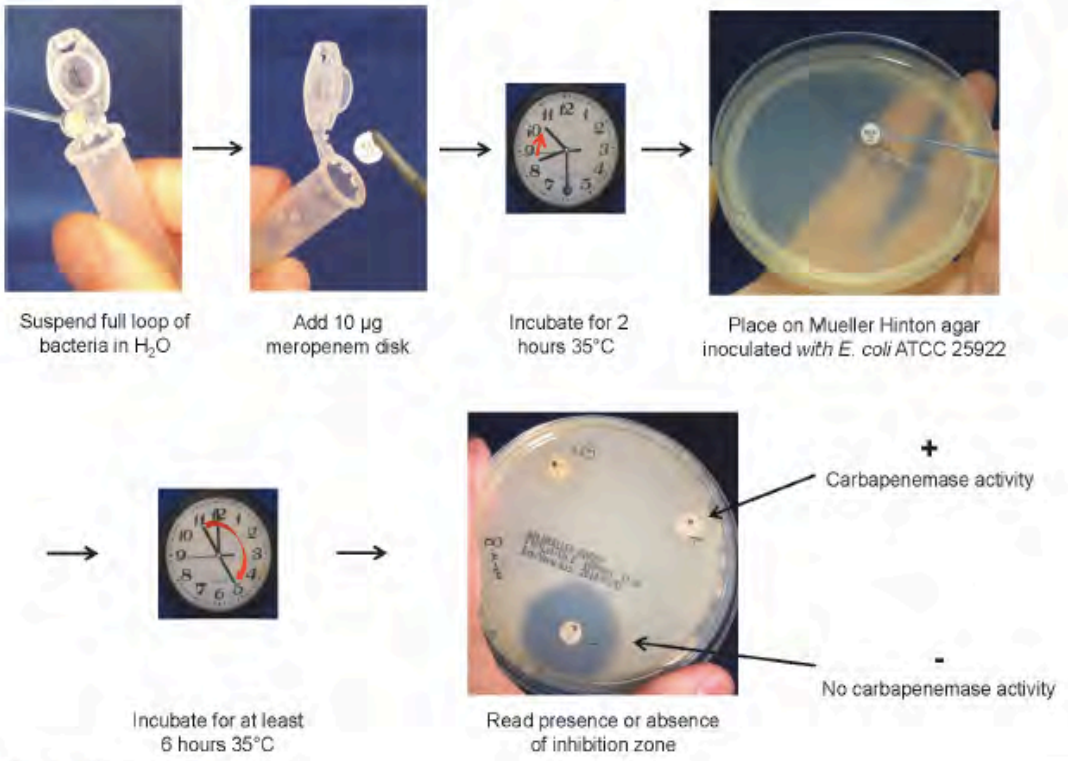

Fig 1. Schematic of the CIM.

doi:10.1371/journal.pone.0123690.g001

van der Zwaluw K, de Haan A, Pluister GN, et al. The Carbapenem Inactivation Method (CIM), a simple and low-cost alternative for the Carba NP Test to assess phenotypic carbapenemase activity in Gram-Negative rods. PLoS ONE 2015; 10(3): e0123690.

Fig. 1. Cepheid GenXpert system. (*A*) Instruments with 1- to 16-cartridge capacity. (*B*) Exploded view of GenXpert cartridge. (*Courtesy of* Cepheid, Sunnyvale, CA; with permission.)

Cepheid GeneXpert

CRE stool Screening

KPC
NDM
(No OXA)

Luminex
complexity simplified.

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HOME / CLINICAL / INFECTIOUS DISEASE TESTING / BLOODSTREAM INFECTION / **VERIGENE® GRAM-POSITIVE BLOOD CULTURE TEST**

Online Assignment Session 9

VERIGENE® GRAM-POSITIVE BLOOD CULTURE TEST

The VERIGENE® Gram-Positive Blood Culture Test (BC-GP) identifies genus, species, and genetic resistance determinants for a broad panel of gram-positive bacteria directly from positive blood culture bottles

Evaluation of the Verigene Gram-Positive Blood Culture Test (BC-GP)

C. Anderson*, K. Kaul* ‡, B. Voss*, and R.B. Thomson* ‡

*NorthS ... on, IL

ASM 2012

Table 1. Verigene BCGP Identifiable Targets

Gram-Positive Blood Culture (BC-GP) Test				Gene target
Genus	*Staphylococcus* spp.	Species	•*Staphylococcus aureus*	*gyrB*
	Streptococcus spp.		•*Staphylococcus epidermidis*	*hsp60*
	Micrococcus spp.		•*Staphylococcus lugdunensis*	*sodA*
tuf gene	*Listeria* spp.		•*Streptococcus pneumoniae*	*gyrB*
Resistance	*mecA*		•*Streptococcus anginosus* Group	*gyrB*
	vanA		•*Streptococcus agalactiae* (GBS)	*hsp60*
gene	*vanB*		•*Streptococcus pyogenes* (GAS)	*hsp60*
			•*Enterococcus faecalis*	*hsp60*
			•*Enterococcus faecium*	*hsp60*

Table 2. Successful Identification Rates of Bacterial Isolates

Isolated Organism	Verigene Result/Micro Lab Result
Staphylococcus	87/87 (100%)
Streptococcus	29/31 (93%)
Enterococcus	8/9 (89%)
Micrococcus	2/2 (100%)
Corynebacterium*	0/4 (0%)
Aerococcus*	0/1 (0%)
Bacillus sp*	0/1 (0%)
Lactobacillus*	0/1 (0%)
Total # of isolates	126/136 (93%)
Total # of identifiable isolates	126/129 (98%)

*Not an intended target of the Verigene BCGP Test

Verigene: BC-GP test (Nanosphere)

blood c/s

multiplex PCR, microarray:

TAT: 2.5 hrs

Limitation

FDA cleared Aerobic bottle only

Mixed infection

Mixed c/s

VERIGENE® GRAM-NEGATIVE BLOOD CULTURE TEST

The VERIGENE® Gram-Negative Blood Culture Test (BC-GN) identifies genus, species, and genetic resistance determinants for a broad panel of gram-negative bacteria directly from positive blood culture bottles

Gram-Negative Blood Culture Test Specifications

Targets	U.S./FDA-Cleared	Outside U.S.
Species		
*Escherichia coli**	•	•
Klebsiella pneumoniae	•	•
Klebsiella oxytoca	•	•
Pseudomonas aeruginosa	•	•
Serratia marcescens		•
Genus		
Acinetobacter spp.	•	•
Citrobacter spp.	•	•
Enterobacter spp.	•	•
Proteus spp.	•	•

Resistance		
CTX-M (ESBL)	•	•
IMP (carbapenemase)	•	•
KPC (carbapenemase)	•	•
NDM (carbapenemase)	•	•
OXA (carbapenemase)	•	•
VIM (carbapenemase)	•	•

* BC-GN will not distinguish *Escherichia coli* from *Shigella* spp. (*S. dysenteriae, S. flexneri, S. boydii*, and *S. sonnei*).

Caution!

Gram-negative bacteria resistance mechanism

= genotypic (enzymatic) and non genotypic (non-enzymatic)

Fig. 6. BioFire FilmArray respiratory panel assay. (*A*) FilmArray RP Pouch. (*B*) FilmArray instrument and pouch. Instrument footprint in inches: 10.00 width × 6.5 height × 15.5 depth. A computer is required for operation. (*Courtesy of* BioFire Diagnostics Inc, Salt Lake City, UT; with permission.)

- **Biofire Filmarray**

Positive

Blood panel

(Multiplex PCR)

(1 h result)

The FilmArray BCID Panel

Simultaneous detection of 27 targets:

Gram + Bacteria

- *Staphylococcus*
- *Staphylococcus aureus*
- *Streptococcus*
- *Streptococcus agalactiae*
- *Streptococcus pyogenes*
- *Streptococcus pneumoniae*
- *Enterococcus*
- *Listeria monocytogenes*

Gram - Bacteria

- *Klebsiella oxytoca*
- *Klebsiella pneumoniae*
- *Serratia*
- *Proteus*
- *Acinetobacter baumannii*
- *Haemophilus influenzae*
- *Neisseria meningitidis*
- *Pseudomonas aeruginosa*
- *Enterobacteriaceae*
- *Escherichia coli*
- *Enterobacter cloacae complex*

Fungi

- *Candida albicans*
- *Candida glabrata*
- *Candida krusei*
- *Candida parapsilosis*
- *Candida tropicalis*

Antibiotic Resistance

- *mecA*
- *vanA / vanB*
- *KPC*

Rapid Diagnostics in Clinical Microbiology and ASP

Direct Testing from BC Bottle	Mortality Benefit	Change in LOS	Cost saving per patient ($)	AS Intervention
FISH probes	ND	2 d less	4005	YES
FISH probes	ND	2.2 d more	ND	NO
FISH probes*	ND	ND	1729	YES
FISH probes	16.8% vs 7.9%	2 d less**	19,441**	NO
GeneXpert MRSA/SA	18% vs 26% **	6.2d less	21,387	YES
MALDI-TOF	5.6% vs 10.7%**	1.8d less	19,547 **	YES
MALDI-TOF	12.7% vs 20.3%	2.8 d less **	ND	YES
Verigene #	NO	21.7d less	60,729	YES

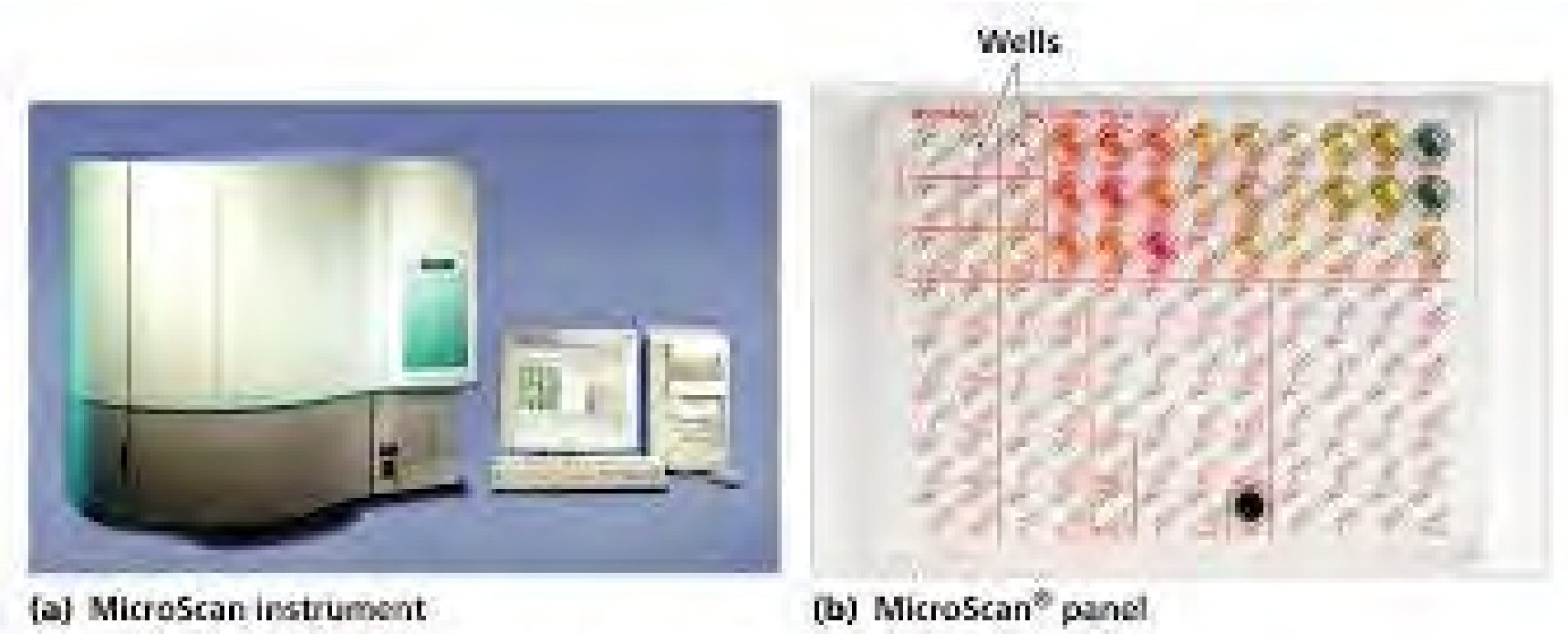
* = Yeast only; ** = difference was not statistically significant; # = enterococci

Kothari A, et al. 2014; CID 59:272-8

Limited data in Thailand

Automated biochemical identification and susceptibility method

MicroScan system (Walkaway system)
VITEK 2 system
BD Phoenix system
Sensititer



MicroScan

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BACTERIOLOGY

Two-Site Evaluation of the Colistin Broth Disk Elution Test To Determine Colistin *In Vitro* Activity against Gram-Negative Bacilli

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February 2019 Volume 57 Issue 2 e01163-18

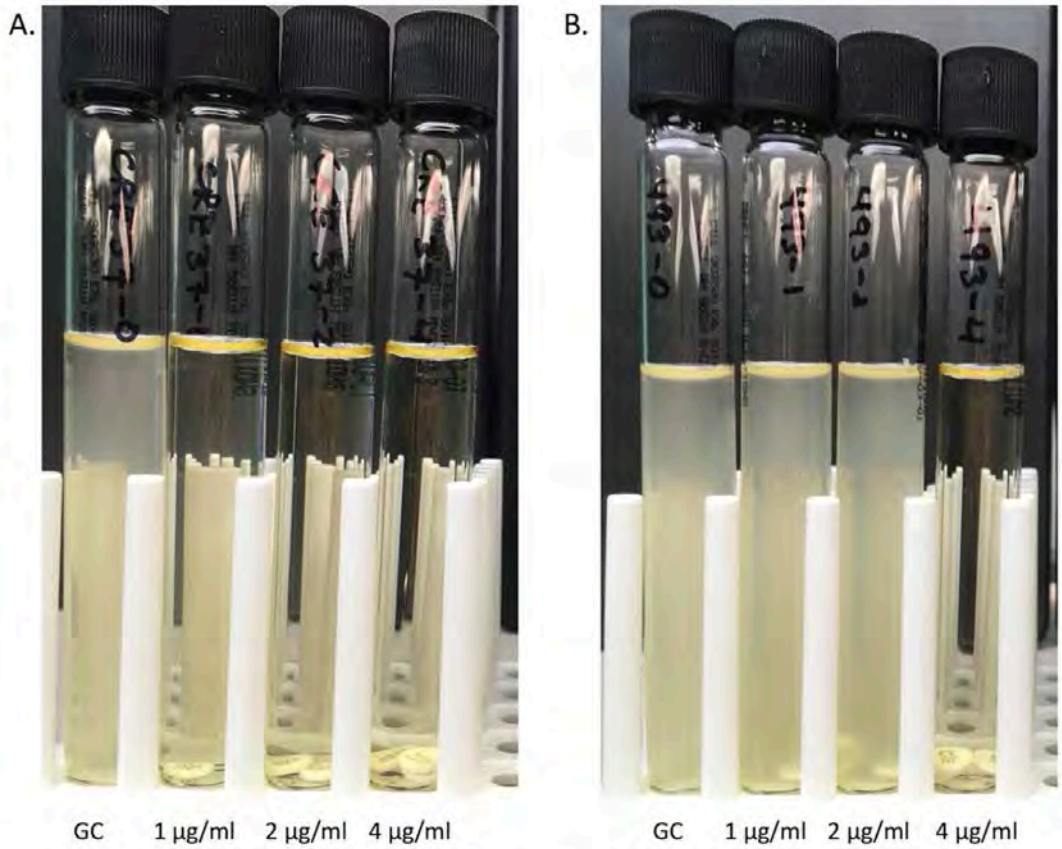

FIG 1 Colistin broth disk elution method. CBDE is performed with four 10-ml cation-adjusted Mueller-Hinton broth tubes per isolate, to which 0, 1, 2, and 4 colistin disks (10 μg) are added, generating final concentrations of 0 (growth control [GC]), 1, 2, and 4 μg/ml, respectively. (A) Tubes for a non-carbapenemase-producing carbapenem-resistant *Klebsiella pneumoniae* isolate with a colistin MIC of $\leq$1 μg/ml. (B) Tubes for an *mcr-1*-producing *Escherichia coli* isolate (CDC AR Bank accession number 493) with a colistin MIC of 4 μg/ml.

TABLE 1 Summary of CBDE results compared to rBMD and BMD results in a two-site study[c]

Site and isolate	No. of isolates with the following BMD result:			CA (%)	EA (%)	VME (%)	ME (%)
	Total	S or WT (N)	R or NWT (N)				
Site 1							
Acinetobacter baumannii	12	5	7	100	100	0	0
Pseudomonas aeruginosa	20	18	2	100	100	0	0
Enterobacteriaceae	24	10	14	100	100	0	0
Site 2							
Retrospective CRE	65	58	7	100	97[a]	0	0
A. baumannii	12	12	0	100	100	0	0
P. aeruginosa	14	14	0	100	100	0	0
Prospective CRE	19	17	2	100	100	0	0
Both sites, *mcr-1*-producing *E. coli*[b]	6	0	6	50	100	50	0
Overall	172	134	38	98	99	8	0

[a]One *Citrobacter freundii* isolate had an MIC of ≤0.25 μg/ml by BMD and an MIC of 2 μg/ml by CBDE, and 1 *Enterobacter cloacae* isolate had an MIC of 0.5 μg/ml by BMD and an MIC of 2 μg/ml by CBDE.

[b]Three *mcr*-1-positive *E. coli* isolates had MICs of 4 μg/ml by BMD and 2 μg/ml by CBDE on initial testing at both sites. These results were reproduced at the 2 sites.

[c]S, susceptible; R, resistant; WT, wild type; NWT, non-wild type; N, number of isolates; CA, categorical agreement; EA, essential agreement; VME, very major error; ME, major error; BMD, broth microdilution; rBMD, reference BMD. Site 1 performed rBMD and site 2 performed BMD. At site 1, the *Enterobacteriaceae* consisted of 8 *Klebsiella pneumoniae* isolates (3 were carbapenem resistant), 7 *E. cloacae* isolates, 4 *Escherichia coli* isolates, 2 *Klebsiella* (*Enterobacter*) *aerogenes* isolates, 1 *C. freundii* isolate, 1 *Citrobacter koseri* isolate, and 1 *Enterobacter hermannii* isolate. At site 2, the retrospective CRE consisted of 32 *K. pneumoniae* isolates, 15 *E. cloacae* isolates, 8 *E. coli* isolates, 4 *C. freundii* isolates, 3 *Serratia marcescens* isolates, 1 *Proteus mirabilis* isolate, 1 *K. aerogenes* isolate, and 1 *Klebsiella oxytoca*/*Raoultella ornithinolytica* isolate. At site 2, prospective carbapenem-resistant *Enterobacteriaceae* consisted of 13 *Klebsiella pneumoniae* isolates, 3 *E. cloacae* isolates, and 3 *Escherichia coli* isolates.

CLINICAL AND LABORATORY STANDARDS INSTITUTE®

29th Edition

M100

Performance Standards for Antimicrobial Susceptibility Testing

New Jan 2019 (CLSI: M100S29)

Interpretive Criteria

Interpretive criteria are the MIC or zone diameter values used to indicate susceptible, intermediate, and resistant breakpoints.

Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)		
		S	I	R	S	I	R
X	30 µg	≥20	15–19	≤14	≤4	8–16	≥32
Y	—	—	—	—	≤1	2	≥4
Z	10 µg	≥16	—	—	≤1	—	—

For example, for antimicrobial agent X with interpretive criteria in the table above, the susceptible breakpoint is 4 µg/mL or 20 mm and the resistant breakpoint is 32 µg/mL or 14 mm.

This document includes updated tables for the Clinical and Laboratory Standards Institute antimicrobial susceptibility testing standards M02, M07, and M11.

Overview of Changes: CLSI 2019

- CoNS: Species identification
- New antibiotics
  - Cefiderocol*
  - Meropenem-vaborbactam*
  - Ceftazidime-avibactam
  - Cetolazane-tazobactam (Thailand)
- Revised MIC breakpoints
  - - Ciprofloxacin/ Levofloxacin (Thailand)
  - - Ceftaroline (Gram-positive) (Thailand)

THE LANCET
Infectious Diseases

Summary

Background

Carbapenem-resistant Gram-negative bacteria represent the highest priority for addressing global antibiotic resistance. Cefiderocol (S-649266), a new siderophore cephalosporin, has broad activity against Enterobacteriaceae and non-fermenting bacteria, such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, including carbapenem-resistant strains. We assessed the efficacy and safety of cefiderocol versus imipenem-cilastatin for the treatment of complicated urinary tract infection in patients at risk of multidrug-resistant Gram-negative infections.

SYMPOSIUM ON ANTIMICROBIAL THERAPY

MAYO CLINIC

Mechanisms of Resistance and Clinical Relevance of Resistance to β-Lactams, Glycopeptides, and Fluoroquinolones

Louis B. Rice, MD

Mayo Clin Proc. ■ February 2012;87(2):198–208

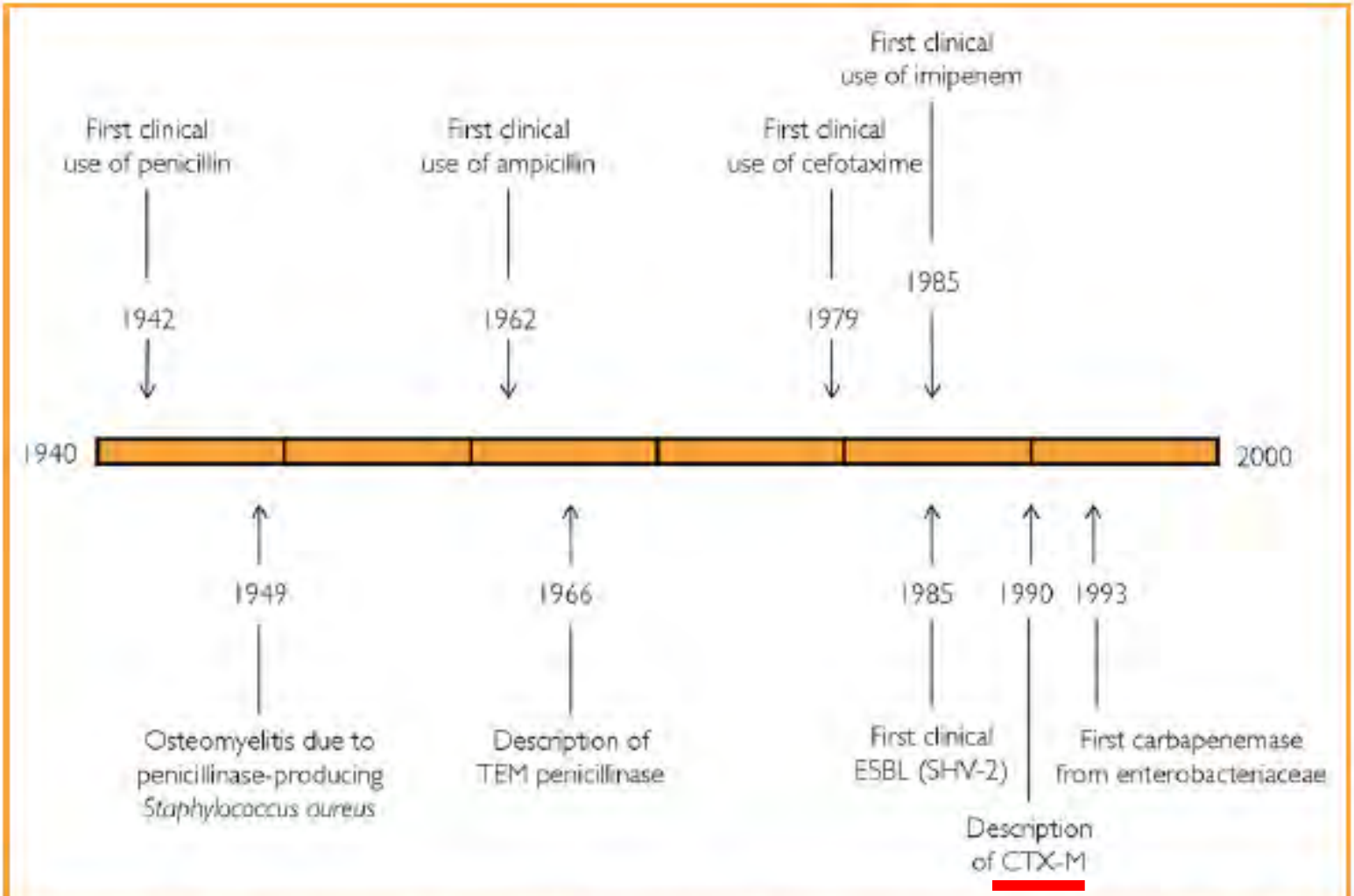

FIGURE 1. Time line showing the use of different classes of antibiotics and the publication of the first article describing resistance (or a new class of β-lactamases conferring resistance) to that class of antibiotics in a previously susceptible organism. It can be seen that emergence of resistance generally follows closely on the heels of clinical introduction of antibiotics. ESBL = extended-spectrum β-lactamase. Data from records of US Food and Drug Administration approvals and PubMed.