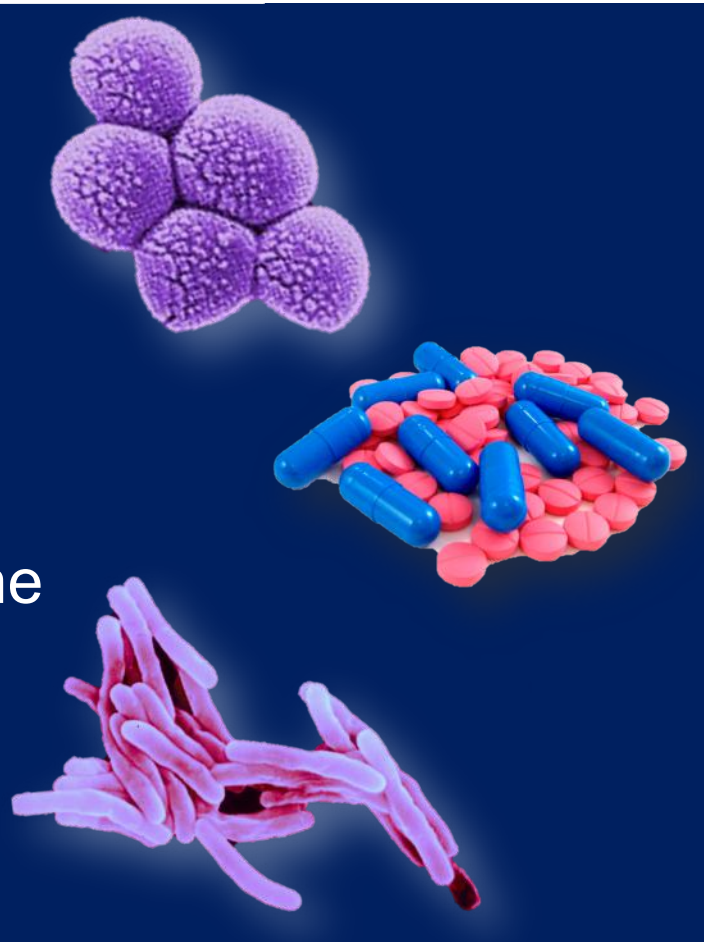
UW TASP
tele-antimicrobial stewardship program

# VISA… Everyplace You DON'T Want to Be!

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UW-TASP

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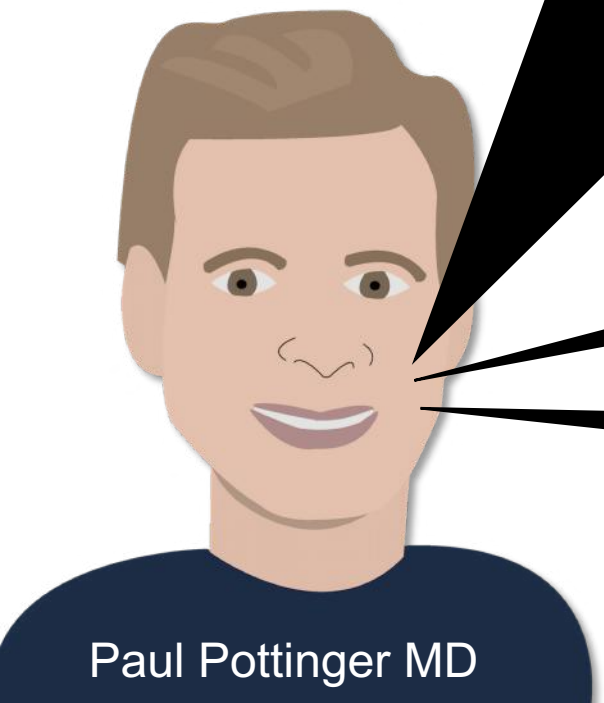
# VISA: *Objectives*

Disclosures
- No financial conflicts of interest

Objective
- Increase your comfort & skill working up possible VISA

Scope
- Hospital & Primary Care



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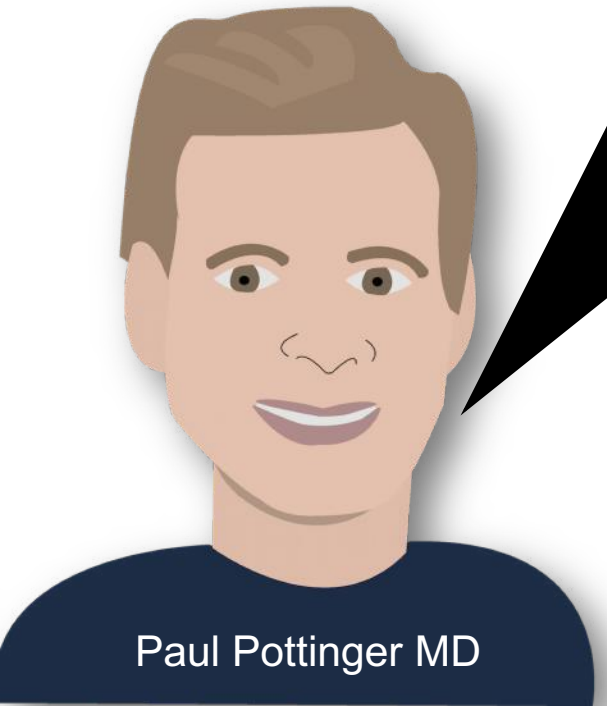
# VISA: *Question*

How comfortable are you with the definition, diagnosis, treatment of VISA?




A. Very Comfortable
B. Kinda Comfortable
C. Not Comfortable
D. Why are we talking about credit cards?

# VISA: *Spoiler Alert!*

- True VISA is uncommon
- Detecting this in lab is challenging
- Most MRSA infections can still be treated well with VANCO, regardless of MIC

Paul Pottinger MD

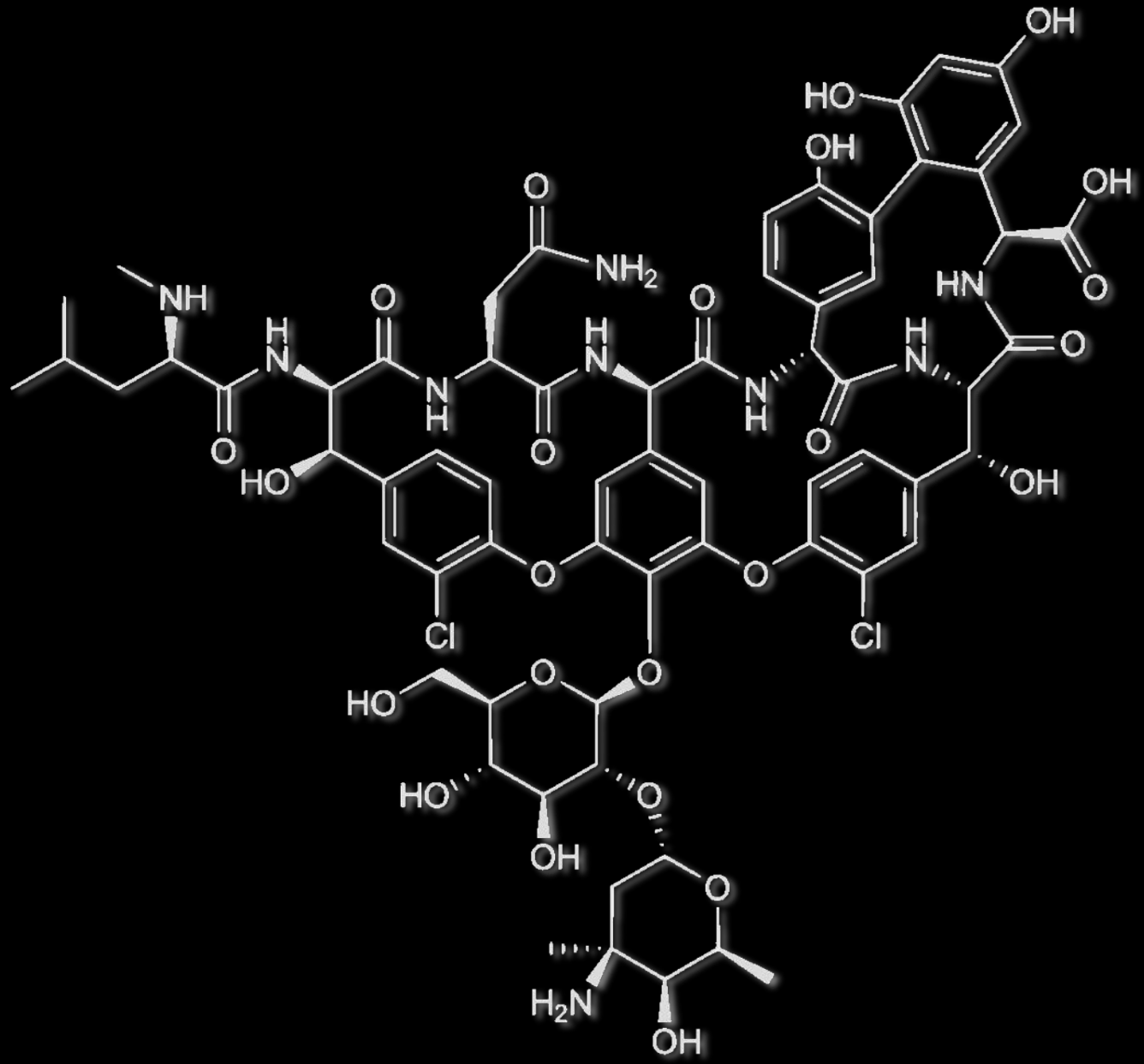
# VISA: *Definition*

"Vancomycin Intermediate *Staph aureus*"

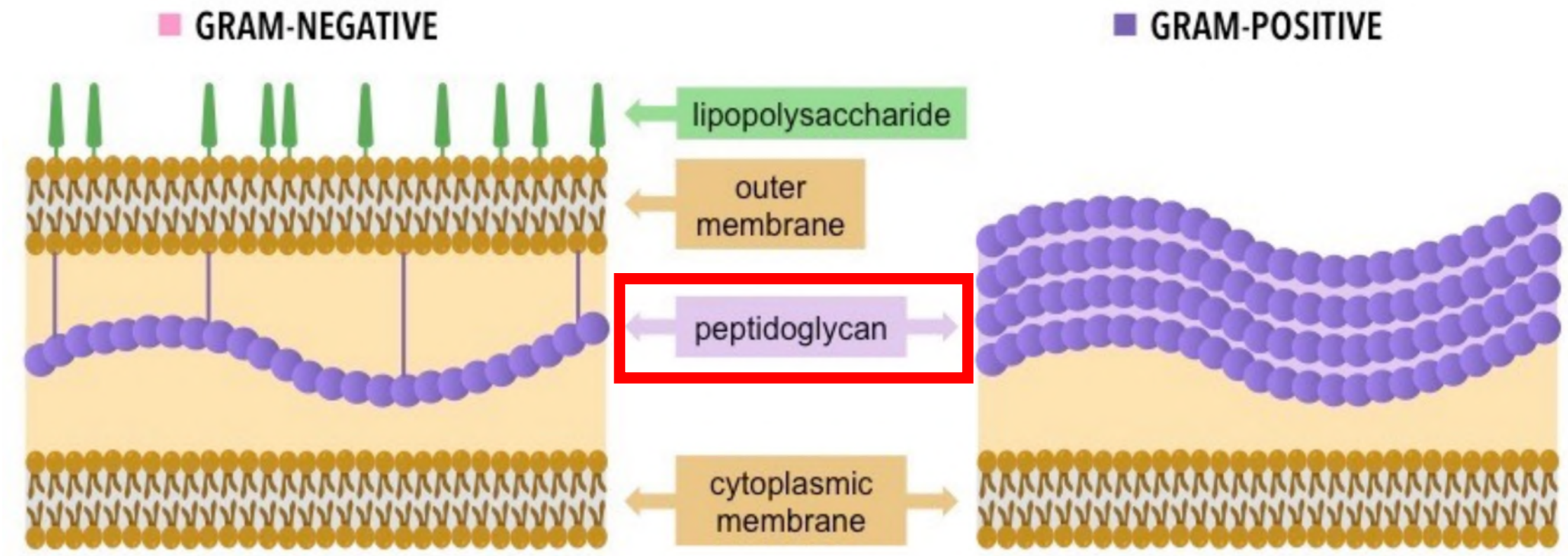
Vanco MIC 4-8 mg/L

Can happen with MRSA or MSSA

# VANCOMYCIN



# Vancomycin: *Mechanism of Action*



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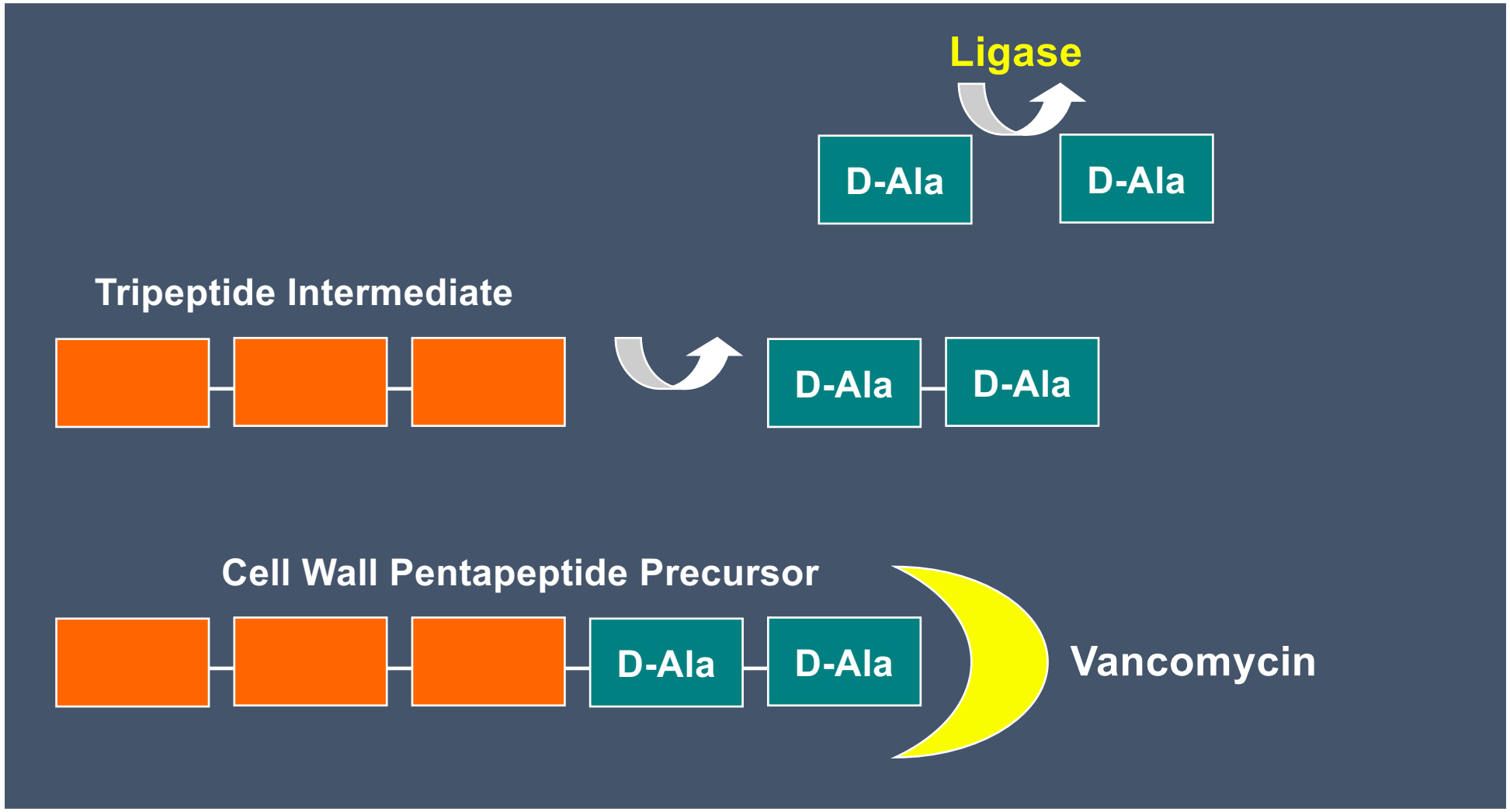
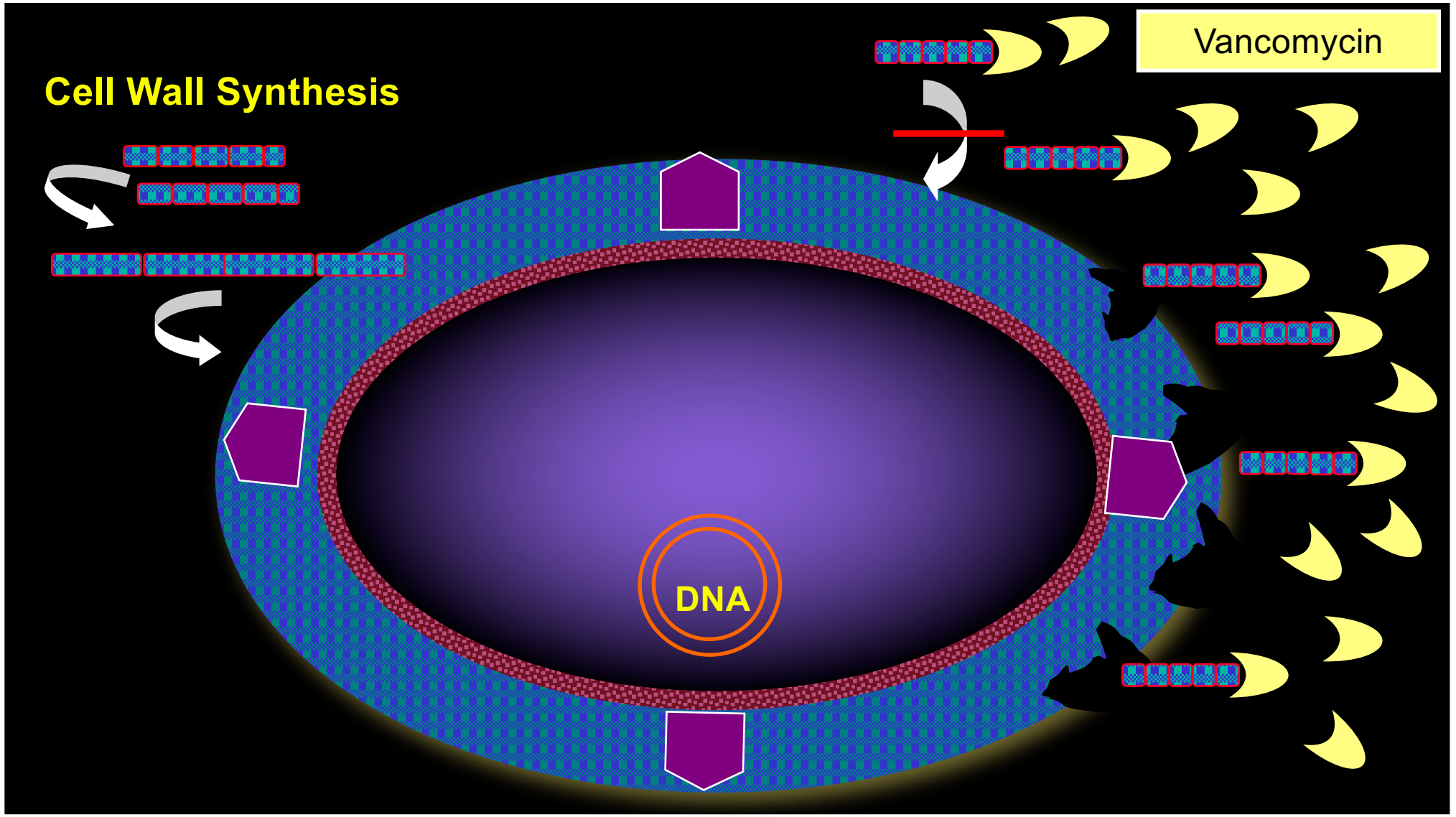


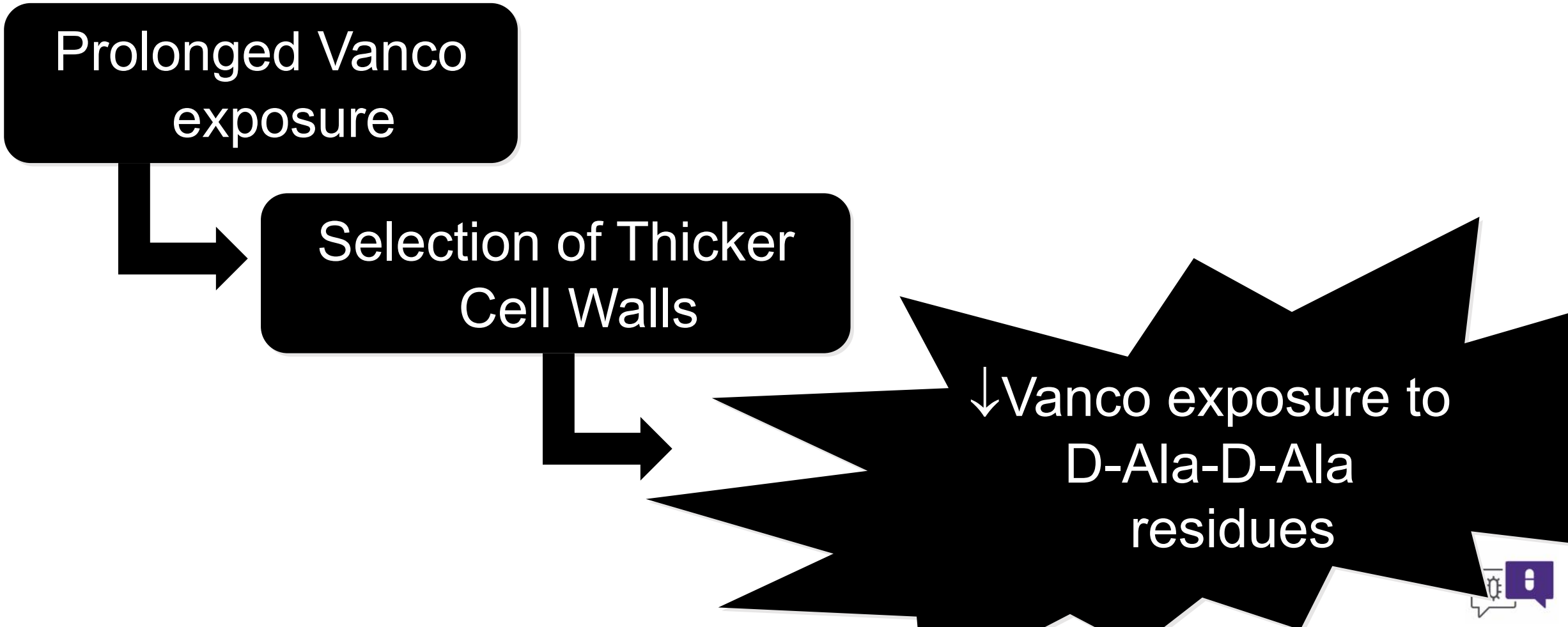
# Vancomycin: *Mechanism of Action*



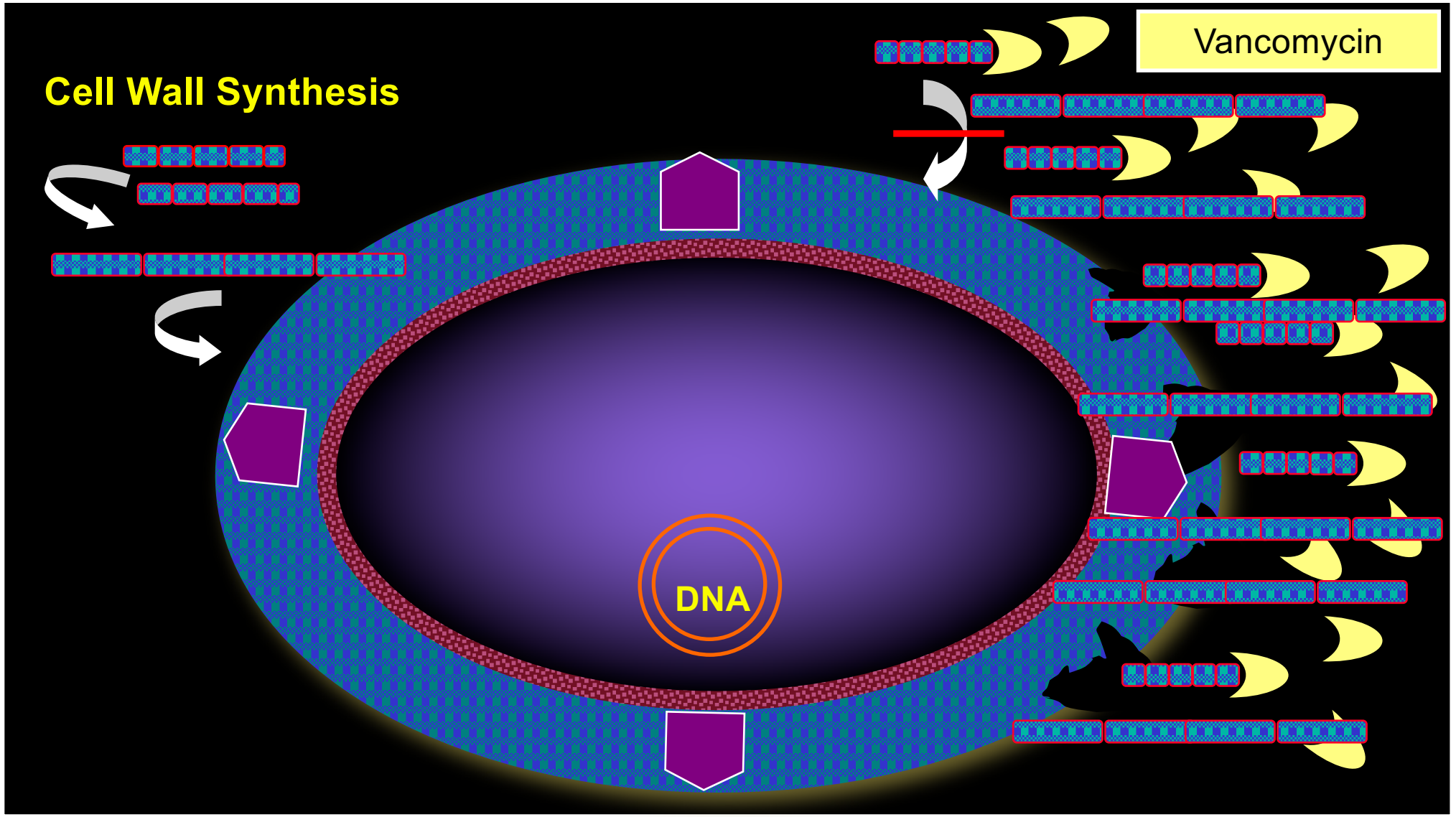

David Spach, MD

# VISA: *Mechanism of Resistance*

Increased D-Ala-D-Ala vancomycin target density



# VISA: *Mechanism of Resistance*



# VISA: *Mechanism of Resistance*

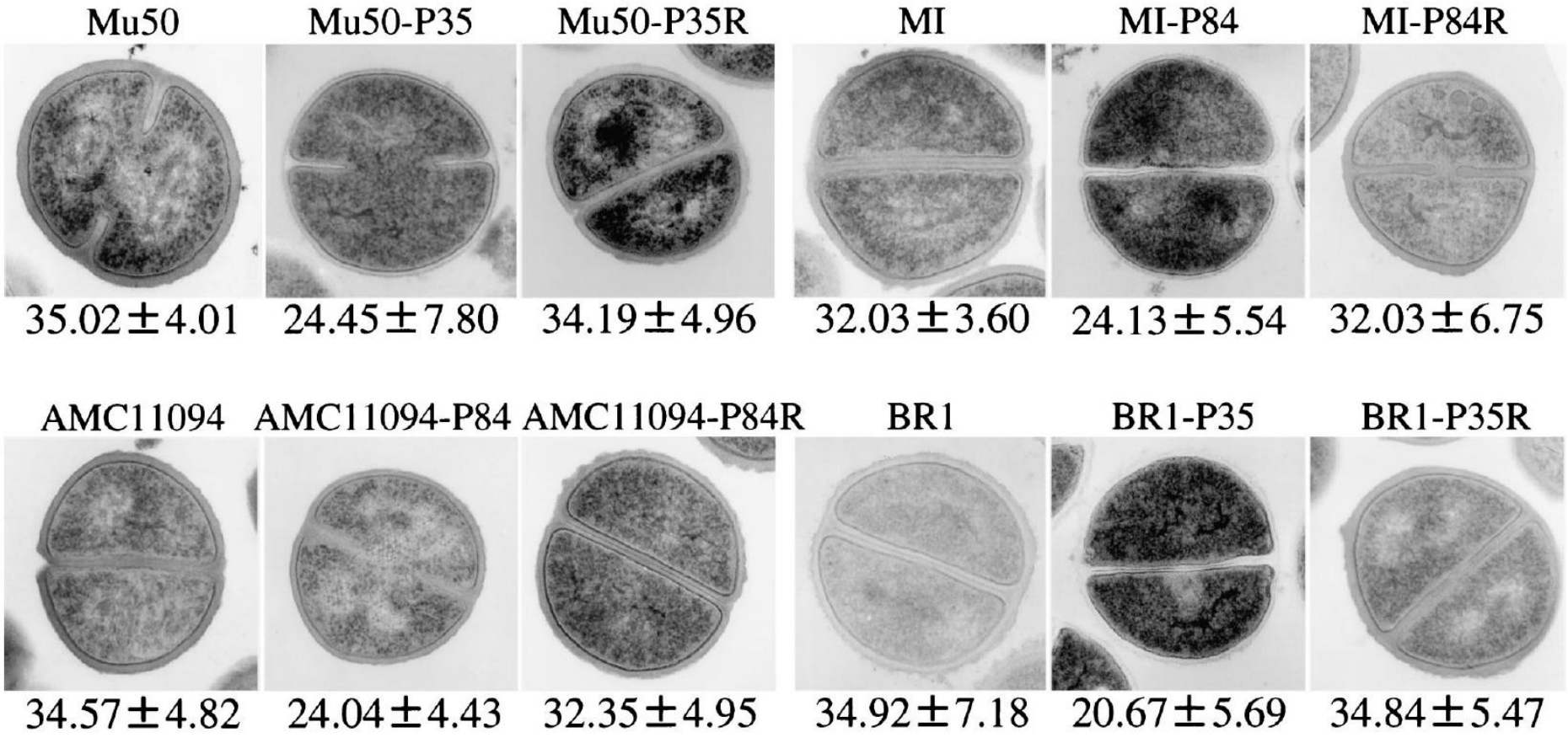



FIG. 3. Transmission electron microscopy of representative VRSA strains, their passage-derived strains, and vancomycin-resistant mutant strains. Magnification, ×30,000. The values given under each panel are the means and SDs of the cell wall thickness of the cells in nanometers. Note that the cell walls of passage-derived strains (with suffix P) were much thinner than those of the parent VRSA strains and vancomycin-resistant mutant strains (suffix PR).

JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 2003, p. 5–14

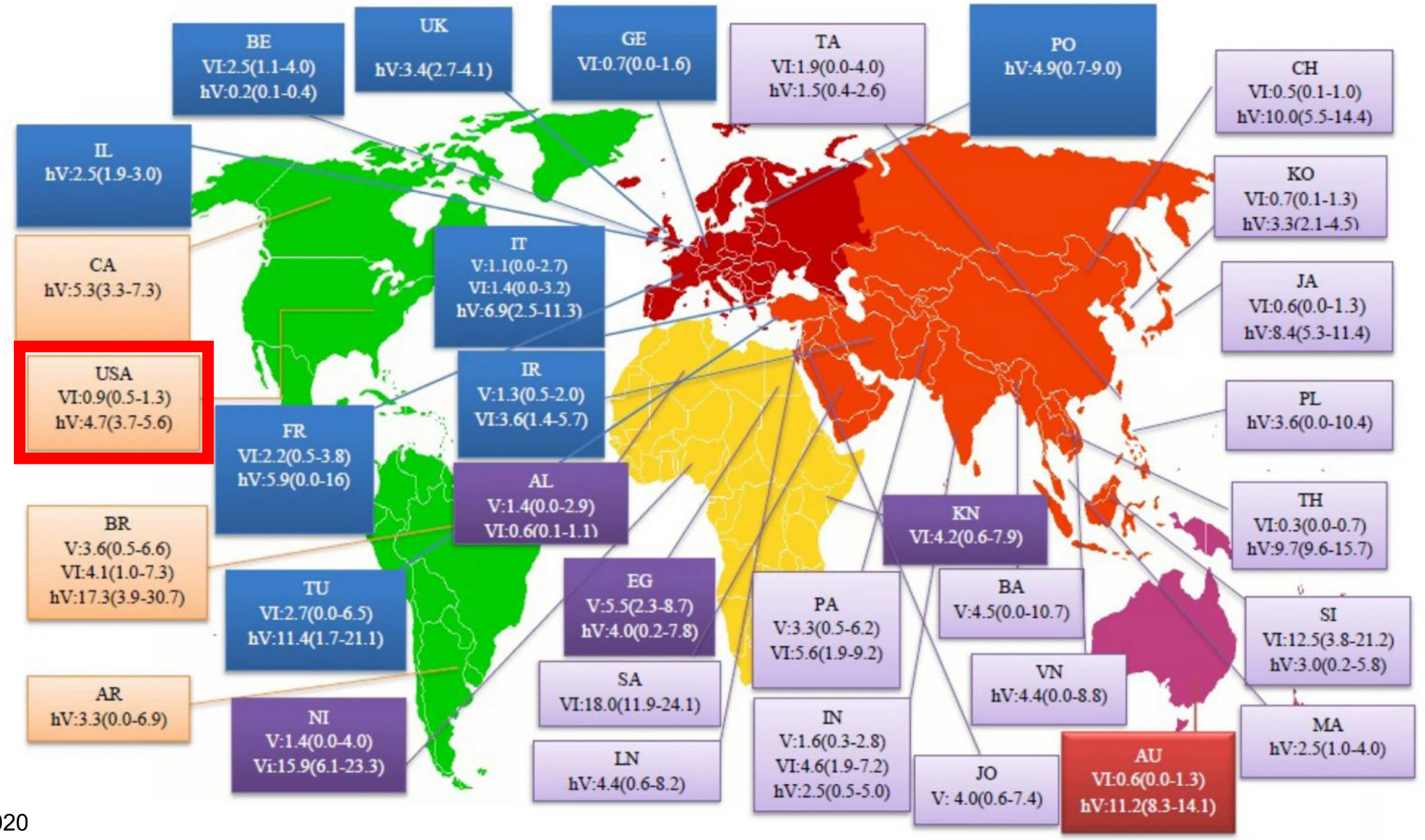
# hVISA: *Definition*

"Heteroresistant Vanco Intermediate *Staph aureus*"

Vanco MIC 4-8 mg/L

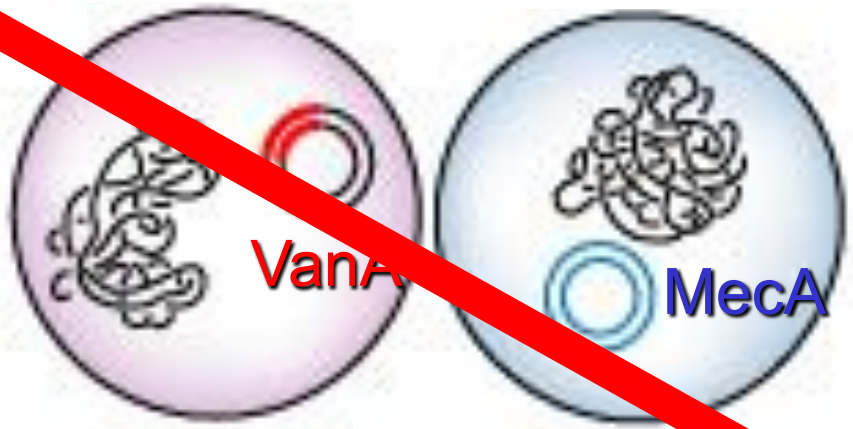
- Can happen with MRSA or MSSA
- Most of a staph isolate grown in lab are good old MRSA… but a minority population are VISA!
- Wild-type tends to out-compete VISA *in vitro*… and probably *in vivo* too!

# VISA: *Incidence*




Shariati *Sci Rev* 2020

VRE MRSA



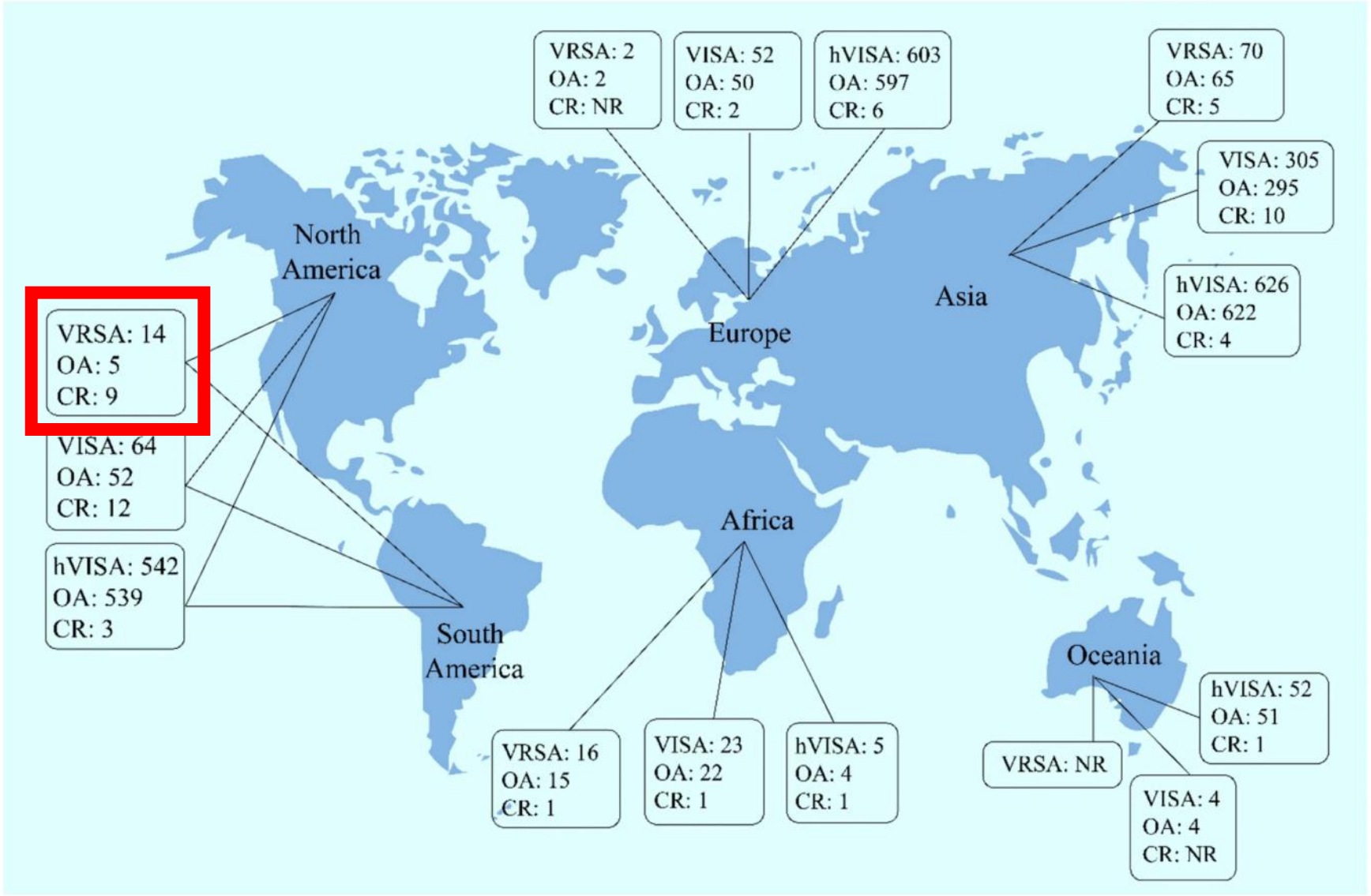
# VRSA: *Definition*

"Vancomycin Resistant *Staph aureus*"

Vanco MIC ≥ 16 mg/L

- Mechanism: Changed target
- (D-ala-D-ala → D-ala-D-lac)
- VRE implicated as the source of new target
- VERY RARE!

# VRSA: *Incidence*




Number of VRSA, VISA and hVISA isolates in different continent based on published original and case report studies. *OA* original article, *CR* case report.

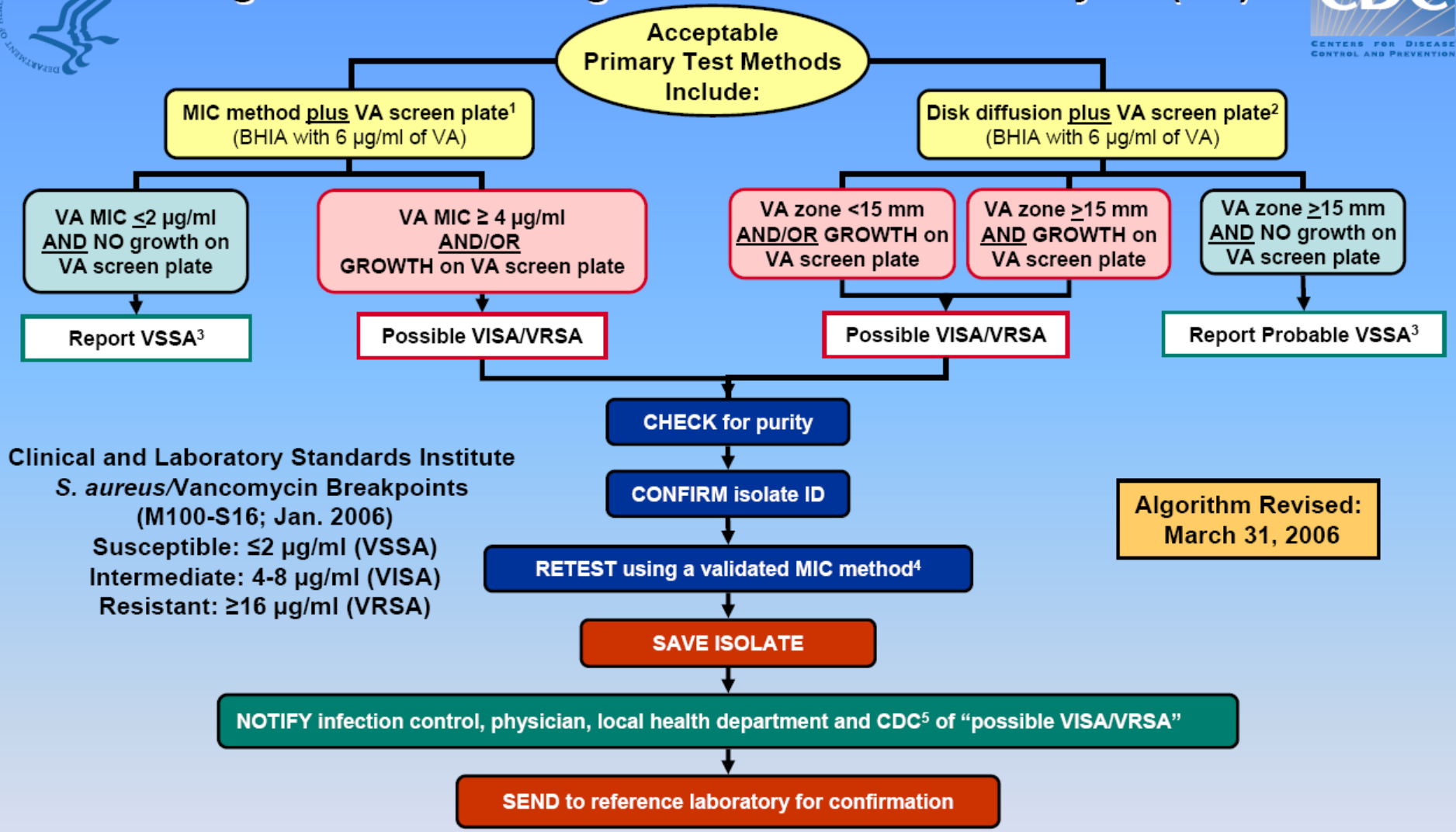
Shariati *Sci Rev* 2020

# hVISA: *Detection Challenges*

- Standard disk diffusion (zone ≤15 mm) and automated systems often *miss* hVISA
- Consider hVISA if pt persistently culture + after 7 d vanco
- Consider 0.5 McFarland starting culture for E-test
- CDC: Vanco plate (6 mg/L) should accommodate all *S.aureus* isolates… but this alone is *not enough*.
- Formal rule-out *not* done routinely.
- Consider sending isolate to state lab

No CLSI-approved detection methods for hVISA!

# Algorithm for Testing *S. aureus* with Vancomycin (VA)




Clinical and Laboratory Standards Institute
*S. aureus*/Vancomycin Breakpoints
(M100-S16; Jan. 2006)
Susceptible: ≤2 µg/ml (VSSA)
Intermediate: 4-8 µg/ml (VISA)
Resistant: ≥16 µg/ml (VRSA)

**Algorithm Revised: March 31, 2006**

Important Footnotes

[1] Laboratories using automated MIC methods that have not been validated for VRSA detection should add a commercial VA agar screen plate (6 µg/ml).

[2] Disk diffusion will not differentiate VISA (MICs 4-8) from susceptible strains (MICs 0.5-2). VA screen plate will not reliably detect strains for which MIC=4.

[3] If concerned about a result based on a patient's history, send to a reference lab for MIC testing.

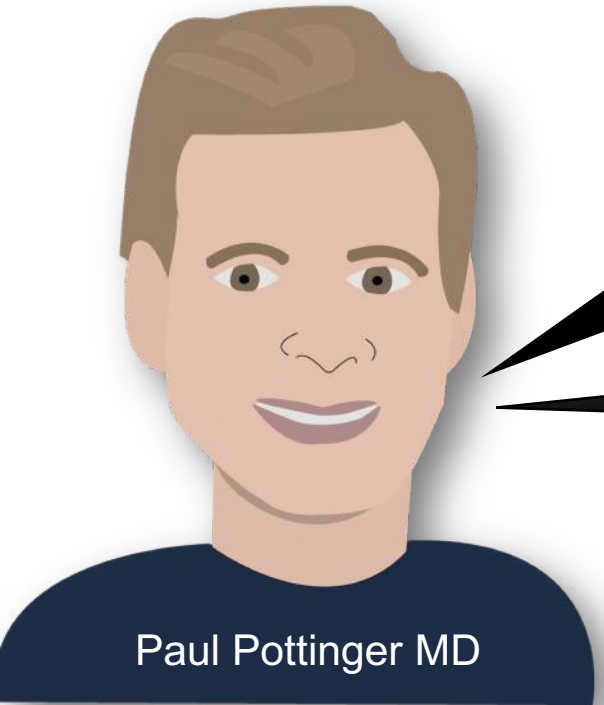
[4] Validated methods: reference broth microdilution, agar dilution, Etest® (0.5 McFarland inoculum, Mueller-Hinton agar), MicroScan® overnight and Synergies plus™; BD Phoenix™ system. For other automated methods, check with the manufacturer about FDA-clearance to detect MICs ≥4 (i.e., VISA/VRSA).

[5] Report to CDC by email: SEARCH@cdc.gov

More VISA/VRSA info: http://www.cdc.gov/ncidod/dhqp/ar_visavrsa.html

# VISA: *Gut Check*

- VISA is *S.aureus* vanco MIC 4-8 mg/L
- It is rare
- Lab detection challenging




- Vanco MIC “creep” sounds scary…
- Do we care?

# Vancomycin: *MIC Creep?*

Meta-Analysis 29,234 isolates: *NO evidence for MIC Creep!*

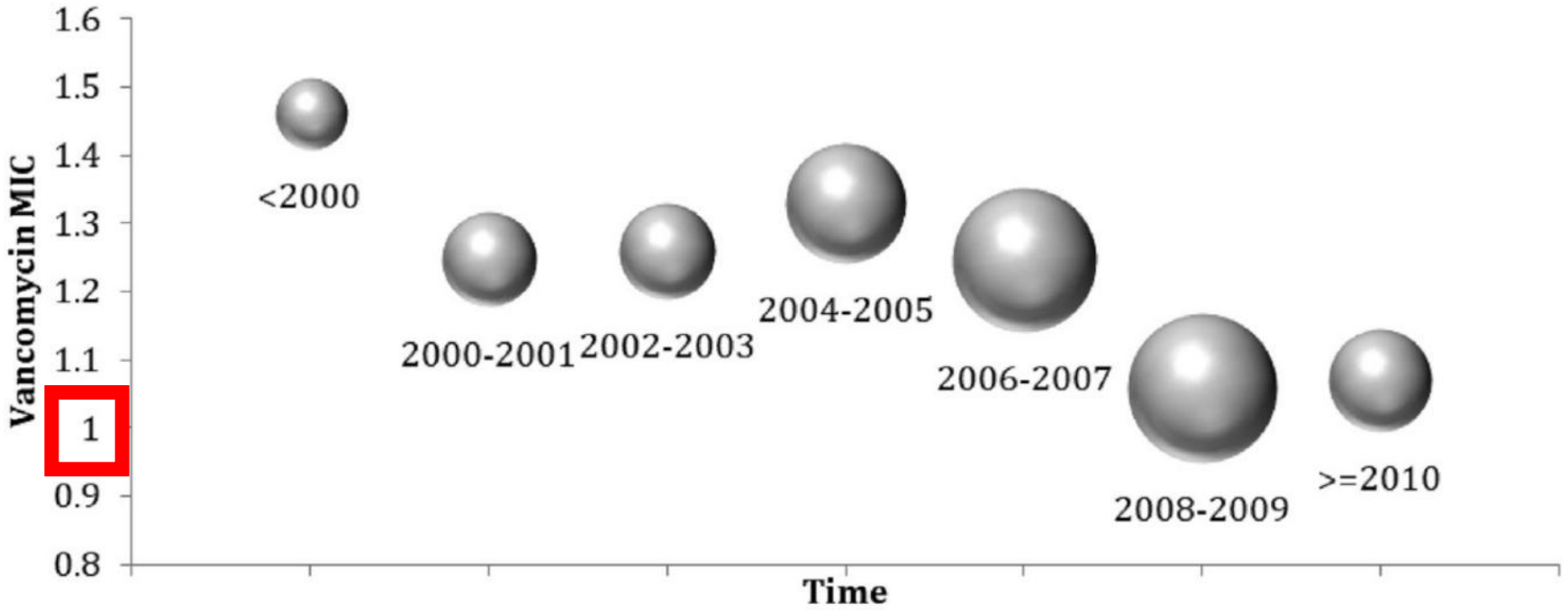



**Fig. 2.** Pooled mean of vancomycin MIC determined by the broth microdilution method over time. The bubble size represents the meta-analysis sub-group weight.

Diaz *Clin Micro Infect* 2018

# Vancomycin: *MIC Creep?*

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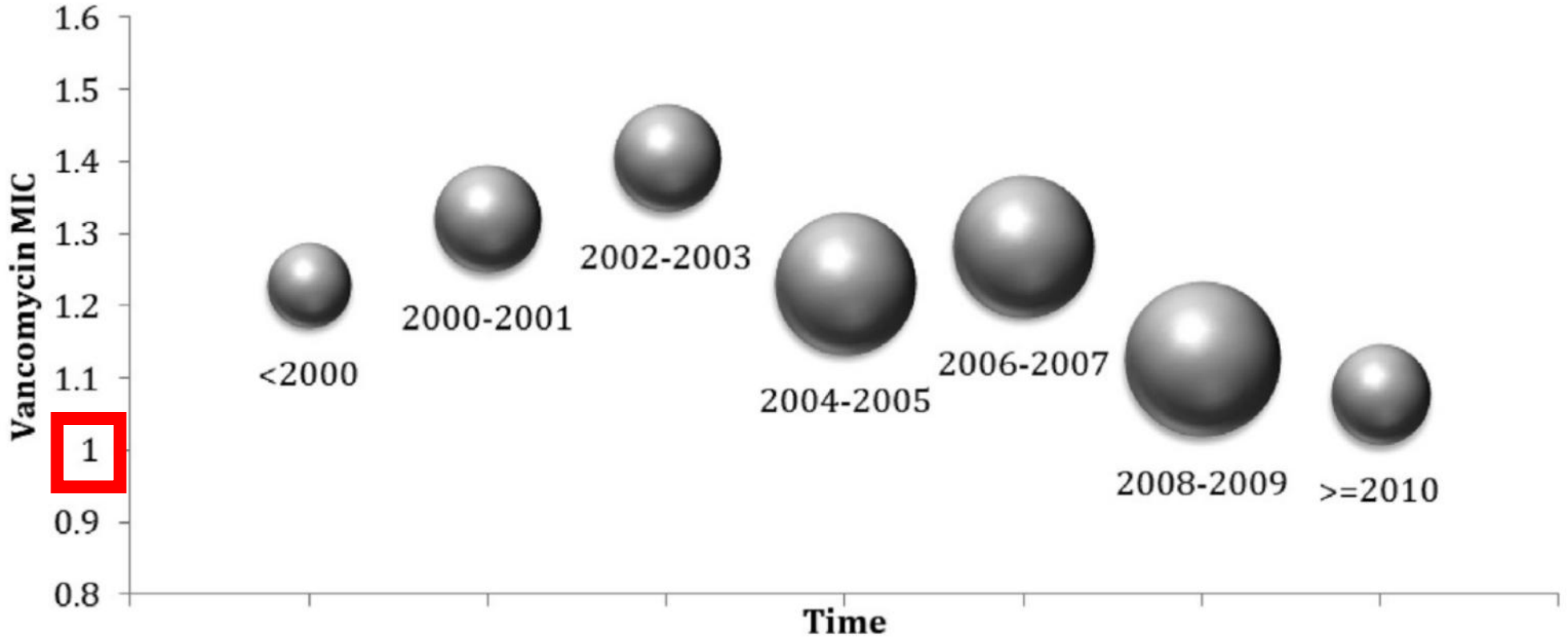


**Fig. 3.** Pooled mean vancomycin MIC determined by the Etest method over time. The bubble size represents the meta-analysis sub-group weight.

Diaz *Clin Micro Infect* 2018

# Vancomycin: *IDSA Guidelines*

ASHP REPORT

Therapeutic monitoring of vancomycin for serious methicillin-resistant *Staphylococcus aureus* infections: A revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists

Rybak *Am J Health-Syst Pharm* 2020

# Vancomycin: *IDSA Guidelines*

- Based on current national vancomycin susceptibility surveillance data, under most circumstances of empiric dosing, the vancomycin MIC should be assumed to be 1 mg/L.
- When the MIC BMD is >1 mg/L, the probability of achieving an AUC/MIC target of ≥400 is low with conventional dosing; higher doses may risk unnecessary toxicity, and the decision to change therapy should be based on clinical judgment.

Rybak *Am J Health-Syst Pharm* 2020

# VISA: *Conclusions*

## Vanco MIC = 4?

- No need to panic!
- Chat with friends in clinical micro lab… repeat the test
- Whether 2 or 4, work hard to achieve source control
- Vanco probably fine if MIC 0.5-2
- If MIC truly 4, you may need to change (e.g. linezolid)… the patient's condition and situation must be considered

*Truly… Thank You*

Paul Pottinger MD