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February 20, 2018

Chloe Bryson-Cahn MD
Robert Cybulski, PhD
Marisa D'Angeli, MD
Zahra Escobar, PharmD
Rupali Jain, PharmD
John Lynch, MD, MPH
Natalia Martinez-Paz, MA, MPA
Paul Pottinger, MD
Erica Stohs MD, MPH
Ted Wright, MD

Agenda

- Paul Pottinger: *What Makes MRSA "MR?"*
- Case Discussions
- Open Discussion

This presentation is intended for educational use only, and does not in any way constitute medical consultation or advice related to any specific patient.

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What Makes MRSA "MR"?

Paul Pottinger, MD, FIDSA
Associate Professor
UW Medical Center &
The University of Washington School of Medicine

February 20, 2018

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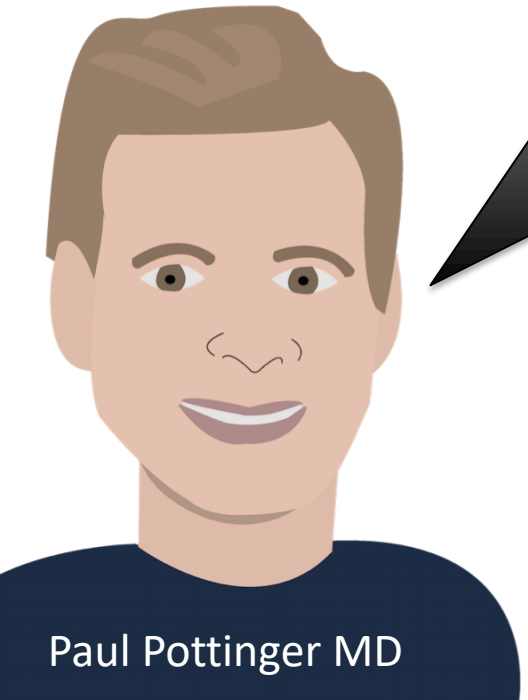
Disclosures

- No financial conflicts of interest
- Everything we discuss is QI, thus protected from legal discovery under WA State Code



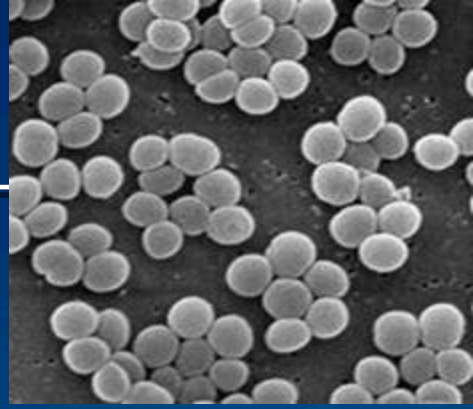
Paul Pottinger MD

Question…

What Makes *S.aureus* resistant to methicillin?

A. Thickened cell wall
B. Beta-lactamase expression
C. Efflux pump expression
D. Altered penicillin binding proteins

MRSA: *What Is It?*



"Methicillin-Resistant Staphylococcus Aureus"

Bacteria

- <10% size of human cells
- Simple chromosome with genes
  - ✓ reproduction
  - ✓ virulence
  - ✓ drug resistance

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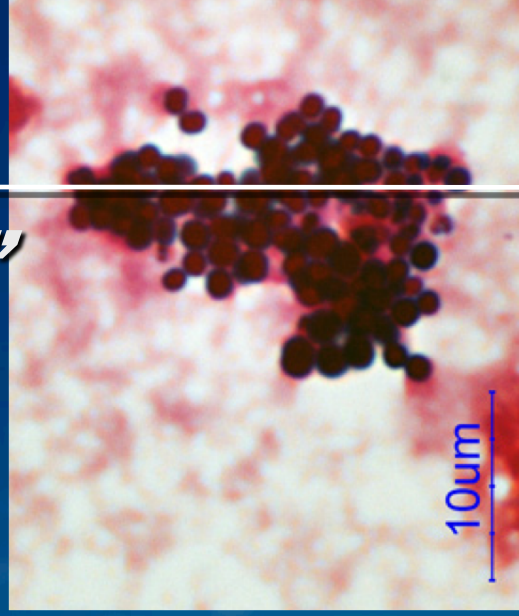
MRSA: *What Is It?*



"Staphylococcus Aureus"

"Staphylo" = Cluster

"Coccus" = Sphere

"Aureus" = Gold color on BAP

Gram-positive

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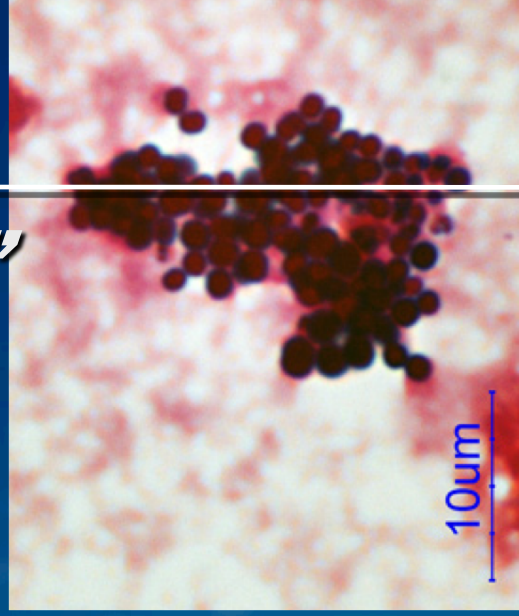
MRSA: *What Is It?*



"Staphylococcus Aureus"

A Scourge:

- ✓ Food Poisoning
- ✓ Toxic Shock
- ✓ Bacteremia / Endocarditis
- ✓ Skin & Soft Tissue Infections
- ✓ Osteomyelitis
- ✓ Meningitis / Epidural Abscess
- ✓ Pneumonia

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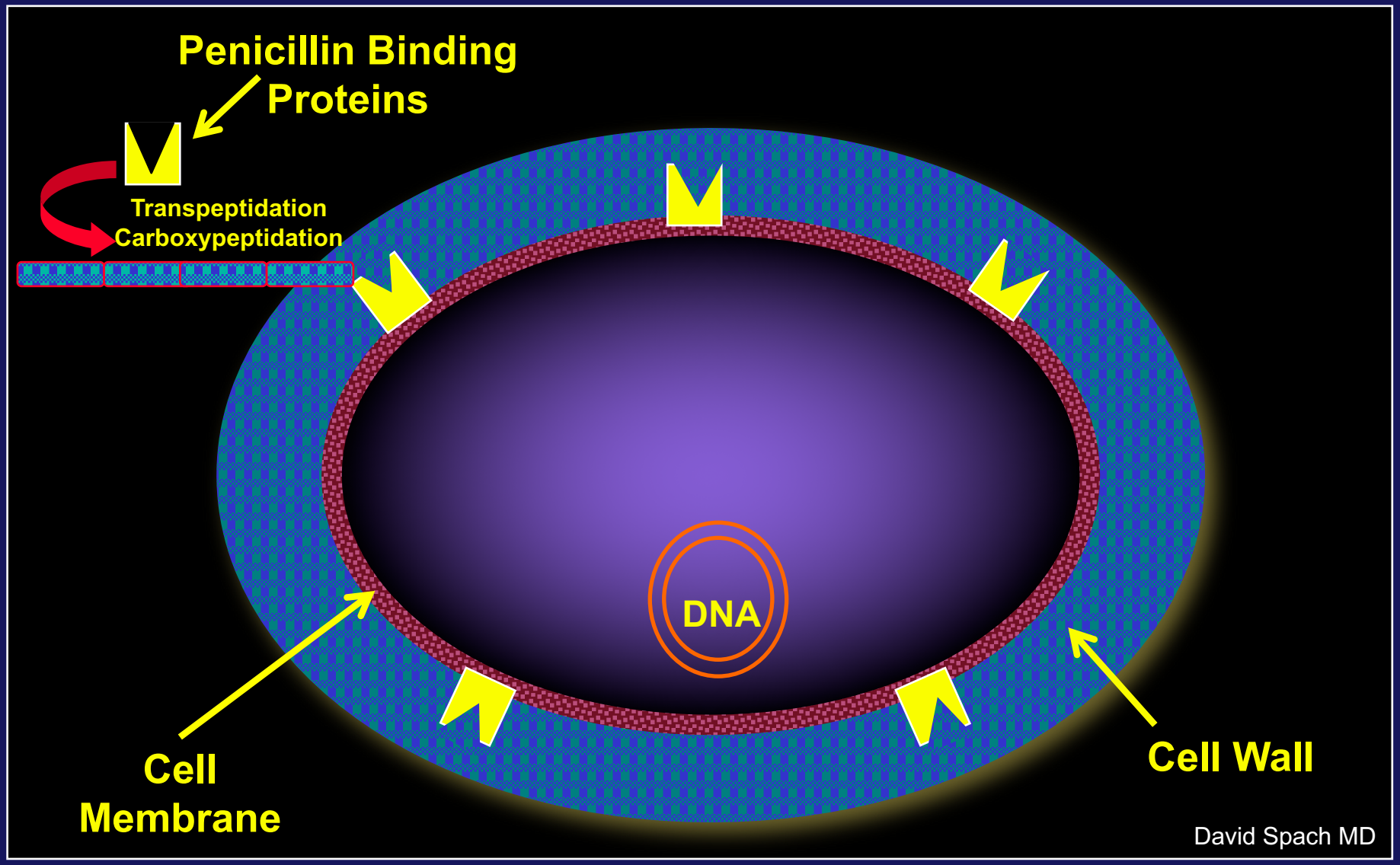
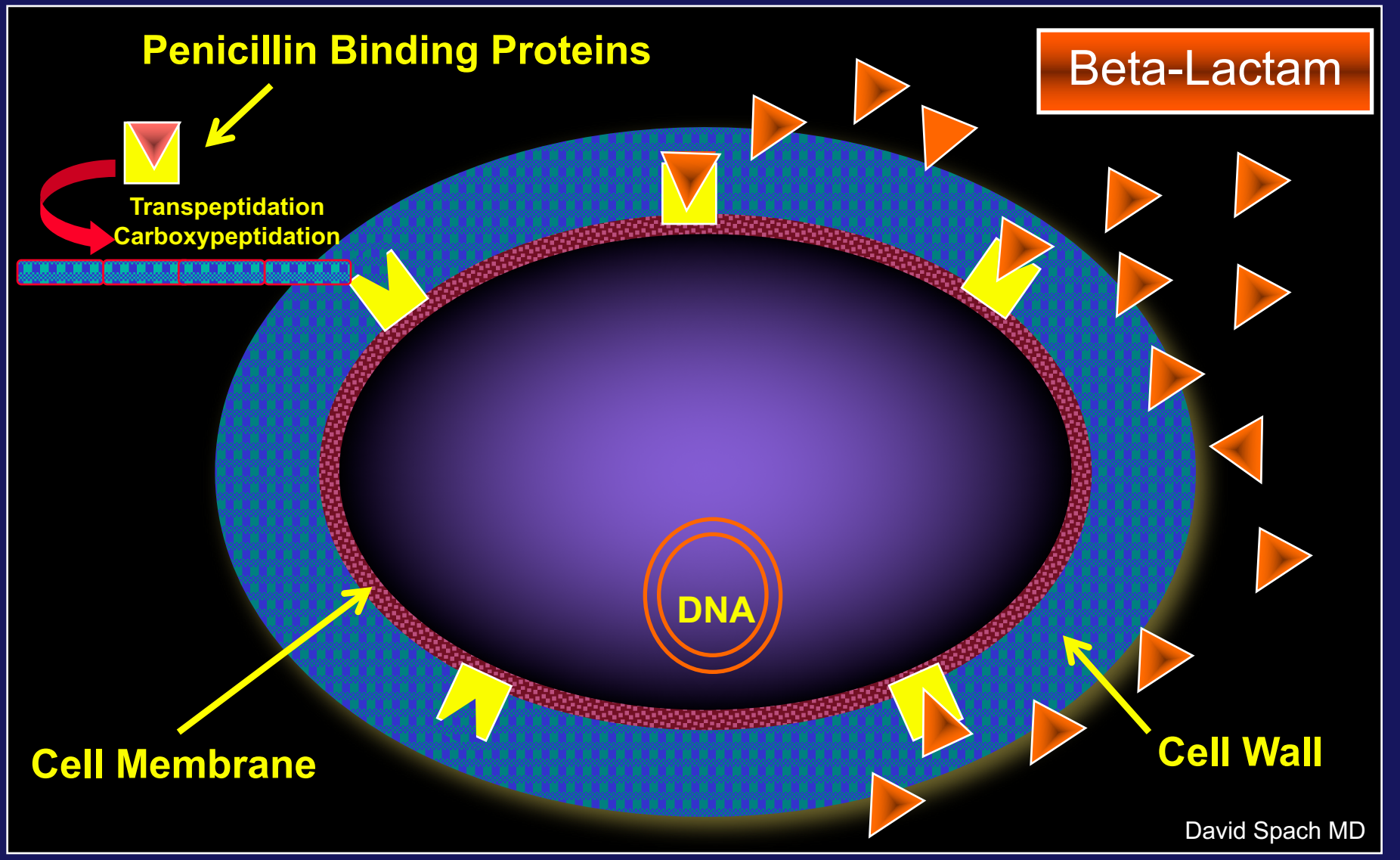
Alexander Fleming (1881 - 1955)

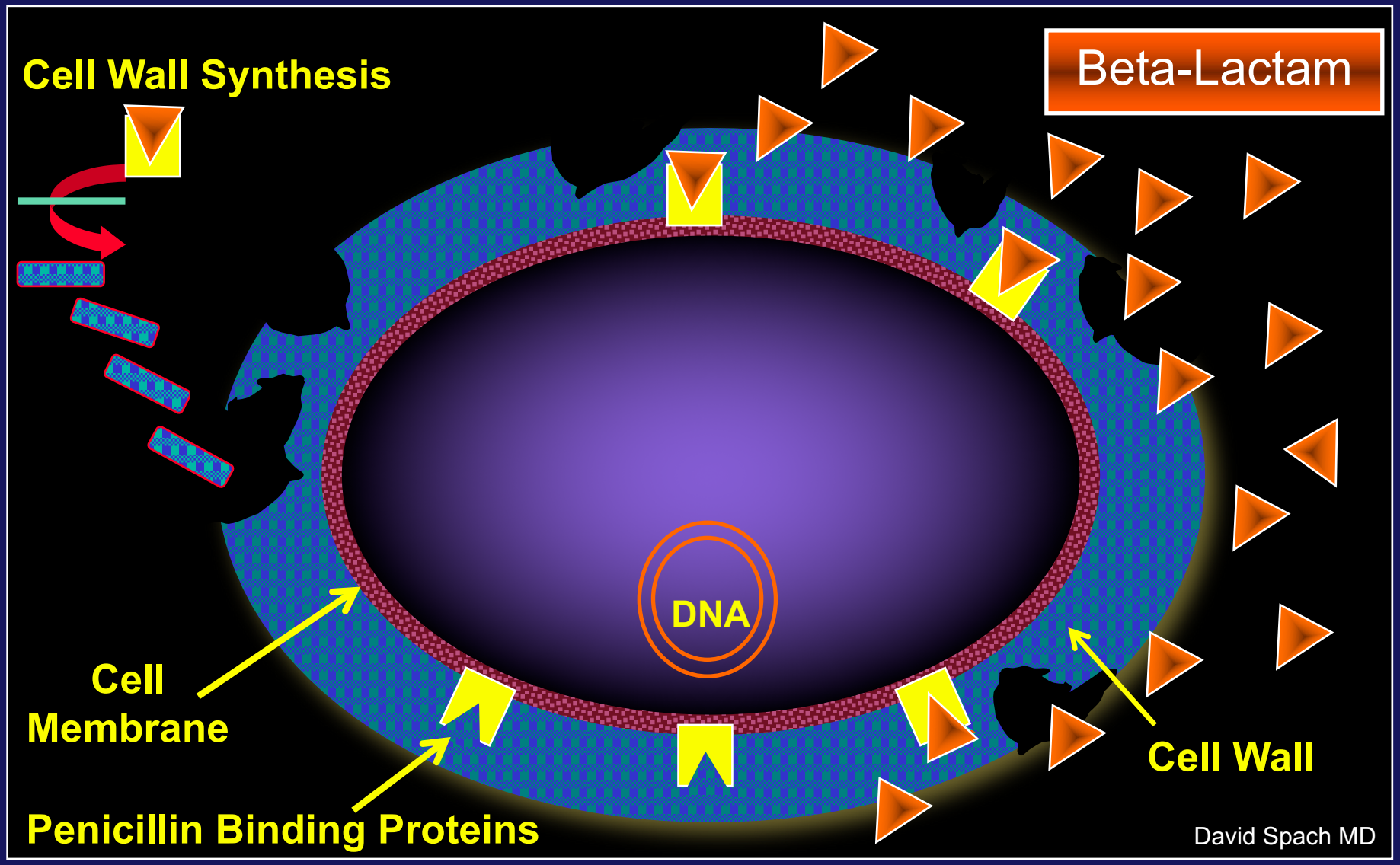
Beta-Lactams: Mechanism of Action

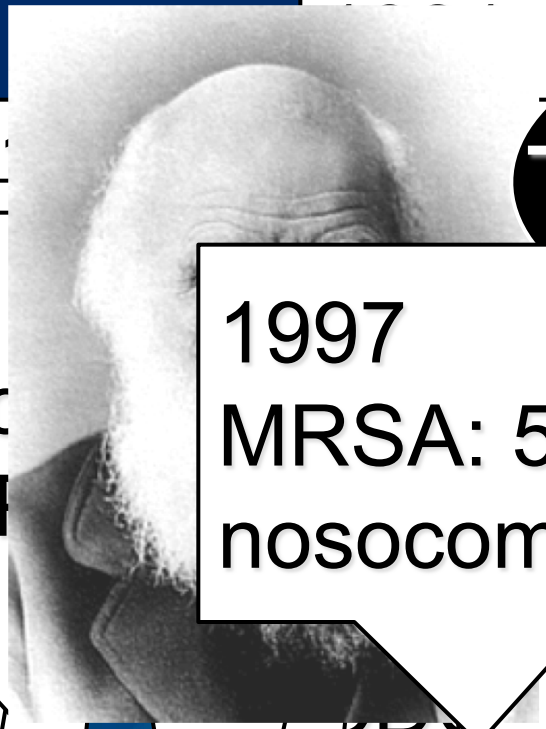


Beta-Lactams: Mechanism of Action



Beta-Lactams: Mechanism of Action





Told you so[d]

1959
Methic
to kill

1997
MRSA: 50% US
nosocomial staph infxns

ealthy kids
-MRSA

Charles Darwin
(1809-1882)

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PRSA: Beta Lactamases

- Original form of PCN resistance: PRSA.
- Hydrolytic enzyme that chews up PCN.
- Still the rule (~5% of MSSA has no beta-lactamase activity… 95% of MSSA is PRSA)
- It's OK… we rarely, RARELY use PCN to treat MSSA!

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MRSA: Altered Target

MRSA: Resistant to all beta-lactams (except ceftaroline), monobactams, carbapenems

MOR:

- ✓ Target Modification: MecA gene encodes altered PCN-binding protein PBP2A
- ✓ Dx by KB-diffusion (Fox best inducer!), robotic microtiter, PBP2A latex agglutination, MALDI-TOF, or MecA PCR

Other resistance genes common!

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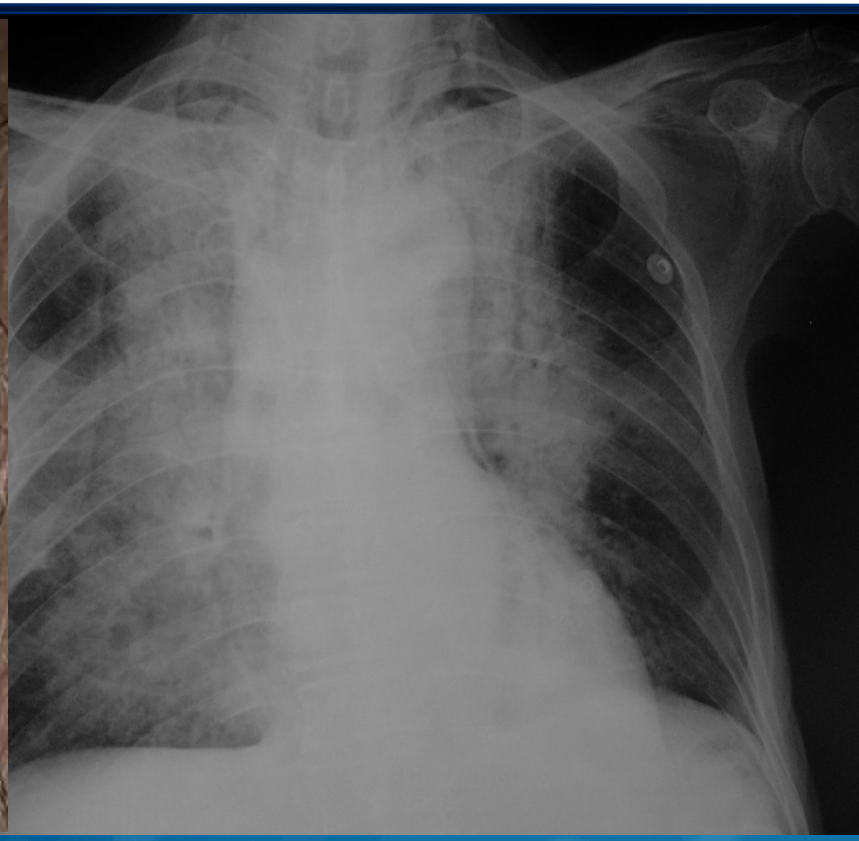
MRSA: *Two Flavors*



CA-MRSA

HA-MRSA

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MRSA: *Two Flavors*

MRSA type	Community	Hospital
Chromosomal Cassette	IV	II
Toxins Produced	Numerous	Few
PVL Toxin	Common	Rare
Common Infections	Skin & Soft Tissue	Lung & Blood
Abx Resistance	Less Resistant	More Resistant

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MRSA Susceptibilities: Seattle 2016

	HMC (45%)	UWMC (32%)
Clindamycin	55%	49%
Levofloxacin	14%	18%
Tetracycline	91%	89%
TMP/SMX	83%	89%
Vancomycin	100%	99%
Linezolid	100%	100%
Daptomycin	100%	100%

At least it's still sensitive to vanco… right?

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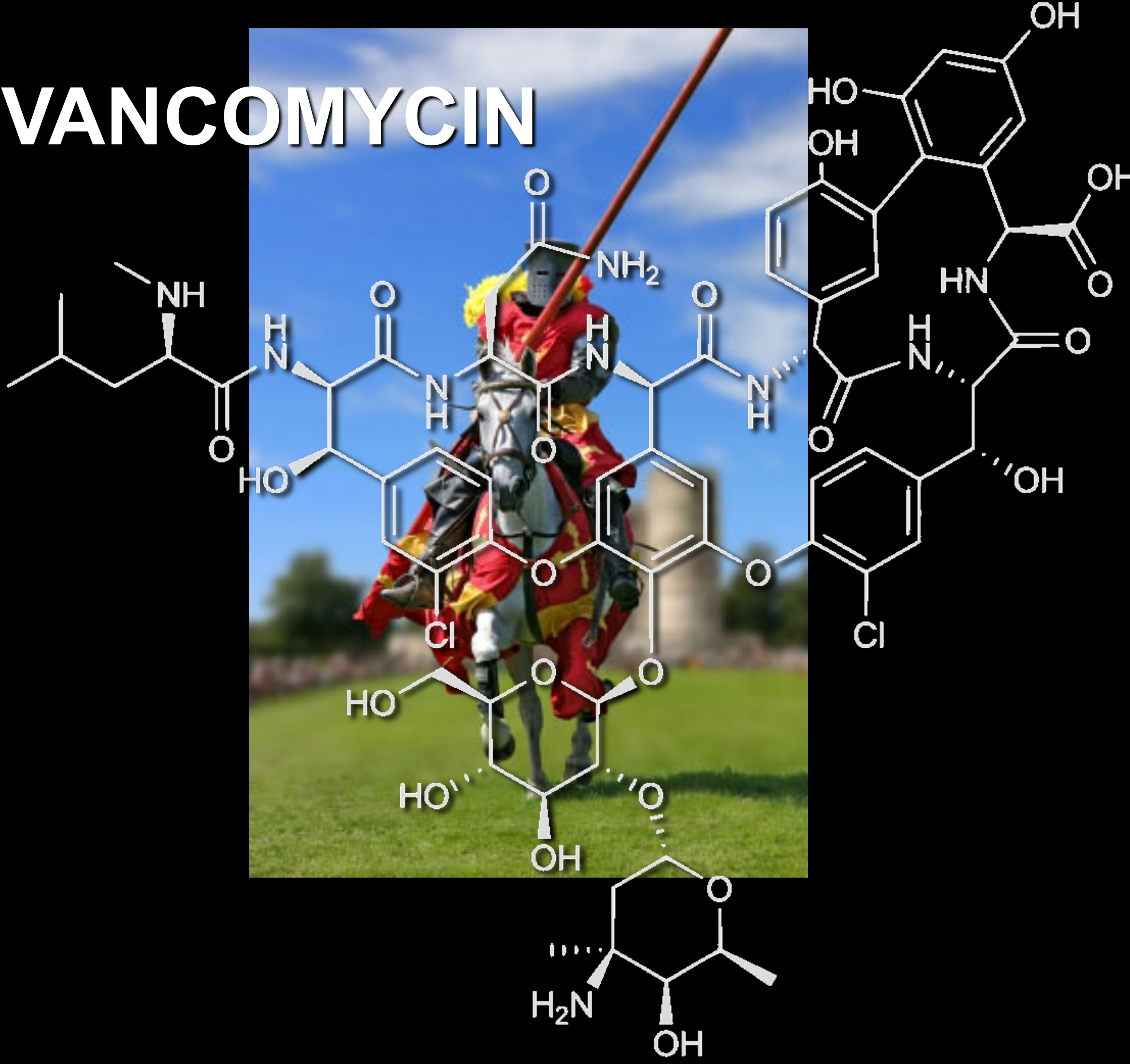
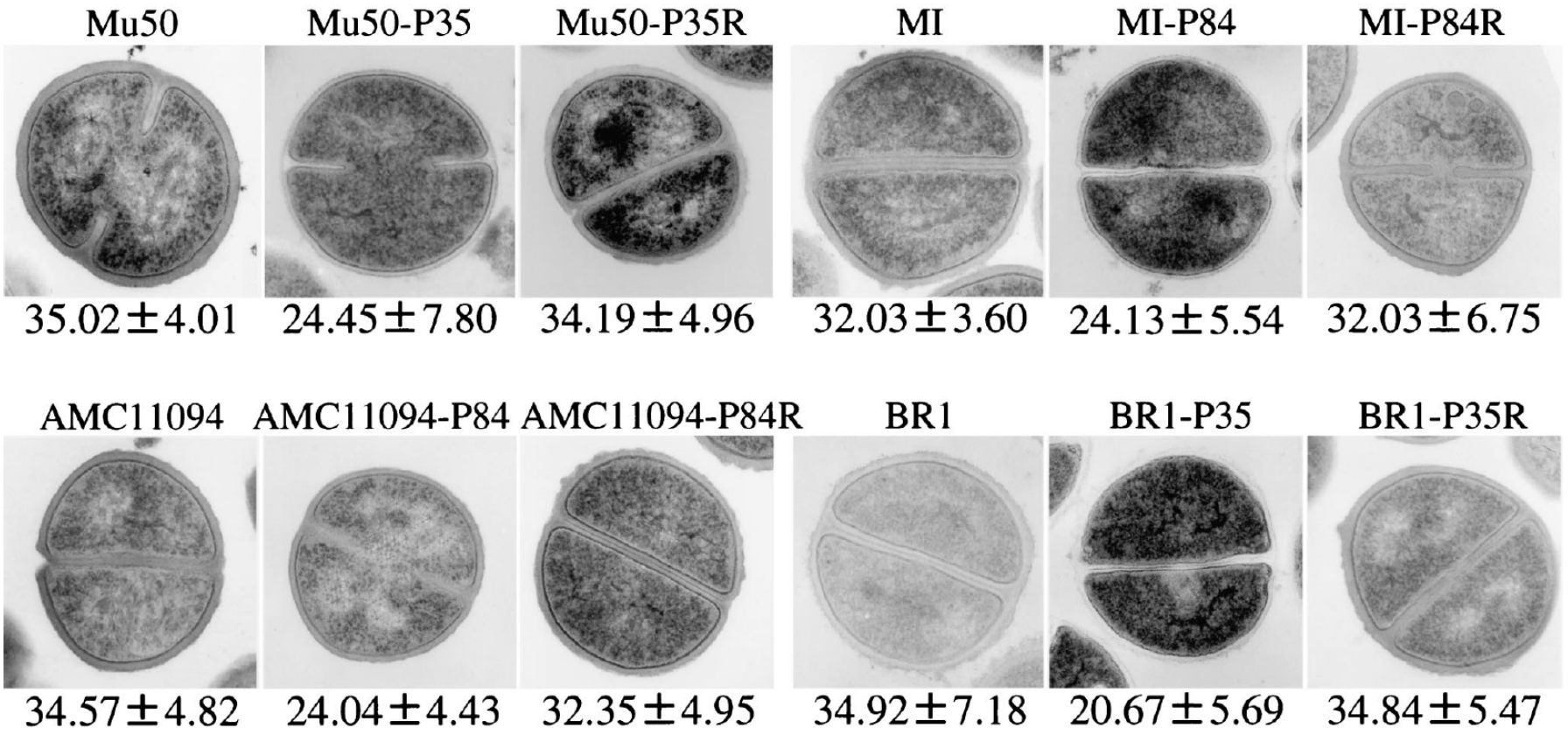
VANCOMYCIN



Vanco's Challenge: VISA

VISA: MIC 4 – 8 mcg/mL

- Increasing # of case reports: MSSA & MRSA



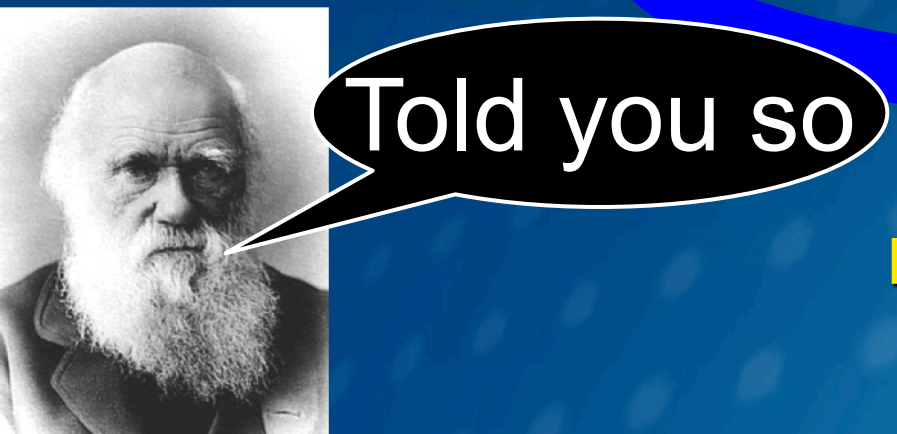
JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 2003, p. 5–14

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).

Emergence of Antimicrobial Resistance

Susceptible Bacteria

Selective Pressure → Upregulation of resistance factors or novel mutations.



New Resistant Bacteria

CDC

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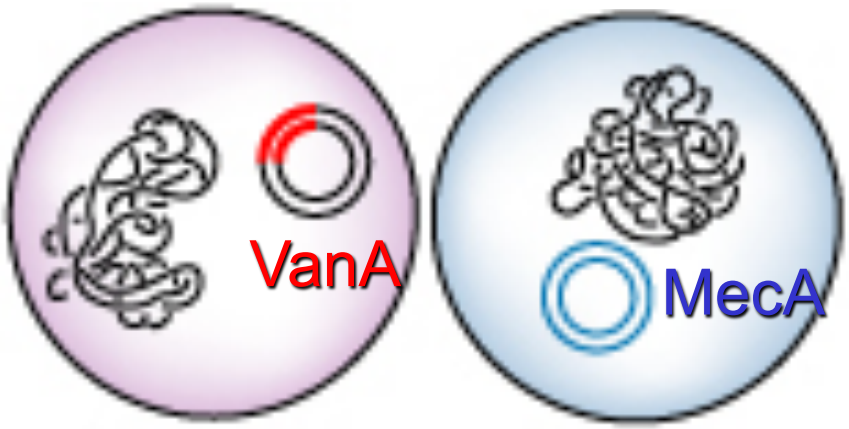
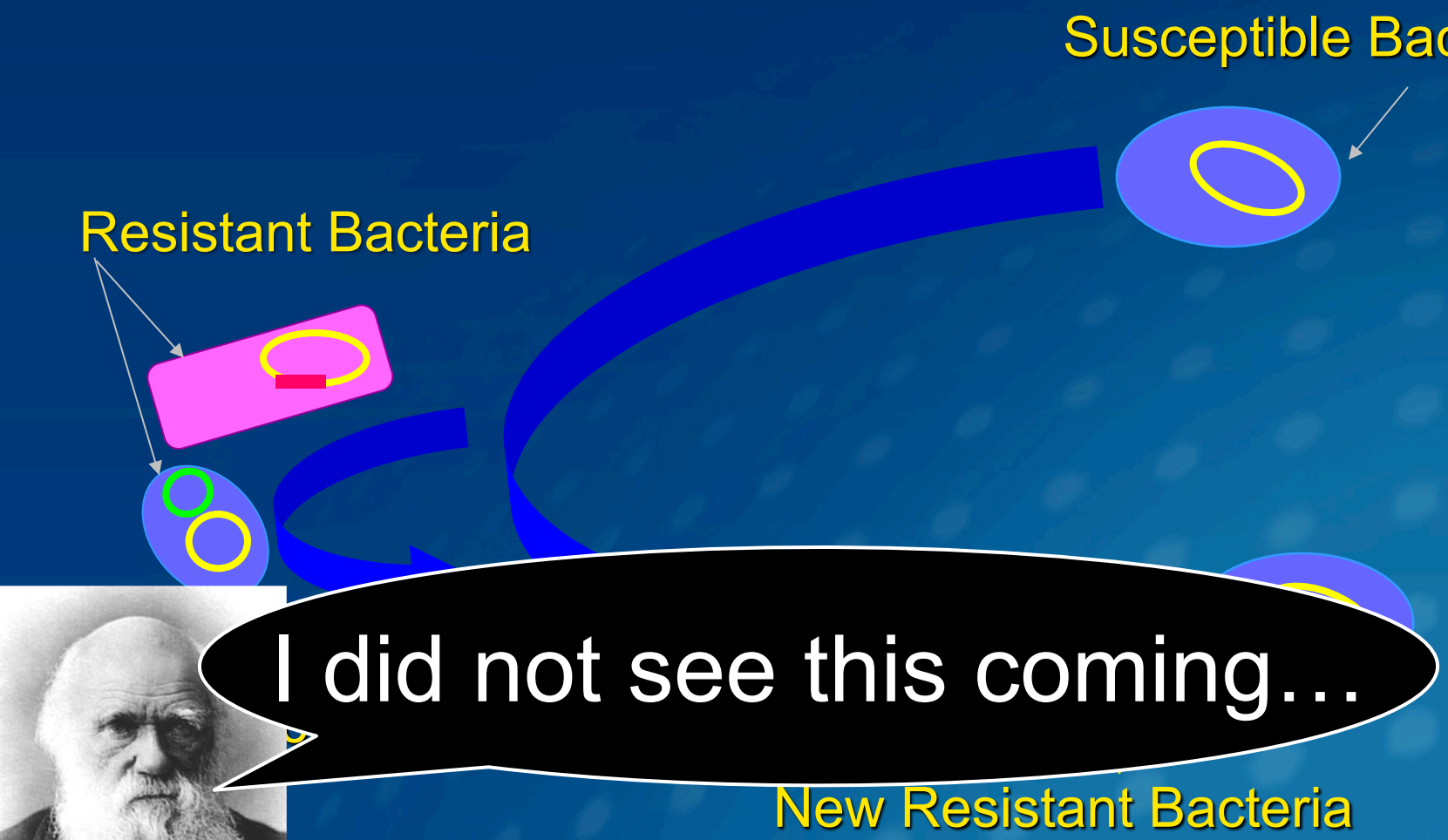
VRE

MRSA



Emergence of Antimicrobial Resistance



CDC

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Armageddon: *VRSA*

VRSA: MIC ≥ 16 mcg/mL

- Few case reports… Under-detected?

14 US cases as of 2014

- **MOR:**

✓Altered target.

✓VRE implicated as source of VanA gene encoding altered cell wall (D-ala-D-ala → *D-ala-D-lac*)

- Treatment Option: Linezolid first-line

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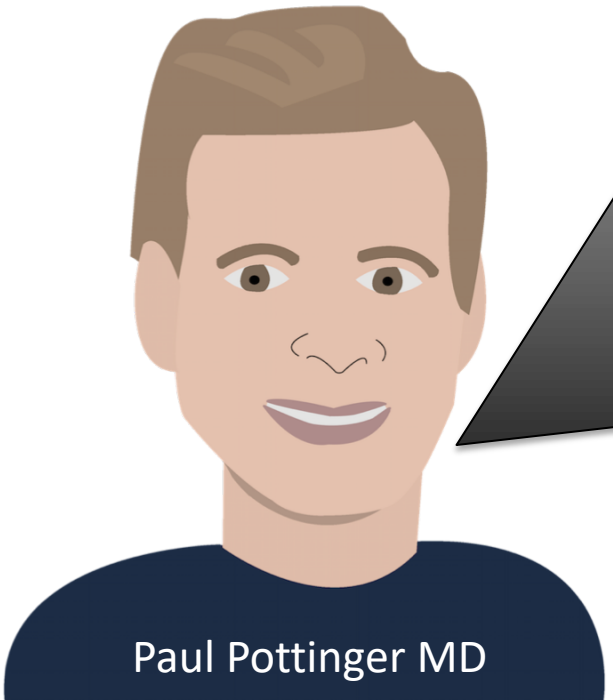
Conclusions



MRSA

- ✓ Altered PCN-binding proteins
- ✓ Still sensitive to some PO abx

VISA

- ✓ Thicker cell wall
- ✓ Do not use vanco!

VRSA

- ✓ VRE + MRSA = altered target
- ✓ Rare… thank goodness