

# CA-MRSA: The New Face of Staphylococcus Aureus

2009 Remington Winter Course

Richard P. Wenzel, M.D., M.Sc.  
Professor and Chairman  
Department of Internal Medicine  
Medical College of Virginia  
Virginia Commonwealth  
University, Richmond





# Legendary Inheritance of Sex, Violence and Tragedy Surrounding Staphylus

## Zeus

Supreme ruler  
Mt. Olympus  
Married to Hera  
Numerous liaisons  
Father to Helen

## Semele

Mortal priestess  
Asked Zeus to reveal  
his glory -  
Bolts of lightning  
led to death

## Minos

King of Crete



## Pasiphaë



## Dionysus

God of wine  
Hera had Titan lure  
and attack him  
remaining heart back  
into Semele. "Twice born"



## Ariadne



Loved Theseus  
who "had no  
joy for her"  
on Naxos

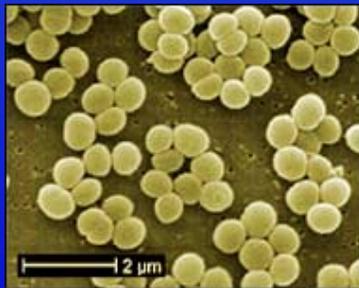
## Staphylus

God of wine  
Traveled with Jason for Golden Fleece

# Staphylococcus Aureus



Dionysus



Sir Alexander Ogston

**100 abscesses**

**Some in chains**

**Some in indigo-colored clumps**

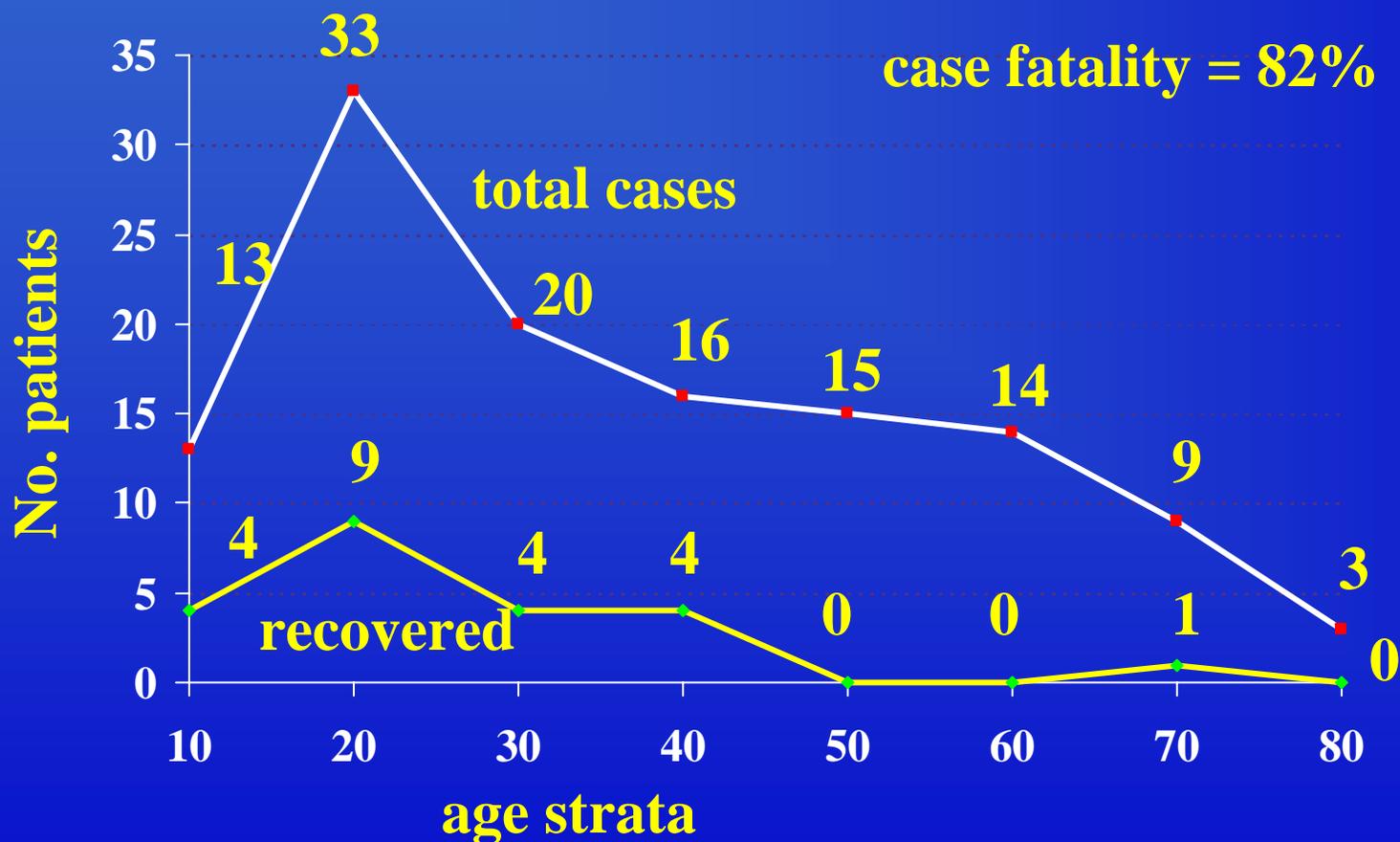
**Reproduce abscess in mice by injection**

**Aureus: Latin – "gold"**

*Scot Med J* 1998; 43:156-7

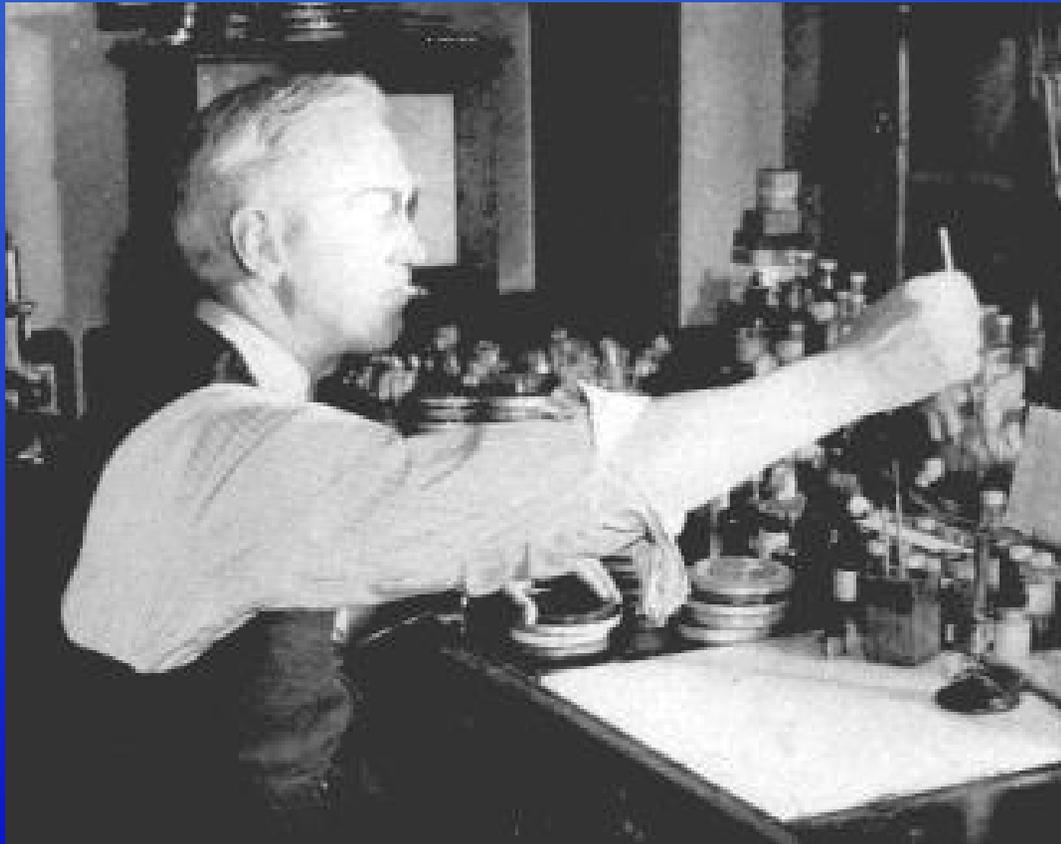
*Arch Klin Chir* 1880; 25:588-

# Significance of Bacteremia Caused by *Staphylococcus Aureus* (n=122)



Skinner & Keefer  
*Arch Int. Med* 1941; 68: 851-75

# Antibiotic Resistance in *S. aureus* Following the Great Discovery of Penicillin



Sir Alexander Fleming

"An enzyme from bacteria  
Able to destroy Penicillin"

Extract of *E. coli* with a  
"substance destroying  
property of penicillin" –  
penicillinase

Abraham and Chain

*Nature* 1940; 146:837-

# S. Aureus Bacteremia and Effective Antibiotic Rx

MIC

Survival

$\geq 6\mu\text{g/ml}$

0/52\*

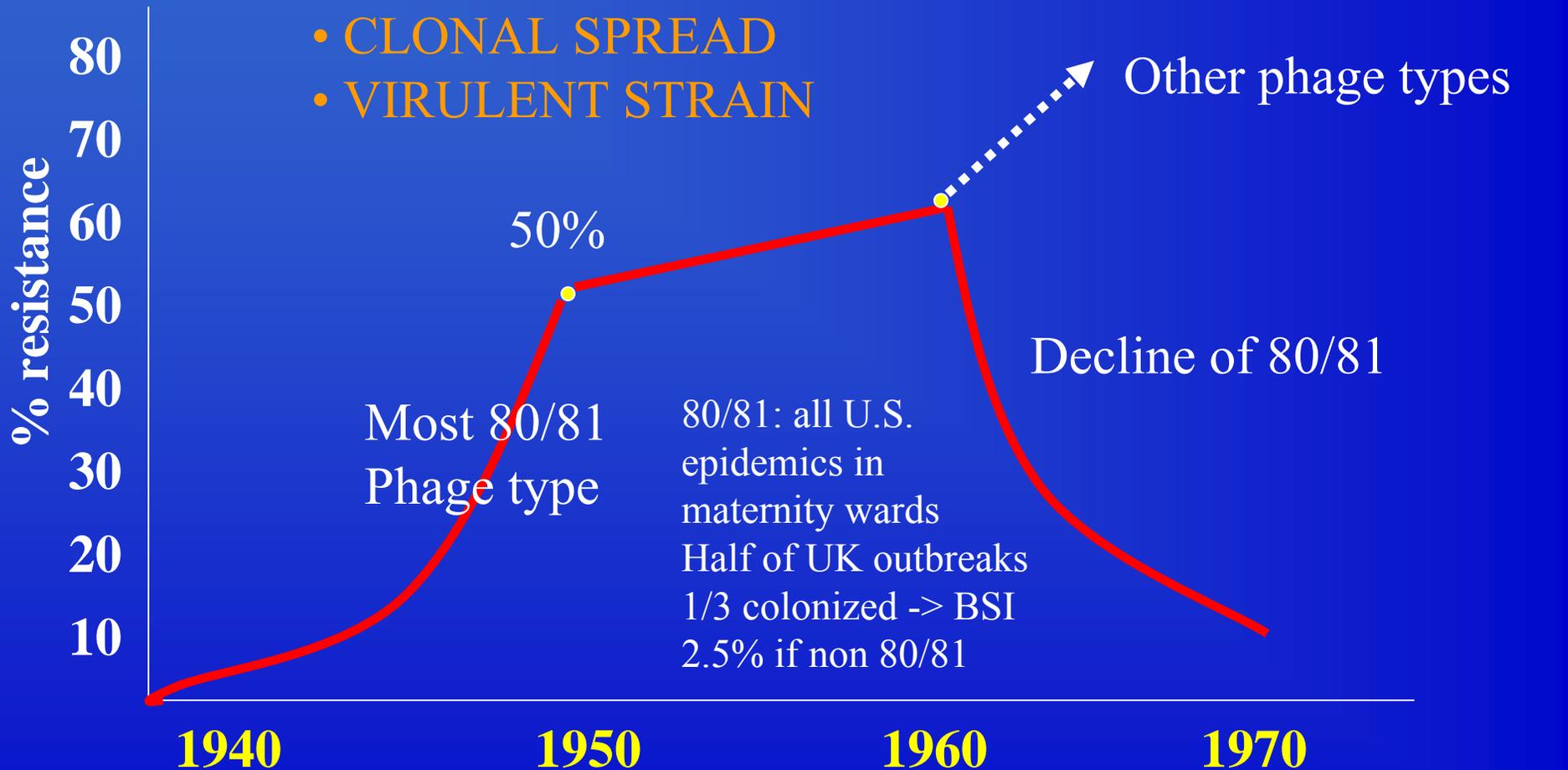
- Despite massive doses of PCN

$<6\mu\text{g/ml}$

20/29 (69%)

Abboud and Waisbren *Arch Intern Med* 1959; 104:226-33

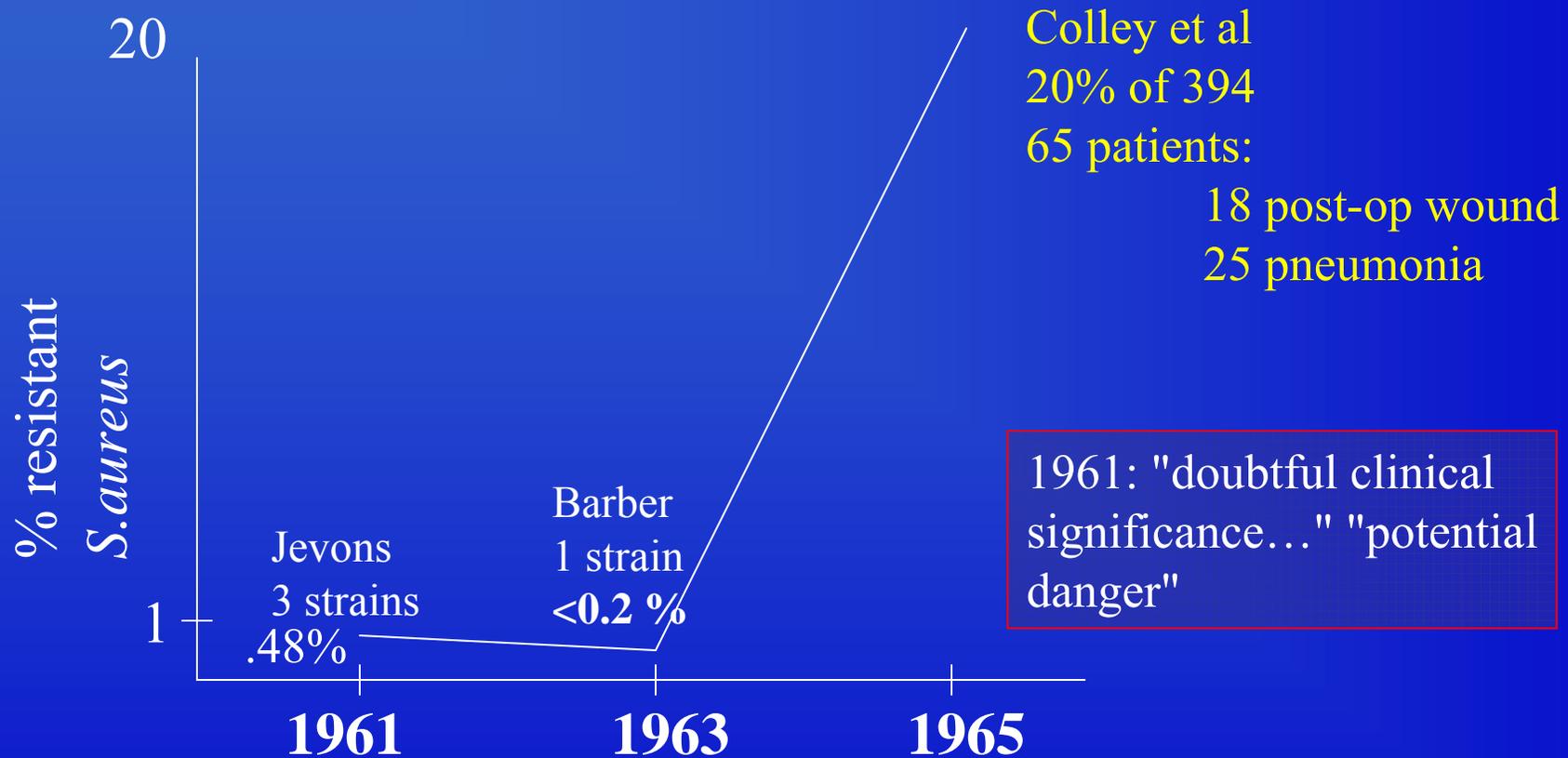
# Penicillin-Resistant *S. aureus*: Lessons after 30 years 1940-70



*Lancet* 1959; 1:190-5  
*BMJ* 1959; 5153:658-62

*Sci Based Med Ann Rev* 1966; 157:73

# Methicillin Resistance Emerges



*BMJ* 1961; 1:124

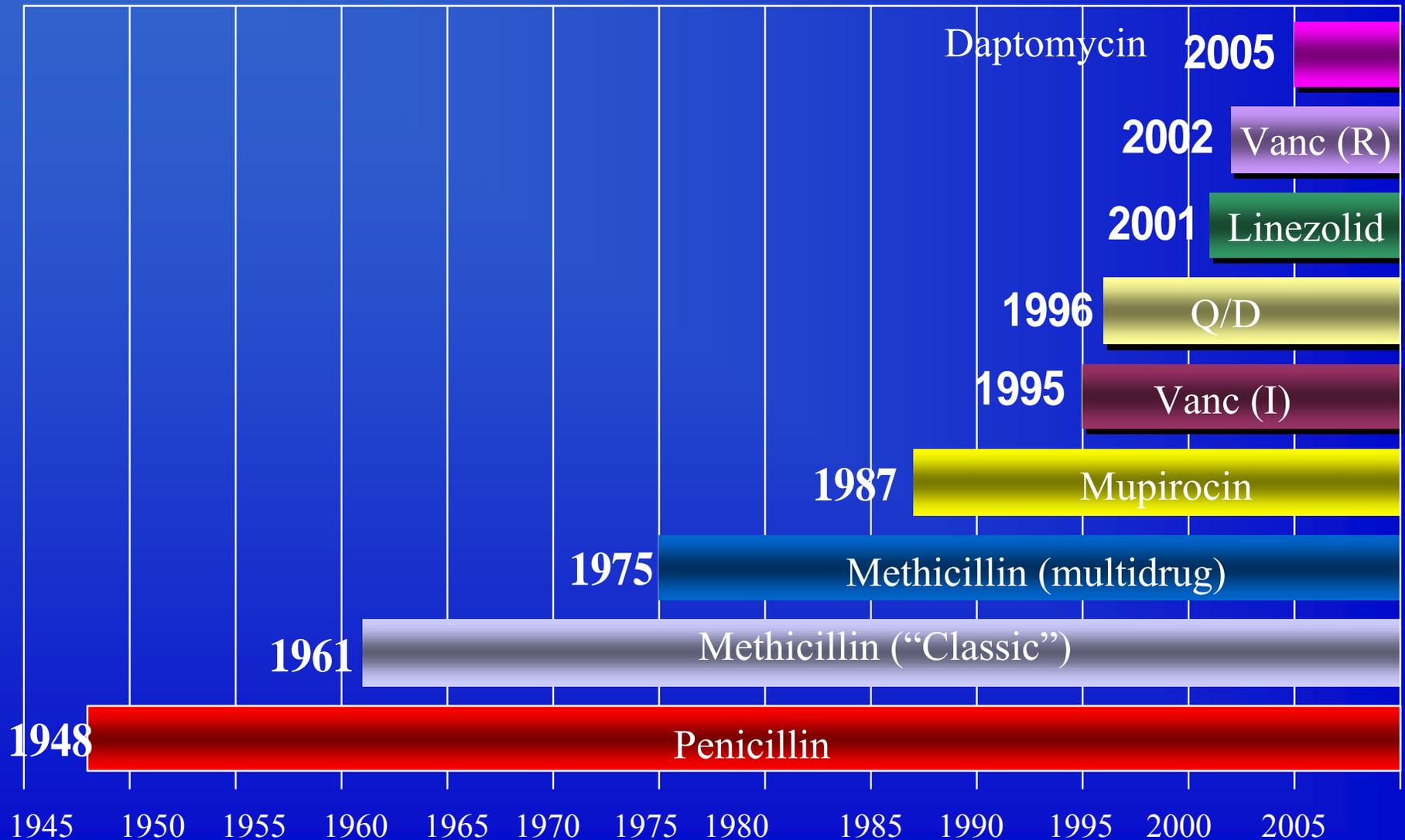
*J Clin Path* 1961; 14:385

*Lancet* 1965; 1:595

*BMJ* 1961; 1:125

*BMJ* 1961; 1:126

# *S. aureus* Resistance Timeline



# Mustarding Resistance in *S. aureus*

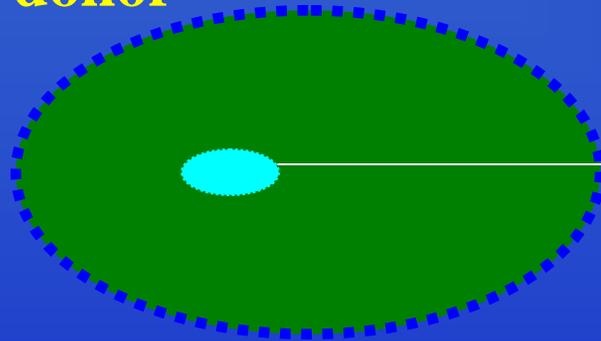
Antibiotic	MSSA (1930)	MRSA (1994)	Resistance Mechanism
Penicillin	S	R	+(1945)
Streptomycin	S	R	+(1948)
Tetracycline	S	R	+(1950)
Methicillin	S	R	+(1961) <i>mecA</i>
Oxacillin	S	R	+
Cephalothin	S	R	+
Cefotaxamine	S	R	+
Imipenem	S	R	+
Chloramphenicol	S	R	+
Ciprofloxacin	S	R	A
Clindamycin	S	R	+
Erythromycin	S	R	+
Gentamycin	S	R	+
Rifampin	S	R	A
Vancomycin	S	S	A (1997) <i>VISA</i>
Vancomycin	S	S	(2002) <i>vanA</i>
Teichoplanin	S	S	+
Trimeth/Sulfa	S	R	A

**Emergence of multidrug resistance in *Staphylococcus aureus*.** The Brazilian clone of methicillin-resistant *S. aureus* (MRSA), isolated in 1994, was resistant (R) to nearly all the antibiotics listed. **Most of the resistance mechanisms were not adaptive (A), but acquired (+) from an extraspecies source.** In contrast, an invasive strain of *S. aureus* (MSSA), recovered in 1930, was susceptible (S) to all the agents.

*Science* 2006; 311:342

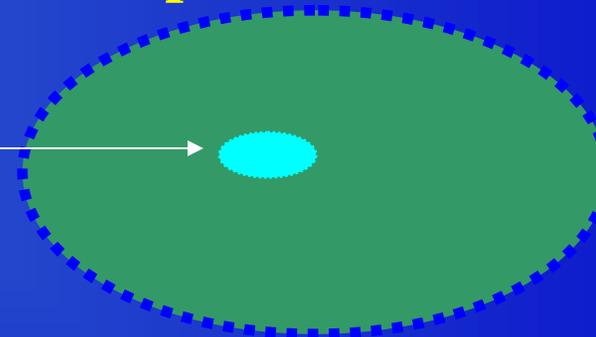
# Enterococci Contain Sex-Pheromone Induced Plasmid Transfer

Plasmid containing  
donor



consenting (responsive)  
- synthesize protein  
adhesin facilitating  
mating

Plasmid free  
recipient



secrete family of heat-stable  
protease **S**  
pheromones (5 to 6) - 7 or 8 AA  
result -  $\uparrow$  transfer  
frequently  $10^5 - 10^6$  fold  
after transfer - specific plasmid  
pheromone shut down

Clewell  
*Cell* 1993; 77: 9-12



# CA-MRSA: The Beginning



CA-MRSA differ from nosocomial strains

- **More susceptible to non- $\beta$ -lactam antibiotics.**

*JAMA* 1998;219:593-8

- **Genotypes differ**

*Emerg Inf Dis* 2003;  
9:978-84

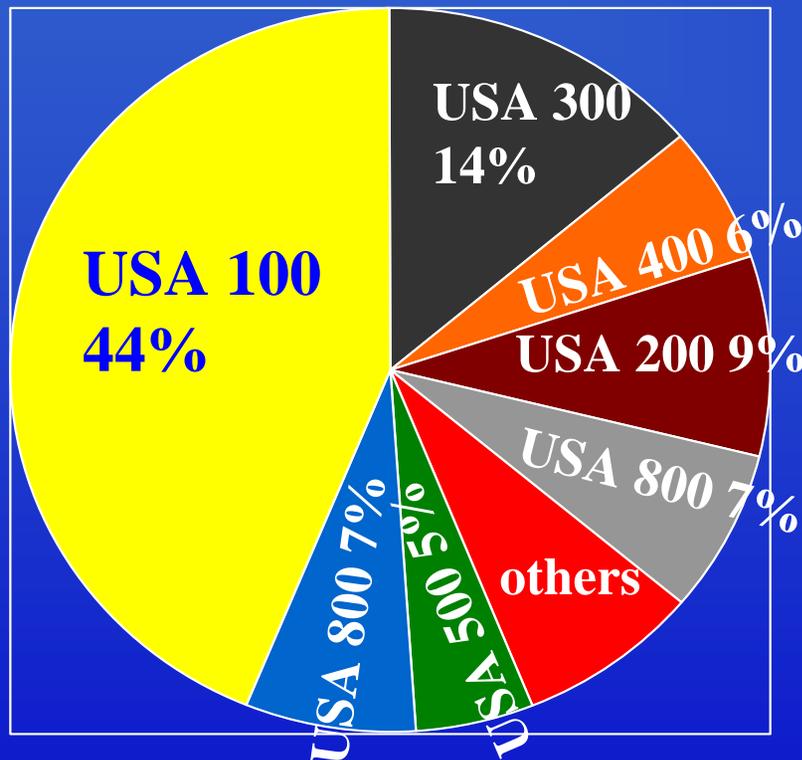
- **More likely encode PVL**

*CID* 2002; 35:819-24

**Indigenous natives with CA-MRSA**

*J Hosp Inf* 1993;25:97-108

# Pulsed-field Electrophoresis Typing (sma 1) of 957 MRSA Isolates in US



## USA 300 – CA-MRSA outbreaks

Athletic teams, nurseries

Prisons: MS, TX, TE, GA

## USA 400 – CA MRSA

Severe, fatal disease in children  
in Minnesota, North Dakota

Skin dis in Native Americans in  
WA

Australian aborigines

# USA 300 is More Virulent than USA 400 – Rat Pneumonia Model

Intra-tracheal inoculation

Inoculum ~  $10^9$  ("high")

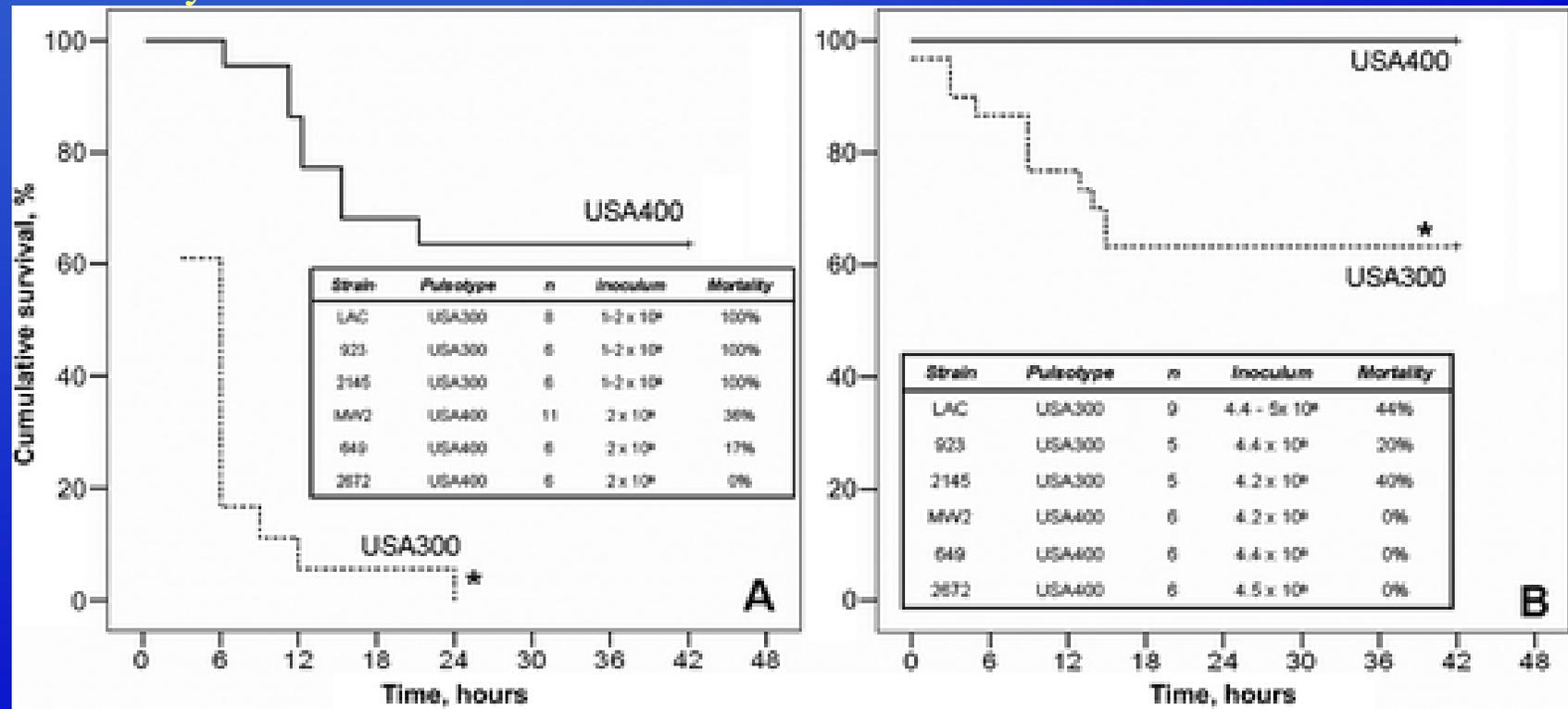
~ $4-5 \times 10^8$  ("low")

Outcome measures:

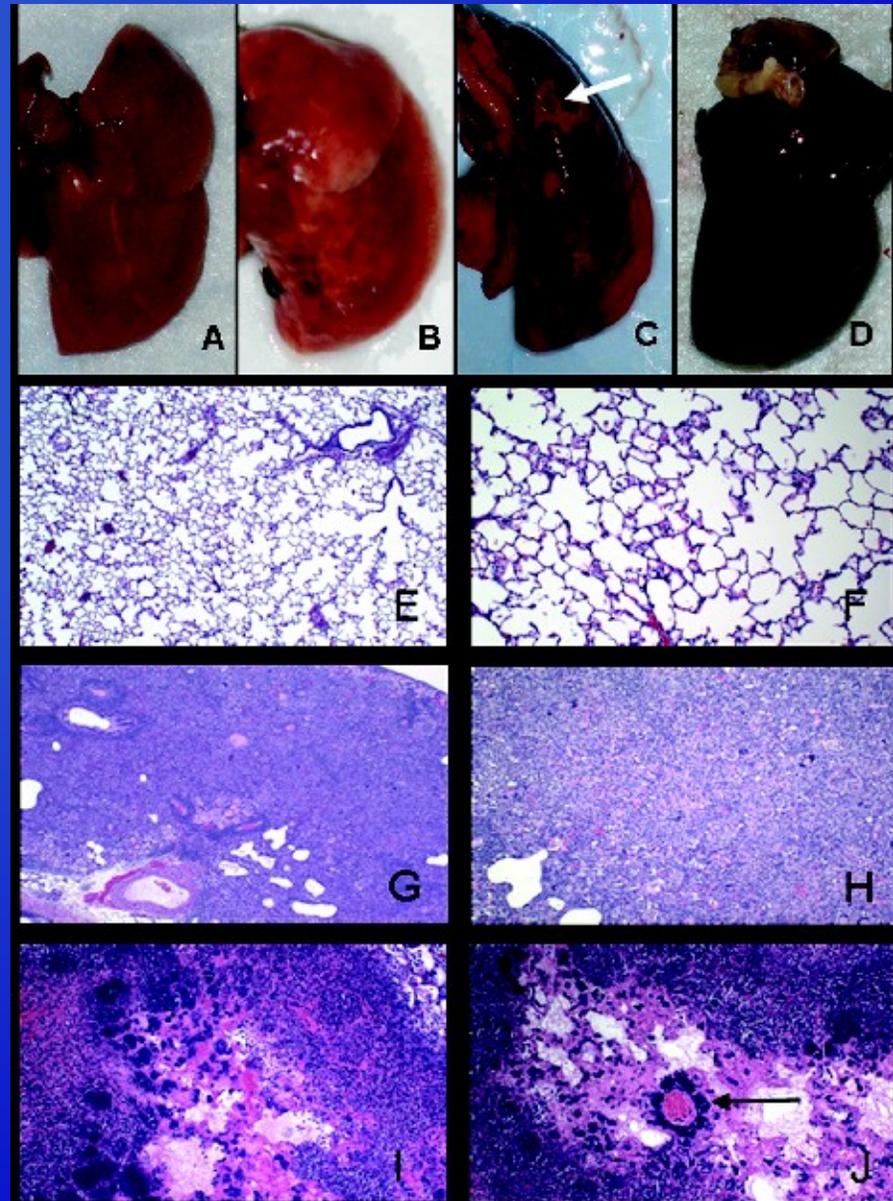
- mortality
- pulmonary bacterial growth
- severity of lung pathology

In vitro expression of toxins, AgR, PVL, saeRS, sarA, hla greater in USA 300

Comparison of USA300 and USA400 lethality. A, USA300 isolates were more lethal than USA400 at the high inoculum. \* $P < .01$ , Fisher's exact test. B, USA300 isolates were also more lethal than USA400 at the low inoculum. \* $P = .02$ , Fisher's exact test. Insert: information for individual strains, including number of animals, size of inoculum, and associated mortality



A, Normal lung from an animal inoculated with PBS. B, Consolidated lung from an animal infected with USA400 isolate. C and D are lungs from animals inoculated with USA300 isolate. C, Overt necrosis (*arrow*) with underlying hemorrhage. D, Dense, congested lung from an animal that died. E and F, Sections of normal lungs; G and H, Alveolar consolidation and neutrophilic infiltration of airspaces in the lungs of animals infected with USA400 strains. I and J, Infection with USA300 strains, showing typical necrotizing pneumonia with multifocal bacterial colonies.



## So Far...

- Evolution of *S. aureus* is clonal
  - Some strains (PEN<sup>®</sup> 80/81 and meth<sup>®</sup> USA 300) are more virulent, spread more rapidly than others, and dominate
- Resistance patterns arise primarily from horizontal gene transfer

# Familial Transmission of CA-MRSA

**2003 and 2004**

**Netherlands**

**10 PVL-MRSA: familial transmissions**

**7/10 (70%) – parent => child or  
child => parent**

**70% skin infections**

**70% USA 300**

*J Clin Micro* 2006; 44:2994-6

## **Case Reports**

- 2 cases of necrotizing pneumonia

*Scand J Infect Dis*  
2002; 34:763-4

- Father to infant in NICU, Saudi Arabia

*ICHE* 2006; 27:636-7

# Heterosexual Transmission of CA-MRSA ( 3 households)

All partners had a history of recurrent CA-MRSA infection (pubic, vaginal, perineal area)  
All isolates: USA 300, PVL(+)  
Nasal swabs negative in 4/5 tested  
8 of 32 females studied (25%) had positive cults of pubic area/vagina

*CID* 2007; 44:410-3



# CA-MRSA: A New Cause of Nosocomial Infections

- Skin/soft tissue infections

8 post-partum women (4-73 days)

*Clin Infect Dis* 2003; 37:1313-9

- Prosthetic hip/knee infections

5 patients (13-29 days)

*Am J Infect Control* 2005; 33:385-91

- 20% of 49 nosocomial BSI with MRSA were USA-300 strain

*Clin Inf Dis* 2006; 42: 647-56

- 65% of 37 MRSA BSI isolates were SCC<sub>MEC</sub> IV.  
22/24 =USA 300

*ICHE* 2006; 27:1081-6

# Two Healthcare-Associated Epidemics with CA-MRSA in Southern Germany

I — 2 hospitals, 5 NH, 1 home for disabled, 1 hemodialysis unit, 1 patient transplant service

52 patients and 21 personnel

NH residents	9%	} carriers
NH personnel	10%	

II - Neonatal unit

5 patients and 3 personnel

*Eur J Clin Micro Infect Dis*  
2005; 24:419-22

# Nosocomial CA-MRSA: New Challenges

**At what prevalence of all *S. aureus* should**

- **Empirical therapy for VAP change?**
- **Perioperative antibiotic prophylaxis  
change?**
- **Empirical therapy for line-related sepsis  
change?**

# CA-MRSA and Nasal Carriage

Prospective cohort (n=51)

only 41% nasal carriers

*ICHE 2007; 28:966-9*

Heterosexual transmission

only 1 of 5 tested was a nasal carrier

*CID 2007; 44:410-3*

Conclusion: screening will underestimate

Carriage – more so than nosocomial MRSA

## So far...CA-MRSA

- Person to person transmission occurs in the community, in families, sexually, and in hospitals now
- Emergence as a nosocomial pathogen very challenging
  - Low rates of nasal carriage
  - Reconsider prevention, empirical treatment strategies

# Staph aureus Pneumonia - 1918

8100  $\bar{c}$  flu

1409 pneumonia (17%)

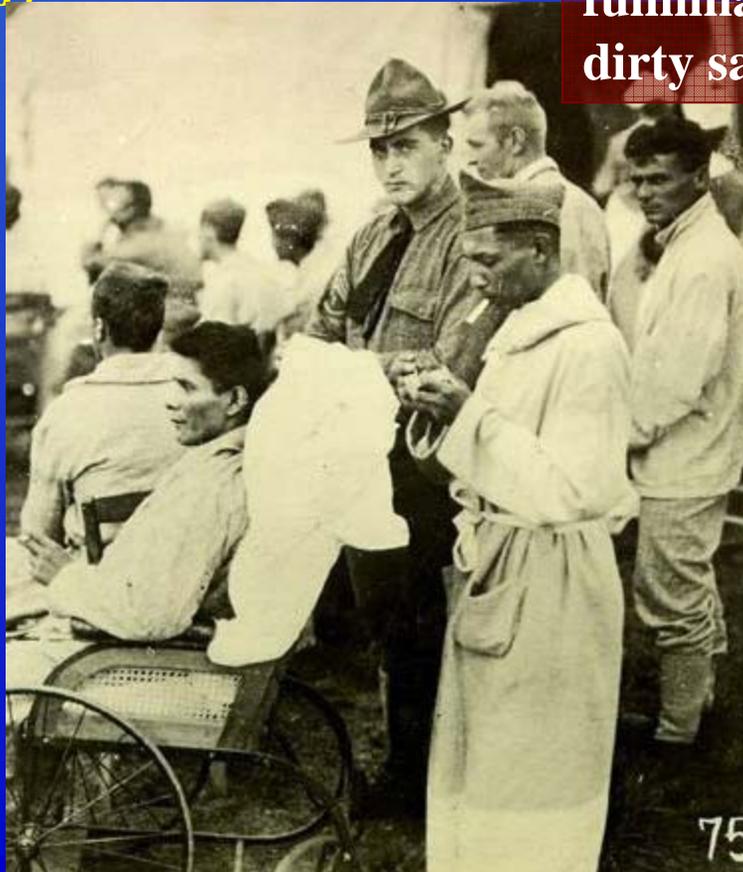
385 died (27%)

~half of deaths (153)

with *S. aureus* cults

92 of 153 (60%) *S. aureus* only

Cherry red indigo blue  
cyanosis  
no chills, localized CP  
no signs consolidation  
fulminating septic course  
dirty salmon-pink sputum



Chickering & Park  
JAMA 1919;  
72:617-26

**Severe CAP Caused by CA-MRSA**  
**2003-04 Influenza Season**  
**(71% lab confirmed)**

17 cases from 9 states

Median age 21

88% MRSA contain PVL

85% USA 300; 15% USA 400

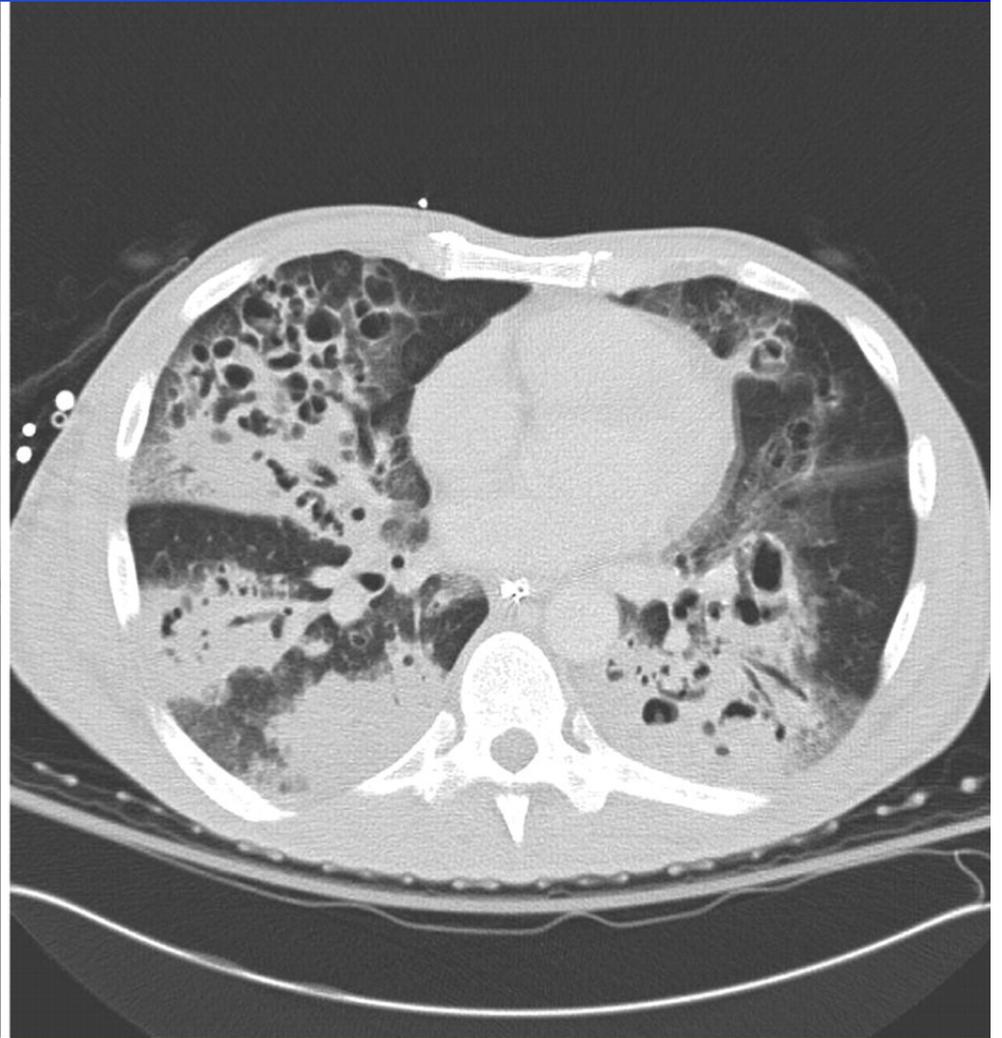
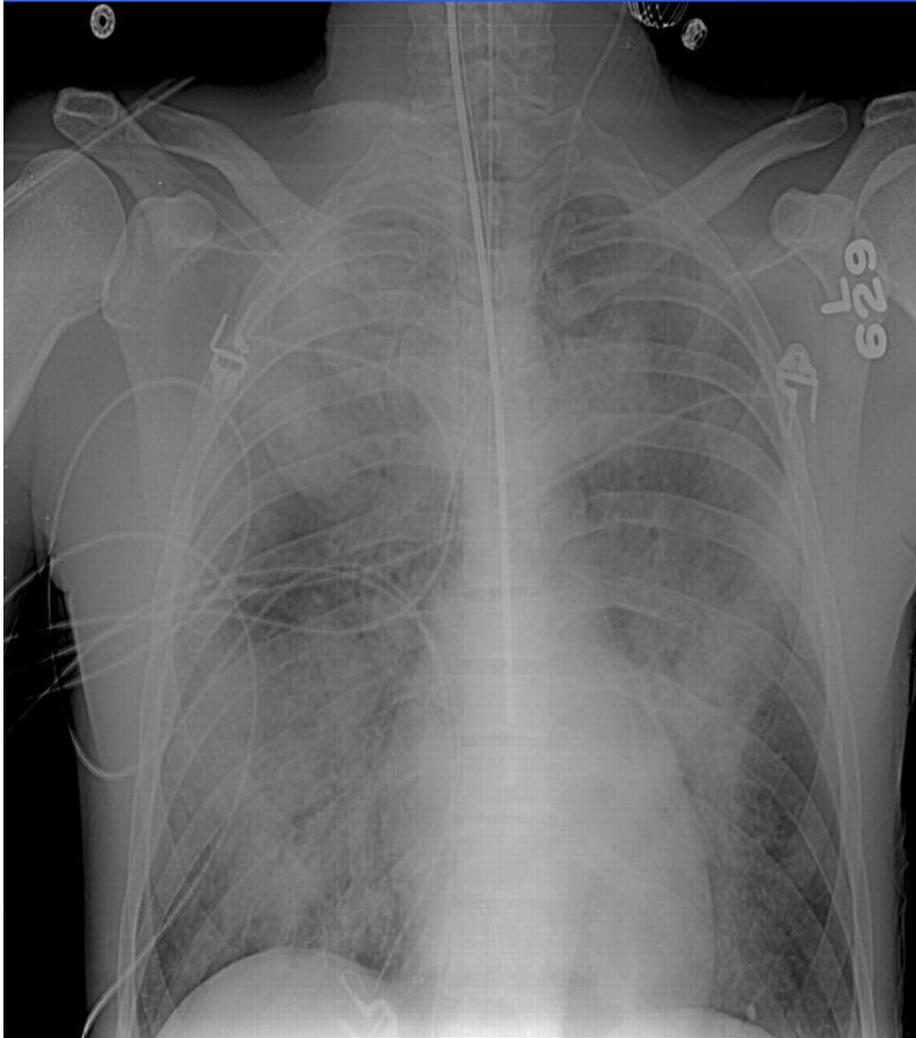
Mortality 5 (4 MRSA) 29%

(SBP)  $\leq$  90: 93%

Leukopenia (23%); Thrombocytopenia (38%)

CXR cavitation 25%; effusion, empyema (31%)

*Emerg Infect Dis* 2006; 12:894-9



Micek et al *Chest* 2005; 128:2732-8

# Four Patients with CA-MRSA PVL-positive, Necrotizing Pneumonia

Age	Sex	Prodrome(d)	(+) Cult	Late AB	Lived
45	M	5	Blood Sputum	Linezolid	Y
40	F	1	Pl fluid Sputum	Rifampin Vanco	Y
34	M	3	Blood/Bal	Vanco, Clinda Linezolid	Y
40	M	?	Blood/Bal* Nasal- on admission	Linezolid, Rifampin	Y

\* Ventilator associated

Micek et al *Chest* 2005; 128:2732-8

**Q: did exotoxin-inhibiting antibiotic effect outcome?**

# Staphylococcal Toxin\*

by P.N. Panton and F.C. O. Valentine

Denys and Van de Velde in 1895 described destruction of WBC after *S. aureus* injected into pleural cavities of rabbits: subsequent anti-leukocidin antibody

7/22 strains: strong leukoidin, weak hemolysis

6/7 severe infections, all 4 "pyemic" cases and

2/4 rapidly fatal after carbuncle

9/22 strains: weak leukocidin, strong hemolysis:  
saprophytes

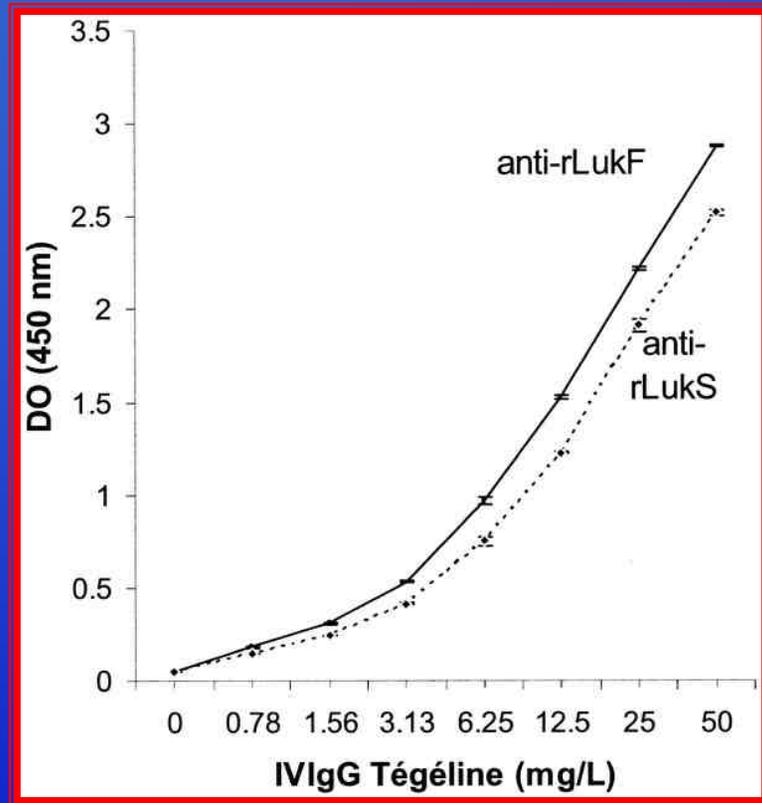
Antisera containing anti-leukocidin antibodies

"chiefly efficacious with pyemic cases" in man

*Lancet* 1932 (March 5): 5068

\* Gene later found to be on a phage virus integrated to Staph

# IVIG Contains PVL-Specific Antibodies



Binding of pooled IgG to LukS-PV and LukF-PV. The presence of IgG antibodies to recombinant (r) LukS PV and rLukF-PV was tested by ELISA at the indicated dilutions. Data are absorbance at 450 nm (mean  $\pm$  SD of duplicate experiments).

IVIG inhibited the cytotoxicity of PVL on PMNs:

- 1) Assay of membrane pore formation
- 2) Transmission EM showing cytoplasmic pore formation and hypervacuolization, loss of granules and thinning of its membrane

Graduchon et al  
*JID* 2004; 189:346-53

# Virulence in CA-MRSA: PVL or $\alpha$ Hemolysin?

Murine models:

- PVL essential for destructive CA-MRSA pneumonia but data not reproducible

Labandeira-Rey et al *Science* 2007; 315:1130-3

- $\alpha$  hemolysin essential, not PVL

Waldenburg et al *Nature Med* 2007; 13:1405-6

PVL and a Hemolysin both are members of family of  $\beta$ -channel, pore-forming toxins that penetrate cell membranes

Recent study shows IVIG has antibody to  $\alpha$  hemolysin

# Considerations in Approaching Life-Threatening CA-MRSA Pneumonia

- 1) One or two drugs active against the organism, at least one of which inhibits protein synthesis (PVL/?  $\alpha$  hemolysin production) unbound toxins
- 2)  $\beta$ -lactam antibiotics increase  $\alpha$  hemolysin production

*JID* 2007; 195:202-11

- 3) IVIG to attempt to neutralize circulating, unbound PVL/?  $\alpha$  hemolysin toxins

**No definitive evidence base for these recommendations**

# Ophthalmic Infections with CA-MRSA: 9 patients with USA 300

**Orbital cellulitis**

**Endogenous endophthalmitis**

**Panophthalmitis**

**Lid abscesses**

**Septic Venous Thrombosis**

**8-good visual**

**outcomes**

**8/9 no prior**

**hospitalization**



Clinical manifestations of ophthalmic infections with the USA300 clone of methicillin-resistant *Staphylococcus aureus*. **C**, Hemorrhagic conjunctival chemosis, corneal edema, and hypopyon in a 61-year-old patient with panophthalmitis. The patient presented with complete ophthalmoplegia. An ultrasound revealed loculated vitreous debris and choroidal thickening. **F**, Dense vitritis and retinal abscess in a 43-year-old human immunodeficiency virus–positive male with endogenous endophthalmitis. Retinal scarring, exudates, and hemorrhage 2 weeks after treatment with intravitreal and IV vancomycin.

*Ophthalmology* 2006; 113:1455-62

# Pathological Fracture in Acute Osteomyelitis from CA-MRSA

- 46 ww fx @ humerus  
4 mo PTA: boil L leg  
Rx trim-sulfa -> resolved  
3 mo PTA: pain @ arm
- 28 woman @ thigh pain  
"skin popper" - > pustules  
Blood cults positive

Geifand et al *Am J Med Sci*  
2006; 332:357-60

26 children – no fracture

*Pediatr Infect Dis J* 2004; 23:701-6



Radiograph demonstrating a permeative appearance of right humerus extending from proximal metaphysis (short arrow) to pathologic fracture of diaphysis (long arrow).



Magnetic resonance imaging scan demonstrating a soft tissue abscess (small arrow) and pathologic fracture of femur (large arrow).

# PVL from S.aureus Cutaneous Infections – Strasbourg, France (n=302)

<u>Source</u>	<u>PVL pos (%)</u>
87 – blood	1(1%)
31 – carriers	0(0%)
35 furuncles*	30(86%)
15 abscesses**	6(40%)
17 superficial folliculitis	1(6%)
37 Impetigo	1(3%)
76 2 skin infections	1(1%)
4 cellulitis	0(0%)



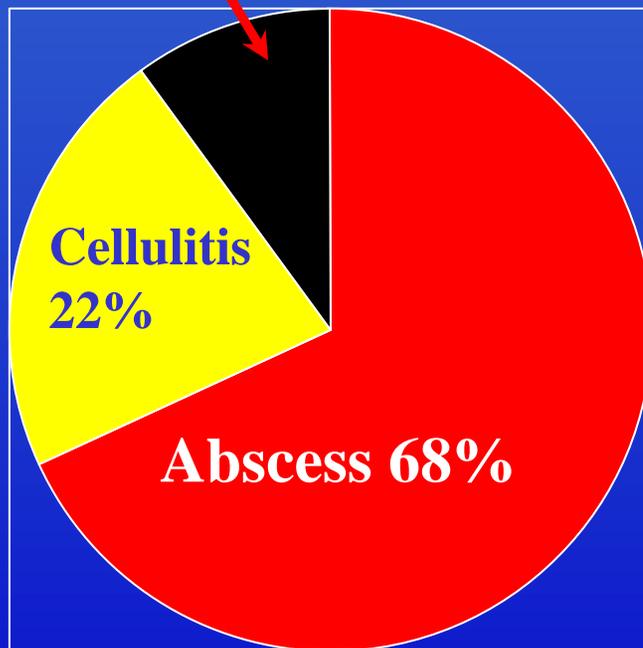
- \* Central area of necrosis => scar
- \*\* Necrotizing lesions

Croupie et al *Arch Derm*  
1994;130:1208-9

# CA-MRSA SSTI: Influence of Rx

retrospective study: 493 adults (531 episodes)

Furuncle or  
Carbuncle – 10%



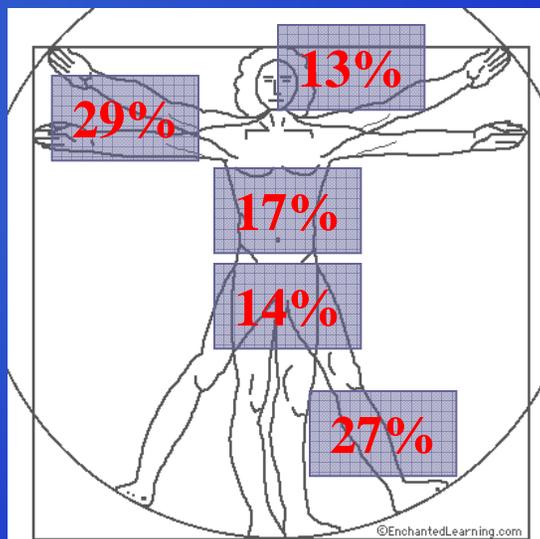
	active AB	inactive AB	p
Success	95%	87%	0.001

Independent predictor – inactive AB  
OR=2.8 (1.26-6.22)

Resistance: vanco,gent –0%; rifampin,  
trim-sulfa-1%; clinda-2%; tetra-  
7%; cipro –27%; erythro – 95%.

Ruhe et al *CID* 2007; 44:777-84

# MRSA Infections in 422 ED Patients - 2004



Moran et al *NEJM* 2006;  
355:666-74

*S.aureus* - 76% SSTI  
(MRSA 59%)

USA 300 - 97%  
SCC IV, PVL - 98%



USA 300 - 31%  
PVL - 42%

# CA-MRSA Bacterial Endocarditis after Furunculosis (n=5)

Age/sex	T°	WBC	Bld cults	Complication
37 M	39	1.5	>4/4	brain infarct/MV sgy
44 M	39 <sup>5</sup>	12	+	pulm septic nodules
44 F	39 <sup>2</sup>	15.6	16/20	sp epidural absow, pulm abscess
19 M	39 <sup>2</sup>	19.8	4/4	cav sinus thrombosis, pulm abscess
47 M	38 <sup>4</sup>	17	8/8	empyema

No mortality; 2/5 diabetes; inappropriate Rx 4/5

# Skin and Soft Tissue Infections: CA-MRSA

- Most patients get well so long as an I + D – if needed – is done
- Appropriate antibiotics may improve outcomes consistent with prior studies of *S.aureus*
- Only rarely will SSTI spread to the bloodstream; PVL-associated organisms causing furuncles may be important

## 22 year old man with CA-MRSA Bloodstream Infections and Rapid Deterioration

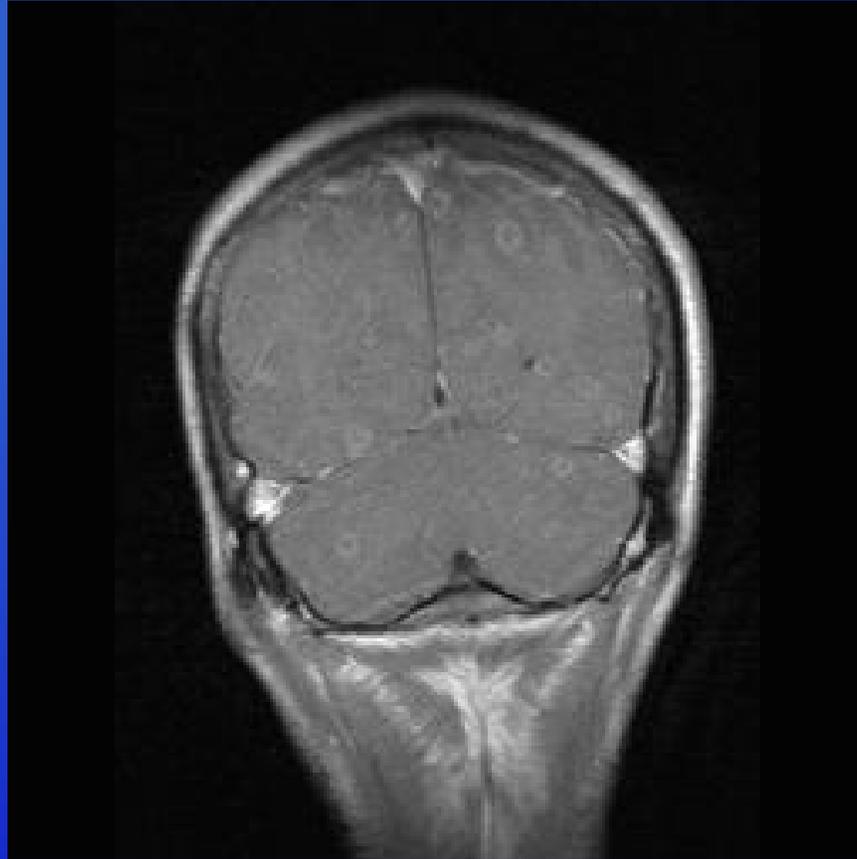
- On the morning after admission, T=104.2° despite ice bath, bladder washes and Tylenol.
- Pt was posturing, with sluggish pupils.
- A new systolic murmur 4/6, heard best at the apex, conjunctival hemorrhages, Janeway lesions on his palms and soles and splinter hemorrhages in his nail beds. Blood and urine cultures drawn the previous night: 4/4 gram + cocci in clusters which was later revealed as CA-MRSA.

# Heart

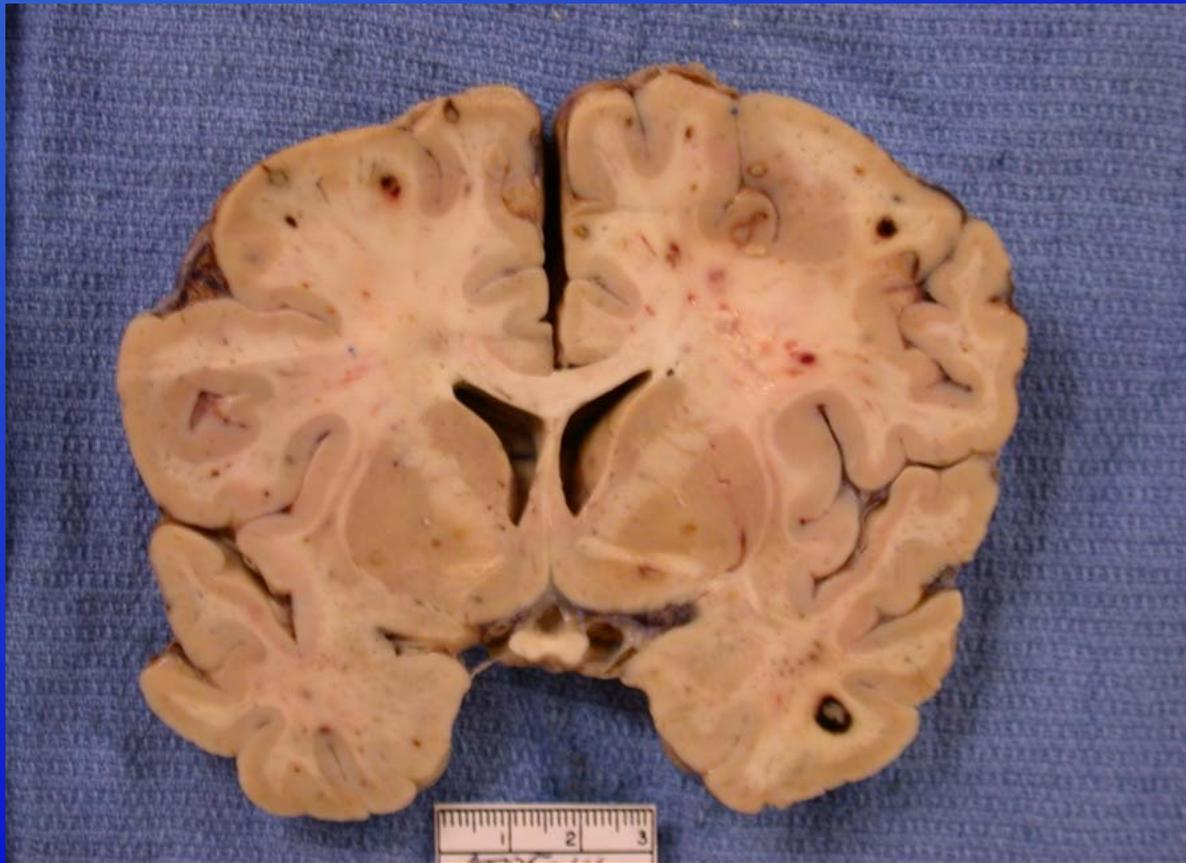


# Heart





# Brain



# Outpatient Treatment Considerations for CA-MRSA

- Doxycycline
  - Trimethoprim-sulfamethoxazole
  - Clindamycin – inducible resistance
  - Levofloxacin – QTc prolongation
  - Linezolid – cost/AE
- } Unreliable for G.A.S.

# Trimethoprim-Induced Hyperkalemia

Reduces K<sup>+</sup> excretion, inhibiting epithelial Na<sup>+</sup> channels in distal nephron

76-100% ↑ 0.36-1.2 MeQ/l

3 to 10 days of R<sub>x</sub>

18-63%: ≥ 5 MeQ/L

10-21%: ≥ 5<sup>5</sup> MeQ/L

If risk factor: ≥6-7 MeQ/L

*Drug Safety* 2000; 22:227-36

*Ann Intern Med* 1996; 124:316-20

*Amer J Neph* 1999; 19:389-94

## Risk factors

- High dose – 20mg/kg/d
- Cr ≥ 1.2

## Probable risk

K-altering drugs:

- NSAIDS
- ACE-I

Age ≥ 60

# Fluroquinolone Associated Tendon Rupture

**Rates reported: 1.2 to 2.4 per 10,000 pts**

*Br J Clin Pharmacol 1996; 41:277-84*

**Rate tendonitis to rupture 3:1**

*Therapie 1994; 49:75-6*

**Average age 64; M:F 2:1**

**50% occur within 1 week**

**85% within 1 month**

**20% on steroids**

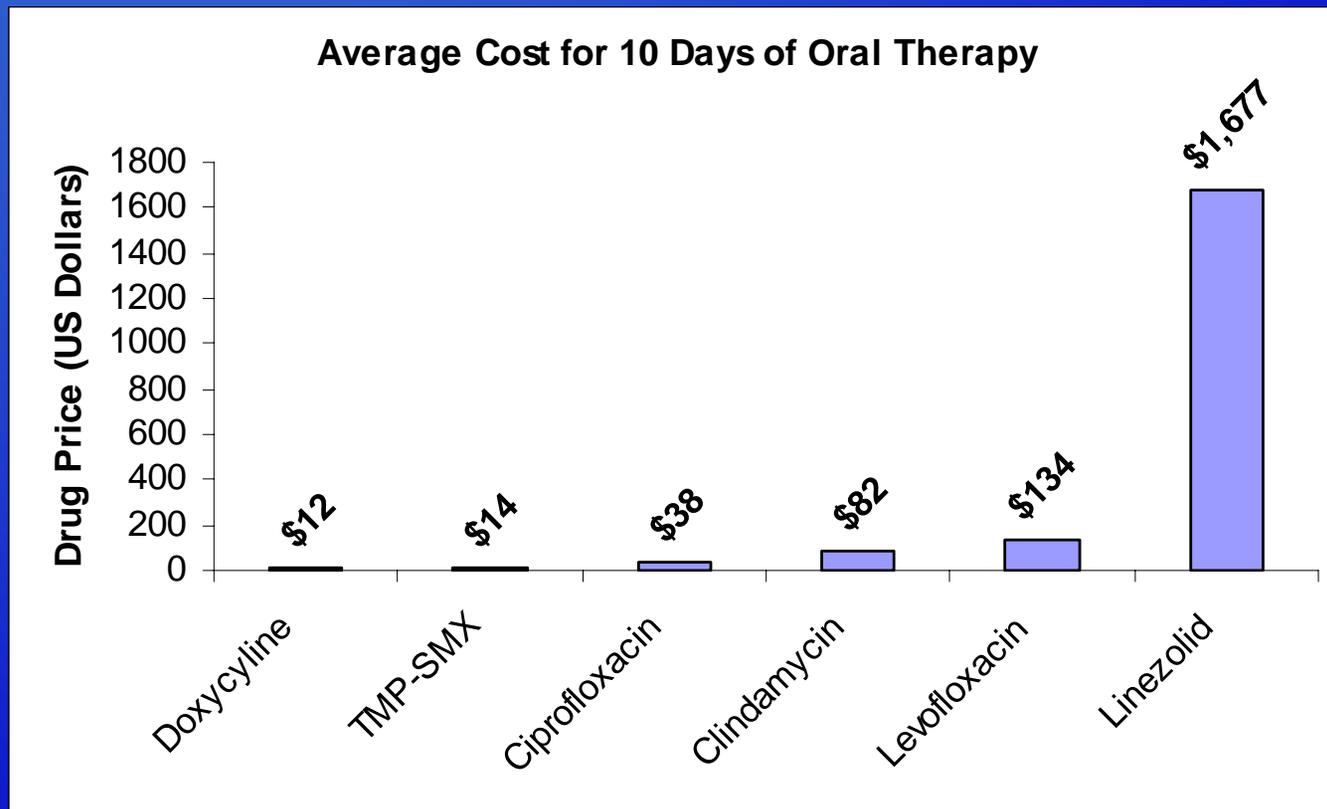
**RR vs other antibiotics 3.7**

*NZ Med J 1983; 96:590*

**RR in Lung Transplant patients 8.0**

*Eur Respir J 2002; 19:469-71*

Drug costs were calculated from survey data obtained through local chain pharmacies. Doxycycline and TMP-SMX costs were low while fluoroquinolones and clindamycin costs were somewhat more expensive. The cash drug cost for linezolid was considerably greater than any other option.



Powell, Wenzel *Expert Rev. Anti Infect Ther.* 2008; 6(3):299-307

# Outpatient Options for CA-MRSA

Favorable

Cost      Susceptibility      Caution

Trim-Sulfa	Low	yes	↓ CL <sub>CR</sub> – older patients:K <sup>+</sup> Renal Adjustment Not if cellulitis
Doxycycline	Low	yes	Not if cellulitis
Clinda	Mod	no	Adjust in severe liver disease
Levo	Mod	no	Renal adjustment
Linezolid	High	yes	Adjust in severe liver disease

If (no): Do not use empirically as a single agent because resistance may be high

# Inpatient Treatment Considerations for CA-MRSA

- **Vancomycin**
- **Linezolid**
- **Daptomycin**
- **Tigecycline**

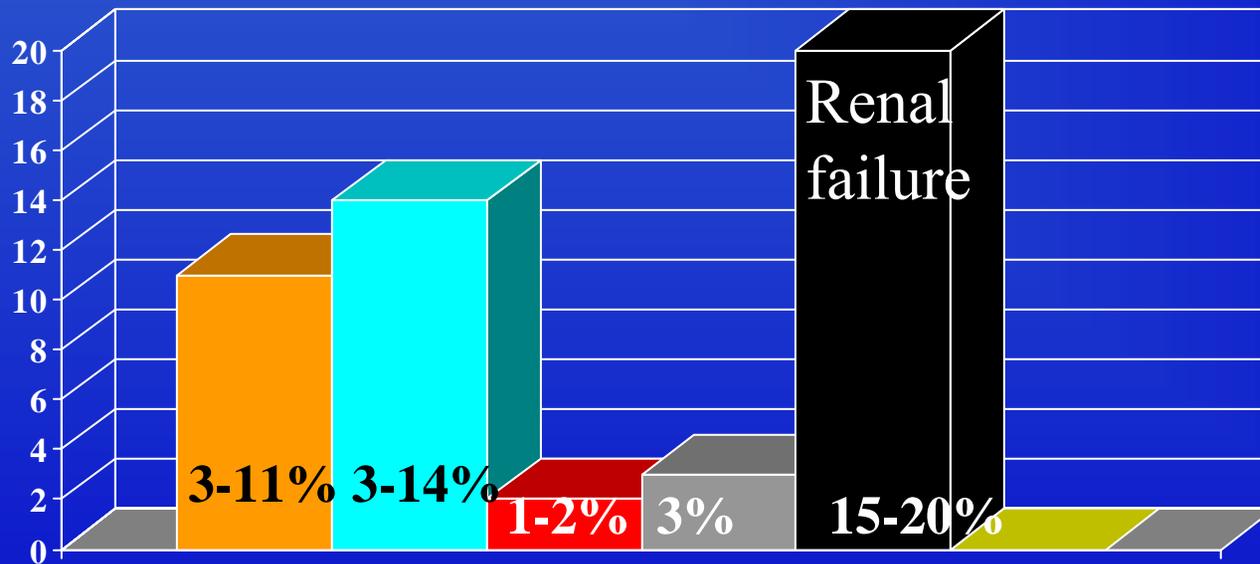
# Vancomycin

Inhibits cell wall synthesis (and RNA synthesis and Cytoplasmic membrane)

Dose: 1 gm q 12h if normal  $Cl_{CR}$

Morbidly obese: base on actual weight  
@ 30 mg/kg/d in normal  $Cl_{CR}$

IDSA/ATS recommend for  
Pneumonia trough of 15-25  $\mu\text{g/mL}$   
*Am J Respir Crit Care Med*  
2005; 171:388-416



"Red Man"  
Syndrome

Phlebitis

Neutropenia

Rash or  
fever

Vanco +  
amino-  
glycoside

Hypotension

PPID 2005

# Daptomycin

FDA approved: *S. aureus*, *E. faecalis*,  $\beta$ -hemolytic streptococci – Skin/soft tissue inf

Bactericidal vs *S. aureus*, VRE

Acts on cell membrane to depolarize =>

$K^+$  ion influx => arrest of NA

and protein synthesis => cell death

$T_{1/2}$  8 h and PAE 6.8 h

Dose: 4 mg/kg/day (q 48 h if  $Cl_{cr} < 30$ )

AE: 3%  $\uparrow$  LFTs,  $\uparrow$  CK; 2.4% hypotension

No Cytochrome p 450 metabolism

2 clinical trials/SST inf: not inferior to nafcilin or Vanco

*JAC* 2005; 55:283-8

**NOT RECOMMENDED FOR PNEUMONIA** because surfactant inhibits antibacterial activity

*JID* 2005; 191:2149-52

# Daptomycin Resistance During Therapy

18 with *S. aureus* BSI

10/18 persistent bacteremia-median 11 d

Initial dapto dose 4 mg/kg in 4/10

MICs 0.125-0.5  $\mu\text{g/ml}$   $\Rightarrow$  2  $\mu\text{g/ml}$  (5/10)

and  $\Rightarrow$  4  $\mu\text{g/ml}$  (1/10) (days 5 of 5)

- Monitor MIC during Rx
- Consider higher dose: 8-10  $\mu\text{g/kg}$

# Vancomycin Intermediate Resistance Identified in a USA 300 Strain in San Francisco

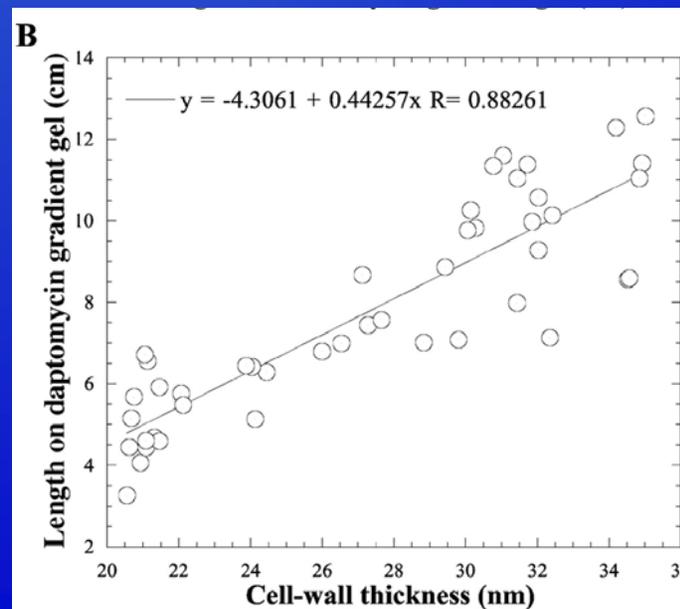
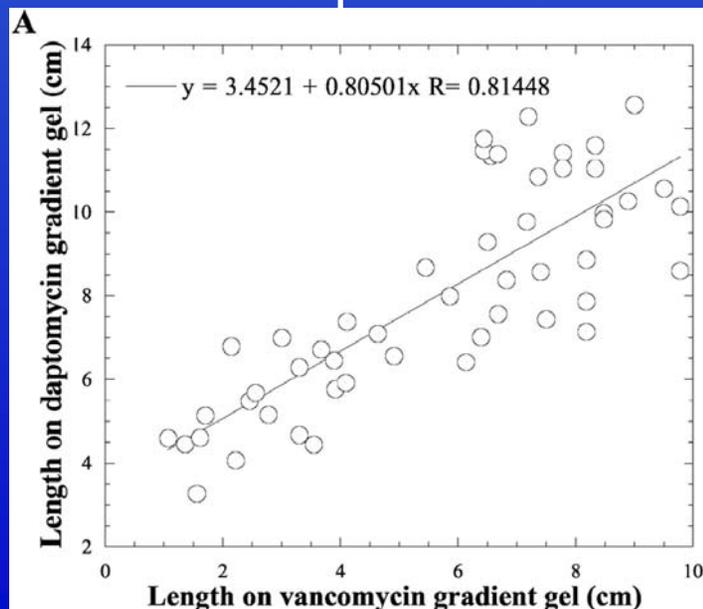
- USA 300-0114 was isolated from bone of a 56 year-old male with lumbar osteomyelitis and diskitis following a 6-week treatment course of vancomycin for catheter-associated septic thrombophlebitis

- Vancomycin 6 ug/ml
- Daptomycin 2 mg/ml

Outcome: clinical failure with vanco and death

# Correlations Between Reduced Dapto Susceptibility, Vanco Resistance, and Cell Wall Thickness in VISA strains

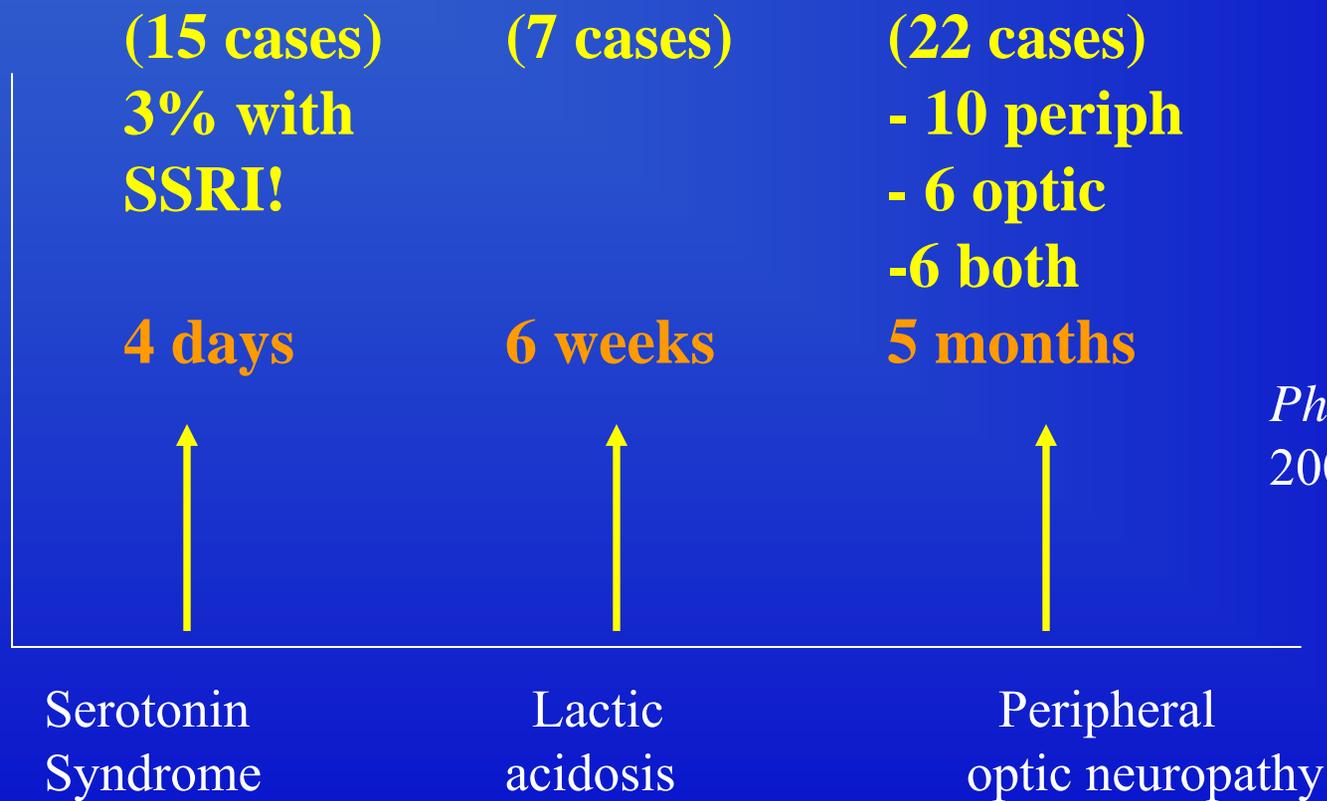
- 16 isogenic triple set of VISA –  
VISA clinical strains, vanco susceptible derivatives grown in drug-free median, and vanco resistant revertants from susceptible derivatives



Regression analysis of correlation between vancomycin and daptomycin susceptibilities and between cell wall thickness and daptomycin susceptibility

AAC 2006; 50:  
1079-82

# Linezolid: Neuropathy, Lactic Acidosis and Serotonin Syndrome



*Pharmacotherapy*  
2007; 27:1189-97

MEDIAN ONSET AFTER THERAPY

# Linezolid: Neuropathy, Lactic Acidosis and Serotonin Syndrome

5 mo: Optic neuropathy: optic disc swelling, edema, pallor, nearby hemorrhage – scotomas. Field defects. Most recover.

Periopheral neuropathy: muscle strength, ankle reflexes, sensation defects; no recovery.

6 wks: Lactic acidosis: levels 10-24.5 (NI $\leq$ 2.2)

~ 28% mortality

4 d: Serotonin syndrome: mental status changes, autonomic hyperactivity, neuromuscular changes

~20% mortality. If SSRI-washout 5 weeks

*Pharmacotherapy 2007; 77:1189-97*

# Tigecycline

Activity: HA and CA-MRSA

Vanc<sup>Ⓢ</sup> + <sup>Ⓜ</sup> *E. faecium* and *E. faecalis*

Skin-soft tissue infection: Clinical end point

100 mg IV => 50 mg q 12 h

Vs Vanco 1 gm q 12/aztreonam 2 q 12

Cure rates 87% and 89%, respectively

AE: No EOF. n/v 35% and 20% vs 8% and 4% (vanc/aztreo)

[www.fda.gov/cder/foi/label/2005](http://www.fda.gov/cder/foi/label/2005)

Reviewed by Wenzel et al

*Nat Rev Drug Disc* 2005; 4:809-10

Few clinical data for CA-MRSA

# Inpatient Options for CA- MRSA

	<u>Cost</u>	<u>Rx SSTI</u>	<u>Pneumonia</u>	<u>Cautions</u>
Vanco	low	yes	yes	renal
Linezolid	high	yes	yes	heme, neuro lactate, serotonin
Dapto	high	yes	no	muscle monitor CPK and withhold statins poor bone penetration
Tigecycl	moderate	yes	no	nausea/vomiting

# On the Horizon: CA-MRSA

<u>Novel Glycopeptides</u>	<u>T ½</u>	<u>Comments</u>
Dalbavacin	8.5 days	↓BP, ↓K, ↑ ALT
Oritavancin	100 h	active in biofilms
Televancin	7-9 h	nausea, taste, insomnia
<u>New Cephalosporins</u>	<u>Dose Interval</u>	<u>Comments</u>
IV Ceftobiprole	12 h	SSTI:non inf to vanco-ceftaz
IV Ceftaroline	12 h	non inf to vanco-aztreonam
<u>New Diaminopyrimidine</u>		
Iclaprim	-	Synergy w/sulfonimides Not reliable for GAS Comparable to Linezolid for SSTI ICAAC 2007; 804

*CID* 2008; 46:577-83

*CID* 2008; 46:March

*CID* 2007; 45:S184-90

*JAC* 2007; 60:1391-4

# Key Points

- 1) Two epidemics of MRSA are occurring with bidirectional movement between the hospital and community
- 2) CA-MRSA strains are increasingly resistant to available options for outpatient care but regional variations exist
- 3) For life-threatening infections, antibiotics that inhibit protein synthesis and IVIG may be useful
- 4) Knowledge of resistance patterns, patients' drugs, and antibiotic adverse events may inform therapy.
- 5) Plans for changing prophylactics and empirical therapy for nosocomial infections need to begin now

