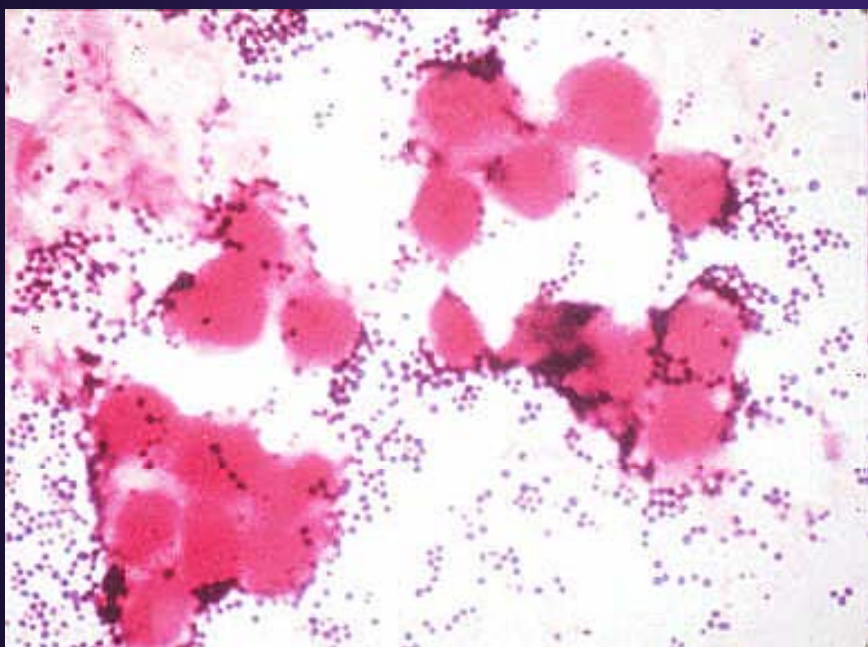


# Reservoirs of infection, prevention and treatment of *S. aureus*

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# Nasal Carriage of *S. aureus* in Healthy Persons

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## Women:

✍️ OB patients:	18%-46%
✍️ GYN patients:	22%-41%

## Healthcare workers:

✍️ Older literature:	22%-47%
✍️ Recent literature:	24%-35%

# Throat Carriage of *S. aureus* in Healthy Adults

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Author	Year	Carriers (%)
Campbell	1948	4
Commission	1949	7
Vogelsang	1958	45
Packalen, et al	1947	63
Vogelsang	1951	60-64

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# Nasal Carriage of *S. aureus* in Patients with Skin Conditions

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## Atopic dermatitis (AD)

- ✍ 93% of children with AD vs 32% of controls carried *S. aureus* ( $P < 0.001$ )
- ✍ Nasal & skin isolates identical in 73% of children with AD vs 7% of controls

## Recurrent skin infections

- ✍ 42%-100% nasal carriers
- ✍ 29%-88% nasal & infection-associated strains had same phage type

# Infection with *S. aureus* in Dialysis Patients

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- ✍ Among hemodialysis (HD) patients, *S. aureus* causes
  - ✍ 67%-90% of vascular access site infections
- ✍ Among peritoneal dialysis (PD) patients, *S. aureus* is responsible for
  - ✍ 25%-85% of exit-site infections (ESI)
  - ✍ 9%-32% of peritonitis episodes

# *S. aureus* Nasal Carriage and Infection in Dialysis Patients

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## ✍ Carriage rates:

✍ 32%-82% in hemodialysis (HD) patients

✍ 23%-65% in peritoneal dialysis (PD) patients

## ✍ Carriage increases risk of *S. aureus* infection:

✍ 4 times for ESI in HD patients

✍ 1.1-13.6 times for ESI in PD patients

✍ 2.5-8.5 times for peritonitis in PD patients

✍ Endogenous strains cause > 75% of infections

# *S. aureus* Nasal Carriage and Infection in PD Patients

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Prospective study of 138 patients

Obtained nares cultures and followed patients for infections

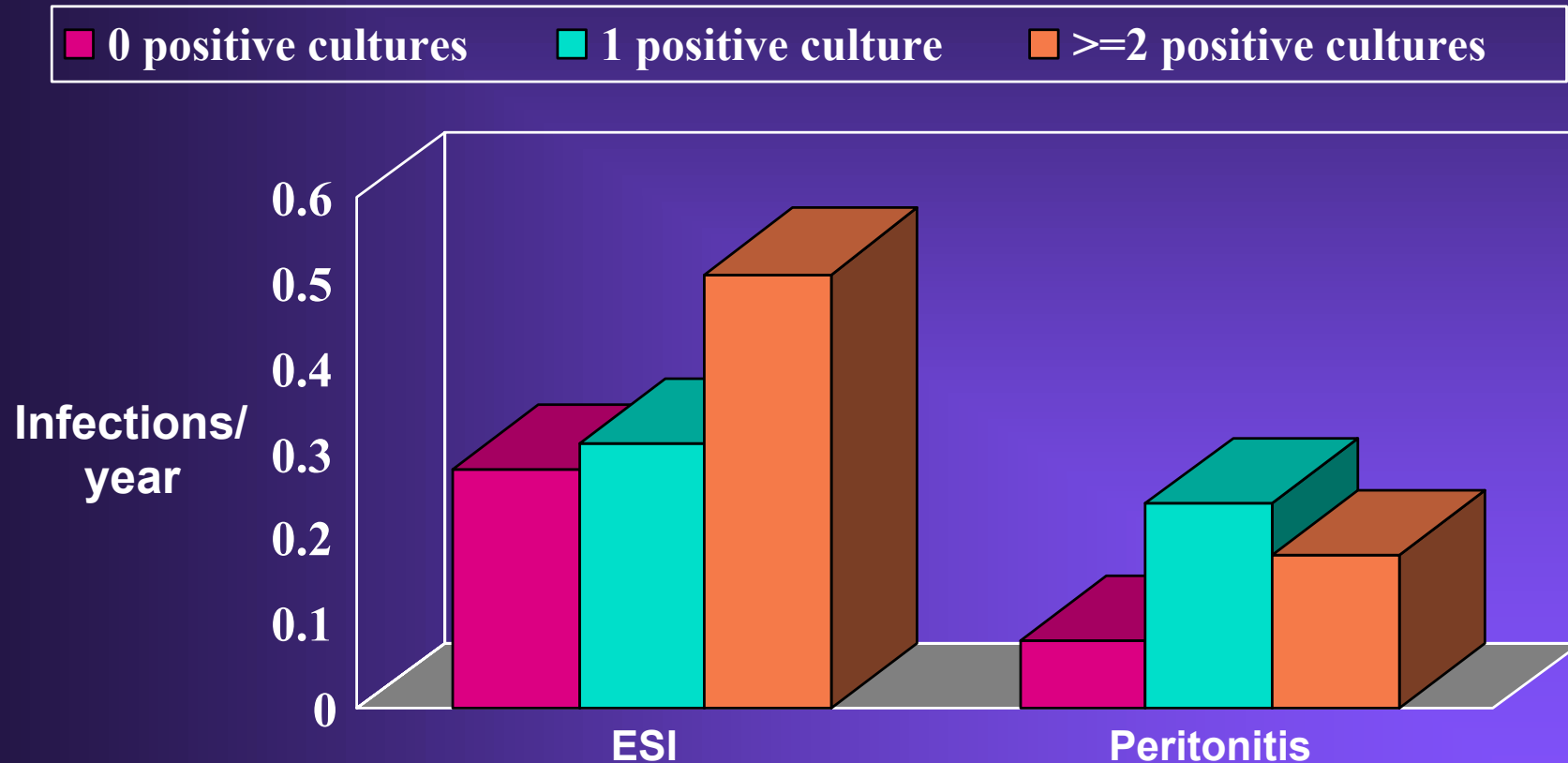
✍ Cultures:

✍ Negative = 49%

✍ One positive culture = 26%

✍ At least 2 positive cultures = 25%

# Infection Rate and the Number of Positive Cultures in Patients on PD



# Independent Risk Factors for Nosocomial *S. aureus* Bacteremia

	RR	95% CI
MRSA nasal carriage	3.9	1.6 – 9.8
Antibiotic therapy	0.04	0.01 – 0.1

# Risk Factors for Nosocomial *S. aureus* Bacteremia among Nasal Carriers

	Bacteremia %	No Bacteremia %	P Value
MRSA carrier	75	34	<0.01
LOS – ICU (Days)	9.7	15.1	0.04
Antibiotic therapy	66	92	<0.01
≥3 IV catheters	63	44	0.06

Not significant - age, gender, severity of illness, primary diagnosis, mechanical ventilation, urinary catheter

LOS = length of stay

Pujol. *Am J Medicine* 1996;100:509.

# The Association Between Nasal and Skin Carriage

Nasal <i>S. aureus</i> (N)	Cultures (N)	Positive Skin Cultures (%)
0	144	4
$10^1$ to $10^3$	25	4
$10^3$ to $10^5$	25	20
$>10^5$	32	34

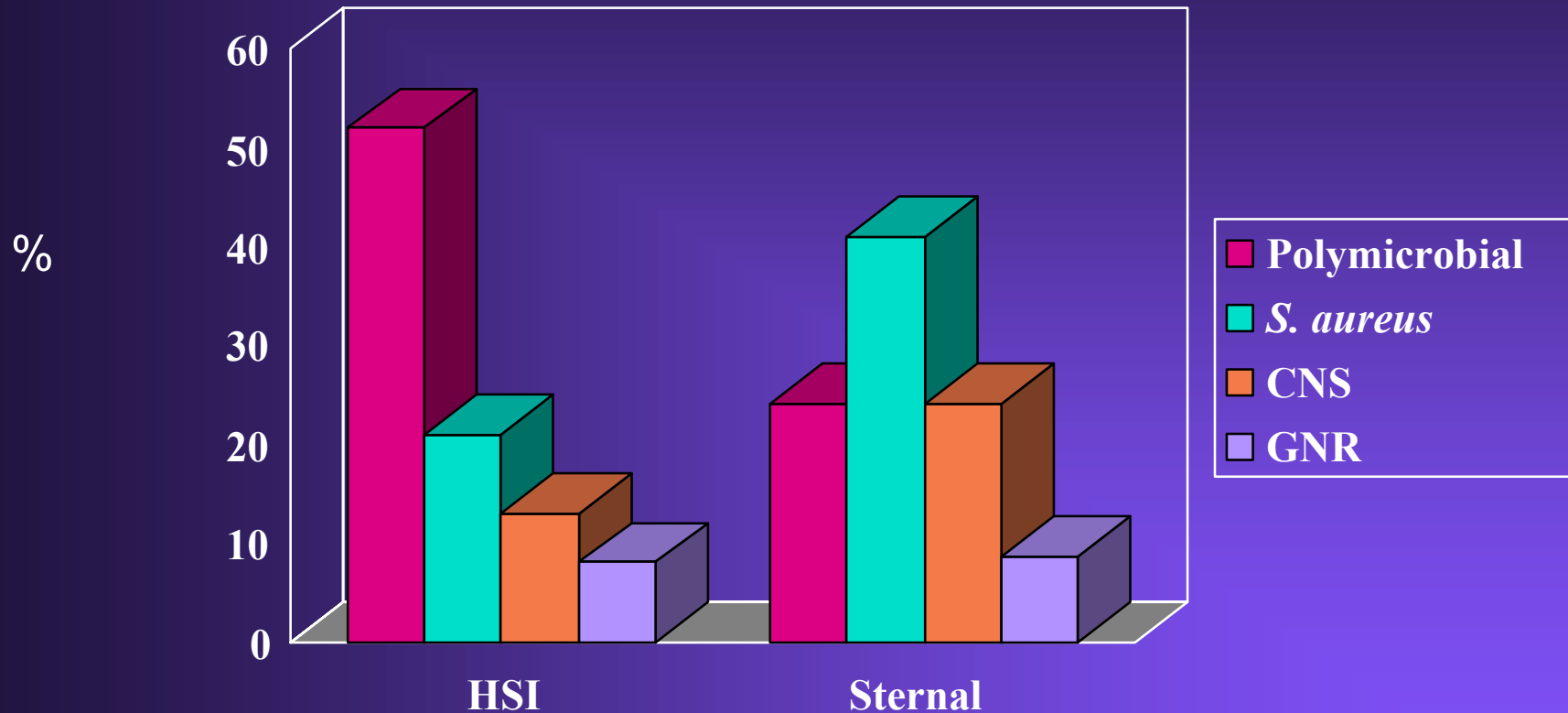
# Nasal Carriage of *S. aureus* and Surgical Site Infections (SSI)

Author	Year	Incidence of SSI (%)		
		Carriers	Noncarriers	Concordance (%)
Williams et al	1959	7.7	2.0	55
Henderson et al	1961	7.8	1.1	47
Bassett et al	1963	5.6	7.6	45
McNeill et al	1961	16.5	5.6	89
White	1963	18.9	8	66
Calia et al	1969	17.0	9	81-100
Perl et al	1998	3.5	1.6	87

# Association between *S. aureus* Nasal Carriage and SSI

Nasal <i>S. aureus</i>	(n)	Patients (n)	Infection Rate (%)
0		345	8
$10^1$ to $10^3$		14	7
$10^3$ to $10^5$		28	11
$10^5$ to $10^6$		26	19
$>10^6$		38	29

# Microbiology of SSI after CABG



Roy et al. Interscience Conference on Antimicrobial Agents and Chemotherapy, 1994.  
CNS=coagulase-negative staphylococci; GNR=gram-negative rods; HSI=harvest site infection.

# *S. aureus* Nasal Carriage & SSIs after CABG

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## ✍ Sternal wound infection

✍ Odds ratio = 9.6, 95% CI 3.9–23.7

✍ Attributable risk = 86.3%

## ✍ Harvest site infection

✍ Relative risk = 7.12, 95% CI 2.22–3.0

✍ Attributable risk = 86%

Kluytmans, et al JID 1995;171:216-19

Morales et al . *Interscience Conference on Antimicrobial Agents and Chemotherapy*, 1994.

# *S. aureus* Surgical Site Infections Associated with Physician Carriers

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- ✍ 14/40 of Surgeon A's patients vs. 1/40 of Surgeon B's patients ( $P = 0.001$ )
- ✍ Both surgeons carried *S. aureus* in their nares
- ✍ Surgeon A's hands were heavily colonized with *S. aureus*
  - ✍ Cultures obtained from gloved fingertips grew *S. aureus*

# Outbreak of *S. aureus* Infections in Pediatric CT Surgery Patients

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- ✍ Between 7/31/95 & 8/17/95, 4 children had *S. aureus* SSI following cardiothoracic surgery (CTS)
  - ✍ 2 had mediastinitis and sepsis
  - ✍ 2 had incisional infections
- ✍ By PFGE, 3 of the isolates were identical (Strain B)

PFGE = pulsed field gel electrophoresis.

# Surveillance Cultures

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- ✍ 14/55 (25%) healthcare workers (HCWs) in OR carried strain B in their nares
- ✍ 2/18 (28%) carried strain B on their hands
  - ✍ 1 surgeon
  - ✍ 1 perfusionist
- ✍ 17/157 (11%) HCWs who cared for pediatric CTS patients on nursing units carried strain B

# Case-Control Study

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<b>Healthcare Worker</b>	<b>Case</b>	<b>Control</b>	<b><i>p</i>-value</b>
<b>Anesthesiologist</b>	<b>3</b>	<b>0</b>	<b>0.0045</b>
<b>Scrub nurse</b>	<b>3</b>	<b>0</b>	<b>0.0045</b>
<b>Perfusionist</b>	<b>2</b>	<b>0</b>	<b>0.045</b>
<b>Surgeon</b>	<b>3</b>	<b>2</b>	<b>0.045</b>

# Synthesis

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- ✍ The anesthesiologist and scrub nurse did not carry epidemic strain
- ✍ Both the perfusionist and surgeon carried epidemic strain in their nares
- ✍ The surgeon also carried the epidemic strain on his hands

# Interventions

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- ✍ All HCWs who carried strain B were treated with intranasal mupirocin
- ✍ HCWs who carried strain B on their hands (N=2):
  - ✍ Were relieved of operative duties
  - ✍ Were instructed to wash their hands with chlorhexidine
  - ✍ Were allowed to return to the OR after two hand cultures were negative

# UIHC Burn Unit MRSA

- ✍ MRSA clusters had not been identified
- ✍ 2 clusters involved 10 patients
- ✍ Isolates: same antibiogram and PFGE pattern
- ✍ Nose culture survey of all staff
- ✍ 3 HCW who carried the epidemic strain were treated with mupirocin
- ✍ No further cases since 6/14/93

PFGE=pulsed field gel electrophoresis.

# Acquisition of MRSA by Staff

- ✍ 26 nurses who cared for 6 patients colonized with epidemic MRSA strains
- ✍ 13 nurses acquired MRSA
  - ✍ 1 nurse persistent carriage
  - ✍ 12 nurses, 40 episodes of transient or short-term carriage
  - ✍ 7/12 carried each epidemic strain at different times, supporting hypothesis of continuous acquisition
- ✍ Acquisition associated with close patient contact, especially wound dressing

# Environmental Contamination With MRSA

- ✍ 42/184 (23%) surfaces positive for MRSA
- ✍ 34% surfaces in rooms of patients with MRSA in wounds and urine positive vs 2% in rooms of patients with MRSA in nose or sputum
- ✍ Gowns, floor, bed linens, blood pressure cuffs, overbed tables
- ✍ HCW should wear gloves for contact with those patients or the environment

# Summary and Conclusions

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- ✍ *S. aureus* nasal carriage increases the risk of infection in several populations
- ✍ Many *S. aureus* infections are caused by the patients' own strains
- ✍ Outbreaks have been related to
  - ✍ Infected or colonized patients
  - ✍ Infected or colonized staff
  - ✍ Environmental contamination

# Interruption of Transmission

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- ✍ Identification of high-risk persons
- ✍ Isolation
- ✍ Cohorting
- ✍ Elimination of source
  - ✍ Colonized persons
    - health care workers
    - high risk patients
  - ✍ Environmental source
    - fomites
    - air
    - hands

# Strategies to Prevent *S. aureus* Transmission: Back to Basics

## Standard precautions

- ✍ Wash hands after contact with the patient and/or environment
- ✍ Wear gloves when touching body fluids and contaminated items
- ✍ Wear a mask and gown when performing activities/procedures likely to generate a splash
- ✍ Handle equipment and laundry carefully to prevent exposures

# Handwashing and *S. aureus*

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- ✍ Handwashing is the single most important strategy to interrupt transmission of organisms between persons
- ✍ Handwashing with ordinary soap does not reduce heavily colonized hands
- ✍ Alcoholic chlorhexidine is superior to alcohol alone ( $P < 0.0002$ ). This disinfectant did not completely eradicate all bacteria

# Strategies to Prevent *MRSA* Transmission: Back to Basics

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## Contact precautions

- ✍ Place patient in private room or cohort patient with another infected patient
- ✍ Wear gloves to enter the patient's room
- ✍ Wear a gown if you anticipate substantial contact with the patient, secretions or the environment
- ✍ Transport patient for essential purposes only
- ✍ Clean equipment/patient care items daily
- ✍ Dedicate non-critical patient equipment and items

# MRSA control: Why Surveillance and “Flagging Systems”

## ✍ 9-year retrospective study

✍ Nares cultures 93% sensitive, NPV 95%

✍ Cutaneous cultures 39% sensitive, NPV 69%

✍ MRSA half life 40 months

✍ 42% of paired isolates had similar plasmids

## ✍ Expert computer based flagging systems

✍ Save ICP time

✍ In one year HCUG increased recognition of cases on admission from 13- 40%

NPV=negative predictive value; ICP=infection control practitioner; HCUG=Hospital Canton Universitaire Geneve

Sanford et al. *Clin Infectious Dis* 1994;19:1123., Pittet et al. *Infect Control Hosp Epidemiol* 1996;17:496.

# Decreasing *S. aureus* Infections: Use of Professional IV Teams

- ✍ After professional, dedicated IV team introduced
- ✍ Primary nosocomial bloodstream infections (BSI) reduced 35% (1.1 to 0.7 BSI/1000 pt days)
- ✍ *S. aureus* BSI reduced 51% ( $P < 0.01$ )
- ✍ Team cost \$253,000
- ✍ Cost per infection saved \$14,000

# Contact Isolation and Preventing Transmission of MRSA

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## ✍ Efficacy of contact isolation-UVA

- ✍ Contact isolation reduced transmission from 0.0140 to 0.009 transmissions/day
- ✍ 16 fold reduction ( $P < 0.002$ )

## ✍ Many investigators have found additional interventions necessary:

- ✍ Intensified surveillance
- ✍ “Flagging” system to identify colonized/infected patients
- ✍ Strict isolation
- ✍ Cohorting of patients and health care workers
- ✍ Cleaning
- ✍ Alternate handwashing agents (0.3% triclosan)

# Nasal Decolonization: Potential Agents/Strategies

## Systemic antibiotics

- ✍ Rifampin
- ✍ TMP/Sulfamethoxazole
- ✍ Ciprofloxacin
- ✍ Combinations
  - ✍ Rifampin and TMP/sulfa

## Systemic and Local antibiotics

- ✍ TMP/sulfa and Bacitracin

## Local antibiotics

- ✍ Bacitracin
- ✍ Mupirocin
- ✍ Provodone Iodine

## Bacterial interference

- ✍ 502 A

# Eliminating Nasal Carriage: Dialysis Patients



# Intranasal Decolonization: Failures

## ✍ Failures

- ✍ Nares not decolonized
- ✍ Nares recolonized quickly

## ✍ Agents

- ✍ Gentamicin
- ✍ Vancomycin
- ✍ Neomycin
- ✍ Bacitracin
- ✍ Chlorohexidine
- ✍ Quinolones
- ✍ Clindamycin
- ✍ Cephalexin
- ✍ Erythromycin

# Trials with Systemic Antibiotics

## ✍ Randomized, controlled trial- 64 CAPD patients

✍ *S. aureus* carriage rate 27%

✍ 0.22 *S. aureus*/ pt year-rifampin; 4 developed resistance

✍ 0.65 *S. aureus*/ pt year-placebo

✍  $P < 0.01$

## ✍ Randomized, clinical trial- 126 MRSA pts

✍ *S. aureus* carriage rate 100%

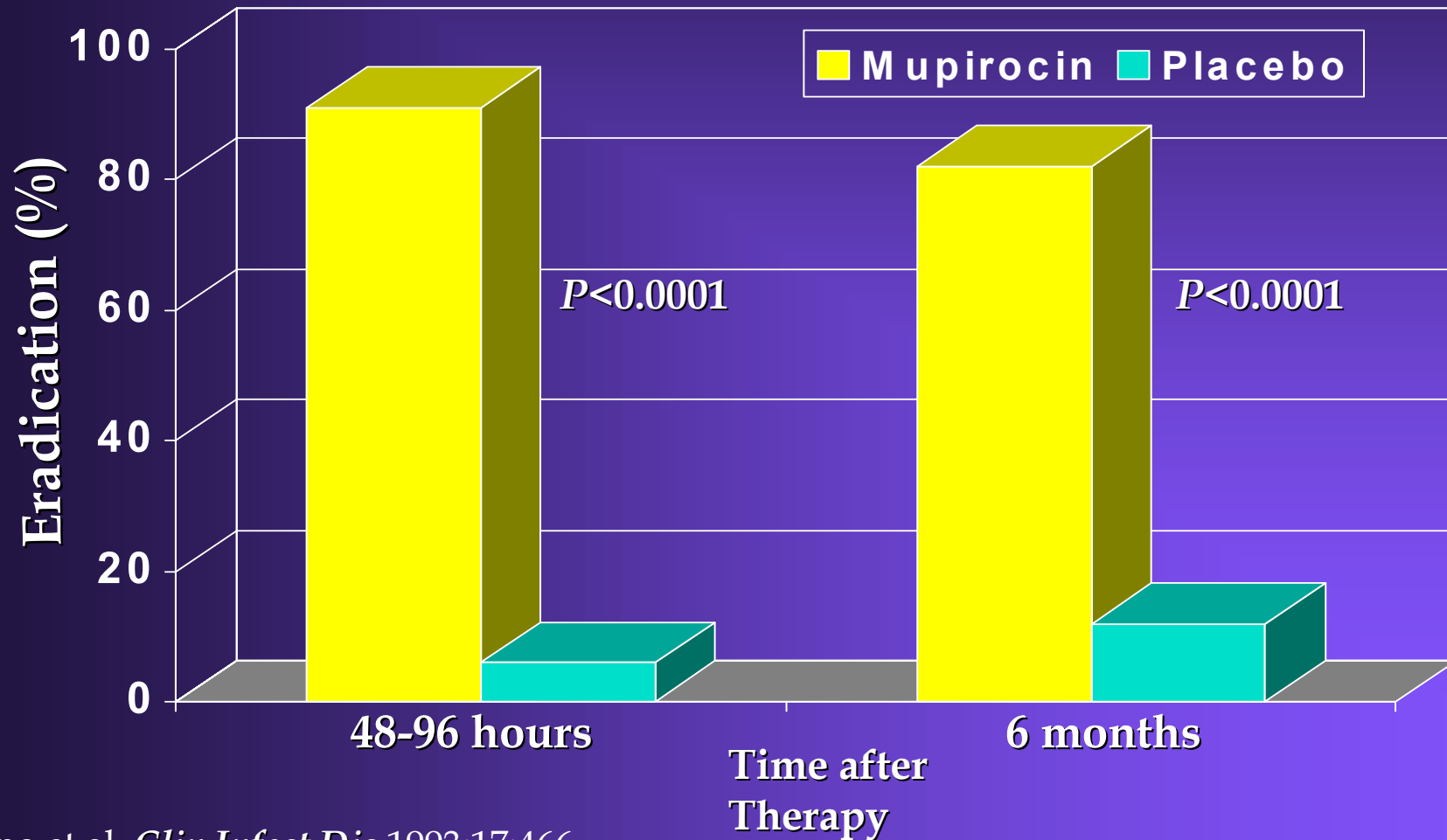
✍ 1.67% cleared - novobiocin + rifampin (1.2% resistance)

✍ 2.53% cleared - TMP/sulfa +rifampin (2.4% resistance)

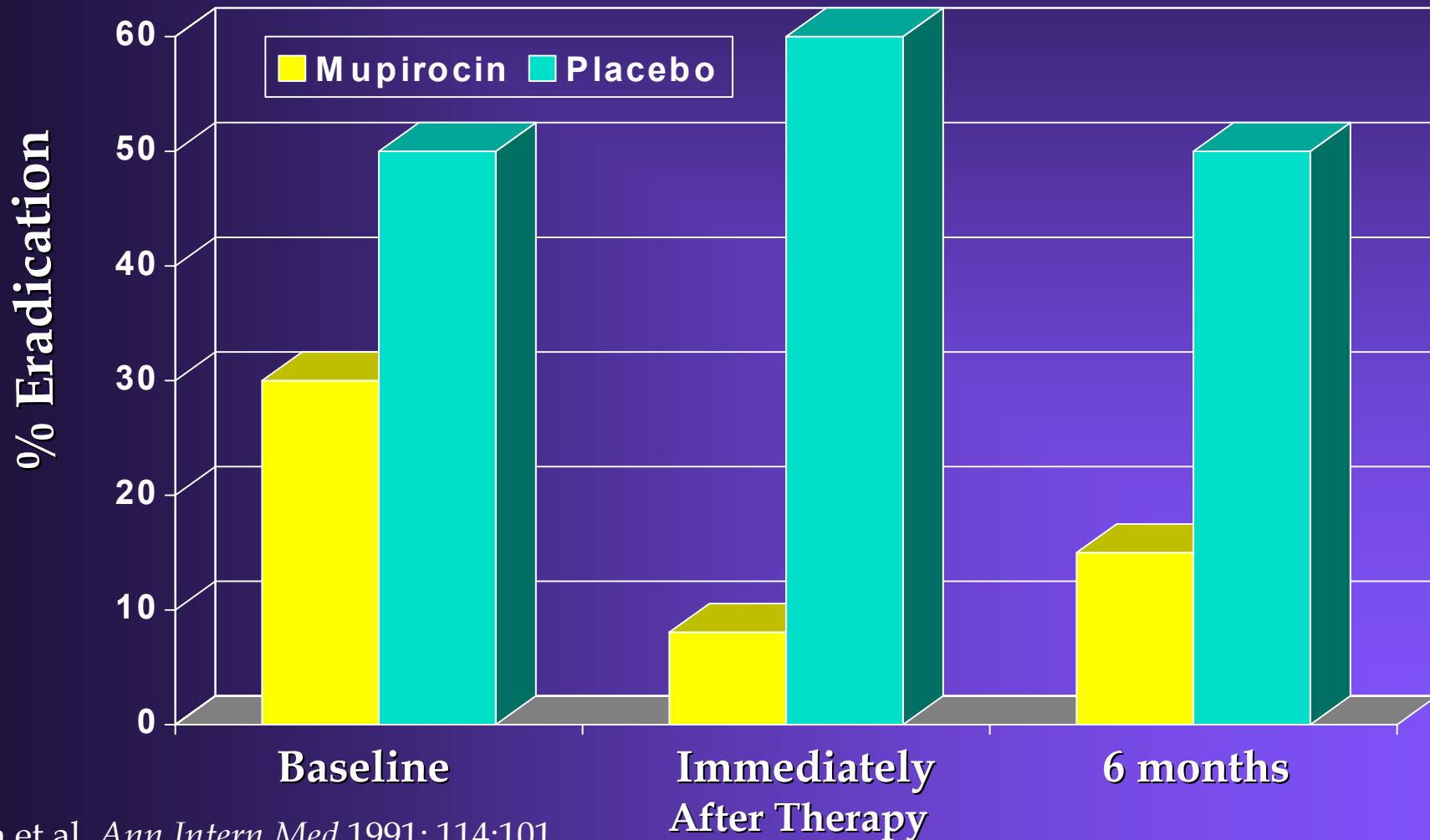
Zimmerman et al. *Am J Kidney Dis* 1993;18:225.

Walsh et al. *Antimicrob Agents Chemother* 1993;37(6):1334.

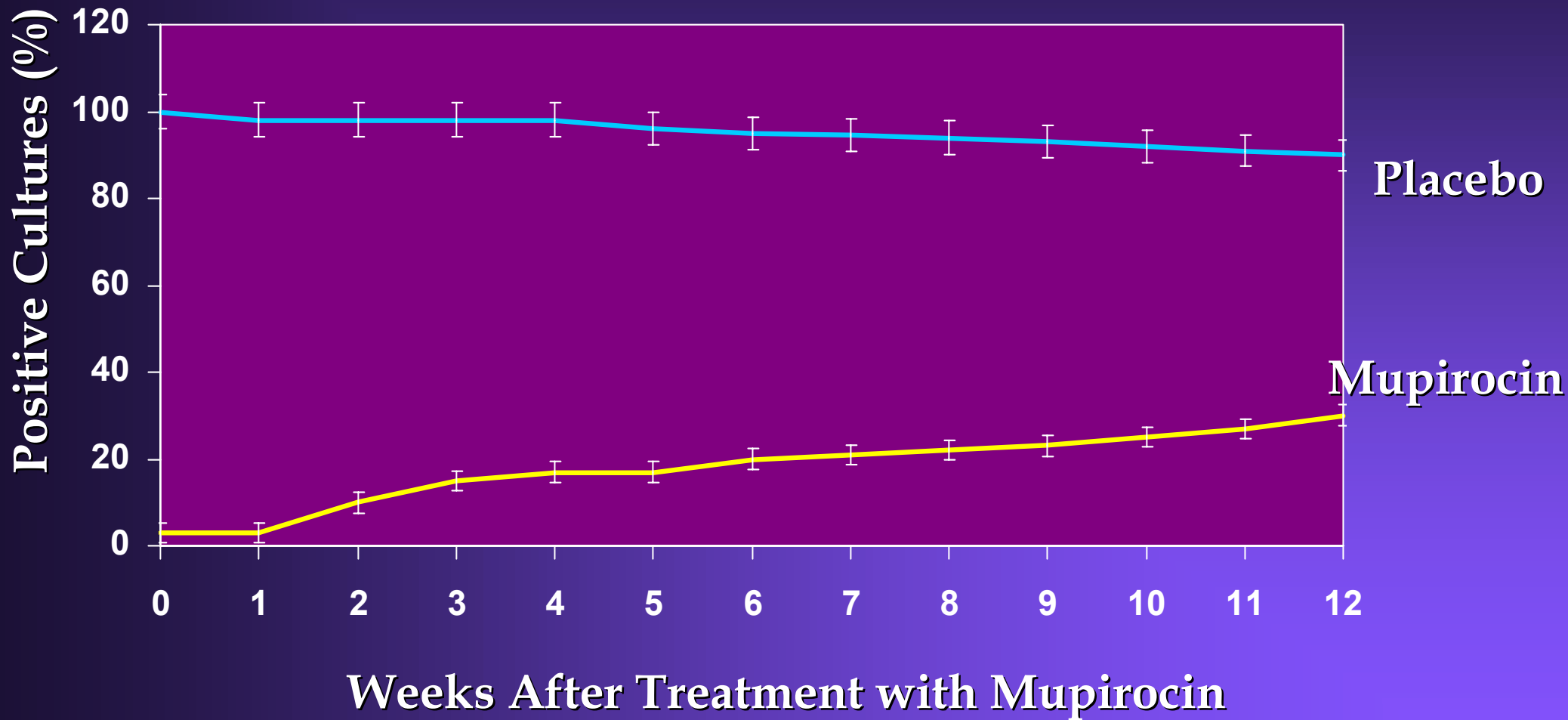
# Mupirocin Efficacy in Healthcare Workers: Nasal Carriage



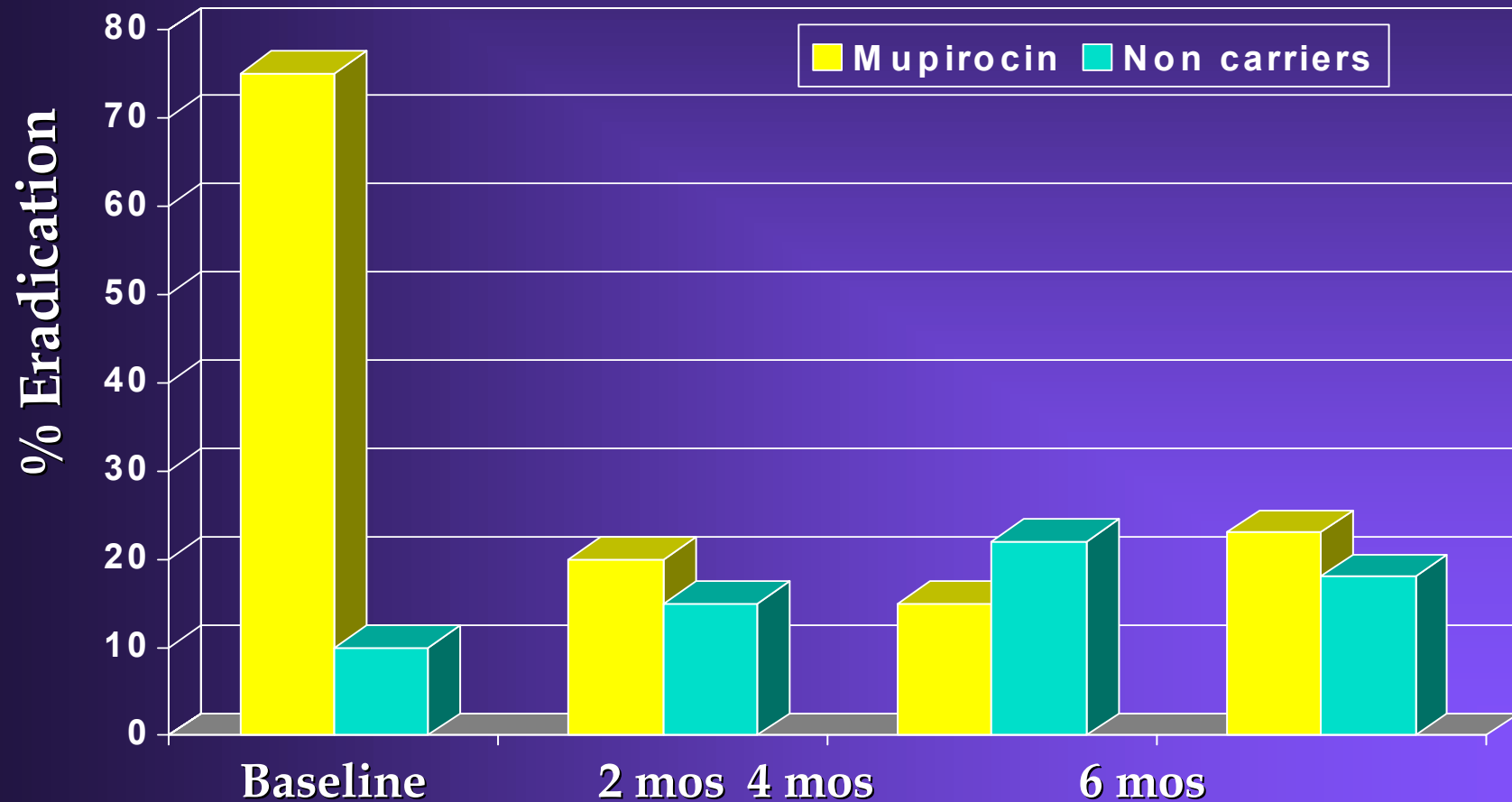
# Mupirocin Efficacy in Healthcare Workers: Hand Carriage



# Duration of Nasal Carriage: Healthcare Workers



# Mupirocin Efficacy in HD Patients: Hand Carriage



# *S. aureus* Bacteremia in HD Patients: Impact of Intranasal Mupirocin

- ✍ Historical controls compared to concurrent cohort
  - ✍ 0.25/patient-year - comparison period
  - ✍ 0.04/patient-year - mupirocin group ( $p < 0.001$ )
- ✍ Randomized double-blind placebo controlled trial
  - ✍ 0.49 BSI/pt-year ( $P = 0.05$  vs. 0.14) - placebo group
  - ✍ 0.12 BSI/pt-year - mupirocin group

Kluytmans et al. *Infect Control Hosp Epidemiol* 1996;17:797.

Boelart et al. *Nephrol Dial Transplant* 1989;4:278.

# Eliminating *S. aureus* nasal carriage with Mupirocin: TCV patients

Characteristic	Historical Controls	Intervention Group	Relative Risk / P value
<b>All patients</b>	<b>983</b>	<b>1003</b>	<b>--</b>
<b>--Cardiac</b>	<b>796</b>	<b>775</b>	<b>--</b>
<b>Infection rate</b>			
<b>--All surgeries</b>	<b>7.5 %</b>	<b>2.5 %</b>	<b>0.33 (.21-.52)</b>
<b>--Cardiac</b>	<b>5.4 %</b>	<b>1.9 %</b>	<b>0.35 (.19-.62)</b>
<b>LOS</b>	<b>12.2 days</b>	<b>12.9 days</b>	<b>ns</b>
<b>--deep SSI</b>	<b>50.7 days</b>	<b>49.5 days</b>	<b>ns</b>
<b>---incision SSI</b>	<b>23.5 days</b>	<b>28.4 days</b>	<b>ns</b>

# Is Eliminating *S. aureus* Nasal Carriage Cost-effective?

<b>Strategies:</b>	<b>Nothing</b>	<b>Mupirocin</b>	<b>Culture</b>
<b>No. infections</b>	<b>313</b>	<b>142</b>	<b>173</b>
<b>Infections prevented</b>	<b>-----</b>	<b>171</b>	<b>140</b>
<b>Total cost</b>	<b>\$2,109,313</b>	<b>\$991,941</b>	<b>\$1,324,450</b>
<b>Total savings/ infections prevented</b>	<b>----</b>	<b>\$1,117,372</b>	<b>\$784,853</b>

75% of *S. aureus* infections attributable to nasal carriage

# Treatment of VRSA

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- ✍ Establish the patient is infected
- ✍ Drain abscesses/pus collections
- ✍ Remove catheters if BSI
- ✍ Test organism for susceptibility to other agents
  - ✍ Trimethoprim/sulfamethoxazole
  - ✍ Tetracycline
  - ✍ Quinupristin/dalfopristin or pristinamycin
  - ✍ Chloramphenicol
  - ✍ Fluroquinolones
  - ✍ ? role of rifampin or use of two antibiotics

# Conclusions

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- ✍ Approach to prevention should include
  - ✍ Handwashing
  - ✍ Isolation
  - ✍ Cleaning the environment
  - ✍ Surveillance & identification of potentially infected pts
- ✍ Several agents eliminate nasal carriage effectively
- ✍ Optimal regimens and settings have not been defined
- ✍ The future challenge is to balance the individual pt needs with impact on a population of pts

# Conclusions

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Decreased *S. aureus* infection rates could:

- ✍ Decrease vancomycin use
- ✍ Decrease the risk of selecting vancomycin-resistant organisms such as enterococci and *S. aureus*
- ✍ Decrease morbidity and mortality
- ✍ Decrease use of healthcare resources and costs

# Conclusions

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- ✍ Further studies are needed to:
  - ✍ Define optimal prophylactic regimens
  - ✍ Define the role of chlorhexidine
  - ✍ Evaluate efficacy of povidone iodine
  - ✍ Monitor for resistance
  - ✍ Determine the most effective strategies to prevent and control VRSA infections

**I**t was the best of times, it was the worst of times, it was the age of wisdom, it was the age of foolishness, it was the epoch of belief, it was the epoch of incredulity, it was the season of Light, it was the season of Darkness, it was the spring of hope, it was the winter of despair, it was the era of people not washing their hands after using the bathroom, it was the era of people eating with their hands after using the bathroom, it was the era of people eating with their hands and falling violently ill after transferring bacteria to each other--in short, it was not a very sanitary period.

Charles Dickens & the Allegheny County Health Department

Scarlett O'Hara was not beautiful, but men seldom realized it when caught by her charm as the Tarleton Twins were. Nor did they realize when they grew frightfully ill that it was the touch of her magnolia-white skin that made them so sick. For, disregarding as all ladylike behavior, Scarlett had frivolously not washed her hands after attending to her business in the lady's parlor. Her delicate hands, being so unguarded, touched those of the twins, causing the unfortunate spread of an atrocious bacterial disease. Shame was brought upon both families, which was the worst disgrace of all.

Margaret Mitchell & the Allegheny County Health Department

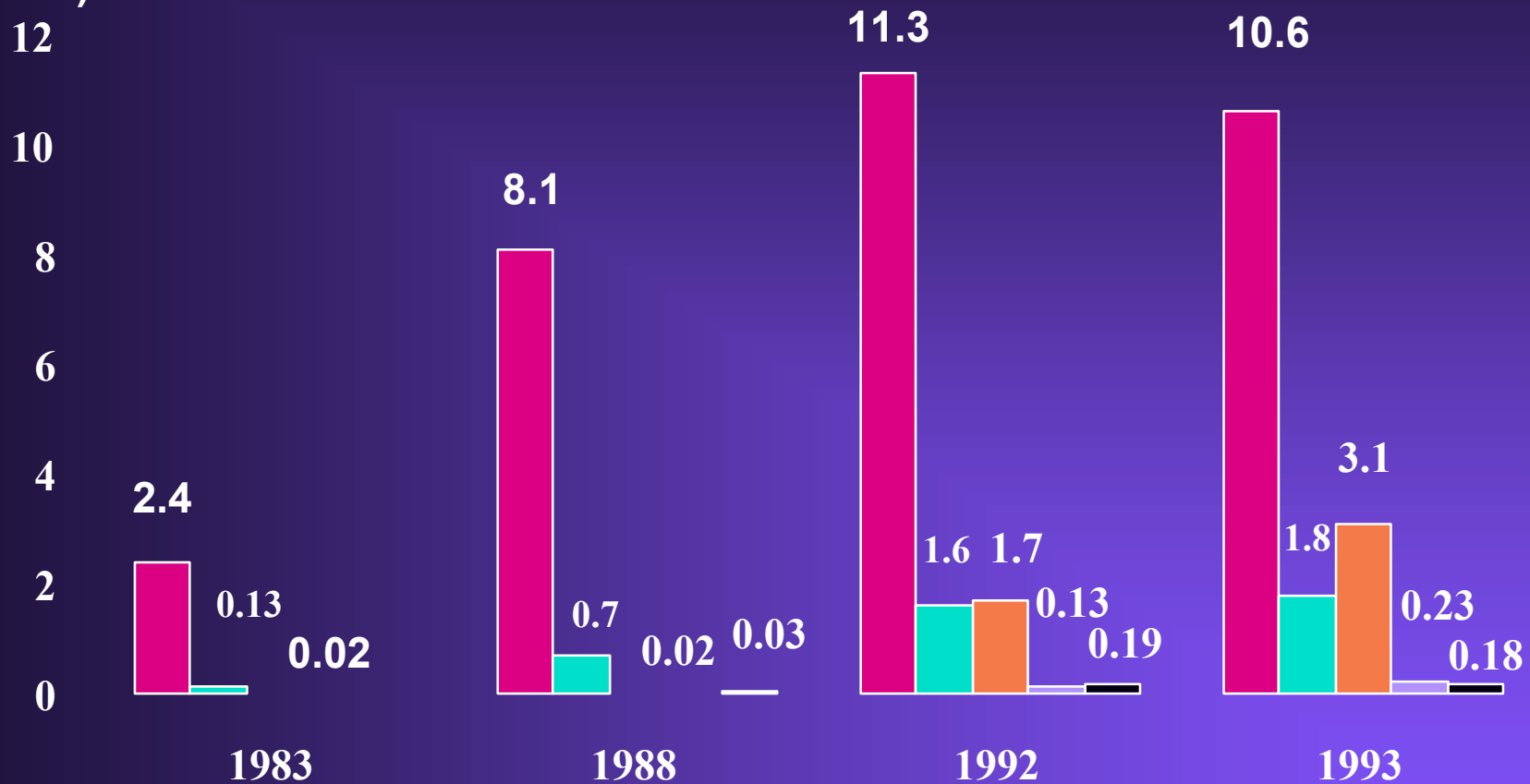
Call me Ishmael. Some years ago--never mind how long precisely--having little or no money in my purse, and nothing particular to interest me on shore, I thought I would sail about a little and see the watery part of the world. Hence I solemnly took to the ship in a blind effort to appease my drizzling soul. Unbeknownst to me was the fateful event this voyage would present. Having a shortage of fresh water, the men resigned themselves to not washing their hands after the moving of their bowels, causing a severe occurrence of stomach cramps and other unpleasant digestive symptoms. Perhaps if I had taken solace in the land, I would never have set foot on that cursed ship.

Herman Melville & the Allegheny County Health Department

# Vancomycin: Injectable

Doses

(Millions)



North America

Europe

Japan

Africa/Asia/Australia

Latin America

12 Month period ending September

Source: IMS MIDAS

# MRSA Nosocomial Bacteremia: JHH

