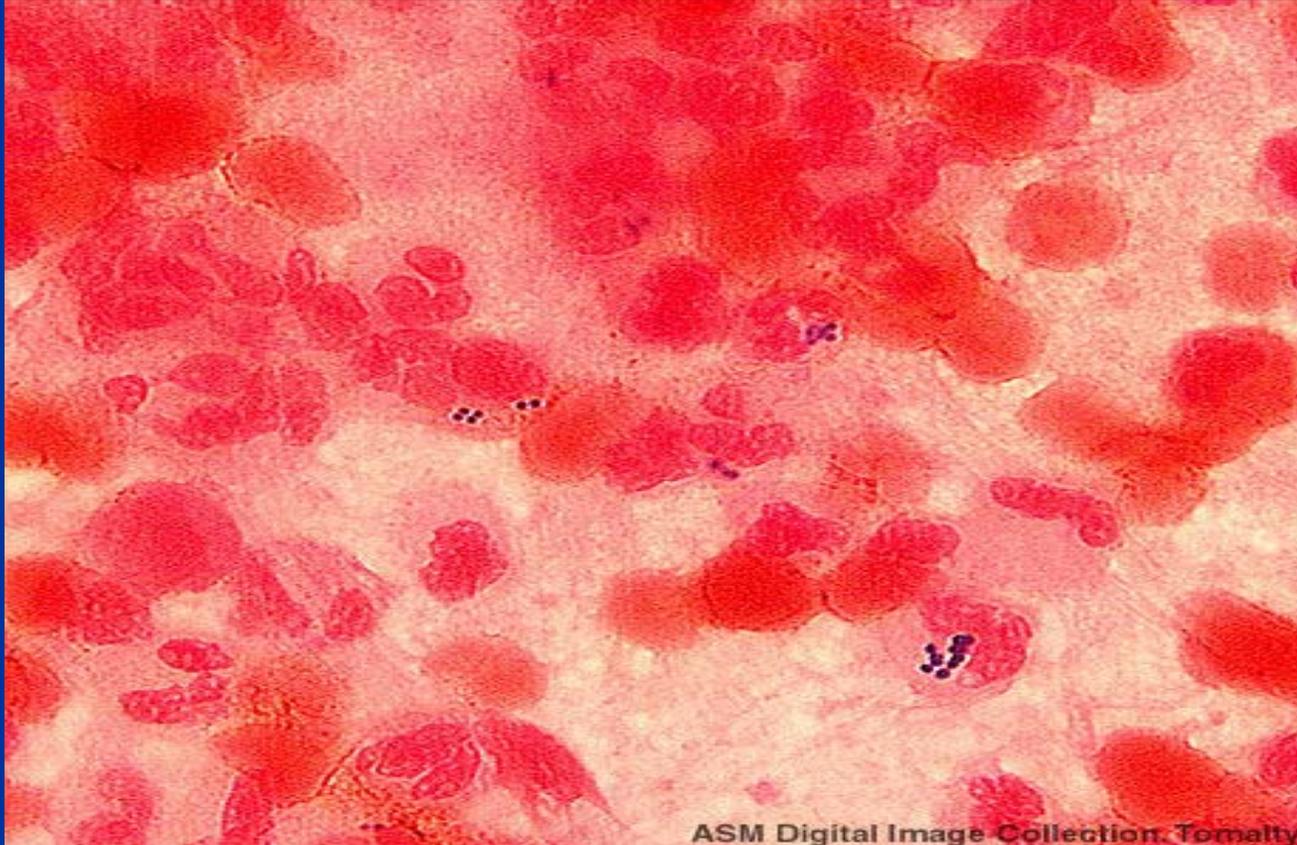
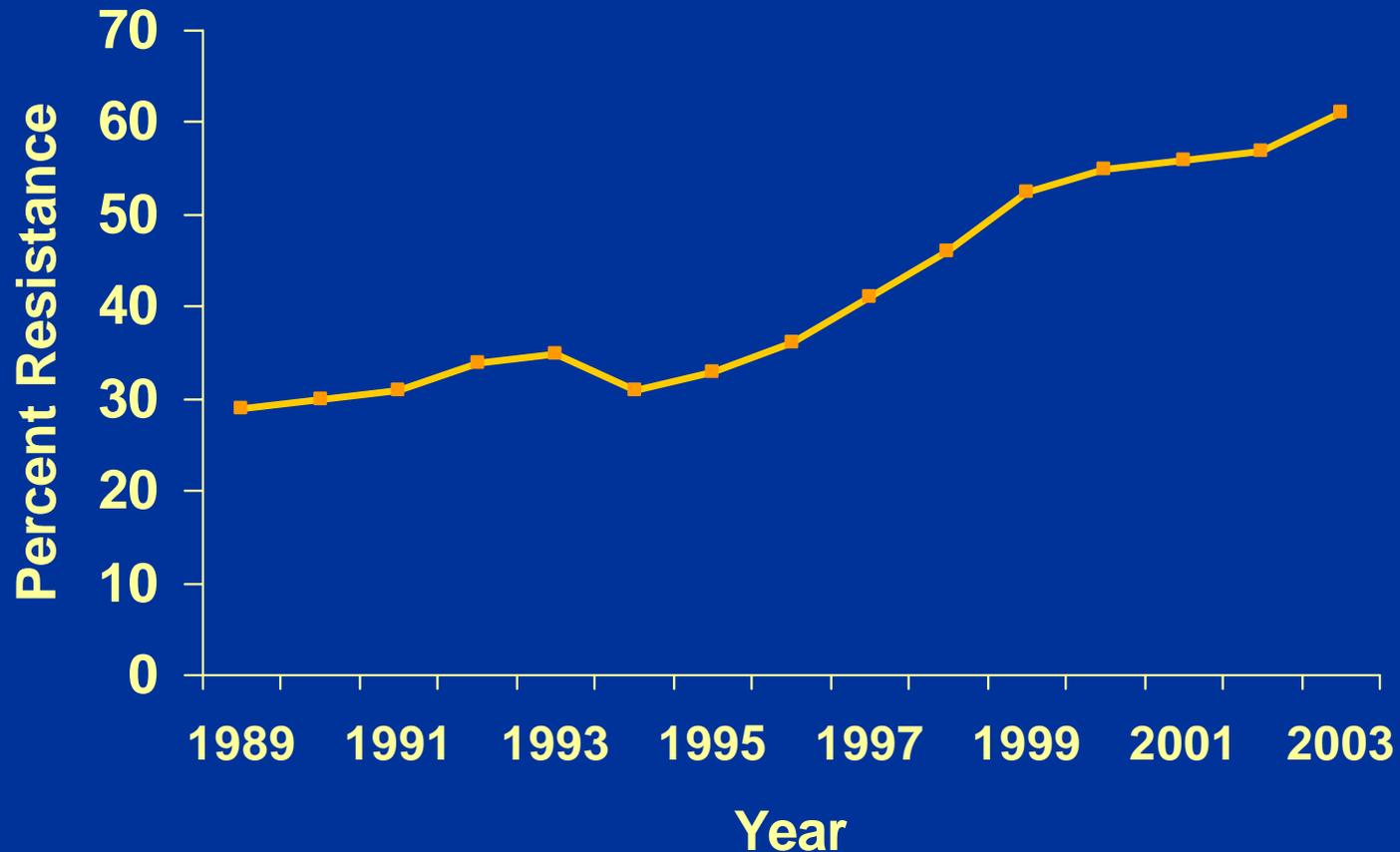


Control and Treatment of MRSA



Proportion of *S. aureus* Nosocomial Infections Resistant to Oxacillin (MRSA) Among Intensive Care Unit Patients, 1989-2003*



*Source: NNIS System

Global MRSA Prevalence

- North America
 - Canada (Ottawa) 1%
- Europe
 - Netherlands 1.5%
 - Switzerland 4 to 68/10,000 adm (Up to 12%)
 - Poland 3-11%
 - UK 25% and Italy, France 30-50%
- Latin America
 - Brazil 70%
- Asia - Japan 60%

Antimicrobial Resistance: **Key Prevention Strategies**

Susceptible Pathogen

*Prevent
Transmission*

*Prevent
Infection*

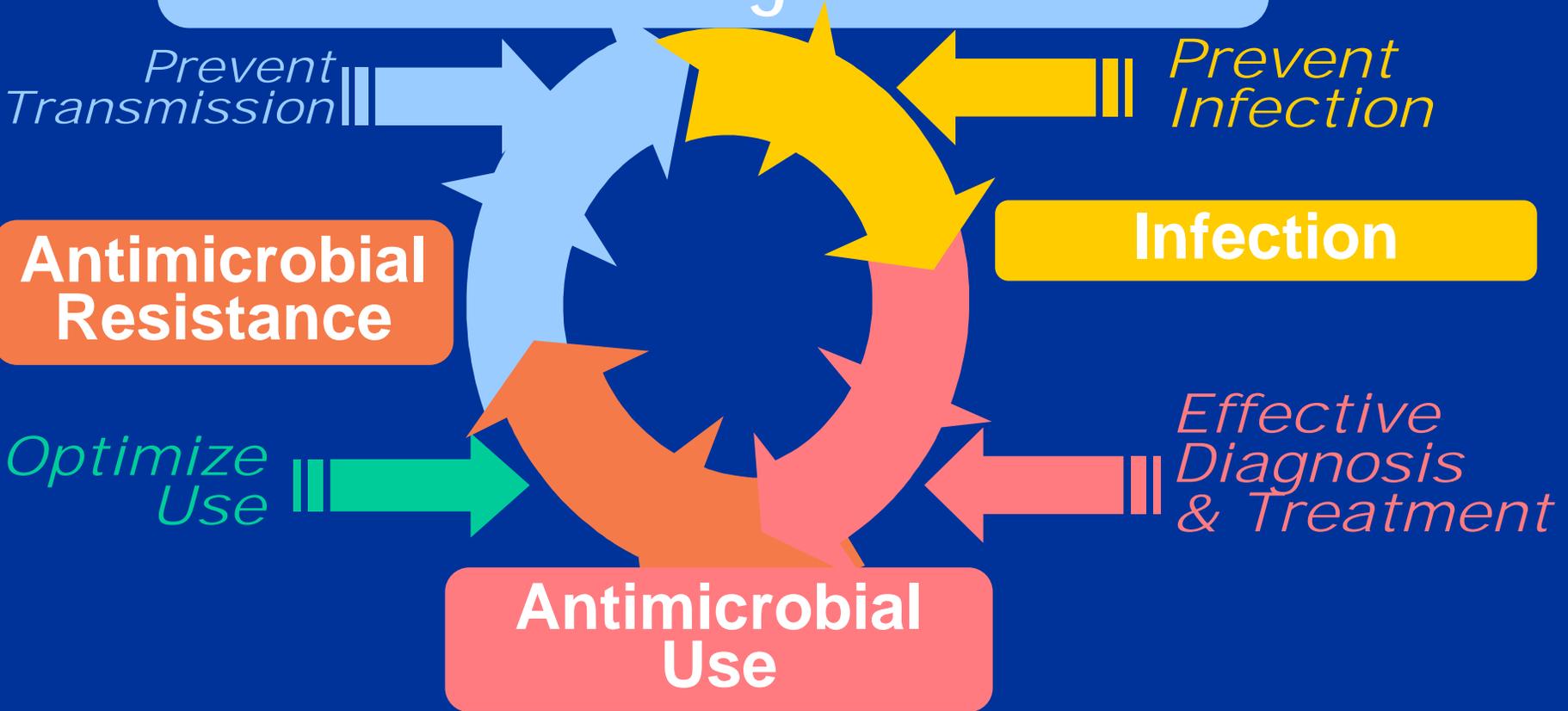
**Antimicrobial
Resistance**

Infection

*Optimize
Use*

*Effective
Diagnosis
& Treatment*

**Antimicrobial
Use**



12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults

- 1 Vaccinate
- 2 Get the catheters out
- 3 Target the pathogen
- 4 Access the experts
- 5 Practice antimicrobial control
- 6 Use local data
- 7 Treat infection, not contamination
- 8 Treat infection, not colonization
- 9 Know when to say "no" to vanco
- 10 Stop treatment when cured
- 11 Isolate the pathogen
- 12 Break the chain

Prevent Transmission

Use Antimicrobials Wisely

Diagnose & Treat Effectively

Prevent Infections



MRSA Transmission

- Clonal spread
 - Transmitted by direct person-to-person contact
 - Sites of colonization
 - Nares, axilla, skin
- Antibiotic selection
 - Methicillin resistance gene chromosomally-mediated
 - Mobilization of gene cassette in recent MRSA
 - Antibiotic selection

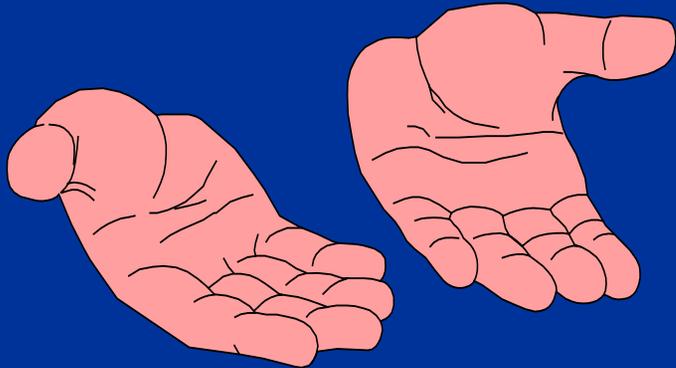
MRSA Transmission

- Transient hand carriage by personnel
 - Infected or colonized patient
 - Infected or colonized HCW
- Environment
 - Burn units
 - Dermatology wards
 - Fomites



"No doubt about it, Bob, you're infected with tiny fighter planes. What's worse — you're a carrier."

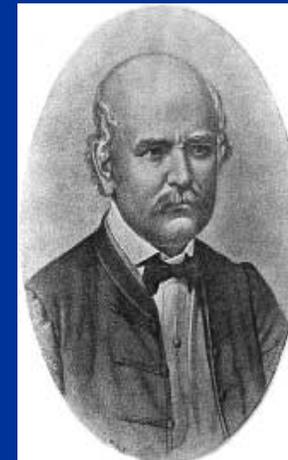
Decrease MRSA Transmission



Hand Hygiene Compliance

- 40% average compliance
 - As low as 10%
- One study showed improvement to 60% with instant antiseptics
- Lowest compliance among physicians and nurses
- JCAHO Pt Safety monitor

Improved Patient Outcomes associated with Proper Hand Hygiene



Ignaz Philipp
Semmelweis
(1818-65)

Chlorinated lime hand antisepsis

➤ [Link to: Ignaz Semmelweis](#)



MRSA Control Measures

- Acute Care Hospital
 - Microbiologic surveillance
 - Standard Precautions
 - Contact Precautions
 - Antisepsis
 - Standard housekeeping
 - Surveillance cultures
 - Standard vs. directed
- Local assessment
- 



Diagnose & Treat Infection Effectively

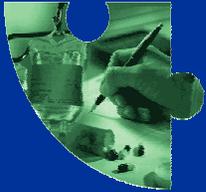
Step 3: Target the pathogen

Fact: Appropriate antimicrobial therapy saves lives.

Actions:

- ✓ culture the patient
- ✓ target **empiric therapy** to likely pathogens and local antibiogram
- ✓ target **definitive therapy** to known pathogens and antimicrobial susceptibility test results

➤ *Link to: [IDSA guidelines for evaluating fever in critically ill adults](#)*



Use Antimicrobials Wisely

Step 6: Use local data

Fact: The prevalence of resistance can vary by locale, patient population, hospital unit, and length of stay.

Actions:

- ✓ know your local antibiogram
- ✓ know your patient population



Prevent Transmission

Step 11: Isolate the pathogen

Fact: Patient-to-patient spread of pathogens can be prevented.

Actions:

- ✓ use standard infection control precautions
- ✓ contain infectious body fluids
(use approved airborne/droplet/contact isolation precautions)
- ✓ when in doubt, consult infection control experts

➤ [Link to: A VRE prevention success story](#)

➤ [Link to: CDC isolation guidelines and recommendations](#)

Surveillance Cultures

- Elimination of MRSA from Finland hospitals
 - 2 outbreaks MRSA 1991-2
 - 1991-2002
 - 202 persons with MRSA in medical district
 - Strict control measures for all 30 district hospitals
 - Contact precautions for colonized patients
 - Systematic screening for contacts of MRSA pts
 - Cohorts of MRSA+ and MRSA exposed pts
 - Continuous staff education

Surveillance Cultures

➤ Cost-effectiveness

➤ NICUs of 2 tertiary care hospitals

➤ 11 month MRSA outbreak in hospital A vs. MRSA bacteremias in hospital B

» Cost of control of outbreak in hospital A

◆ \$60,000 range

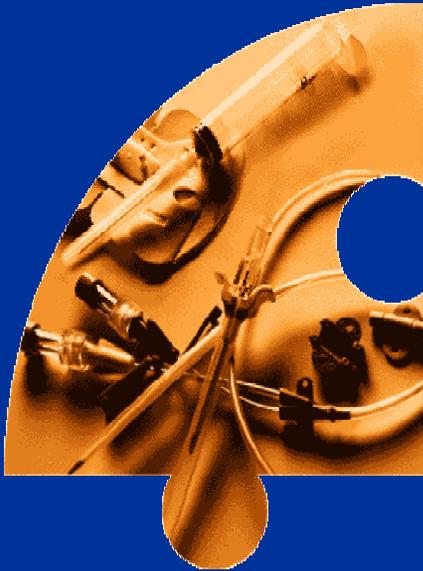
» Attributable excess cost of MRSA bacteremias in hospital B

◆ \$1.3 million

Risk Factors for MRSA

- Invasive devices
- Time at risk
- ICU stay
- Coma
- Surgery

Law. Epidemiol Infect 1988; Ascensio. ICHE 1996
Crowcroft JHI. 1996; Crossley. JID. 1979
Peacock. Ann Intern Med 1980



Prevent Infection

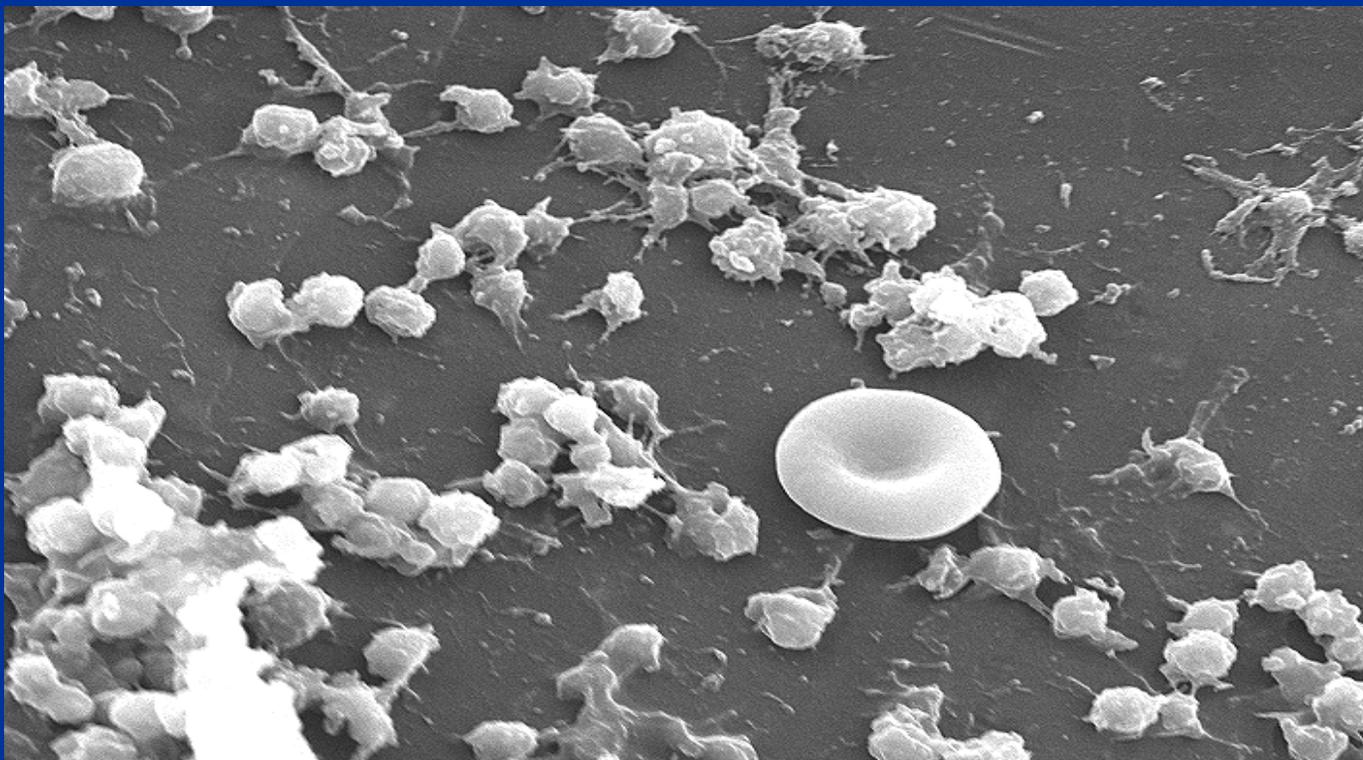
Step 2:

Get the catheters out

Fact:

Catheters and other invasive devices are the # 1 exogenous cause of hospital-onset infections.

Biofilm on Intravenous Catheter Connector 24 hours after Insertion



Scanning Electron
Micrograph



Prevent Infection

Step 2: Get the catheters out

Fact: Catheters and other invasive devices are the # 1 exogenous cause of hospital-onset infections.

Actions:

- ✓ use catheters only when essential
- ✓ use the correct catheter
- ✓ use proper insertion & catheter-care protocols
- ✓ remove catheters when not essential

➤ Link to: [New IV Guideline](#)

➤ Link to: [Urinary catheter infection prevention](#)

➤ Link to: [Guidelines for the Prevention of Intravascular Catheter-related Infections](#)

VISA (GISA)

- Intermediate resistance to vancomycin
 - MIC 8 $\mu\text{g/ml}$
 - Japan: $\leq 20\%$ prevalence among noso MRSA
 - Cases in all continents
 - ?Continuum of strains with decreasing susceptibility to vancomycin
- Risk factors
 - Exposure to vancomycin
 - Prior MRSA infection
 - Renal failure

Hiramatsu 1997, CDC 1997-98

Vancomycin-Resistant *S. aureus*

- 3 VRSA isolates reported in US, 2002
- June 2002
 - Catheter exit infection
 - MRSA, vanco MIC 1024 µg/ml
 - Susc TMP/S, Clinda, tetracycline, minocycline, linezolid, quinu/dalfo
 - VRE *vanA* gene detected in the VRSA isolate
 - Rx TMP/S and removal of catheter

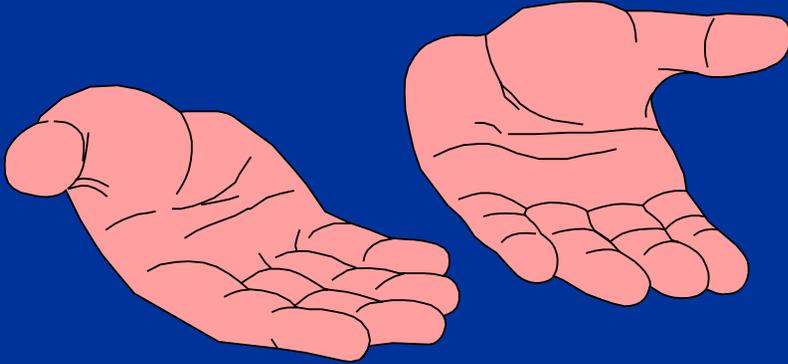
VRSA/VISA Control Measures

- Laboratory detection
 - Revised NCCLS standards
 - broth dilution, agar dilution, agar-gradient diffusion
 - Strains with MIC $\geq 4\mu\text{g/ml}$
 - Confirm genus and species; repeat vanco MIC
 - Report state health dept, CDC
- May be missed by automated systems
 - Add vancomycin screening plates
- Antimicrobials
- Prevent spread with Contact Precautions

VRSA/VISA Control Measures

- Prevent spread
 - Lab to notify infection control, attending MD
 - Initiate epidemiologic investigation
 - Contact Precautions
 - Good antisepsis; gloves, gown
 - Monitor compliance
 - Surveillance cultures HCWs, pt roommates
 - Consider: mupirocin for nasal eradication

Prevention is Primary!





Diagnose & Treat Infection Effectively

Step 3: Target the pathogen

Fact: Appropriate antimicrobial therapy saves lives.

Actions:

- ✓ culture the patient
- ✓ target **empiric therapy** to likely pathogens and local antibiogram
- ✓ target **definitive therapy** to known pathogens and antimicrobial susceptibility test results

➤ *Link to: [IDSA guidelines for evaluating fever in critically ill adults](#)*



Diagnose & Treat Infection Effectively

Step 3:

Target the pathogen

Appropriate antimicrobial therapy (correct regimen, timing, dosage, route, and duration) saves lives.

Step 4:

Access the experts

Infectious diseases expert input improves the outcome of serious infections.

Therapy of Hospital MRSA Infections

- Vancomycin
 - Good safety record
 - 10-15 mg/kg; trough levels 12-15
 - Monitor ototoxicity in elderly
 - No po or IM route
 - Resistance now reported
 - Tolerance more widespread problem

Linezolid

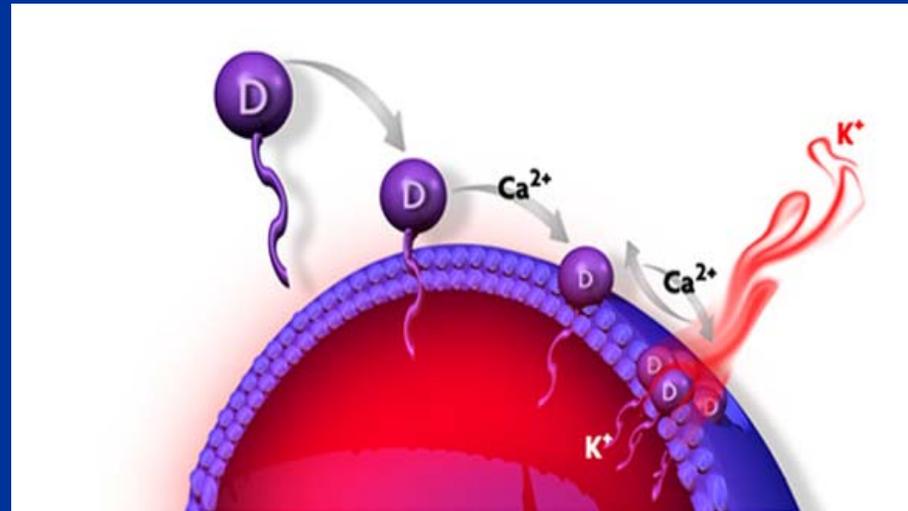
- Oxazolidinone; IV and po
- Broad Gram-positive activity
- Mechanism – protein synthesis inhibitor
 - Bacteriostatic
- Adverse effects
 - Marrow suppression, weak MAOI
 - Uveitis, peripheral neuropathy
 - Rare serotonin syndrome with concurrent SSRI

Daptomycin

- Cyclic lipopeptide
- Broad Gram-positive activity
- Bactericidal, including enterococci
- Unique mechanism – disrupts plasma membrane function
- Adverse effect – myopathy

Daptomycin Mode of Action

- Binds to Gram-positive bacterial cell membrane
 - Calcium-dependent insertion of lipid tail
- Rapidly depolarizes the cell membrane
 - Efflux of potassium
 - Destroys ion-concentration gradient
- Cell death
 - Multiple failures in biosystems, DNA, RNA, protein synthesis



Therapy of HA MRSA Infections

- Minocycline
 - Most active tetracycline to date
 - IV or po form
 - Used in Japan for MRSA and MRCNS
- TMP/S or Clinda if susceptible

Fluoroquinolones and MRSA

- In vitro and in vivo rapid emergence of FQ resistance in MRSA
- Duration of exposure and serial passages may yield conflicting results
- Cipro > Levo > Gati ≥ Moxi
- FQ use associated with clinical isolates of MRSA?

Venezia RA, et al. *J Antimicrob Chemother.* 2001;48:375-381.

Venezia RA, et al. 7th International Symposium on New Quinolones (abstract). UK, 2001.

Gilbert DN, et al. *Antimicrob Agents Chemother.* 2001;45(3):883-892.

Evans ME, Titlow WB. *J Antimicrob Chemother.* 1998;41:285-288.











Community MRSA Infections

- Therapy skin & soft tissue infection
- Local drainage
- 2 drugs: clinda + TMP/S
- Chlorhexidine baths
- Mupirocin nasal eradication
- Treat affected family members

MRSA Nasal Eradication

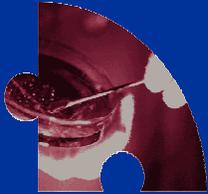
Route and efficacy

➤ Intranasal

- Mupirocin anterior nares BID X 7 days
 - 95%

➤ Oral +/- intranasal

- RIF +TMP/SMX + Bacitracin (intranasal) X 5 days
 - 90%
- RIF + TMP/SMX X 5 days
 - 50-75%
- MIN + RIF X 14 days + MUP X 3 days
 - 90%



Diagnose & Treat Infection Effectively

Step 4: Access the experts

Fact: Infectious diseases expert input improves the outcome of serious infections.

Action:

- ✓ consult infectious diseases experts about patients with serious infections

➤ [Link to: SHEA / IDSA: Guidelines for the Prevention of Antimicrobial Resistance in Hospitals](#)



Summary

- Major nosocomial pathogen
- Community onset cases increasing
- Controlled by antiseptics
- Contact vs. Standard Precautions
- Surveillance cultures in some settings
- New options for therapy
- Vancomycin resistance

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