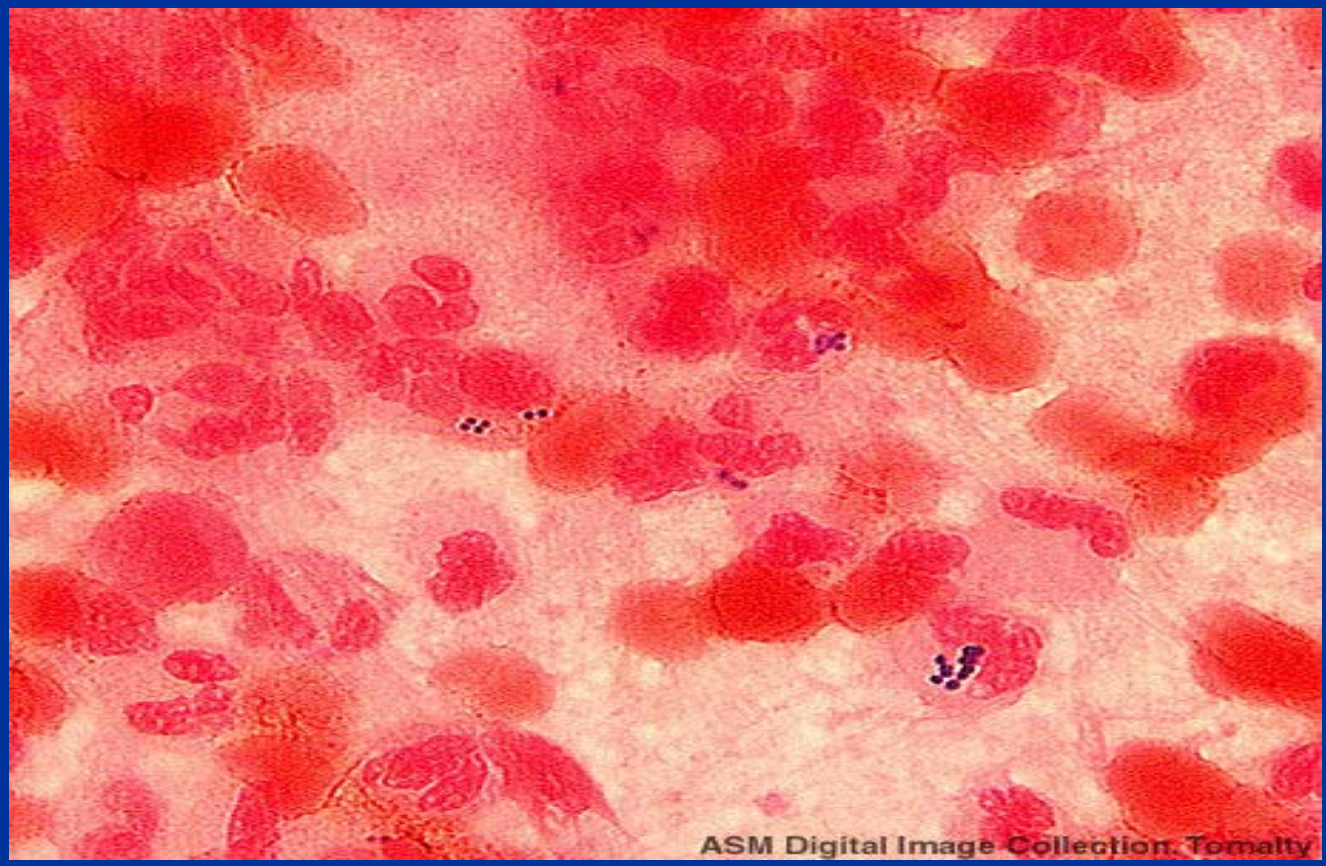
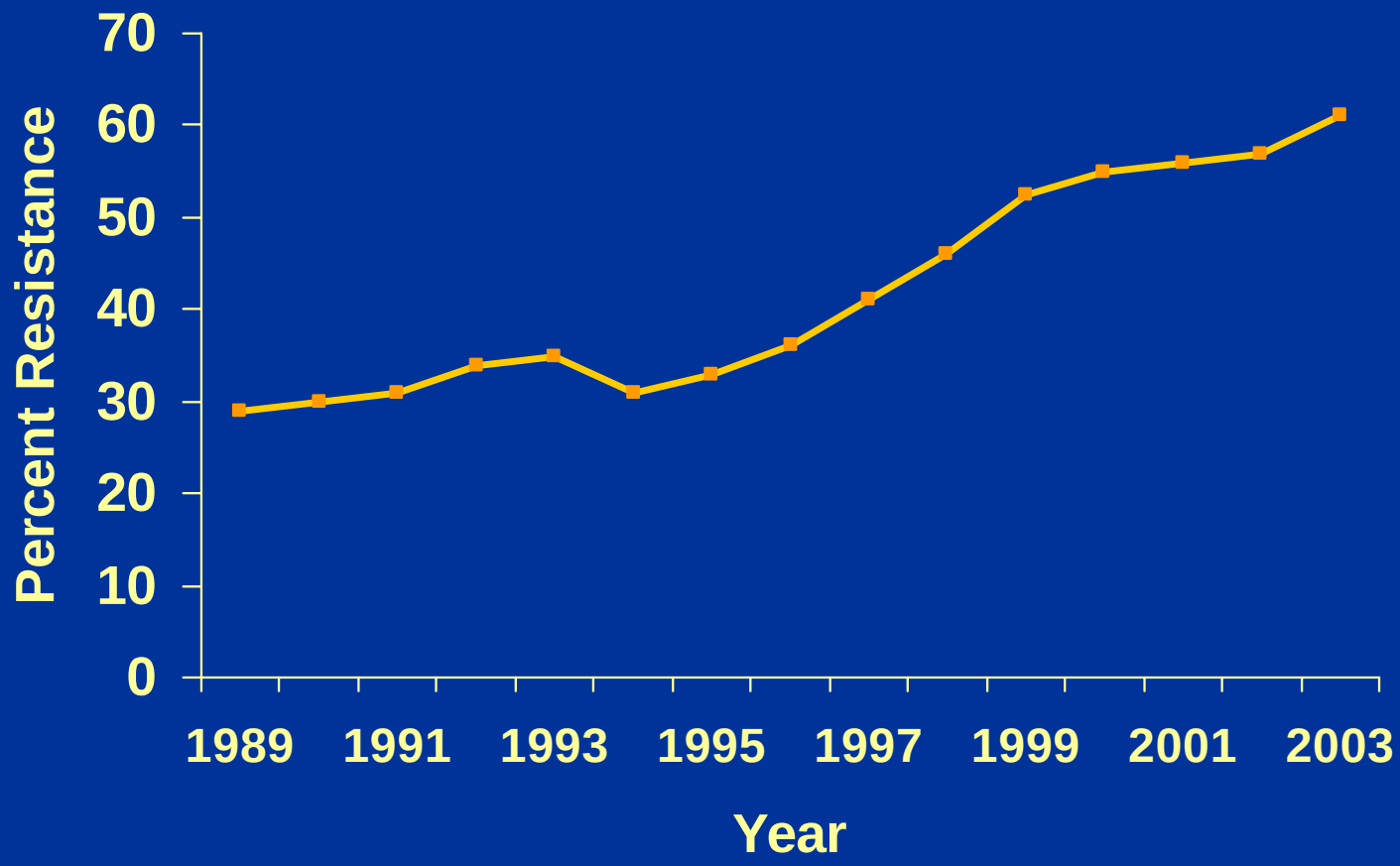
Control and Treatment of MRSA



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



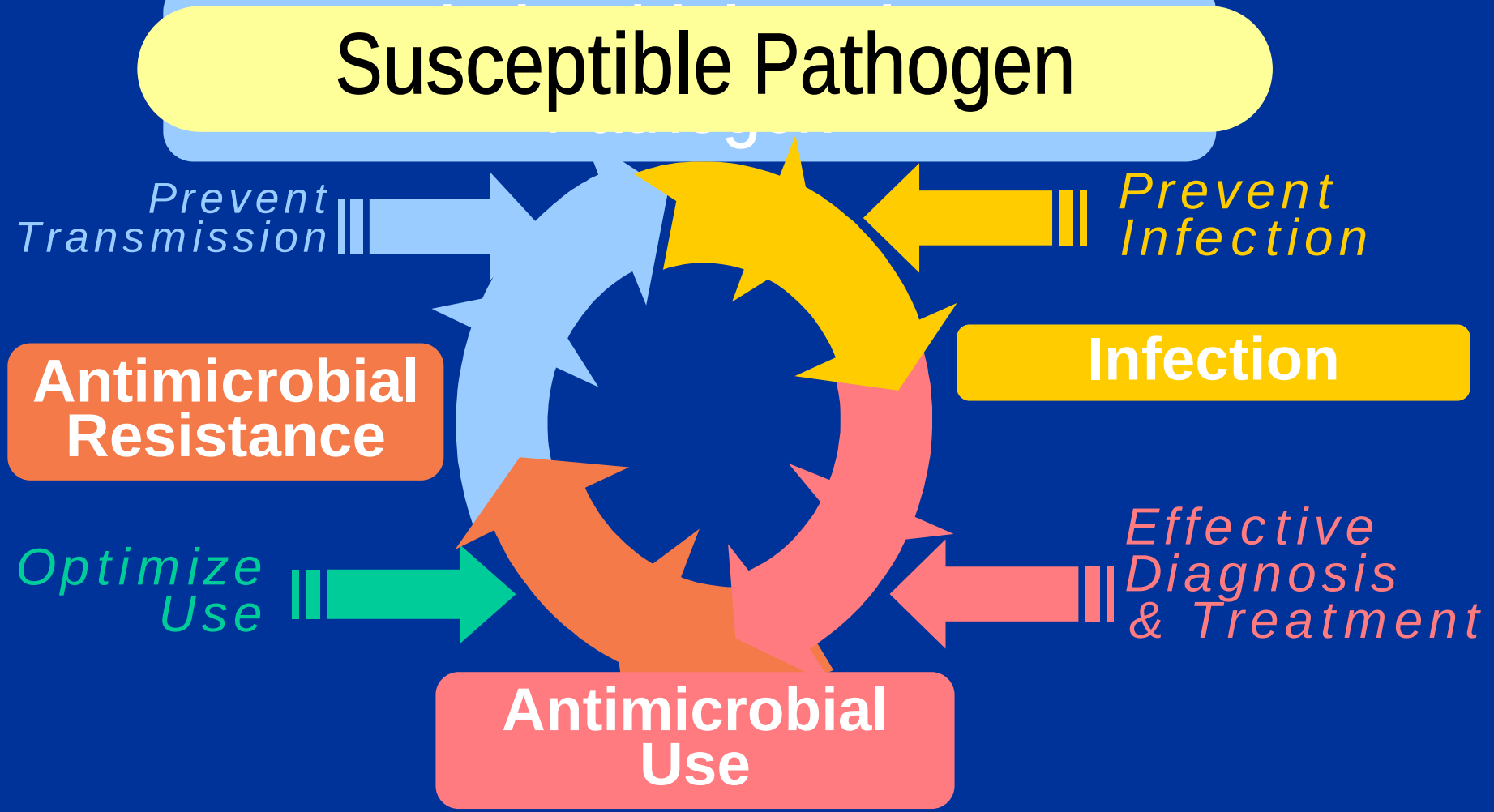
*Source: NNIS System

Global MRSA Prevalence

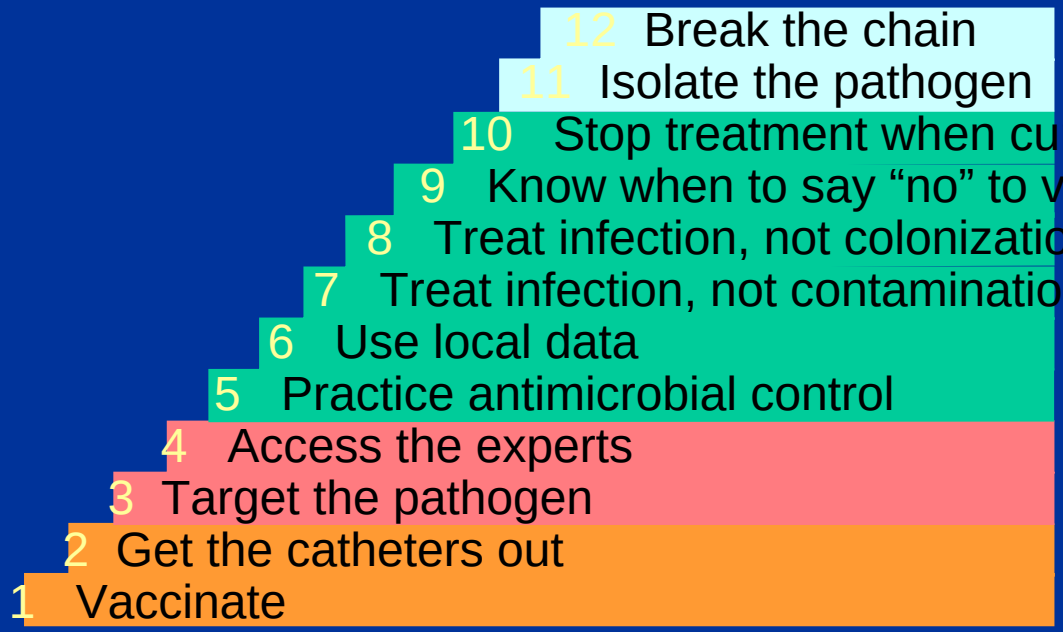
- North America
  - Canada (Ottawa) 1%
- Europe
  - Netherlands 1.5%
  - Switzerland 4 to 68/10,000 adm (Up to 12%)
  - Poland 3-11%
  - UK 25% and Italy, France 30-50%
- Latin America
  - Brazil 70%
- Asia - Japan 60%

Johnson 1998, HIS 1998, Wey 1990, Suh 1998

Antimicrobial Resistance: Key Prevention Strategies



12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults



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MRSA Transmission

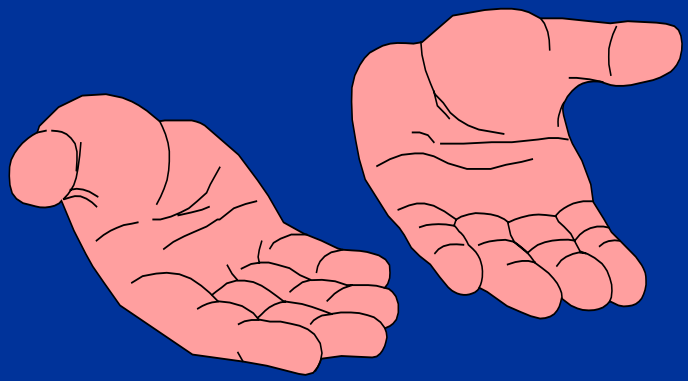
- Clonal spread
  - Transmitted by direct person-to-person contact
  - Sites of colonization
    - Nares, axilla, skin
- Antibiotic selection
  - Methicillin resistance gene chromosomally-mediated
  - Mobilization of gene cassette in recent MRSA
  - Antibiotic selection

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

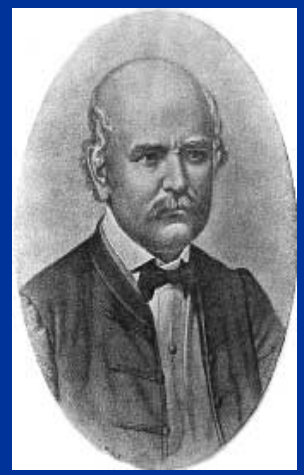


Hand Hygiene Compliance

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

Improved Patient Outcomes associated with Proper Hand Hygiene

Chlorinated lime hand antisepsis



Ignaz Philipp Semmelweis (1818-65)

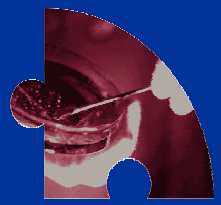
➢ *Link to: Ignaz Semmelweis*


DIDN'T WASH HANDS
MEN

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*

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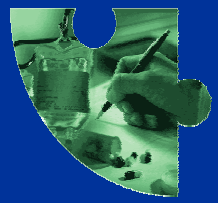

Use Antimicrobials Wisely

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

➢ *Link to: NCCLS Proposed Guidance for Antibiogram Development*

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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*

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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

Kotilainen EID 2003

Surveillance Cultures

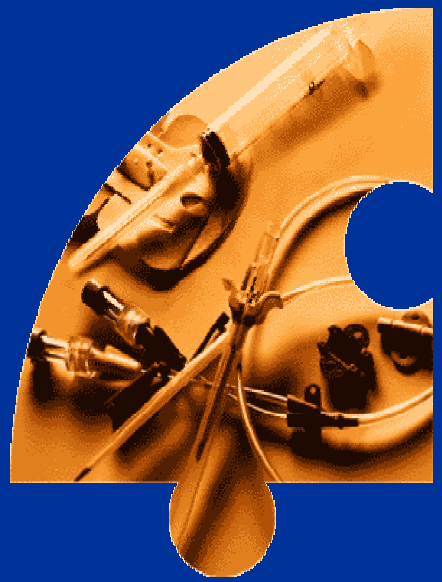
- Cost-effectiveness
  - NICUs of 2 tertiary care hospitals
  - 11 month MRSA outbreak in hospital A vs. MRSA bacteremias in hospital B
    - » Cost of control of outbreak in hospital A
      - $60,000 range
    - » Attributable excess cost of MRSA bacteremias in hospital B
      - $1.3 million

Karchmer T et al. JHI 2002

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.

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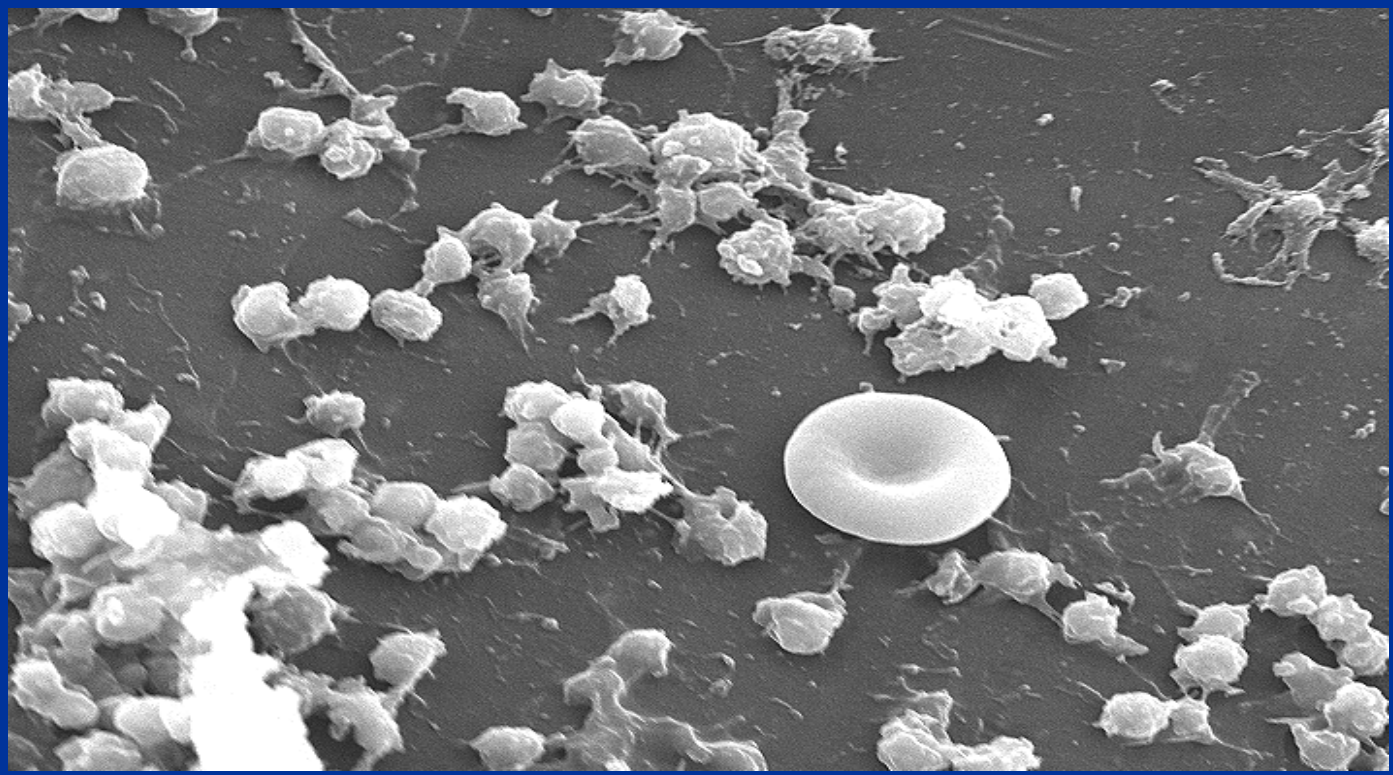
➢ *Link to: NNIS Online at CDC*

Biofilm on Intravenous Catheter Connecter 24 hours after Insertion



Scanning Electron Micrograph

➢ *Link to: Biofilms and device-associated infections*

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*

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VISA (GISA)

- Intermediate resistance to vancomycin
  - MIC 8 μg/ml
  - Japan: ≤ 20% prevalence among noso MRSA
  - Cases in all continents
  - ?Continuum of strains with decreasing susceptibility to vancomcyin
- 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

MMWR 2002;51(26):565 MMWR 2002;51(40):902

VRSA/VISA Control Measures

- Laboratory detection
  - Revised NCCLS standards
    - broth dilution, agar dilution, agar-gradient diffusion
  - Strains with MIC $\geq$ 4μg/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

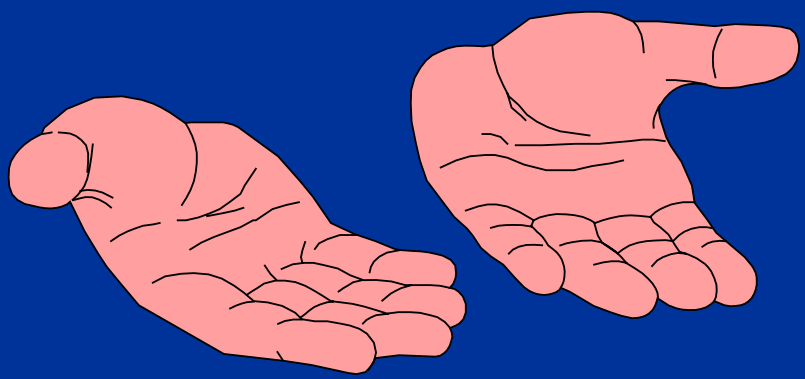
CDC, 1997; 2003

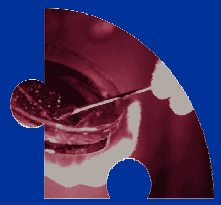
VRSA/VISA Control Measures

- 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

CDC, 1997; 2003

Prevention is Primary!





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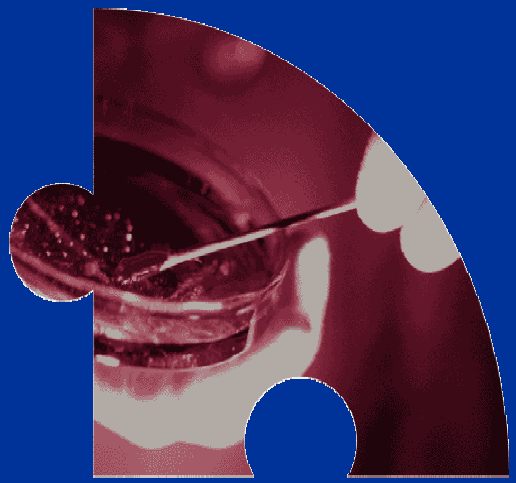

Diagnose & Treat Infection Effectively

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.

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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

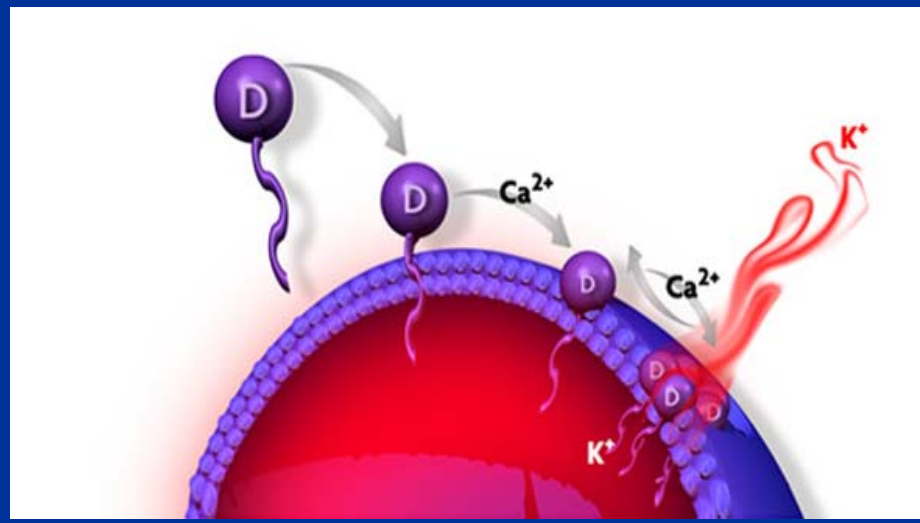
- Oxazolidinone; IV and po
- Broad Gram-positive activity
- Mechanism – protein synthesis inhibitor
  - Bacteriostatic
- Adverse effects
  - Marrow suppression, weak MAOI
  - Uveitis, peripheral neuropathy
  - Rare serotonin syndrome with concurrent SSRI

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.

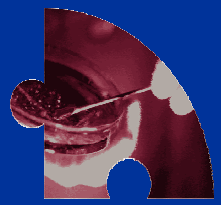
Community MRSA Infections

- 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*

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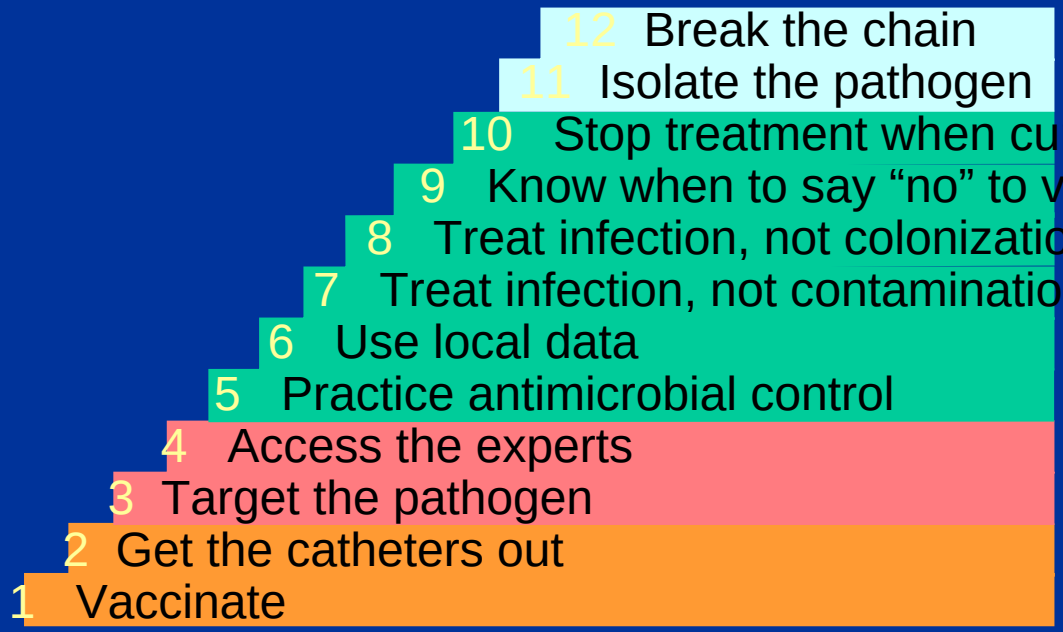
Summary

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

12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults



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